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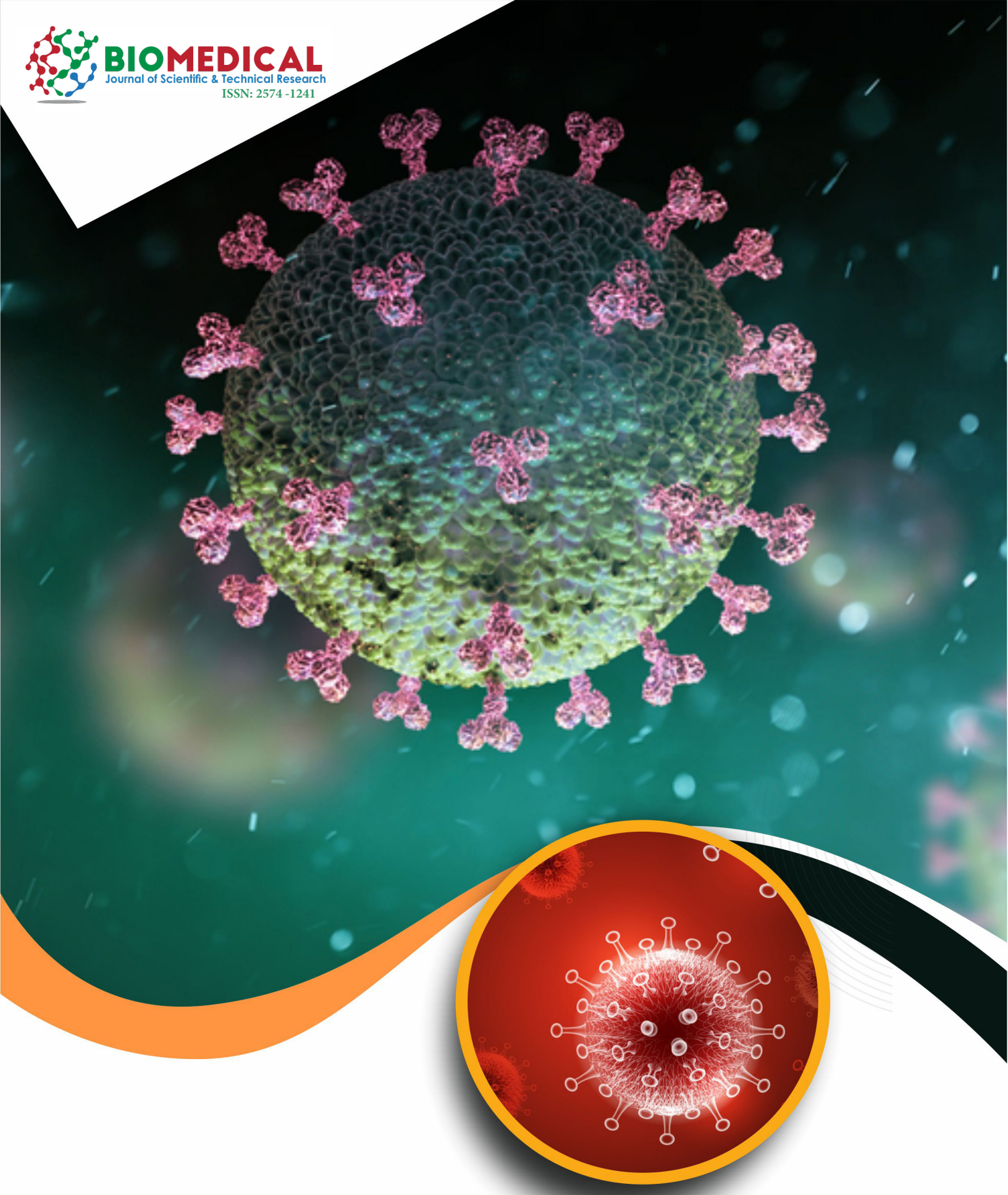

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A LITERATURE REVIEW: BOOK REVIEW ON COVID 19 EPIDEMIOLOGY; DATA; CONTROL AND CLINICAL PREVENTION

A Literature Review: Book Review on COVID 19 Epidemiology; Data; Control and Clinical Prevention

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Acknowledgement

COVID19 Pandemic has taught us great lesson that we could not under estimate the power and control of the nature. Although in this current 21st century scientists and researchers claim that we have developed the treatment of almost all medical diseases accept few and COVID19 comes in those few diseases. Till date 1st October 2020 More than 1 Million people are dead and approximately 34 Million people are COVID19 Positive around the globe due to COVID19 pandemic.

I have started writing this systematic literature review about COVID19 Epidemiology; incidence; distribution; preventions; current treatment and development of vaccination four months ago. I have also published 44 articles including 18 articles on COVID19 Epidemiology and its preventions during current pandemic time. I would say that I am really grateful and thankful to Almighty God who made it possible for me to finish this book on COVID19 Epidemiology and its preventions. Also; I am thankful to my wife; 2 daughters; my beloved parents and siblings specially to my wife Suraya Umabong Siddiqui. My wife Suraya helps me during the current COVID19 pandemic to keep our family healthy; wealthy and fine. Those sleepless nights to finish the 18 articles and this book; only my wife; my mother; father and daughters help me emotionally and morally by their presence; calling and by emailing in the Kingdom of Saudi Arabia.

This achievement is completely dedicated to my beloved Wife Mrs Suraya Umabong Siddiqui; My daughters Fatima Zahra Siddiqui and Aminah Ahsan Siddiqui and my beloved parents Mr. Muhammad Ali Siddiqui and Mrs. Khalidah Siddiqui. I want to specially mention my sister Mrs Sawat wasi and My brother in law Mr Wasi who were with me during this time. Without their emotional and moral support; it could not be possible to complete this book in the short period of time. Their physical presence and verbal support made it possible for me to ignore all the fears and worries of covid19 pandemic and focus on this research book.

Abbreviations and Acronyms

SARS: Severe Acute Respiratory Syndrome; DM: Diabetes Mellitus; HTN: Hypertension; CHD: Coronary Heart Disease; CDC: Centres for Disease Control and Prevention;

NHS: National Health Services; NGO: Nongovernmental Organization; ACE2: Angiotensin-Converting Enzyme-2; ARDS: Acute Respiratory Distress Syndrome; CDCC: The Center for Disease Control in China; COVID-19: Coronavirus disease 2019; ELISA: Enzyme-Linked Immunosorbent Assay; GISAID: Global Initiative on Sharing All Influenza Data; INF: Interferon; MERS: Middle East respiratory syndrome; MHC-I: Major Histocompatibility Complex I; ORF: Open Reading Frames; PDB: Protein Data Bank archive; PDCs: Plasmacytoid Dendritic Cells; RCSB: Research Collaboratory for Structural Bioinformatics; RNA: Ribonucleic Acid; RdRp: RNA-Dependent RNA polymerase; RBD: Receptor-Binding Domain; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; SARS: Severe Acute Respiratory Syndrome; TCGA: The Cancer Genome Atlas; TLRs: Endosomal Toll-Like Receptors; WHO: World Health Organization; FDA: Food and Drug Administration; AlphaCoV: Alpha-Coronavirus; BetaCoV: Beta-Coronavirus; DeltaCoV: Delta-Coronavirus; GammaCoV: Gamma-Coronavirus; CDC: Centers for Disease Control and Prevention; RT-PCR: Real-Time Reverse Transcription Polymerase Chain Reaction; CT; Computed Tomography; VLP: Virus-Like Particle; IL-6; Interleukin-6

Keywords

Severe acute respiratory syndrome coronavirus-2; Epidemiology; Clinical; Pathology; Treatment; COVID-19; SARS-CoV-2; Saudi Arabia; Pandemic; Racial and ethnic disparities; Basic reproduction number; Incubation period; Serial interval; Beta coronavirus; Coronaviridae; MERS-CoV; SARS-CoV; bats; ecology; phylogenetic; receptor-binding domain; sequencing; 2019-nCoV; Betacorona virus; Coronaviridae; ecology; phylogenetic; review; sequencing; Italian Regions; Model; Outbreak Progression; Peak; cytokine storm; immunotherapy; leukocyte; Severe acute respiratory syndrome; Pathogenesis; Therapy; Vaccines; ACE2; acute kidney injury; blood pressure; catepsin; coronavirus; COVID; cytokine storm; endothelium; heparin; Kawasaki disease; allergy; children; lymphocyte subsets; pneumonia; ELISA - human - IgG antibodies - microneutralization test - SARS-CoV-2 – standardization; Armed groups; Covid-19; Colombia; Deforestation; Forest fires; Lockdown; SEIR model; COVID-19; Simulation model; Basic reproduction number; Lyapunov function; biostatistics and bioinformatics; coronavirus; data processing; epidemiology; infection; test statistics; virus classification; Tracheostomy; Tracheotomy; SARS-CoV-2; Pandemic; Guideline; pulmonary embolism; deep vein thrombosis; D-dimer; DOAC; cancer; Virology; Diagnostic Equipment; Infection Control in Health Technology; Analytical Chemistry; Public health; Prevention; Disease control; Population immunity; Herd immunity; Epidemic; Vaccination stockpile; SIS; Stochastic disease

Abstract Summary

Background and objective: The main aim of this book is to find the proven cure/Vaccine development for COVID19 Novel corona virus in current pandemic to save human lives. The author has done systematic literature review of approximately 500 Pubmed Indexed articles related to COVID19 Epidemiology distribution; available treatment and preventions.

Methods: The author of this book has chosen systematic literature review of 500 Pubmed indexed articles. The author has done comparison between Bray and Rees (1995) critiquing frame work and Critical Appraisal Skills Programme (CASP) of 10 randomly selected articles. 12 Questions has been answered by using technique of Bray and Rees 1995 critiquing frame work. Then next 50 other articles are randomly selected to answer 3 other questions about the COVID19 Epidemiology; prevention and Vaccine development. MS EXCEL Tables; graphs and SPSS Diagrams are used to present the results and explain the observations. Mind Maps using diagrams and flow charts are used to show the positive steps for the preventions of COVID19 Novel corona virus in this current pandemic.

Results: The author has used SPSS; MS Excel and other software's to present the results and observation regarding the Systematic literature review about COVID19 Epidemiology and Vaccine development. Bray and Rees 1995 critiquing frame work and Critical Appraisal Skills Programme (CASP) of 10 randomly selected articles are used to answer 12 questions. And then 3 questions are answered about COVID19 Epidemiology; prevention and Vaccine development by using 50 articles data from Pubmed Central. Mind maps are drawn by flow charts to discuss preventions and outcomes of COVID19 novel corona virus.

Conclusion: The traces of COVID19 Pandemic starts from Wuhan province; China where it was initially reported to WHO in November 2019 and it was given the name COVID19 Novel corona virus. Current COVID19 pandemic has taught us a great lesson and it is similar to other SARS viruses but till date October 2020 there is no proven medical treatment or approved Vaccine to prevent against COVID19 Virus. Remdesivir; Lopinavir- Ritonavir; Ceftriaxone; Cephalexin; Azithromycin; Clarithromycin; Continuous Oxygen therapy; Dexamethasone; Plasma therapy has shown positive results in some of the patients and treated them well. Human trials for approved COVID19 Vaccination are conducted in Russia; USA; Europe and the UK; UAE; China and Pakistan; India and Saudi Arabia but still time is needed to be recommended by WHO; FDA USA; EU to use on mass scale to vaccinate local people. The author of this article has done systematic literature review of more than 450 articles and selected 60 articles for Critical literature review by Bray and Rees criteria of 12 Questionnaire to answer them and critically explain the articles and their written matter. The author has written and presented this book for the research on Epidemiology of COVID19 Virus; its Distribution; Incidence; Prevention and treatment; use of PPE to save the precious human lives. The aim is to provide the reliable research to find the treatment and approved vaccination for the COVID19 Novel corona virus.


1
Chapter

Introduction

Epidemiology of the COVID-19 in Incidence and Distribution Among the Community

In December 2019 the outbreak of [1] the novel coronavirus disease-COVID-19 in China spread worldwide becoming an emergency of major international concern. SARS-CoV-2 infection causes clusters of severe respiratory illness similar to severe acute respiratory syndrome coronavirus. Human-to-human transmission via droplets contaminated hands or surfaces has been described; with incubation times of 2-14 days. Early diagnosis quarantine; and supportive treatments are [1] essential to cure patients. Constant efforts at individual national [2] and international level are being made in order to understand the genomics hosts modes of transmission and epidemiological link of nCoV-2019. As of now; whole genome sequence of the newly discovered coronavirus has already been decoded. Genomic characterization nCoV-2019 have shown close homology with bat-derived severe acute respiratory syndrome-SARS like coronaviruses bat-SL-CoVZC45 and bat-SL-CoVZXC21. Structural analysis of the receptor binding site has confirmed that 2019-nCoV binds with the same ACE 2 receptor protein as human SARS virus. Remdesivir originally [2] develop as a treatment for Ebola virus disease and Marburg virus infections is being studied for its effectiveness against 2019-nCoV infection.

By 27 February 2020 the [3] outbreak of coronavirus disease 2019- COVID-19 caused 82 623 confirmed cases and 2858 deaths globally more than severe acute respiratory syndrome-SARS (8273 cases; 775 deaths) and Middle East respiratory syndrome-MERS (1139 cases; 431 deaths) caused in 2003 and 2013 respectively. COVID-19 has spread to [3] 46 countries internationally. SARS-CoV-2 shares highly homological sequences with SARS-CoVs causing highly [4] lethal pneumonia with respiratory distress and clinical symptoms similar to those reported for SARS-CoV and MERS-CoV infections. Notably; some COVID-19 patients also expressed neurologic signs like nausea; headache; and vomiting. Several studies have reported that coronaviruses are not only causing respiratory illness but also invade the central nervous system [4] through a synapse-connected route.

Thus far no proven and specific antiviral treatments for COVID-19 are available. Thus [5] what could we do to fight COVID-19? The most important goal is to control infectious sources. The Chinese government rapidly initiated serial measures such as isolating Wuhan and then the whole Hubei Province improving epidemic information monitoring and reporting and detecting isolating [5] and curing patients. The third epidemic which turned into a COVID-19 pandemic [6] caused by SARS-CoV-2 virus; emerged in China (Hubei Province) in the autumn 2019. This review focuses on ecological and genetic aspects that lead to the emergence of new human zoanthroponous coronaviruses. Appearance of SARS-CoV; SARS-CoV-2 (subgenus Sarbeco virus); and MERS (subgenus Merbeco virus) viruses is a result of evolutionary events occurring in bat populations with further transfer of viruses to the human directly or through [6] the intermediate vertebrate hosts; ecologically connected with bats.

COVID-19 is a variant of SARS-2002 [7] and is different from MERS-2012 outbreak which were caused by coronavirus belonged to the subgenus Merbeco virus of the same genus- according to the results of phylogenetic analysis of 35 different betacorona viruses. Isolated from human and from wild animals in 2002-2019 the natural source of COVID-19 and SARS-CoV (2002) is bats of Rhinolophus genus (Rhinolophidae) and probably some species of other genera. An additional reservoir of the virus could be an intermediate animal species (snakes; civet; hedgehogs; badgers; etc.) that are infected by [7] eating of infected bats. Our results also revealed that [8] the BetaCoV/bat/Yunnan/RaTG13/2013 virus was more similar to the SARS-CoV-2 virus than the coronavirus obtained from the two pangolin samples (SRR10168377 and SRR10168378). We also identified a unique peptide (PRRA) insertion in the human SARS-CoV-2 virus; which may be involved in the proteolytic cleavage of the spike protein by cellular proteases and thus [8] could impact host range and transmissibility.

The possibility of an intermediate host [9] facilitating the emergence of the virus in humans has already been shown with civet cats acting as intermediate hosts for SARS-CoVs; and dromedary camels for MERS-CoV. The coronaviral genome contains four major structural proteins: the spike (S); membrane (M); envelope (E) and the nucleocapsid (N) protein; all of which are encoded within the 3' end of the genome. The S protein mediates attachment of the virus to the host cell surface receptors resulting in fusion and subsequent [9] viral entry. Here we show that a coronavirus which we [10] name pangolin-CoV isolated from a Malayan pangolin has 100%; 98.6%; 97.8% and 90.7% amino acid identity with SARS-CoV-2 in the E; M; N and S proteins respectively. In particular the receptor-binding domain of the S protein of pangolin-CoV is almost identical to that of SARS-CoV-2 with one difference [10] in a noncritical amino acid.

Metagenomic sequencing identified pangolin [11] associated coronaviruses that belong to two sub-lineages of SARS-CoV-2-related coronaviruses including one that exhibits strong similarity in the receptor-binding domain to SARS-CoV-2. The discovery of multiple lineages of pangolin coronavirus and their similarity to SARS-CoV-2 suggests that pangolins should be considered as possible hosts in the emergence of new coronaviruses and should be removed [11] from wet markets to prevent zoonotic transmission. The pandemic of coronavirus disease 2019 [12] (COVID-19) caused by SARS-CoV-2 has posed a severe threat to global public health. Yet; the origin of SARS-CoV-2 remains mysterious. Several recent studies (e.g.; Lam et al. Xiao et al.) identified SARS-CoV-2-related viruses in pangolins; providing novel insights into the evolution and [12] diversity of SARS-CoV-2-related viruses (Figure 1).

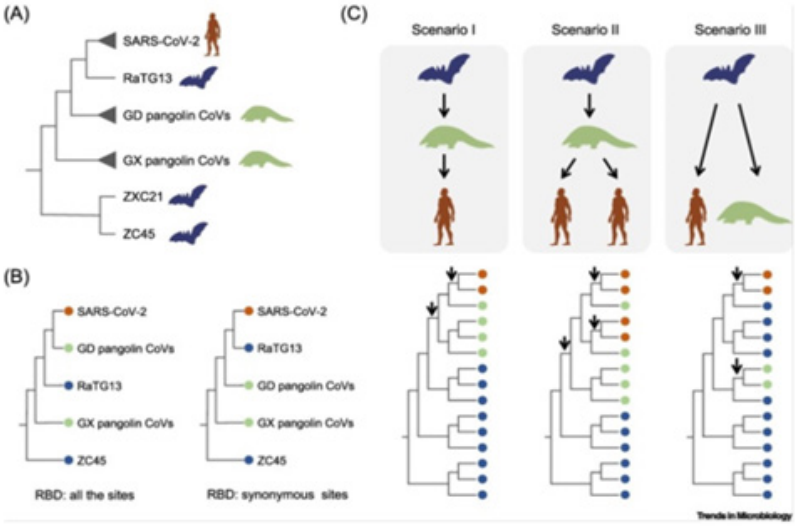


Figure 1: (Guan-ZhuHan, 2020).

The transmission of COVID-19 is [13] potent and the infection rate is fast. Since there is no specific drug for COVID-19 the treatment is mainly symptomatic supportive therapy. In addition; it should be pointed out that patients with severe illness need more aggressive treatment and meticulous care. Recently; accurate RNA detection [13] has been decisive for the diagnosis of COVID-19. Importantly; increasingly evidence showed [14] sustained human-to-human transmission along with many exported cases across the globe. The clinical symptoms of COVID-19 patients include fever cough fatigue and a small population of patients appeared gastrointestinal infection symptoms. The elderly and people with underlying diseases are susceptible to infection and prone to [14] serious outcomes which may be associated with acute respiratory distress syndrome (ARDS) and cytokine storm (Figure 2).

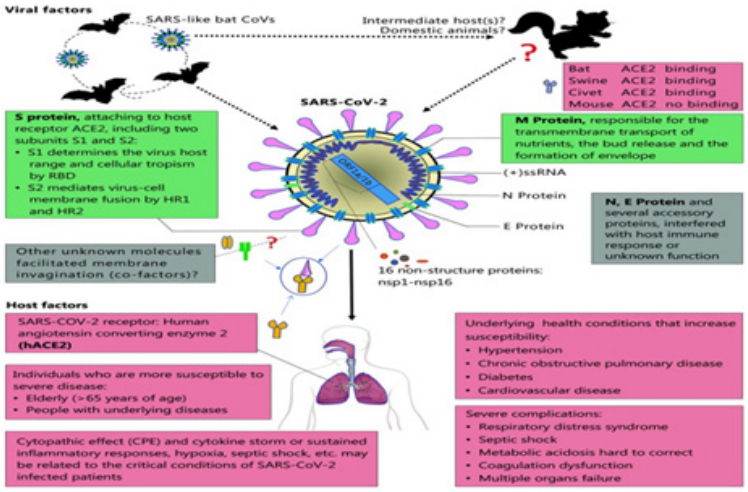


Figure 2: (Yan-Rong Guo, Qing-Dong Cao, Zhong-Si Hong, Yuan Tan, 2020).

The case fatality rate is [15] estimated to range from 2 to 3%. Diagnosis is by demonstration of the virus in respiratory secretions by special molecular tests. Common laboratory findings include normal/ low white cell counts with elevated C-reactive protein (CRP). The computerized tomographic chest scan is usually abnormal even in those with no symptoms or mild disease. Treatment is essentially [15] supportive role of antiviral agents is yet to be established. In terms of the prevention and control strategies vaccine development [16] as the primary prevention should be accelerated. Regarding the secondary prevention ongoing efforts of the infected patients and close contacts quarantine mask wearing promotion regular disinfection in public places should be continued. Meanwhile rapid detection kit for serological monitoring of the virus in general population is expected so as to achieve early detection [16] early diagnosis; early isolation and early treatment.

Although the Advancement in Medical Technology [17] and Sciences still a lot of Research and hard work needed as still scientists could not find the appropriate and proven treatment and Vaccine of COVID-19. From Human beings to Animals all are getting benefits to enjoy better health in twenty first century by modern treatment and surgical procedures for humans and Animals. The Human Doctor and Veterinary Doctor are getting modern medicines and technology [17] to save the lives of their patients. COVID19 is transmitted human [18] to human by droplet and contact routes but some doubt about airborne; fecal or intrauterine transmission also should be removed. Its R0 value is 2.3 but it could be as high as 5.7. Its case fatality rate was 6.3; but it was different in different ages and counties and it could be over 15%. While different countries show different daily case numbers total number of cases; case mortality rates or R0 it seems they show a similar epidemic curve. Every day [18] we learn new data about the current outbreak (Figure 3).

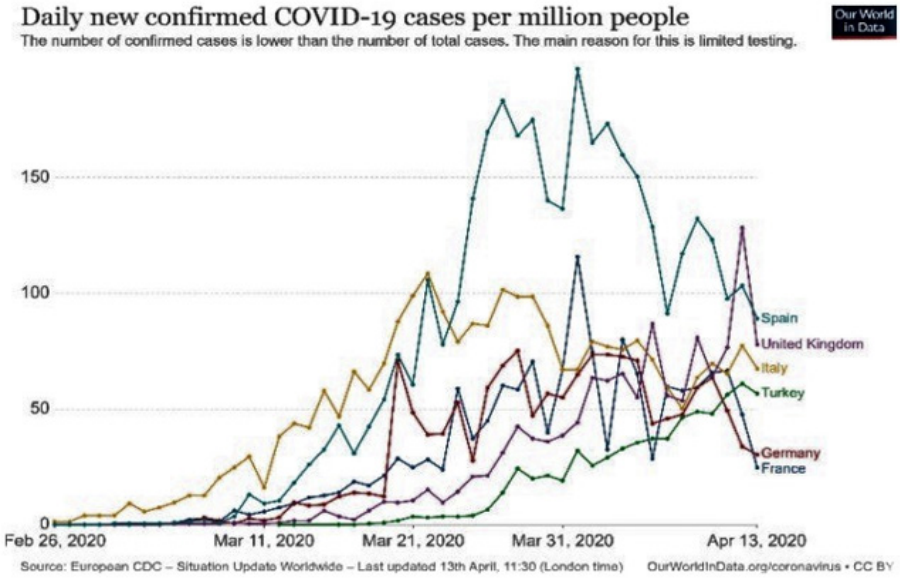


Figure 3: (Cemal Bulut, Yasuyuki Kato, 2020).

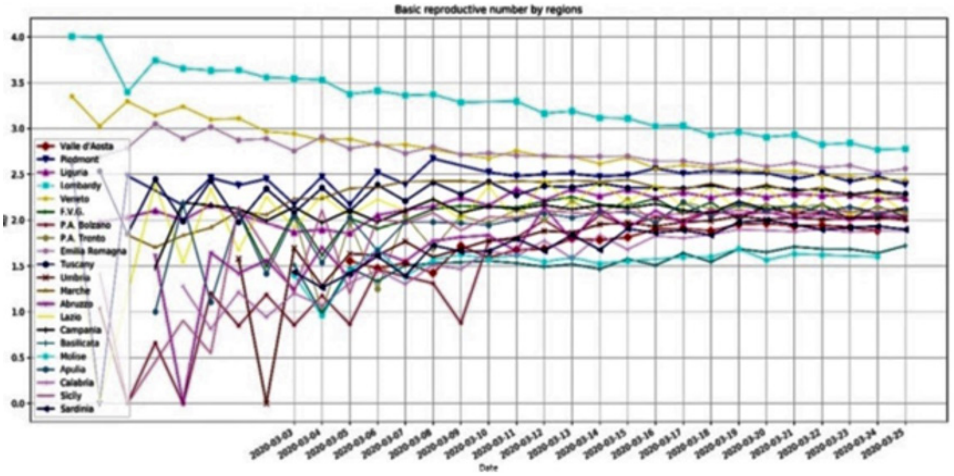


Figure 4: (Cosimo Distante, Prisco P, Alessandro M, 2020).

Epidemiological figures of the [19] SARS-CoV-2 epidemic in Italy are higher than those observed in China. Our objective was to model the SARS-CoV-2 outbreak progression in Italian regions vs. Lombardy to assess the epidemic's progression. Our setting was Italy; and especially Lombardy which is experiencing a heavy burden of SARS-CoV-2 infections. cording to our model Piedmont; Veneto; Emilia Romagna; Tuscany and Marche will reach an R0 value of up to 3.5. The R0 was 3.11 for Lazio and 3.14 for the Campania region; where the latter showed the highest value among the Southern Italian regions; followed by Apulia (3.11); Sicily (2.99); Abruzzo (3.0); Calabria (2.84); Basilicata (2.66); and Molise (2.6). The R0 value is decreased in Lombardy and the Northern regions [19] while it is increased in Central and Southern regions (Figure 4).

Severe acute respiratory syndrome coronavirus-2 [20] which began in Wuhan; China; has spread throughout the country and many countries around the world. The number of children with coronavirus disease-2019 (COVID-19) has also increased significantly. Although information regarding the epidemiology of COVID-19 in children has accumulated; relevant comprehensive reports are lacking. Soon after the number of cases [21] soared dramatically spreading across China and worldwide. Italy has had 12;462 confirmed cases according to the Italian National Institute of Health (ISS) as of March 11; and after the "lockdown" of the entire territory; by May 4; 209;254 cases of COVID-19 and 26;892 associated deaths have been reported (Figure 5).

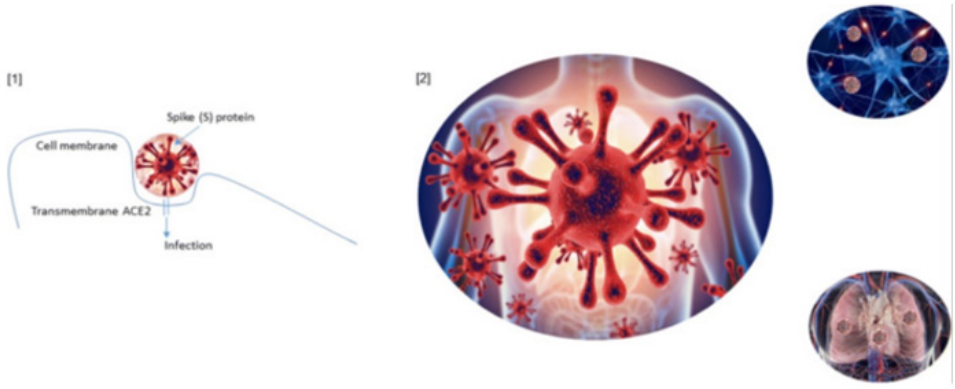


Figure 5: (Carla Prezioso, Maria Marcocci, Anna Palamara, Giovanna C et al, 2020).

World health organization has issued the [22] warning in December 2019 for the Novel corona virus in Wuhan China. The lesson learned from the Pandemic COVID-19 is that our health systems and health agencies do not have abilities to save their citizens and they have to work [22] hard to improve their abilities to save their citizens. Here; we report three children [23] cases of SARS-CoV-2 infected children diagnosed from 3 February to 17 February 2020 in Tianjin; China. All of these three cases experienced mild illness and recovered soon after the treatment; with the nucleic acid of throat swab turning negative within 14; 11; and 7 days after diagnosis; respectively. However; after been discharged all three cases were tested SARS-CoV-2 positive in the stool samples within 10 days in spite of their remained negative nucleic acid in throat swab specimens. Therefore; it is necessary to be aware of the possibility of fecal-oral [23] transmission of SARS-CoV-2 infection; especially for children cases (Figure 6).

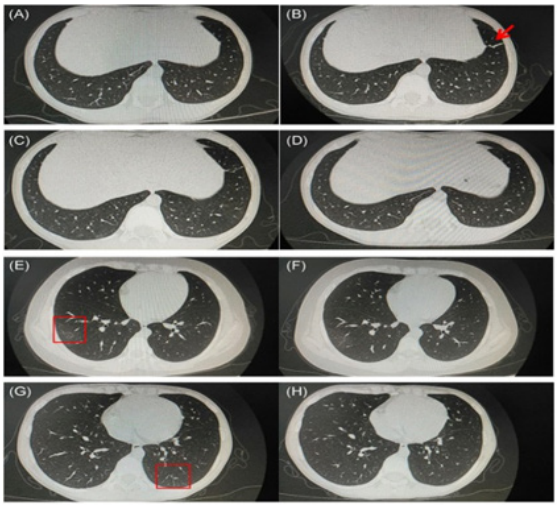


Figure 6: Imaging characteristics of children with COVID-19. (Tongqiang Zhang, Xiaojian Cui, Xue Zhao, Jinhu Wang et al, 2020).

COVID-19- Epidemiological Triangle made up of Three Parts: Agent; Host and Environment

The disease triangle; disease outbreaks depend [24] on the "disease triangle" Scholthof said. Scholthof said a simple form of McNew's disease triangle is helpful to explain the key role of environment in the success of pathogens such as SARS-CoV-2; the virus that causes COVID-19. In the case of COVID-19; people are the susceptible hosts and SARS-COV-2; the virulent pathogen. The constant and close contact between people is the hospitable environment needed to keep this pandemic going strong. The novel coronavirus; having jumped from an animal host; has become [24] extraordinarily successful at infecting humans [25] (Figures 7 & 8).

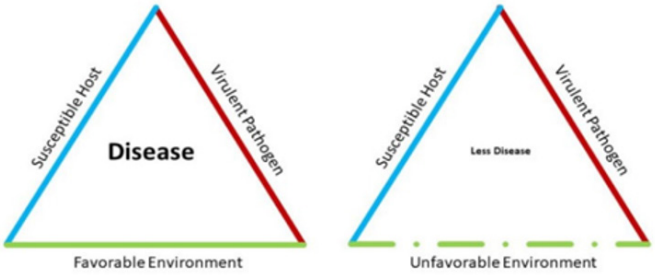


Figure 7: News wise [24].

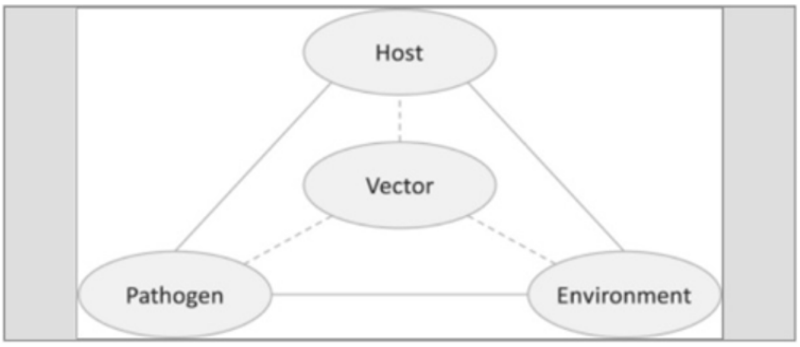


Figure 8: Epidemiological triad. The main infection components are host, agent and environment. The vector is frequently related to all components making it a hub node in the transmission network, and hence a good target for infection control approaches. (Openi.nlm.nih.gov, 2020).

The epidemiologic Triangle [26] includes chain of infection requirement as mentioned. Here infectious agent is corona virus which leaves its reservoir source or host through a portal of exit. COVID-19 Virus is conveyed by some mode of transmission and enters the host through an appropriate portal of entry. Virus infects the susceptible person; and the newly-infected individual becomes [26] a new reservoir and the whole process starts over. The Epidemiologic Triangle [27] is a model that scientists have developed for studying health problems. It can help your students understand infectious diseases and how they spread; study the facts (Figure 9).

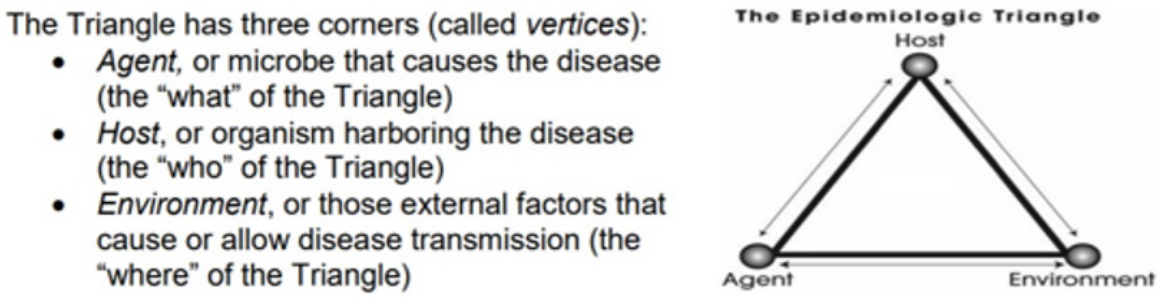


Figure 9: (CDC.GOV, 2020).

It plays a crucial role in curbing disease [28] burden by breaking the chain of transmission through a preventive or curative mechanism. This arm of public health detects disease and decides on appropriate intervention. The case of COVID-19 disease is a typical example of the

role of epidemiology in the news. The descriptive epidemiologic study of COVID-19 is currently giving the world a sense of direction on the incidence; virulence; fatality rate; and possible interventions to curb this pandemic virus. In epidemiology; both the health-care provider and the non-health-care provider are stakeholders as they work in synergy to create [28] the news. This game-changing role of epidemiology can create a healthy nation (Figure 10).

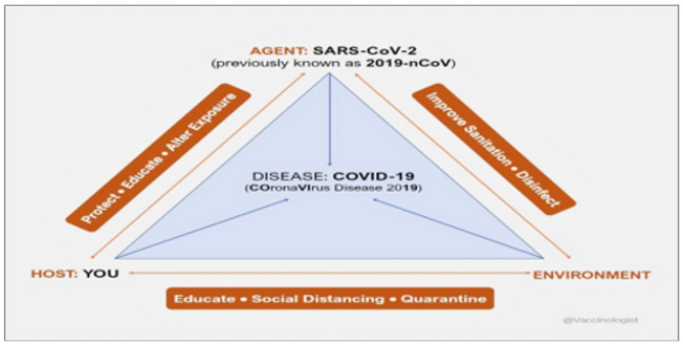


Figure 10: RG Epidemiology in the News [28].

Aims and Objectives

The author of this book has discussed the Epidemiology; Incidence; distribution; control and preventions of the current COVID-19 Pandemic. The main aim of writing this short book is to discuss COVID-19 Pandemic treatment available for sick patients and how long time it would take to develop and approve vaccination. This book also discusses the latest articles literature review about the topic COVID-19 Pandemic which has taken grasp on the whole world and become disaster for all the governments. Since the start of COVID-19 in Wuhan China in November 2019 till present August 2020 where WHO declared it COVID-19 Pandemic. Approximately 16.5 Million people all around the world in 215 countries are sick due to COVID-19 Pandemic and 660;000 people died because of COVID-19 illness. The articles selected for the Literature reviews are mostly from PubMed central; well known Journals; websites and books. This books also discusses the importance of Epidemiology; Prevention medical science and data collection to control the epidemic or Pandemic (Figure 11).

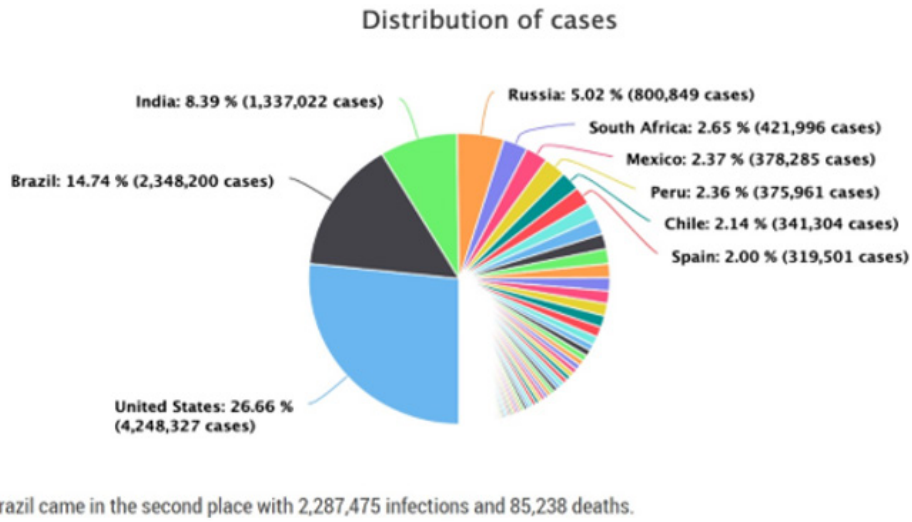


Figure 11: Countries Covid-19 cases distribution 26 July [32].

Epidemiology is the study of the emergence [29] distribution and control of disease; disability and death among groups of people. "Epidemiology is a tool in many ways to understand the distribution of disease in populations; and the factors that lead to higher or lower rates of disease and ways of effectively preventing disease" Lewis Kuller; according to professor of epidemiology. Epidemiologists can be thought of as doctors of the masses. An epidemiologist focuses on the collective health of communities and sometimes global populations of people. As a disease detective; every epidemiologist needs an extensive toolbox to find and investigate clues. [29] And at the center of every epidemiologist's toolbox is the so-called epidemiologic triangle [30] (Figures 12 & 13).

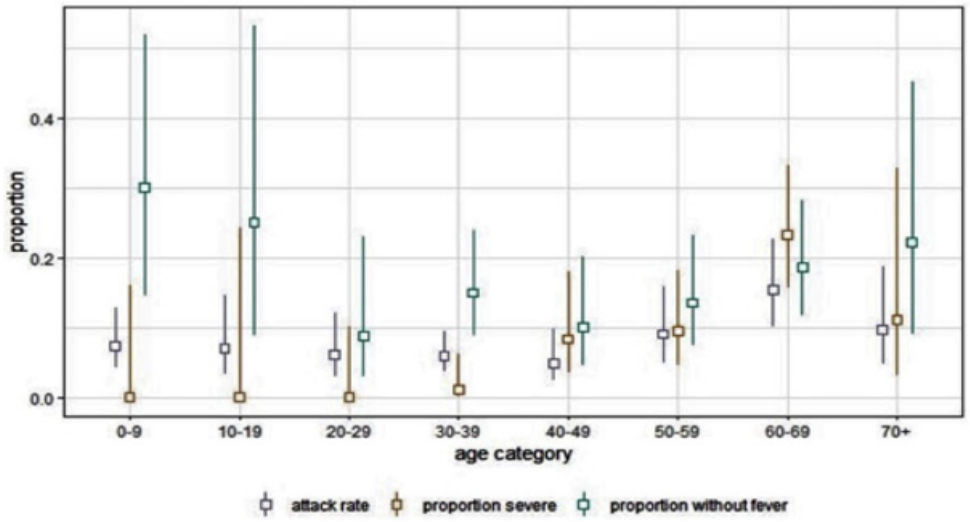


Figure 12: Attack rate among close contacts, baseline severity, and proportion without fever at initial assessment by age group. (RG Epidemiology and Transmission, 2020).

		Outcome: symptom-based surveillance						Outcome: moderate/severe symptom					
		Univariate regression			Multivariate regression			Univariate regression			Multivariate regression		
		OR	2.5%	97.5%	OR	2.5%	97.5%	OR	2.5%	97.5%	OR	2.5%	97.5%
sex	female	ref			ref			ref			ref		
	male	3.23	1.93	5.53	3.06	1.77	5.44	1.30	0.82	2.07	1.37	0.85	2.22
age	0-9	0.07	0.02	0.23	0.08	0.02	0.25	0.88	0.30	2.77	0.67	0.22	2.23
	10-19	0.19	0.05	0.77	0.17	0.04	0.76	1.08	0.28	5.27	0.88	0.22	4.40
	20-29	0.33	0.12	0.89	0.37	0.13	1.02	0.65	0.28	1.56	0.61	0.26	1.49
	30-39	0.75	0.31	1.77	0.8	0.32	1.93	1.17	0.58	2.37	1.15	0.57	2.33
	40-49	0.86	0.32	2.33	0.79	0.29	2.19	1.27	0.58	2.83	1.21	0.55	2.72
	50-59	ref			ref			ref			ref		
	60-69	0.48	0.2	1.08	0.44	0.18	1.04	1.50	0.72	3.16	1.43	0.68	3.03
	70+	0.56	0.16	2.25	0.45	0.12	1.89	1.41	0.45	5.43	1.28	0.40	4.96
severity	mild	ref			ref			-	-	-	-	-	-
	moderate	0.6	0.33	1.05	0.51	0.26	0.94	-	-	-	-	-	-
	severe	2.2	0.68	9.84	1.51	0.42	7.23	-	-	-	-	-	-
fever	no	ref			-	-	-	ref			-	-	-
	yes	3.06	1.69	5.49	-	-	-	0.94	0.49	1.75	-	-	-
symptomatic	no	ref						ref					
	yes	8.62	3.68	21.89	-	-	-	0.51	0.15	1.39	0.55	0.29	1.01
surveillance method	contact-based	ref			-	-	-	ref			-	-	-
	symptom-based	-	-	-	-	-	-	0.67	0.37	1.17	-	-	-

Figure 13: Association of clinical and demographic factors with mode of detection. (RG Epidemiology and Transmission, 2020).

The aim of this book writing is to identify the mistakes and ignorance made by Governments of the countries to contain or tackle the COVID-19 Pandemic. How does the COVID-19 SARS Cov get out of Wuhan China and spread to the whole world 215 countries till now? Why did not WHO; UN; UNICEF; EU Health commission; US CDC act as fast as possible in November 2019 to stop the virus spread? Rather than act quickly as it could be the Governments of EU; the UK and the USA politicises the Pandemic issue and started blame game on the WHO current secretary general. Now the public is paying the price of ignorance by their lives and dying due to COVID-19 Pandemic. The statistics should be noticed that currently USA; Brazil; India and the Russia is highest victim of COVID-19 and China has controlled the COVID-19 spread as early in February 2020.

Context Setting

The Author has chosen the Critical Literature review as the methodology for this book. The articles are chosen by selected words such as "Epidemiology of COVID-19; COVID-19 Epidemiological Triangle; COVID-19 Vaccination; COVID-19 Treatment; others for the PubMed; Google others search engines. The First chapter of the book "introduction" discusses the Epidemiology of the COVID-19 in Incidence and distribution among the community. Also; in the chapter first there are details about COVID-19 as Epidemiological Triangle made up of three parts: agent; host and environment.

First chapter also discusses about aims and objectives of writing this book and the difficulties during literature review; publishing the book.

The second chapter discusses following points:

1) What is COVID-19 pathophysiology?

2) What are the effects of COVID-19 in the Adults patients?

3) What are the effects of COVID-19 in children?

4) Statistics about children affected by COVID-19.

5) Role of PPE specially wearing mask all the time.

6) Public health message of hand washing several times in a day and social distancing in COVID-19 Pandemic.

7) Actions taken against not following the orders of prevention from COVID-19 in the USA.

8) Intervention strategies for reducing the spread of COVID-19 among the community.

9) The role of COVID-19 Testing and self-quarantine in the COVID-19 Pandemic.

10) The need of Vaccine development for COVID-19 and the progress made till August 2020.

11) Treatment for COVID-19 Pandemic or the supportive treatment available till August 2020.

12) Patients again get infected by COVID-19 after some time when they have tested Positive and then Negative; later again tested Positive after few months.

13) How long the COVID-19 Pandemic would last may be till 2030?

The third and the fourth chapter tells us that the author of this book has chosen the critical analytical literature review as the methodology. The author has chosen method as "Key word searches" in the Pubmed central; Google and other search engines to find the research articles and other discussions on the websites for referencing. Key word search focused the search to Epidemiology of COVID-19 or COVID-19 Vaccination or treatment available which proves to be right method.

The fifth and sixth chapter include the results and analysis of the study of Epidemiology of COVID-19 for the book. The fifth chapter includes the results of the study and the presentation of the findings which includes 10 articles and papers (different articles from preliminary literature review) which will be used for critical literature review (CLR) and to present the results.

The sixth chapter includes analysis of the studies reviewed for the Epidemiology of COVID-19; crucial data; control and prevention. It also includes the tables of aim and objective and common themes across the articles in critical literature review.

The seventh chapter discusses the points below in the discussion chapter:

1) COVID-19 in context of 5 W's of Epidemiology (diagnosis or health event (what); person (who); place (where); time (when); and causes; risk factors; and modes of transmission (why/how).

2) COVID-19 How did it start?

3) Policies; Programmes and their implications - WHO; CDC and other government action plan against the COVID-19 Pandemic.

4) COVID-19 surveillance and tracking in the community.

5) COVID-19 Economic impact on the countries and statistics.

6) COVID-19 Awareness; body temperature;

7) Critical care for the COVID-19 Patients.

8) Death rate in COVID-19?

9) World Dashboard of COVID-19 and global statistics.

10) COVID-19 free countries and affected countries.

11) COVID-19 Guidelines; covid-19 kit;

12) COVID-19 Genome sequence.

13) COVID-19 Herd immunity.

14) COVID-19 mode of transmission and mortality rate.

15) COVID-19 Second wave and when it is happening?

16) COVID-19 and Zip code in the USA?

Eighth chapter includes the conclusion of the study of the articles and author views on them. The book includes so many references from the different articles from different journals; papers from the different health websites; reference books and newspapers. The referenced articles discuss the current COVID-19 Pandemic and the proactive approach towards preventions of COVID-19. As we all know that there is no approved Vaccine and treatment specifically available for COVID-19 pandemic. The author wishes to contribute the research book for the successful availability of COVID-19 Vaccine and treatment available to help the vulnerable sick and ill because of COVID-19 Pandemic.


2
Chapter

Preliminary Literature Review

Overview of "Epidemiology of COVID-19 in incidence distribution and prevention; availability of possible vaccination and treatment. A Battle against the Pandemic while whole world is fighting the COVID 19 novel corona Virus [31] possibly originated from Wuhan; Hubei Province China."

What is COVID-19 Definition and Pathophysiology?

The coronavirus disease- COVID-19 [30] is an infectious disease caused by a new strain of coronavirus. This new virus and disease were unknown before the outbreak began in Wuhan China in December 2019. Although for most people COVID-19 causes only mild illness; it can make some people very ill. More rarely; the disease can be fatal. Older people and those with pre- existing medical conditions such as high blood pressure heart problems [31] or diabetes appear to be more vulnerable [32] (Figures 14 & 15).

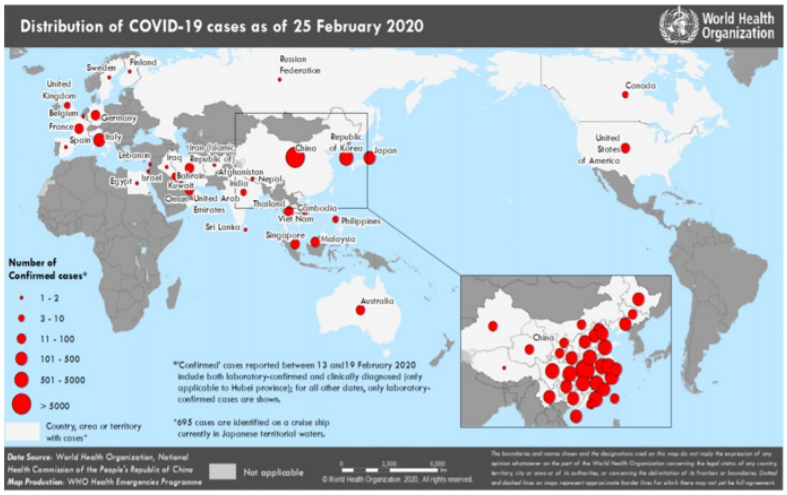
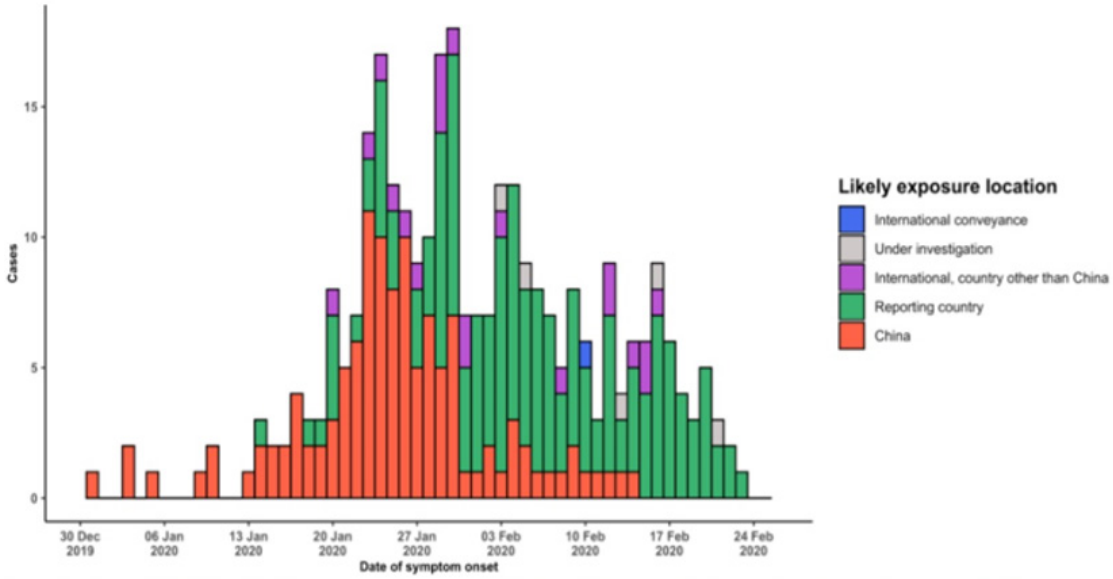


Figure 14: Countries, territories or areas with reported confirmed cases of COVID-19, 25 February 2020. (WHO, 2020).



Note: Of the 2459 cases reported outside china, 86 were detected while apparently asymptomatic. For the remaining 2373 cases, information on date of onset is available only for the 303 cases presented in the epidemiologic curve.

Figure 15: Epidemic curve of COVID-19 cases (n=303) identified outside of China. (WHO, 2020).

COVID-19 a respiratory disease caused [33] by the SARS-CoV-2 virus was declared a pandemic by the World Health Organization (WHO) on 11 March 2020. The rapid spread of the disease has taken the scientific and medical community by surprise. Latest figures from 20 May 2020 show more than 5 million people had been infected with the virus causing more than 330;000 deaths in over 210 countries worldwide. Current COVID-19 Pandemic; [34] MERS; SARS; EBOLA and other epidemics teaches us the lesson than as the world population grows; we need more research and technology to handle Pandemic such as COVID-19. More resources and advance technology are needed to battle diseases and training for medical staff is needed. Nuclear Radiotherapy; Nuclear radiology; MRI Scan; CT Scan; X Rays; Ultrasound; Angioplasty and Angiography others made [34] the diagnosing and treatment easier for the patients [35] (Figure 16).

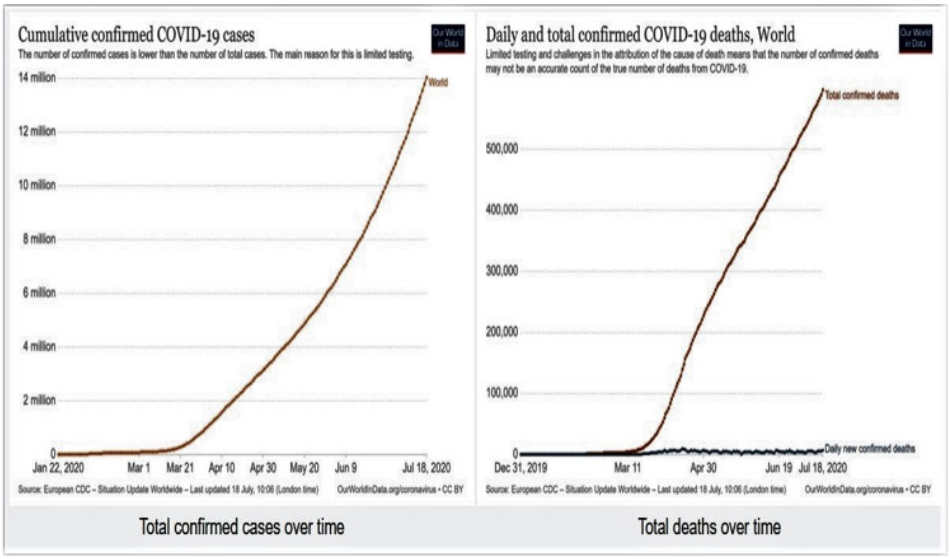


Figure 16: (Wikipedia coronavirus disease 2019, 2020).

A novel coronavirus named severe acute [36] respiratory syndrome coronavirus-2 (SARS-CoV-2) was isolated from lower respiratory tract sample as the causative agent. The current outbreak of infections with SARS-CoV-2 is termed Coronavirus Disease 2019 (COVID-19) by the World Health Organization (WHO). COVID-19 rapidly spread into at least 114 countries and killed more than 4;000 people by March 11 2020. WHO officially declared COVID-19 a pandemic on March 11 2020. There have been 2 novel coronavirus outbreaks in the past 2 decades. The outbreak of severe acute respiratory syndrome (SARS) in 2002-2003 caused by SARS-CoV had a case fatality rate of around 10% (8;098 confirmed cases and 774 deaths) while Middle East respiratory syndrome [36] (MERS) caused by MERSCoV killed 861 people out of a total 2;502 confirmed cases between 2012 and 2019 (Figure 17).

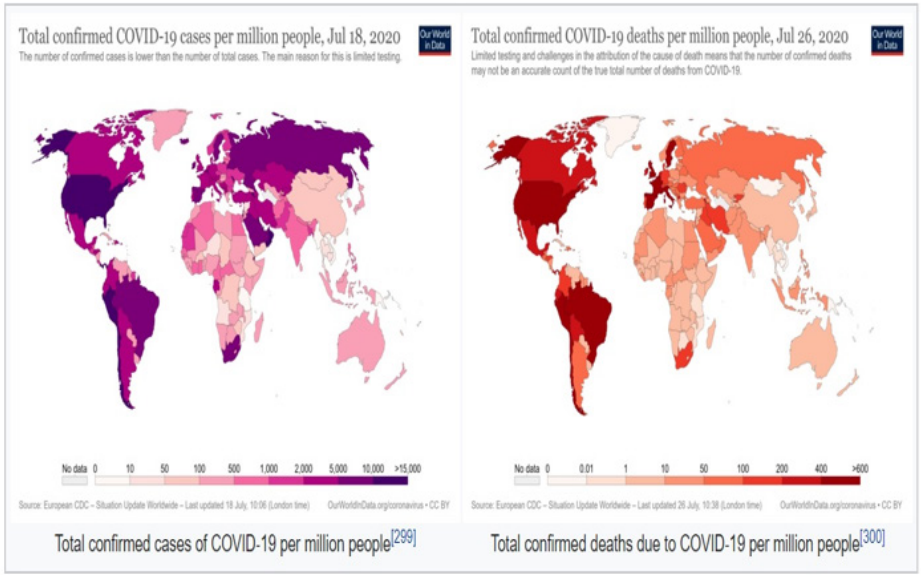


Figure 17: (Wikipedia coronavirus disease 2019, 2020).

Clinical evidence indicates that the fatal [37] outcome observed with severe acute respiratory syndrome-coronavirus-2 infection often results from alveolar injury that impedes airway capacity and multi-organ failure-both of which are associated with the hyperproduction of cytokines; also known as a cytokine storm or cytokine release syndrome. Clinical reports show that both mild and severe forms of disease result in changes in circulating leukocyte subsets and cytokine secretion; particularly IL-6; IL-1β; IL-10; TNF; GM-CSF; IP-10 (IFN-induced protein 10); IL-17; MCP-3; and IL-1ra. Not surprising; therapies that target the immune response and curtail the cytokine storm [37] in coronavirus 2019 (COVID-19) patients have become a focus of recent clinical trials (Figure 18).

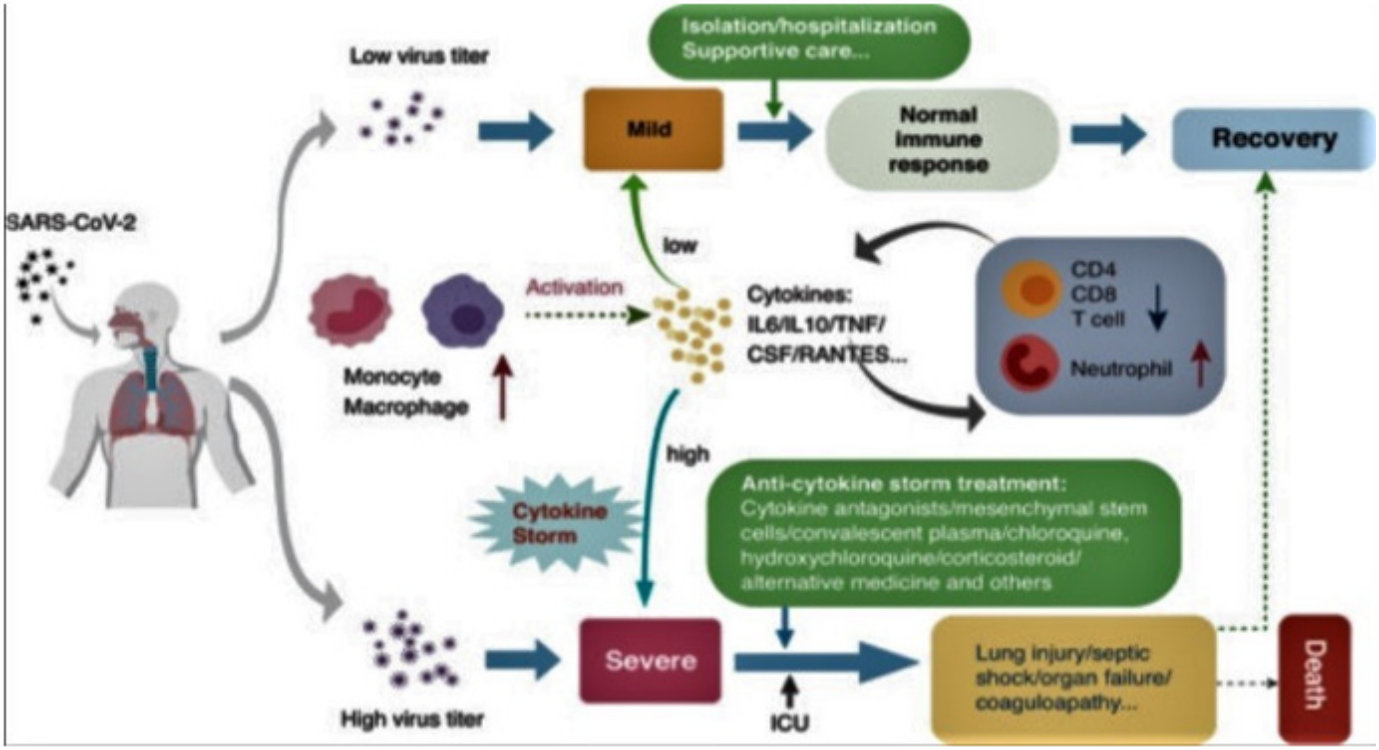


Figure 18: (Jin Wang, Mengmeng Jiang, Xin Chen, Luis M, 2020).

Mortality in COVID-19 patients [38] has been linked to the presence of the so-called "cytokine storm" induced by the virus. Excessive production of proinflammatory cytokines leads to ARDS aggravation and widespread tissue damage resulting in multi-organ failure and death. Targeting [38] cytokines during the management of COVID-19 patients could improve survival rates and reduce mortality. For instance; strategy [39] high IL-6 concentration predicted mortality in patients with MERS. In patients infected with pathogenic human coronaviruses cytokine storm contributes to acute lung injury and acute respiratory distress syndrome-ARDS. Therefore; controlling the cytokine storm might be a strategy [39] for treating patients with COVID-19 especially for those severe cases.

In a retrospective study of 41 patients with COVID-19 [40] most patients with SARS-CoV-2 infection developed mild symptoms; whereas some patients later developed aggravated disease symptoms; and eventually passed away because of multiple organ dysfunction syndrome (MODS) [40] as a consequence of a severe cytokine storm. At present some therapies such as interleukin-6 antibody blocker stem cell therapy and transfusion of convalescent plasma have been applied to counteract the [41] cytokine storm with some progresses being achieved.

Clinical studies have also reported [42] an association between COVID-19 and cardiovascular disease. Pre-existing cardiovascular disease seems to be linked with worse outcomes and increased risk of death in patients with COVID-19 whereas COVID-19 itself can also induce myocardial injury arrhythmia; acute coronary syndrome and venous thromboembolism. Potential drug disease interactions affecting patients with COVID-19 and [42] comorbid cardiovascular diseases are also becoming a serious concern (Figure 19).

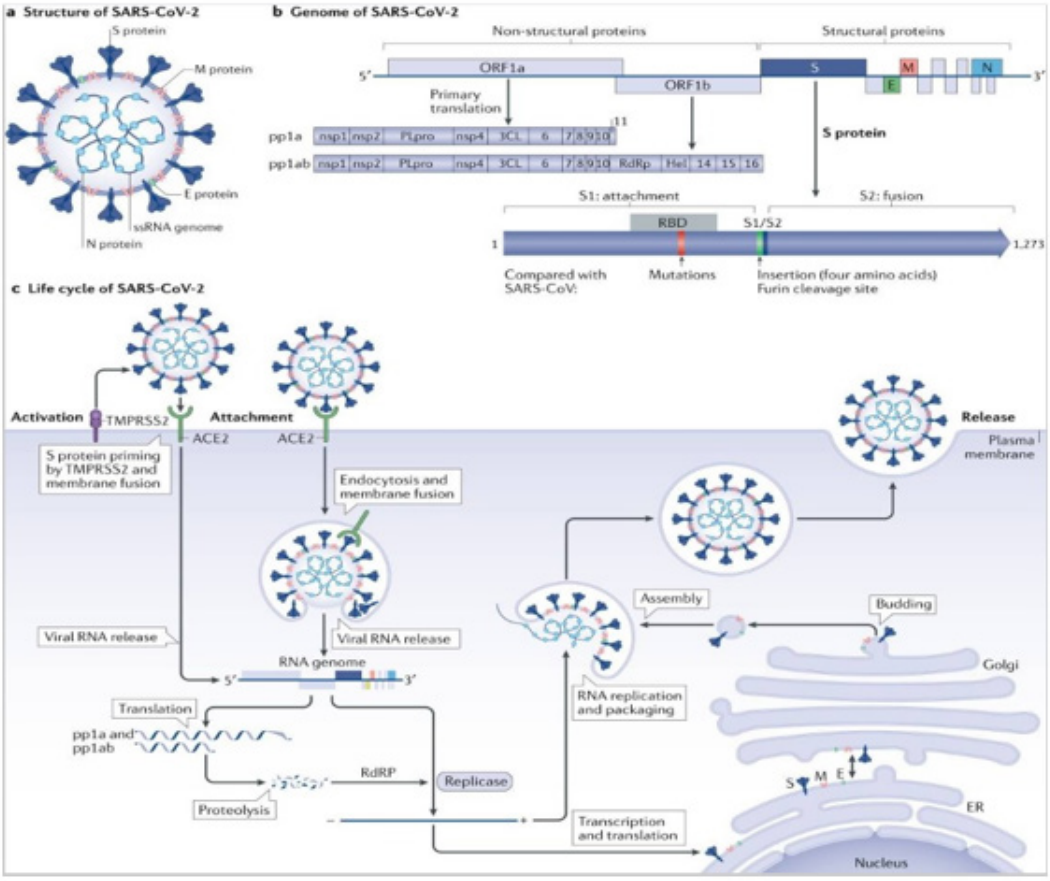


Figure 19: (Masataka Nishiga, Dao Wang, Yaling Han, David L et al, 2020).

SARS-CoV-2 is closely related to two bat-derived [43] severe acute respiratory syndrome like coronaviruses bat-SL-CoVZC45 and bat-SL-CoVZXC21. Among patients with pneumonia caused by SARS-CoV-2 (novel coronavirus pneumonia or Wuhan pneumonia) fever was the most common symptom followed by cough. Bilateral lung involvement with ground-glass opacity was the [43] most common finding from computed tomography images of the chest. The treatment guidelines for COVID-19 [44] vary [45] between countries yet there is no approved treatment to date. A systematic review protocol was developed based on the PRISMA statement. Four hundred and forty-nine articles were identified in the literature search of these 41 studies were included in this review. These were clinical trials (N=3); case reports (N=7); case series (N=10); and retrospective (N=11) and prospective (N=10) observational studies. Thirty-six studies were conducted in China (88%). Corticosteroid treatment [45] was reported most frequently (N=25); followed by lopinavir (N=21) and oseltamivir (N=16).

Despite rigorous global containment and [46] quarantine efforts the incidence of COVID-19 continues to rise with more than 1;948;617 laboratory-confirmed cases and over 121;846 deaths worldwide. Currently; no specific medication is recommended to treat COVID-19 patients. Favilavir is an antiviral drug that is approved in Japan for common influenza treatment and is now approved to treat symptoms of COVID-19 in China. Moreover; Chloroquine and hydroxychloroquine; drugs used to treat malaria and arthritis; respectively; were recommended by the National Health Commission of the People's Republic of China for treatment of COVID-19. Presently; chloroquine and hydroxychloroquine are under investigation by the US Food and Drug Administration (FDA) as a treatment for COVID-19. The first COVID-19 vaccine is not expected to be ready [46] for clinical trials before the end of the year.

What are the Effects of COVID-19 in the Adults Patients?

No drugs are currently approved [47] for Coronavirus Disease-2019 (COVID-19) although some have been tried. In view of recent studies and discussion on chloroquine and hydroxychloroquine (HCQ) we aimed to review existing literature and relevant websites regarding these drugs and COVID-19 adverse effects related to drugs and related guidelines. The elderly may represent a specific [48] cluster of high-risk patients for developing COVID-19 with rapidly progressive clinical deterioration. Indeed; in older individuals [48] immune senescence and comorbid disorders are more likely to promote viral-induced cytokine storm resulting in life-threatening respiratory failure and multisystemic

involvement. Our review examines the pathogenesis and clinical implications of ageing in COVID-19 patients finally we discuss the evidence and controversies in the management in the long-stay residential care homes [48] and aspects of end-of-life care for elderly patients with COVID-19 [49] (Figure 20).

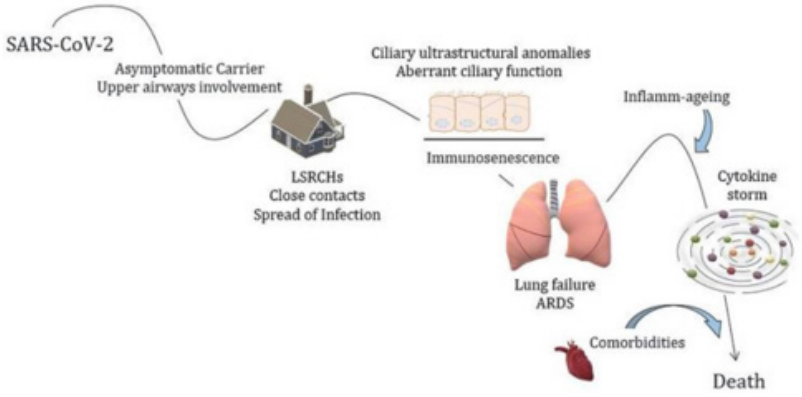


Figure 20: Proposed risk factors and pathogenetic mechanisms underlying increased mortality among elderly with SARS-CoV-2 infection. (Fabio Perrotta, Graziamaria Corbi, Grazia Mazzeo, Matilde B et al, 2020).

COVID-19 has become [50] a global pandemic immune dysregulation has been implicated but immune responses remain poorly understood. We analysed 71 COVID-19 patients compared to recovered and healthy subjects using high dimensional cytometry. Integrated analysis of 200 immune and >30 clinical features revealed activation of T cell and B cell subsets but only in some patients. A subgroup of patients had T cell activation characteristic of acute viral infection and plasma blast responses could reach >30% of circulating B cells. However; another subgroup had lymphocyte activation comparable to uninfected subjects. These analyses identified three "immunotypes" associated with poor clinical trajectories versus improving health. These immunotypes may have [50] implications for therapeutics and vaccines (Figure 21).

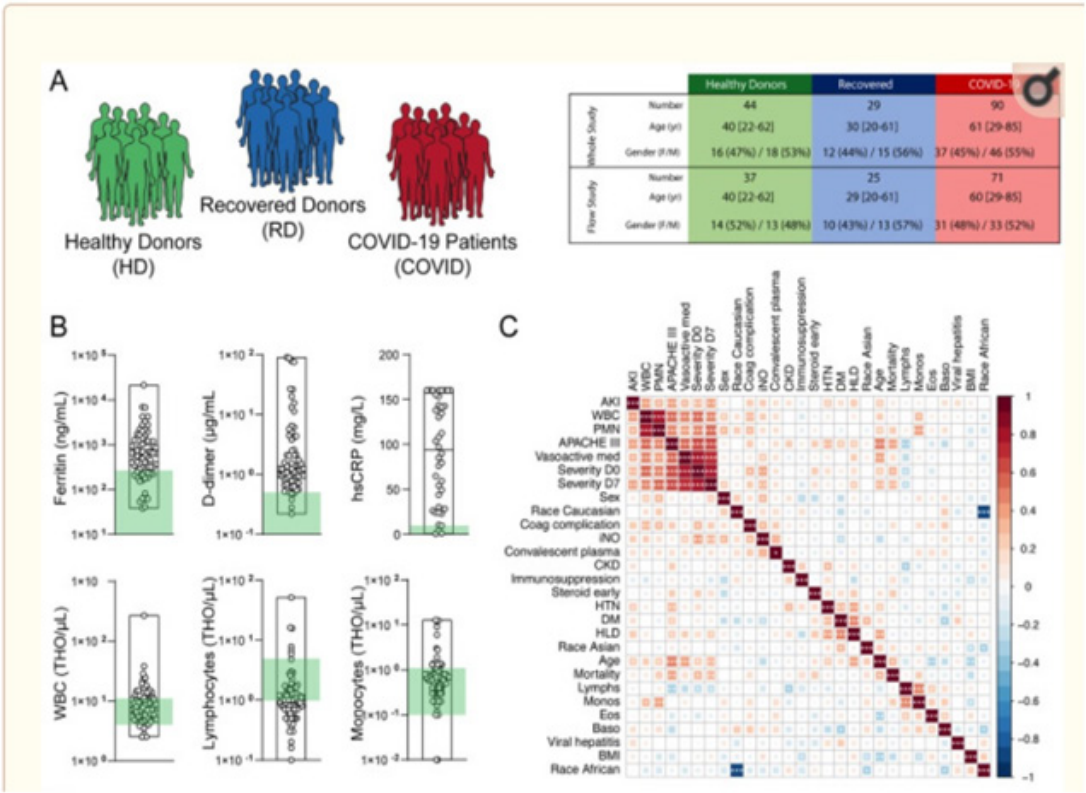


Figure 21: Clinical characterization of cohort, inflammatory markers, and quantification of major immune subsets. (Divij Mathew, Josephine Giles, Amy E. Baxter, Allison G et al, 2020).

Along with its high infectivity and fatality [51] rates the 2019 Corona Virus Disease (COVID-19) has caused universal psychosocial impact by causing mass hysteria economic burden and financial losses. Mass fear of COVID-19 termed as "corona phobia" has generated a plethora of psychiatric manifestations across the different strata of the society. The psychosocial aspects of older people their caregivers; psychiatric patients and marginalized communities are affected by this pandemic [51] in different ways and need special attention. COVID-19 mortality rate is higher in [52] the elderly and in those with pre-existing chronic medical conditions. The elderly also suffers from increased morbidity and mortality from seasonal influenza infection and thus annual influenza vaccination is recommended for them. The significant public health implications of this possibility point to an urgent need for studying the relationship between influenza vaccination and COVID-19 mortality at the individual level to [52] investigate both the epidemiology and any underlying biological mechanism.

The fact that the virus- Coronavirus disease-2019 (COVID-19) uses [53] angiotensin-converting enzyme (ACE)-2 as the cell entry receptor and that hypertension as well as cardiovascular disorders frequently coexist with COVID-19 have generated considerable discussion on the management of patients with hypertension. In addition; the COVID-19 pandemic necessitates the development of and adaptation to a New Normal lifestyle which will have a profound impact not only on communicable diseases but also on noncommunicable diseases including hypertension. Summarizing what is known and what requires further investigation in this field may help to address the challenges we face [54] (Figure 22).

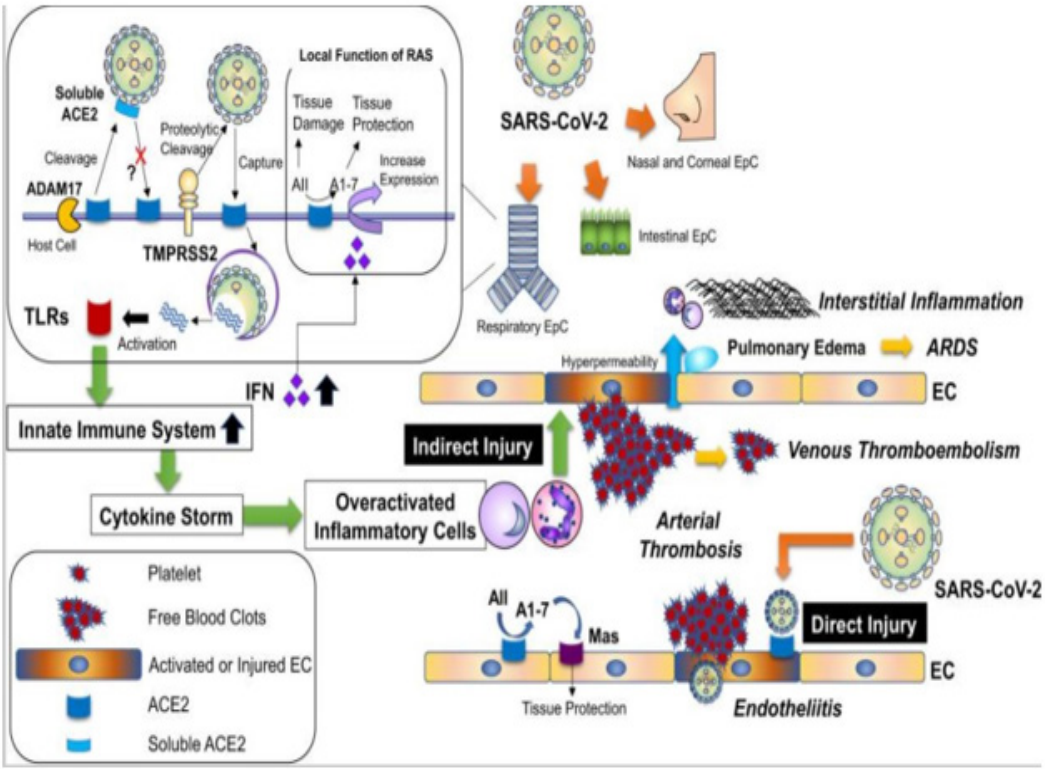


Figure 22: Possible mechanism of SARS-CoV-2-induced vascular complications. ACE2 angiotensin-converting enzyme 2, ADAM17 a disintegrin and metalloprotease 17, AII angiotensin II, A1-7 angiotensin 1-7, ARDS acute respiratory distress syndrome, EC endothelial cell, EpC epithelial cell, IFN interferon, SARS-CoV-2 severe acute respiratory syndrome coronavirus 2, TLRs Toll-like receptors, TMPRSS2 transmembrane serine protease 2, RAS renin-angiotensin system. (Shigeru Shibata, Hisatomi Arima, Kei Asayama, Satoshi H et al. 2020).

What are the Effects of COVID-19 in Children?

Eighty three percent of the children were within [55] family clusters of cases and 19% had no symptoms. At least 7% with digestive symptoms and the main symptoms of children were fever 48%; 95% confidence interval 39%; 56% and cough (39%; 95% CI: 30%; 48%). The lymphocyte count was below normal level in only 15% (95% CI: 8%; 22%) of children which is different from adult patients. 66% (95% CI: 55%; 77%) of children had abnormal findings in CT imaging. Most children with COVID-19 have only mild symptoms and many children are asymptomatic. Fever and cough are the most common symptoms in children. Vomiting and diarrhoea were not common in children. [55] The lymphocyte count is usually within the normal range in children (Figure 23).

Symptoms and imaging results of patients with COVID-19

Variable	ES	I^2 (%)	P value
The overall symptoms			
No Symptom	19% (14%, 23%)	70.7	<0.10
Mild symptom	94% (90%, 98%)	89.9	<0.10
Severe symptom	3% (2%, 4%)	22.5	0.24
More than one sign or symptom	35% (21%, 48%)	80.8	<0.10
Specific symptoms			
Fever	48% (39%, 56%)	85.7	<0.10
Cough	39% (30%, 48%)	84.4	<0.10
Fever and cough	30% (18%, 42%)	67.4	<0.10
Sputum production	19% (0%, 44%)	97.5	<0.10
Rhinorrhea	9% (6%, 12%)	0.0	0.64
Shortness of breath/dyspnea	9% (0%, 19%)	91.8	<0.10
Myalgia or fatigue	8% (5%, 12%)	56.7	<0.10
Diarrhea	7% (5%, 9%)	0.0	0.62
Nausea or vomiting	6% (4%, 9%)	0.0	1.00
Nasal obstruction	6% (3%, 9%)	0.0	0.59
Sore throat	6% (2%, 10%)	35.2	0.13
Headache	4% (1%, 6%)	0.0	0.61
Imaging findings			
Abnormal	66% (55%, 77%)	89.6	<0.10
Unilateral pneumonia	31% (20%, 43%)	81.5	<0.10
Bilateral pneumonia	28% (20%, 36%)	81.3	<0.10
Ground-glass opacity	35% (26%, 44%)	84.7	<0.10

ES, effect size.

Figure 23: (Zijun Wang, Qi Zhou, Chenglin Wang, Qianling Shi et al, 2020).

We aim to investigate the clinical characteristics [56] of COVID-19 children with different severities and allergic status. The majority (97.8%) of infected children were not severe and 24 (13.2%) of them had asymptomatic infections. Compared to children without pneumonia (manifested as asymptomatic and acute upper respiratory infection) children with pneumonia were associated with higher percentages of the comorbidity history symptoms of fever and cough and increased levels of serum procalcitonin alkaline phosphatase and serum interleukins (IL)-2; IL-4; IL-6; IL-10 and TNF-α. All the hospitalized COVID-19 children had recovered except one death due to intussusception and sepsis [56]. Eighty-seven percent (95% CI: 77%-95%) [57] of patients had household exposure to COVID-19. The most common symptoms and signs were fever (53%; 95% CI: 45%-61%) cough (39%; 95% CI: 30%-47%) and sore throat/pharyngeal erythema (14%; 95% CI: 4%-28%) however 18% (95% CI: 11%-27%) of cases were asymptomatic. The most common radiographic and computed tomography (CT) findings were patchy consolidations (33%; 95% CI: 23%-43%) and ground glass opacities (28%; 95% CI: 18%-39%) but 36% (95% CI: 28%-45%) [57] of patients had normal CT images (Figure 24).

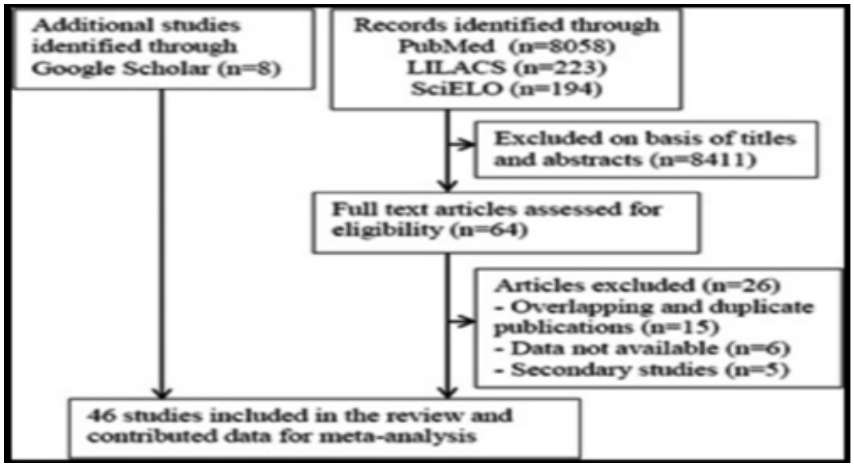


Figure 24: Flow chart for studies: (Linjie Zhang, Tyele G Peres, Marcus Silva, Paulo C et al, 2020).

According to the available data children [58] appear to be at lower risk for COVID-19 as adults constitute for maximum number of the confirmed cases (308;592) and deaths (13;069) as on 22nd March (https://www.worldometers.info/coronavirus). However; rapid publications and information of the adult patients with COVID-19 is in progress and published on the contrary almost no comprehensive data or discussion about the COVID-19 in children is available. Therefore; in this review we outline the epidemiology clinical symptoms; diagnosis; treatment; prevention [58] possible immune response and role of thymus in children to combat the COVID-19 outbreak (Figure 25).

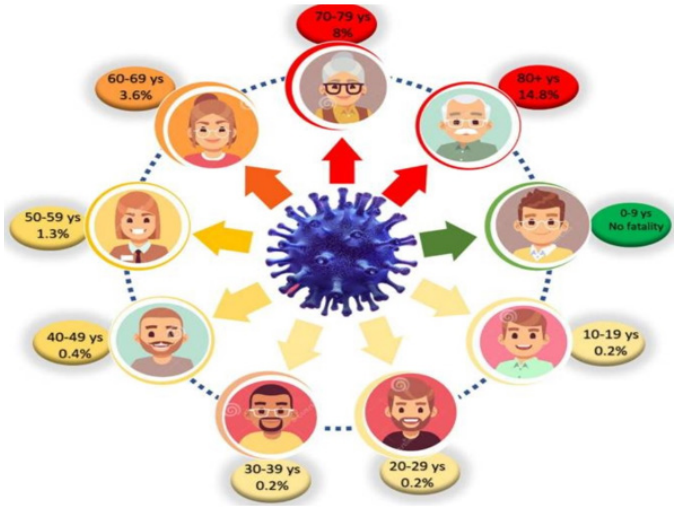


Figure 25: Illustration of fatality rate (percentage) among different age group in COVID-19. The sources of data presented is https://www.worldometers.info/coronavirus (Suriya Rehman, Tariq Majeed, Mohammad Ansari, Uzma Ali et al 2020).

In this Canadian study [59] only 4.8% (2.8% girls; 6.5% boys) of children and 0.6% (0.8% girls; 0.5% boys) of youth were meeting combined movement behaviour guidelines during COVID-19 restrictions. Children and youth had lower PA levels less outside time higher SB (including leisure screen time); and more sleep during the outbreak. Parental encouragement and support [59] parental engagement in PA and family dog ownership were positively associated with healthy movement behaviours. Four human coronaviruses (hCoVs)-229E; HKU1; NL63 and OC43-circulate globally [60] commonly infect children and typically cause mild upper respiratory tract infections. Consistent with what has been observed during the outbreaks of SARS and MERS; children with COVID-19 are more likely to be asymptomatic or to have mild-to-moderate illness with few deaths reported in children globally thus far. Clinical trials for therapeutics and vaccine development should include paediatric considerations. Children may play an important role in [60] the transmission of infection and outbreak dynamics and could be a key target population for effective measures to control outbreaks (Figure 26).

Measure	Total No Studies	Sample Size	WMD	95 CI	I^2 %	Cochran's Q, p-value
Hematologic						
WBC	8	71	1.34 × 10^9/L	0.09, 2.60	45	0.08
Neutrophils	4	33	1.83 × 10^9/L	0.99, 2.67	57	0.07
Lymphocytes	7	62	0.37 × 10^9/L	−0.41, 1.15	0	0.54
Platelets	4	34	32.59 × 10^9/L	−14.08, 79.26	0	0.93
Hemoglobin	5	42	−4.37 g/L	−9.94, 1.19	0	0.62
Biochemical						
ALT	7	62	−2.89 U/L	−6.71, 0.94	0	0.62
AST	7	61	−2.30 U/L	−8.46, 3.86	7	0.37
BUN	2	19	−0.57 mmol/L	−1.42, 0.27	0	0.99
Creatinine	3	24	0.74 μmol/L	−6.58, 5.09	0	0.41
CK	3	23	−47.52 U/L	−94.63, −0.4	0	0.91
CK-MB	4	35	2.61 U/L	−5.41, 10–64	44	0.14
LDH	5	41	37.06 U/L	10.76, 63.35	0	0.84
Inflammation/Coagulation						
D-Dimer	3	24	0.04 mg/L	−0.06, 0.13	36	0.21
Procalcitonin	4	30	−0.01 ng/mL	−0.03, 0.01	0	0.61
CRP	5	42	0.03 mg/L	−0.04, 0.10	58	0.05

*WMD: Weighted Mean Difference.

Figure 26: (Brandon Henry, Stefanie Benoit, Maria de Oliveira, Wan Hsieh et al, 2020).

Statistics about Children Affected by COVID-19

Children suspected of COVID-19 should not be [61] imaged routinely. Imaging should be performed only when expected to alter patient management depending on symptoms pre-existing conditions and clinical evolution. In order to prevent disease transmission; it is important to manage the inpatient caseload effectively by triaging children and carers outside the hospital re scheduling nonurgent elective procedures and [61] managing symptomatic children and carers as COVID-19 positive until proven otherwise (Figure 27).

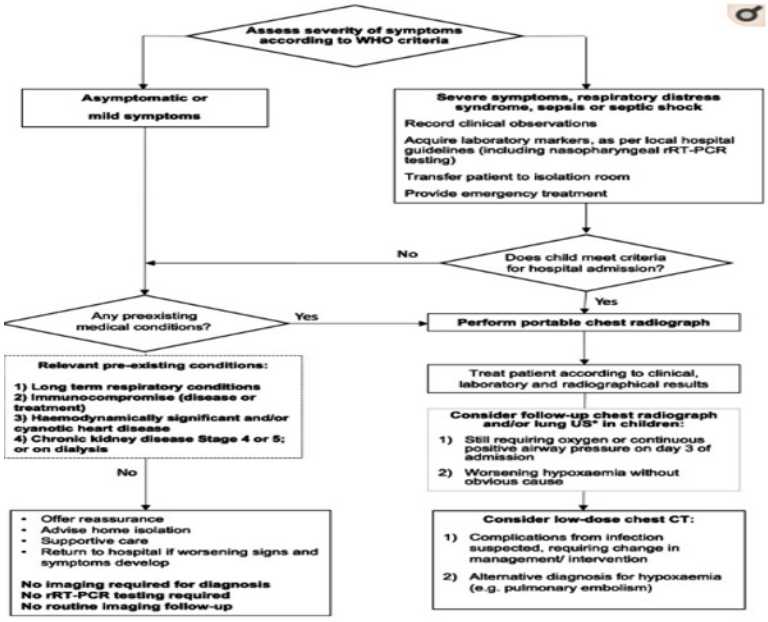


Figure 27: WHO Criteria: Huan Wu, et al. [399].

Although information [62] regarding the epidemiology of COVID-19 in children has accumulated relevant comprehensive reports are lacking. Special attention should be devoted to children because they are a special group of patients. Through analysis of the epidemiological history of a small number of child cases of COVID-19 and a fuller grasp of the epidemiological characteristics of SARS-CoV-2 it will be possible to provide more effective preventive measures and treatment policies and lay a solid foundation for winning [62] the battle against this epidemic (Figure 28).

Epidemiologic and clinical characteristics in pediatric series of COVID-19.

Diarrhea	2	0	6
Milk rejection	1	0	0
Feeding intolerance	1	0	0
Sneezing	0	1	4
Stuffy nose	0	1	4
Running nose	0	4	2
Fatigue/malaise	0	0	1
Lethargy	1	0	0
Sore throat	0	0	10
Shortness of breath	1	2	8
None	1	1	9
Case severity			
Mild	2	0*	3
Moderate	4	5*	33
Severe	0	1*	4
Critical	1	1*	4
Epidemiologic history			
Linkage to Wuhan**	6	14	30*
Contact with infected family member	2	15*	16*
Complication	1	3	3
Radiographic evidence	5	6*	28*
Positive nucleic acid test			
Pharyngeal swab	7	16	43
Stool/anal swab	5*	4*	5*
Sputum	NA	NA	1*
Urine	NA	0*	0*
Blood	NA	0*	0*
Treatment			
Oxygen therapy	1*	3	6*
Antiviral therapy	1*	5*	19*
Use of corticosteroid	0*	1*	9*
Antibiotic therapy	2*	4*	16*
Outcome			
Discharge	6	13	27
In hospital	1	3	17
Died	0	0	0

Figure 28: Yuanqiang Yu, et al. [398].

Children more often have gastrointestinal symptoms [63] compared with adults. Most children with SARS-CoV present with fever but this is not the case for the other novel CoVs. Many children affected by MERS-CoV are asymptomatic. The majority of children infected by novel CoVs have a documented household contact often showing symptoms before them. In contrast; adults more often have a nosocomial exposure. In this review we summarize epidemiologic clinical and diagnostic findings as well as treatment and [63-65] prevention options for common circulating and novel CoVs infections in humans with a focus on infections in children (Figure 29).

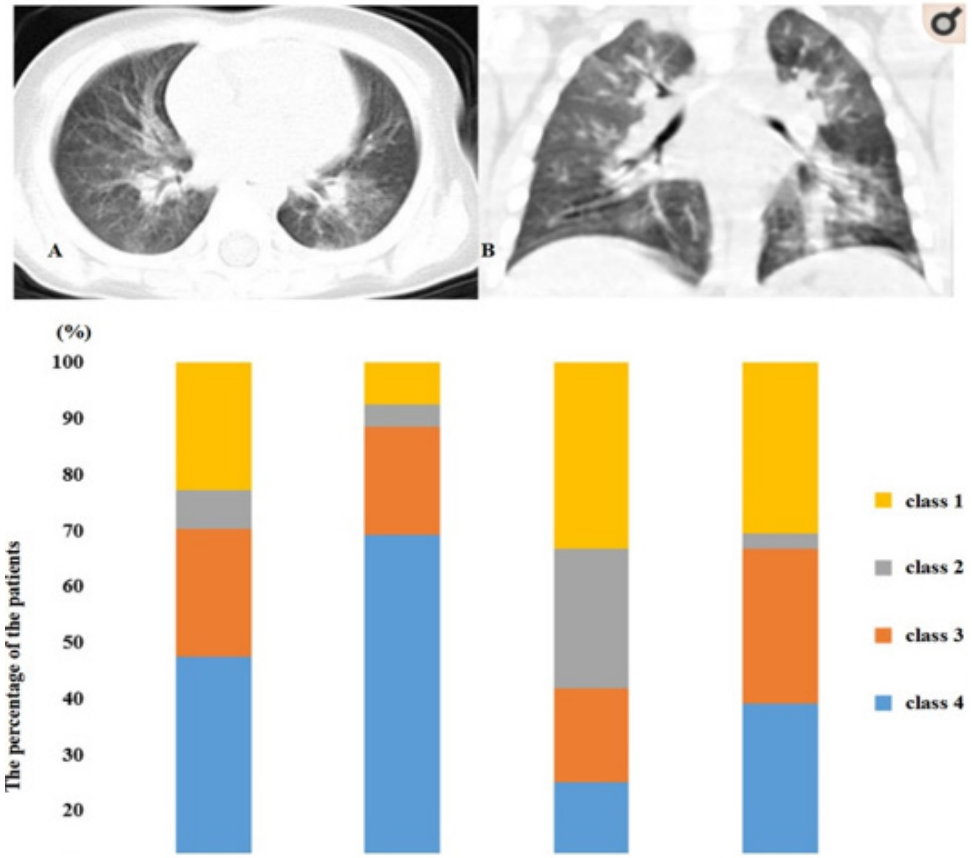


Figure 29: (A, B) Multifocal ground-glass opacities are shown in the lung. (C) Distribution of clinical symptoms and typical manifestations of viral pneumonia in chest CT. Class 1, symptom (+) CT (+); Class 2, symptom (+) CT (–); Class 3, symptom (–) CT (+); Class 4, symptom (–) CT (–). (Dan Sun, Feng Zhu, Cheng Wang, Jing Wu et al,2020).

Severe acute respiratory syndrome [66] coronavirus 2 (SARS-CoV-2) cause china epidemics with high morbidity and mortality the infection has been transmitted to other countries. About three neonates and more than 230 children cases are reported. The disease condition of the main children was mild. There is currently no evidence that SARS-CoV-2 can be transmitted trans placentally from mother to the new-born. The treatment strategy for children with Coronavirus disease (COVID-19) is based on adult experience. Thus far; no deaths have been reported in the paediatric age group. The disease condition of the neonates was also minor. Though this new virus comes out without specific antiviral drugs treatment neonatologist [64] needs to more virologic epidemiological and clinical data to treat and manage COVID-19.

Role of PPE Specially Wearing Mask All the Time

Thirteen patients with coronavirus disease 2019-COVID-19 [65] visited a university hospital in Seoul before recognizing their disease infections causing contact with 184 hospital workers. We classified the patients into four risk levels and provided corresponding management measures. The average age of study participants was 35.8 years [66] and 68.1% (286/420) were women. All 420 study participants had direct contact with patients with covid-19 and performed at least one aerosol generating procedure. During the deployment period in Wuhan none of the study participants reported covid-19 related symptoms. When the participants returned home; they all tested negative for SARS-CoV-2 specific nucleic acids and IgM or IgG antibodies (95% confidence interval 0.0 to 0.7%). Healthcare systems must give priority to the procurement and distribution of personal protective [66] equipment and provide adequate training to healthcare professionals in its use (Figures 30 & 31).

Aerosol generating procedures performed by healthcare professionals. Values are numbers (percentages)

Aerosol generating procedures	Cumulative procedures performed by doctors (n=116)				Cumulative procedures performed by nurses (n=304)			
	0	<10	10-20	>20	0	<10	10-20	>20
Tracheal intubation*	53 (45.7)	43 (37.1)	14 (12)	6 (5.2)	304 (100)	0 (0.0)	0 (0.0)	0 (0.0)
Ventilation	18 (15.5)	67 (57.8)	22 (19)	9 (7.7)	77 (25.3)	138 (45.4)	62 (20.4)	27 (8.9)
Gastric intubation	116 (100)	0 (0.0)	0 (0.0)	0 (0.0)	156 (51.3)	141 (46.4)	7 (2.3)	0 (0.0)
Sputum aspiration	116 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	61 (20)	127 (41.8)	116 (38.2)
Aerosol inhalation	116 (100)	0 (0.0)	0 (0.0)	0 (0.0)	107 (35.2)	116 (38.2)	34 (11.2)	47 (15.4)
Oral care	116 (100)	0 (0.0)	0 (0.0)	0 (0.0)	83 (27.3)	120 (39.5)	68 (22.4)	33 (10.8)
Tracheostomy care	116 (100)	0 (0.0)	0 (0.0)	0 (0.0)	88 (29)	135 (44.4)	52 (17.1)	29 (9.5))

*Combined tracheostomy and intubation.

Figure 30: Min Liu, et al. [66].

Personal protective equipment provided to study participants for prevention of covid-19

Personal protective equipment	Ward*			AGP† exposure	
	Intensive care units	Regular wards	No covid-19 contact area	AGPs	Non-AGPs
Mask:					
N95 respirator	+	+	-	+	+
Surgical mask	+	+	+	+	+
Medical suit	+	+	-	+	+
Isolation gown	+	+	-	+	+
Apron	-	-	-	+	-
Gloves	+	+	-	+	+
Eye protection	+	+	-	+	+
Hair cover	+	+	-	+	+

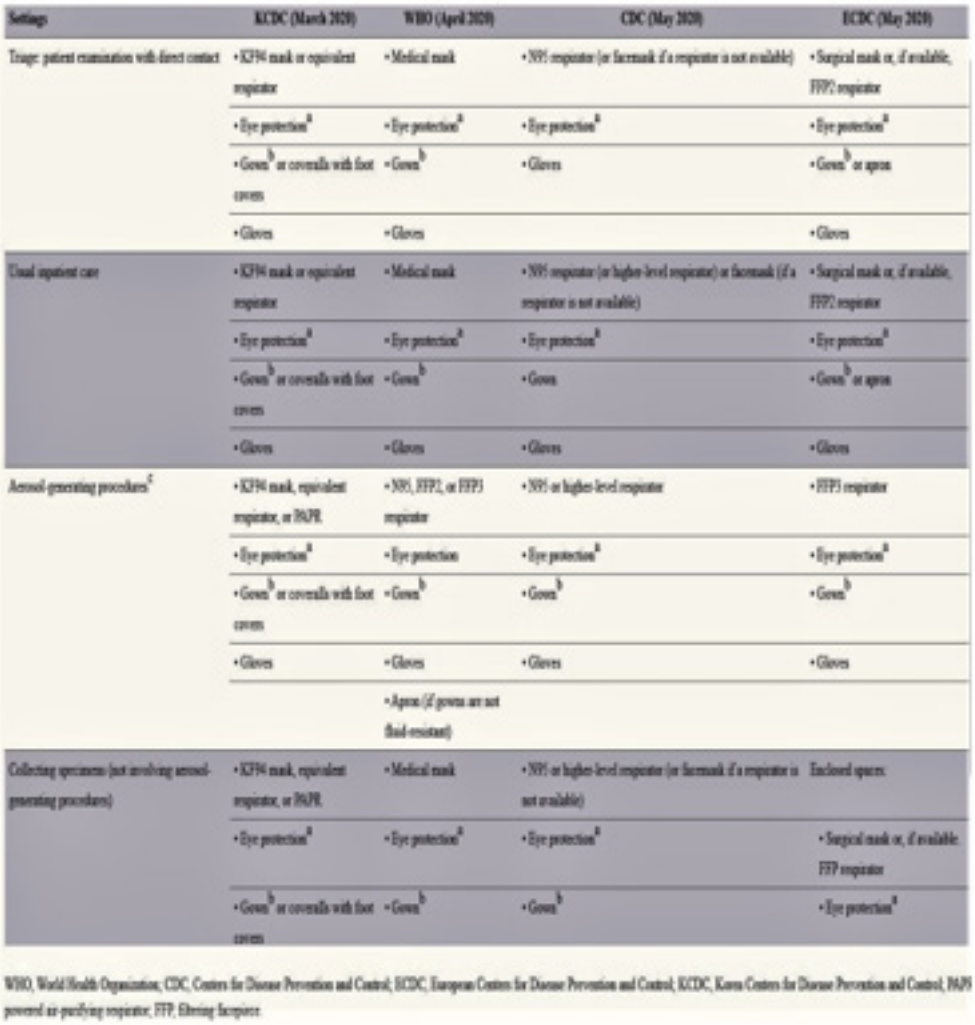
AGP–aerosol generating procedure; covid-19–coronavirus disease 2019.

*Overlap existed between the different wards.

†Powered air purifying respirator used when performing tracheal intubation.

Figure 31: Min Liu,et al [66].

Adequate personal protective equipment [67] is needed to reduce the rate of transmission of COVID-19 to health care workers. Otolaryngology groups are recommending a higher level of personal protective equipment for aerosol generating procedures than public health agencies. Otolaryngologists are likely at high risk of contracting COVID-19 during aerosol generating procedures because they are likely exposed to high viral loads in [67] patients infected with the virus. Even low-cost interventions such as facemasks for patients [68] with a cough and water supplies for handwashing may be challenging as is physical distancing in overcrowded primary health care clinics. The continent has learnt invaluable lessons from Ebola and HIV control. HIV counsellors and community healthcare workers are key resources and could promote social distancing and related interventions dispel myths support healthcare workers [68] perform symptom screening and trace contacts [69] (Figure 32).



Settings	KCDC (March 2020)	WHO (April 2020)	CDC (May 2020)	ECDC (May 2020)
Triage: patient examination with direct contact	• KF94 mask or equivalent respirator	• Medical mask	• N95 respirator (or facemask if a respirator is not available)	• Surgical mask or, if available, FFP2 respirator
	• Eye protection[a]	• Eye protection[a]	• Eye protection[a]	• Eye protection[a]
	• Gown[b] or coveralls with foot covers	• Gown[b]	• Gloves	• Gown[b] or apron
	• Gloves	• Gloves		• Gloves
Usual inpatient care	• KF94 mask or equivalent respirator	• Medical mask	• N95 respirator (or higher-level respirator) or facemask (if a respirator is not available)	• Surgical mask or, if available, FFP2 respirator
	• Eye protection[a]	• Eye protection[a]	• Eye protection[a]	• Eye protection[a]
	• Gown[b] or coveralls with foot covers	• Gown[b]	• Gown	• Gown[b] or apron
	• Gloves	• Gloves	• Gloves	• Gloves
Aerosol-generating procedures[c]	• KF94 mask, equivalent respirator, or PAPR	• N95, FFP2, or FFP3 respirator	• N95 or higher-level respirator	• FFP3 respirator
	• Eye protection[a]	• Eye protection	• Eye protection[a]	• Eye protection[a]
	• Gown[b] or coveralls with foot covers	• Gown[b]	• Gown[b]	• Gown[b]
	• Gloves	• Gloves	• Gloves	• Gloves
		• Apron (if gowns are not fluid-resistant)		
Collecting specimens (not involving aerosol-generating procedures)	• KF94 mask, equivalent respirator, or PAPR	• Medical mask	• N95 or higher-level respirator (or facemask if a respirator is not available)	Enclosed spaces
	• Eye protection[a]	• Eye protection[a]	• Eye protection[a]	• Surgical mask or, if available FFP respirator
	• Gown[b] or coveralls with foot covers	• Gown[b]	• Gown[b]	• Eye protection[a]

WHO, World Health Organization; CDC, Centers for Disease Prevention and Control; ECDC, European Centers for Disease Prevention and Control; KCDC, Korea Centers for Disease Prevention and Control; PAPR powered air-purifying respirator; FFP, filtering facepiece

Figure 32: Comparisons of personal protective equipment recommendations from the World Health Organization, the US Centres for Disease Prevention and Control (CDC), the European CDC, and Korea CDC. Sun Hee Park, [69].

Transmission of viruses was lower with physical distancing [70] of 1 m or more compared with a distance of less than 1 m protection was increased as distance was lengthened. Face mask use could result in a large reduction in risk of infection (n=2647; aOR 0·15; 95% CI 0·07 to 0·34; RD −14·3%; −15·9 to −10·7 low certainty) with stronger associations with N95 or similar respirators compared with disposable surgical masks or similar (eg; reusable 12-16-layer cotton masks pinteraction=0·090; posterior probability >95%; low certainty). Eye protection also was associated with less infection (n=3713; aOR 0·22; 95% CI 0·12 to 0·39; RD −10·6%; 95% CI −12·5 to −7·7; low certainty). The findings of this systematic review and meta-analysis support physical distancing of 1 m or more and provide quantitative estimates for models and contact tracing to inform policy. Optimum use of face masks respirators and eye protection in public and [70] health-care settings should be informed by these findings and contextual factors.

Public Health Message of Hand Washing Several Times in a Day and Social Distancing in COVID-19 Pandemic

The world is facing a medical crisis amid the [71] CoViD-19 pandemic and the role of adequate hygiene and hand sanitisers is inevitable in controlling the spread of infection in public places and healthcare institutions. A consequent increase of substandard products in the market has raised safety concerns. This review also provides a range of hand sanitisation product formulations and manufacturing instructions to allow for extemporaneous preparations at the community and hospital pharmacies [71] during this urgent crisis. In hospital transmission is one of the main routes [72] of the covid19 novel coronavirus spreading among health care workers who are the frontline fighters. However; coming into contact with COVID-19-positive patients is unavoidable. Therefore; hand hygiene is of utmost importance for the prevention of COVID-19 among HCWs. This purpose can be achieved by applying alcohol-based hand rubs washing hands properly with soap and water and applying other antiseptic agents.

A shortage of essential equipment (G Kampf; S. Scheithauer; S. Lemmen; P. Saliou; 2020) such as alcohol-based hand rubs- ABHRs medical gloves and face masks is currently being experienced by more and more healthcare facilities worldwide due to the coronavirus disease 2019-COVID-19 pandemic. Although it is still highly desirable to use commercially produced quality hand rubs and single-use medical gloves and face masks the current shortage of some articles is so profound that it results in uncertainty among healthcare workers-HCWs as to whether it is safe for them to care for COVID-19 patients. The coronavirus disease 2019 (COVID-19) pandemic has caused a huge demand for alcohol-based hand rubs medical gloves face masks and gowns in healthcare and from the public. More and more hospitals face a serious shortage of these articles. (G Kampf; S. Scheithauer; S. Lemmen; P. Saliou; 2020) We propose a risk-adapted approach to ensure adequate patient and healthcare worker safety for as long as possible (Figure 33).

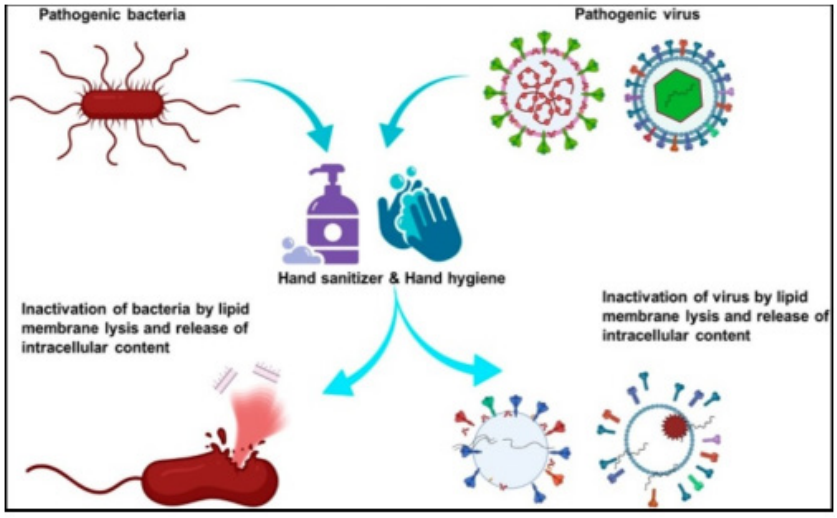


Figure 33: Illustration of alcohols antiviral mechanism (Jane Jing, et al. [400].

When hand washing [73] with soap and water is unavailable a sufficient volume of sanitizer is necessary to ensure complete hand coverage and compliance is critical for appropriate hand hygiene. By extrapolating effectiveness of hand sanitizers on viruses of similar structure to SARS-CoV-2; this virus should be effectively inactivated with current (Andrew Golin; Dexter Choi; Aziz Ghahary; 2020) hand hygiene products though future research should attempt to determine this directly. Hands can be a vector for transmitting pathogenic microorganisms [73] to foodstuffs and drinks and to the mouths of susceptible hosts. Hand washing is the primary barrier to prevent transmission of enteric pathogens *via* cross-contamination from infected persons. Water and soap appear to be more effective than waterless products for removal of soil and microorganisms from hands. Alcohol-based products achieve rapid and effective inactivation of various bacteria; but their efficacy is generally lower against nonenveloped viruses. The presence of food debris [74] significantly affects the microbial inactivation rate of hand sanitizers.

Soap with an antimicrobial agent in particular CHG [75] was observed to be more effective than regular soap. Hot air drying had the capacity to increase the amount of bacterial contamination on hands while paper towel drying caused a slight decrease in contamination. There was little difference in the efficacy of alcohol and alcohol-free sanitizers. Ring wearing caused a slight decrease in the efficacy [75] of hand washing. A non-pathogenic nalidixic acid resistant [76] Enterobacter aerogenes surrogate for Salmonella was used to assess the efficacy of using soap or no soap for 5 or 20 s on hands with or without ground beef debris and drying with paper towel or air. Each experiment consisted of 20 replicates each from a different individual with 6 log CFU/ml E. aerogenes on their hands. A reduction of 1.0 ± 0.4 and 1.7 ± 0.8 log CFU of E. aerogenes was observed for a 5-s wash with no soap and a 20-s wash with soap respectively. A significantly greater reduction ($P < 0.05$) in E. aerogenes (0.5 log CFU greater reduction) was [76] observed with soap when there was ground beef debris on the hands.

Alcohol based hand rub the [77] World Health Organization (WHO) defines an alcohol-based hand rub as "An alcohol containing preparation (liquid; gel or foam) designed for application to the hands to inactivate microorganisms and/or temporarily suppress their growth. Alcohol-based hand antiseptics mostly contain isopropanol ethanol n-propanol or a mixture of these as their active ingredients. The antimicrobial activity of alcohols is attributed to their ability to denature and coagulate proteins. This causes microbes to lose their protective coatings and become non-functional. The Centre for Disease Control and Prevention recommends formulations containing 80% (percent volume/volume) ethanol or 75% isopropyl alcohol however; generally speaking sanitizers [77] containing 60 to 95% alcohol are acceptable. Many countries have implemented [78] social distancing as a measure to "flatten the curve" of the ongoing epidemics. Evaluation of the impact of government-imposed social distancing and of other measures to control further spread of COVID-19 is urgent especially because of the large societal and economic impact of the former.

Actions taken Against Not Following the Orders of Prevention from COVID-19 in the USA

Fear anxiety and even paranoia can [79] proliferate during a pandemic. Such conditions even when subclinical tend to be a product of personal and predisposition factors as well as shared cultural influences including religious literary; film; and gaming; all of which can lead to emotional and less than rational responses. They can also lead people to give credence to simplistic and unscientific misrepresentations about medications and devices which are claimed to prevent treat or cure disease. This article notes the eruption of quackery during the 1889-1892 Russian Flu and the 1918-1920 Spanish Flu and the emergence during 2020 of spurious claims during the COVID-19 pandemic. It identifies consumer protection [79] strategies and interventions formulated during the 2020 pandemic. The four-tier emergency management system [80] and the joint prevention mechanism established in China have provided various resources to control the epidemic but there is still weakness in dealing with the spread of COVID-19. The quantitative and qualitative analysis shows that the public health [80] emergency response system constructed in China plays a significant role in controlling the epidemic in a certain period of time.

Global Health and other organizations such as [81] WHO; UNHCR; UN; UNESCO; UNICEF did not act fast to Prevent and Control the COVID-19 Pandemic. Other Governments of the countries in the world act very slowly for the warnings given by WHO and other scientists. Later since November 2019 till now approximately 350;000 people have lost their lives due to COVID-19 and approximately 5 Million people are infected by this COVID-19 disease. The vaccine of COVID-19 is under development and there is no approved [81] treatment for COVID-19 by medical sciences till now. The present study aimed at [82] assessing the impact of demographic characteristics maladaptive personality traits. And causal beliefs about COVID-19 on perceived emotional problems in a sample of Italian community-dwelling adults (N = 1043) in the first month of the social distancing period due to the COVID-19 pandemic in Italy. Our data supported the importance of considering the impact of quarantine measures on psychological well-being while [82] suggesting possible risk factors related to individual differences in personality and causal beliefs.

At the beginning of a public health crisis [83] such as the coronavirus disease 2019 (COVID-19) pandemic it is important to collect information about people's knowledge worries and behaviours to examine their influence on quality of life and to understand individual characteristics associated with these reactions. Results suggested that during the first week of the COVID-19 outbreak in Italy people were well informed and had a relatively stable level of worries. Quality of life did not vary across the areas although mental well-being was challenged by the social appraisal and worries related to the contagion. [83] Increased scores for worries and concerns were associated with more cognitive rigidity and emotional instability.

As coronavirus disease 2019 (COVID-19) spreads [84] across the world it is critical to understand the psychological factors associated with pandemic-related behaviours. Outcomes included COVID-19 news monitoring social distancing disinfecting and hoarding behaviours during the 7 days after the United States declared a national emergency. The psychological factors were attitudes about COVID-19 severity social responsibility values social trust; and self-interest. Emphasizing the severity of COVID-19 and the social implications of pandemic related behaviours [84] may be important for teens particularly for those who are not following preventive health behaviours or who are engaging in hoarding. In Indianapolis the USA this is another reminder [85] that starting on Thursday July 9 everyone in Marion County over the age of 2 will need to wear a mask in an effort to prevent the spread of the coronavirus. That goes for anyone in public indoors or even outdoors where social distancing is not possible. It also includes workspaces where people don't have their own office. You are also asked to wear them in [85] all stores and restaurants when you're not eating.

South Africa Cape Town will penalize [86] people for not wearing masks in public places as part of efforts to curb the rapid spread of the COVID-19 pandemic in the country the government announced on Monday. Should people not take all reasonable measures to ensure masks are worn they will face a fine or imprisonment for a period not exceeding six months or to both such fine and imprisonment said Nkosazana Dlamini-Zuma Minister of Cooperative Governance and Traditional Affairs. We have introduced provisions that enforce the mandatory wearing of face masks particularly in a public setting said the minister while elaborating on the Amendment of Level Three Coronavirus COVID-19 Regulations. The amended regulations announced by President Cyril Ramaphosa on Sunday evening reinforce the mandatory wearing of masks in public or in public places. Under the new regulations any employer manager or owner of a building used by the public to obtain goods or services will be responsible if any person enters [86] and remains in such building place or premises without wearing a mask.

Intervention Strategies for Reducing the Spread of COVID-19 Among the Community

Long-term care facilities are high-risk settings [87] for severe outcomes from outbreaks of Covid-19 owing to both the advanced age and frequent chronic underlying health conditions of the residents and the movement of health care personnel among facilities in a region. Most cases among residents included respiratory illness consistent with Covid-19 however in 7 residents no symptoms were documented. In the context of rapidly escalating Covid-19 outbreaks proactive steps by long-term care facilities to identify and exclude potentially infected staff

and visitors actively monitor for potentially infected patients and implement appropriate [87] infection prevention and control measures are needed to prevent the introduction of Covid-19.

Approximately 10 Million People are Infected with COVID-19 [88] Corona virus and More than Half Million are Dead with current COVID-19 Pandemic till July 2020. Scientists are trying to manufacture COVID-19 Vaccine and Treatment as soon as possible to help the Mankind. In the current 21st century still people are dying with diseases without the treatment available as still we lack knowledge and research facilities to tackle the diseases.

International health organizations for example WHO; UNICEF and UN should invest more on Medical research and pharmaceuticals to find the upcoming Epidemics or Pandemics and prepare their available Vaccines and Treatment. Without taking serious steps and proper design and management [88] the Task for Medical research for disease Preventions could not be completed.

Countries have developed strategies [89] to deal with the COVID-19 pandemic that fit their epidemiological situations capacities and values. We believe that case finding and management with identification and quarantine of close contacts are vitally important containment measures and are essential in China's pathway forward. We describe the next steps planned in China that follow the containment effort. We believe that sharing countries experiences will help the global community manage the COVID-19 pandemic by [89] identifying what works in the struggle against SARS-CoV-2 [90] (Figure 34).

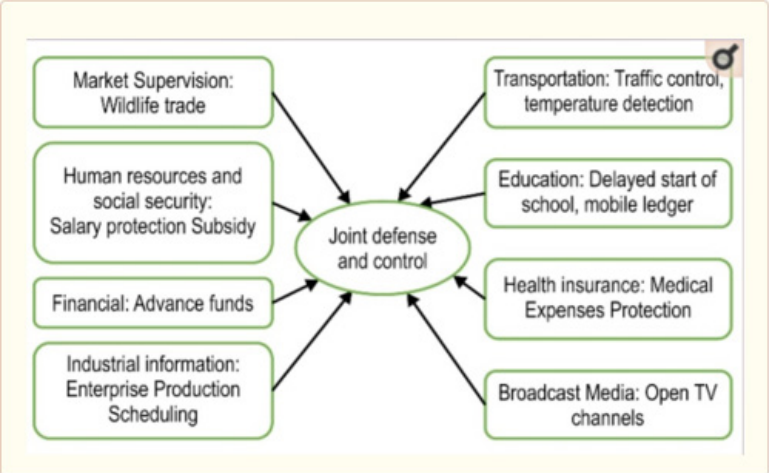


Figure 34: Coronavirus (COVID-19) epidemic joint prevention and control in various departments. (Jia Wang, Zhifeng Wang, 2020).

China banned travel to and from Wuhan city [91] on 23rd January 2020 and implemented a national emergency response. We investigated the spread and control of COVID-19 using a data set that included case reports human movement and public health interventions. The Wuhan shutdown was associated with the delayed arrival of COVID-19 in other cities by 2.91 days. Cities that implemented control measures preemptively reported fewer cases on average (13.0) in the first week of their outbreaks compared with cities that started control later (20.6). Suspending intracity [91] public transport closing entertainment venues and banning public gatherings were associated with reductions in case incidence (Figure 35).

Figure 35: The COVID-19 checkpoint at rural entrance (left) and 5G base stations in a designated hospital (right) (Bao Fu, Xiaoyun Fu (2020) The model of epidemic (COVID-19) prevention and control in rural of China. Crit Care).

Coronavirus disease 2019 (COVID-19) has [92] rapidly spread not only in China but throughout the world. Children with kidney failure (chronic kidney disease-CKD stage 5) are at significant risk for COVID-19. In turn a set of recommendations for the prevention and control of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and COVID-19 in pediatric hemodialysis (HD) centers and in-home peritoneal dialysis (PD) settings have been proposed. The recommendations are based on the epidemiological features of the SARS-CoV-2 virus and COVID-19 disease [92] susceptibility factors and preventive and control strategies.

Unfortunately; the current unavailability of an [93] effective antiviral drug and approved vaccine worsen the situation more critical. Implementation of an effective preventive measure is the only option left to counteract CoVID-19. The effectiveness of preventive measures completely relies on the strength of surface disinfectants the composition of hand sanitizer appropriate material for the manufacture [93] of personal protective equipment (PPE). Various preventive measures were implemented [94] including flight restrictions to certain countries gradually expanded to suspending all flights and prohibiting the entry of foreign nationals 14-day isolation and symptom monitoring for those that came from countries under risk. Persons with chronic diseases have been granted an administrative leave on campus education at schools and activities of public rest and entertainment areas were temporarily suspended. In accordance with the pandemic plan actions have been carried out with a [94] multi-sectoral approach and preventive measures have been implemented to cover the society as a whole.

Early implementation of quarantine and [95] combining quarantine with other public health measures is important to ensure effectiveness. In order to maintain the best possible balance of measures; decision makers must constantly monitor the outbreak situation and the impact of the measures implemented. Testing in representative samples in different settings could help assess the true prevalence of infection and would reduce [95] uncertainty of modelling assumptions. This review was commissioned by WHO and supported by Danube-University-Krems.

Unfortunately; there is no medication that has been approved [96] by the FDA gone through controlled studies and demonstrated an effect on the virus for this global pandemic. Although there are cures for illnesses and developments made by leaps and bounds in our day the strongest and most effective weapon that society has against this virus that is affecting not just health but also economics politics and social order is the prevention of its spread. The main points in preventing the spread in society are hand hygiene social distancing and quarantine. With increased testing capacity detecting more COVID-19 positive patients in the community will also enable the [96] reduction of secondary cases with stricter quarantine rules.

The dialysis population is vulnerable and [97] the dialysis facility is critical in maintaining operations and avoiding disease transmission. The present information regarding the clinical features of COVID-19 infection in the dialysis population was collected and the useful measures of COVID-19 infection prevention and infection control in the dialysis facilities were summarized. Leadership education preparedness management and recovery phase were determined to be the critical procedures. It is hoped this updated interim review might provide information for medical professionals to take proactive action to best prepare and mitigate damage [97] when facing the COVID-19 pandemic challenge.

Containment measures in the event of pandemic [98] due to infective agents should be well known by healthcare professionals and promptly applied in order to mitigate the risk of nosocomial transmission and outbreak. A full reorganization of ophthalmology services is mandatory according to current existing infection containment measures in order to continue dispensing urgent procedures without endangering the community with amplification of the diffusion chain. Ophthalmologists are considered at elevated risk of exposure when caring patients and vice versa due to their close proximity during eye examination. High volumes of procedures typically generated by ophthalmologists with concurrent implications on the risk of [98] infection are considered when re-assessing healthcare facilities reorganization.

The Role of COVID-19 Testing and Self-Quarantine in the COVID-19 Pandemic

On the same date also the date of this review [99] Africa had reported 5;999 confirmed cases of which 3;838 (almost 65%) occurred in South Africa Algeria; Egypt; Morocco and Tunisia; with the remaining 2;071 cases distributed unevenly across the other African countries. We speculate that while African nations are currently experiencing much lower rates of COVID-19 relative to other continents their significantly lower testing rates may grossly underestimate incidence rates. Failure to grasp the true picture may mean crucial windows of opportunity shut unutilized while limited resources are not deployed to maximum effect. In the absence of extensive testing data an overestimation of spread may lead to disproportionate measures being taken [100] causing avoidable strain on livelihoods and economies. To date the FDA has given emergency (Lauren Ching; Sandra Chang; Vivek N; 2020) use authorization (EUA) to 48 COVID-19 *in vitro* diagnostic tests and 21 high complexity molecular based laboratory developed tests. Currently there are 2 types of diagnostic tests available for the detection of SARS-CoV-2;

(1) Molecular and

(2) Serological tests.

Molecular detection of nucleic acid (RNA or DNA) sequences relating to the suspected pathogen is indicative of an active infection with the suspected pathogen. Serological tests detect antibodies against the suspected pathogen which are produced by an individual's immune system. A positive serological test result indicates recent exposure to the suspected pathogen but cannot be used to determine if the individual [100] is actively infected with the pathogen or immune to reinfection. So far confirmation of COVID-19 infection is based [101] on the detection of virus RNA in a sample taken from a person meeting the suspected case definition. However; in the laboratory diagnosis of SARS-CoV-2 infections in addition to genetic tests serological methods can also be used to detect specific antibodies of the IgM; IgG and IgA class produced after contact with antigens or to detect viral antigen. Currently a number of rapid immunochromatographic chemiluminescent and ELISA immunoassay tests developed by different manufacturers for the diagnosis of COVID-19 are available on the market. Despite this fact so far there is no WHO or ECDC recommendations or even reliable research regarding the usefulness of [101] serological investigations in the laboratory diagnosis of infections caused by SARS-CoV-2.

The currently available diagnostic tools [102] for the diagnosis of COVID-19 are mainly based on molecular assays. Real time reverse transcription-polymerase chain reaction is the only diagnostic method currently recommended by the World Health Organization for COVID-19. Considering the need for the development of such a screening test an attempt was made to develop and evaluate an IgG-based ELISA for COVID-19. A total of 513 blood samples (131 positive; 382 negatives for SARS-CoV-2) were collected and tested by microneutralization test (MNT). Antigen stock of SARS-CoV-2 was prepared by propagating the virus in Vero CCL-81 cells. An IgG capture ELISA was developed for serological detection of anti-SARS-CoV-2 IgG in serum samples. The developed ELISA was found to be 92.37 per cent sensitive 97.9 per cent specific robust [102] and reproducible. The positive and negative predictive values were 94.44 and 98.14 per cent respectively.

The sensitivity of antibody tests is too low [103] in the first week since symptom onset to have a primary role for the diagnosis of COVID-19. But they may still have a role complementing other testing in individuals presenting later when RT-PCR tests are negative or are not done. Antibody tests are likely to have a useful role for detecting previous SARS-CoV-2 infection if used 15 or more days after the onset of symptoms. However; the duration of antibody rises is currently unknown and we found very little data beyond 35 days post symptom onset. COVID-19-positive cases who are RT-PCR-negative should be included as well as those confirmed RT-PCR in accordance with the World Health Organization (WHO) and China National Health Commission of the People's Republic of China (CDC) case definitions. We were only able to obtain data from a small proportion of available tests; and action is needed to [103] ensure that all results of test evaluations are available in the public domain to prevent selective reporting.

Simple and rapid immunodiagnostic [104] methods are urgently needed to identify positive cases. Here we report the development of a rapid and sensitive lateral flow immunoassay (LFIA) that uses lanthanide-doped polystyrene nanoparticles (LNPs) to detect anti-SARV-CoV-2 IgG in human serum. A recombinant nucleocapsid phosphoprotein of SARS-CoV-2 was dispensed onto a nitrocellulose membrane to capture specific IgG. Mouse anti-human IgG antibody was labelled with self-assembled LNPs that served as a fluorescent reporter. A 100-μL aliquot of serum samples (1:1000 dilution) was used for this assay and the whole detection process took 10 min. We tested 7 samples that were positive by reverse-transcription (RT-)PCR and 12 that were negative but clinically suspicious for the presence of anti-SARS-CoV-2 IgG. One of the negative samples was determined to be SARS-CoV-2 IgG positive [104] while the results for the other samples were consistent with those obtained by RT-PCR.

A retrospective validation study was [105] conducted including the serum of 125 patients in order to determine the analytical and clinical performances of the LIAISON SARS-CoV-2 from DiaSorin detecting anti-SARS-CoV-2 IgG. And to compare its clinical performance with the enzyme linked immunosorbent assay (ELISA) test from Euroimmun one of the first commercially available tests allowing the detection of anti-SARS-CoV-2 IgA and IgG. Comparison between the LIAISON SARS-CoV-2 and the ELISA method did not reveal any difference between the two techniques in terms of sensitivities and specificities regarding the determination of the IgG. This study reports the validation of the LIAISON SARS-CoV-2 allowing to detect IgG antibodies specifically directed against SARS-CoV-2. The analytical and clinical performances are excellent and the automation [105] of the test offers important rates ideal for absorbing an extension of testing.

There is global lockdown for [106] containment of the virus transmission. Testing of symptomatic patient's healthcare workers and suspected individuals and mass screening is vital. WHO recommends nasopharyngeal (NP) and oropharyngeal (OP) swab for the quantitative assessment of SARS-CoV-2 RNA level through real-time reverse transcription polymerase chain reaction (rRT-PCR)?. The virus is shown to be consistently present in saliva and rRTPCR of saliva specimens and have advantages over NP and OP swabs such as self-collection of saliva

avoidance of healthcare workers for specimen collection cost effectiveness etc. This article explores the current literature and suggests saliva as an [106] emerging potential diagnostic specimen for COVID-19 testing.

We evaluated six different RT-qPCR [107] alternatives for SARS-CoV-2/COVID-19 diagnosis based on standard RNA extractions. That of best sensitivity was also assessed with direct nasopharyngeal swab viral transmission medium (VTM) heating overcoming the RNA extraction step. We found a wide variability in the sensitivity of RT-qPCR solutions that associated with a range of false negatives from as low as 2% (0.3-7.9%) to as much as 39.8% (30.2-50.2). Direct preheating of VTM combined with the best solution provided a sensitivity of 72.5% (62.5-81.0) in the range of some of the solutions based on standard RNA extractions. Our results will help to calibrate the impact of false negative diagnoses of COVID-19 and to [107] detect and control new SARS-CoV-2 outbreaks and community transmissions.

The Need of Vaccine Development for COVID-19 and the Progress Made till August 2020

As the world is witnessing the epidemic of COVID-19; a [108] disease caused by a novel coronavirus; SARS-CoV-2; emerging genetics and clinical evidence suggest a similar path to those of SARS and MERS. The rapid genomic sequencing and open access data together with advanced vaccine technology are expected to give us more knowledge on the pathogen itself; including the host immune response as well as the plan for therapeutic vaccines in the near future [109] (Figure 36).

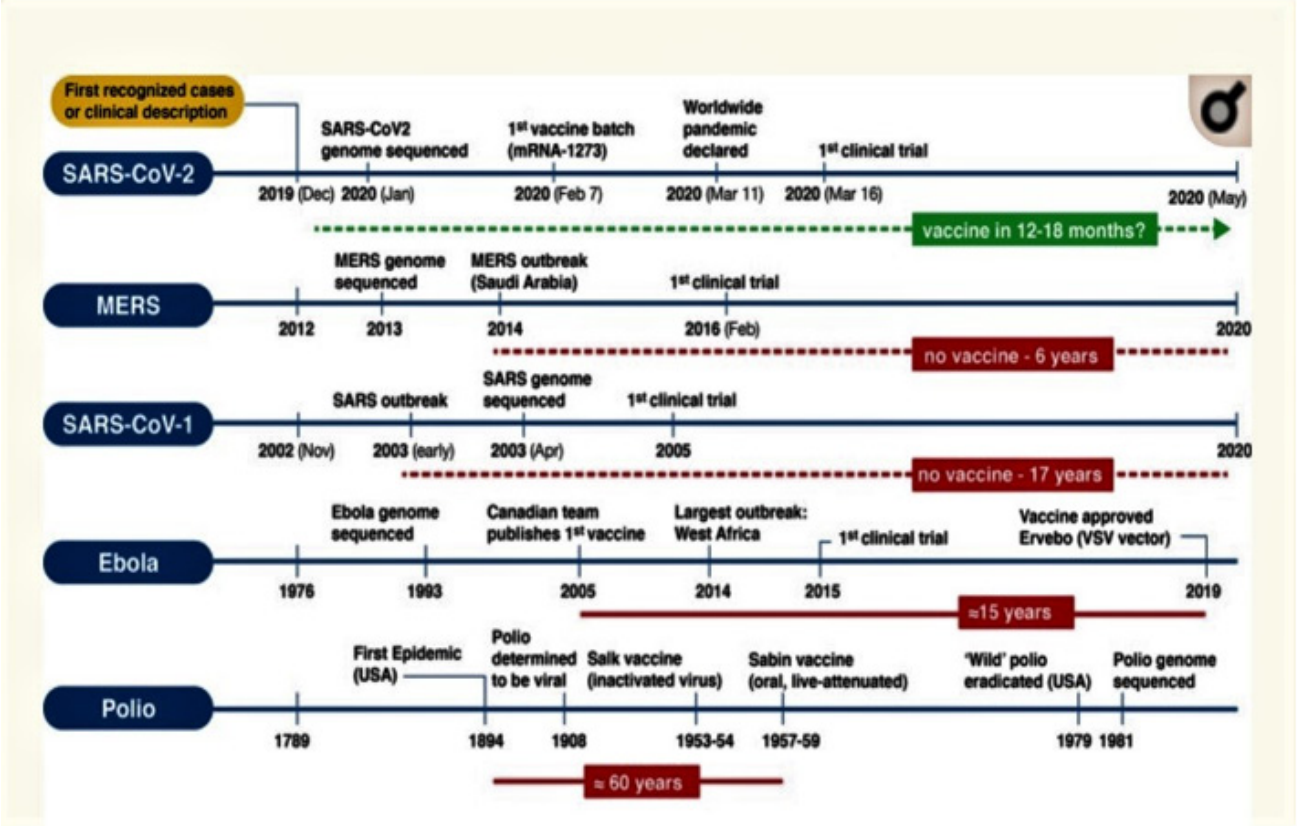


Figure 36: Timelines for the development of various vaccines for polio, Ebola virus, and three beta coronaviruses (SARS-CoV-1, MERS-CoV and SARS-CoV-2). Colin D et al. [109].

Through online search direct communication [110] with network members and an internal survey engagements of developing countries vaccine manufacturers network members in the research and development of COVID-19 vaccines and their capacities in the manufacturing fill-finish and distribution of vaccines were assessed. Currently 19 network members engaged in research and development of COVID-19 vaccines using six principal technology platforms. In addition; an internal survey showed that the number of vaccines supplied collectively by 37 members in 2018-19 was about 3.5 billion doses annually The use of existing manufacturing fill-finish and distribution capabilities can support an efficient roll-out of vaccines against COVID-19 while maintaining [110] supply security of existing vaccines for on-going immunization programmes (Figure 37).

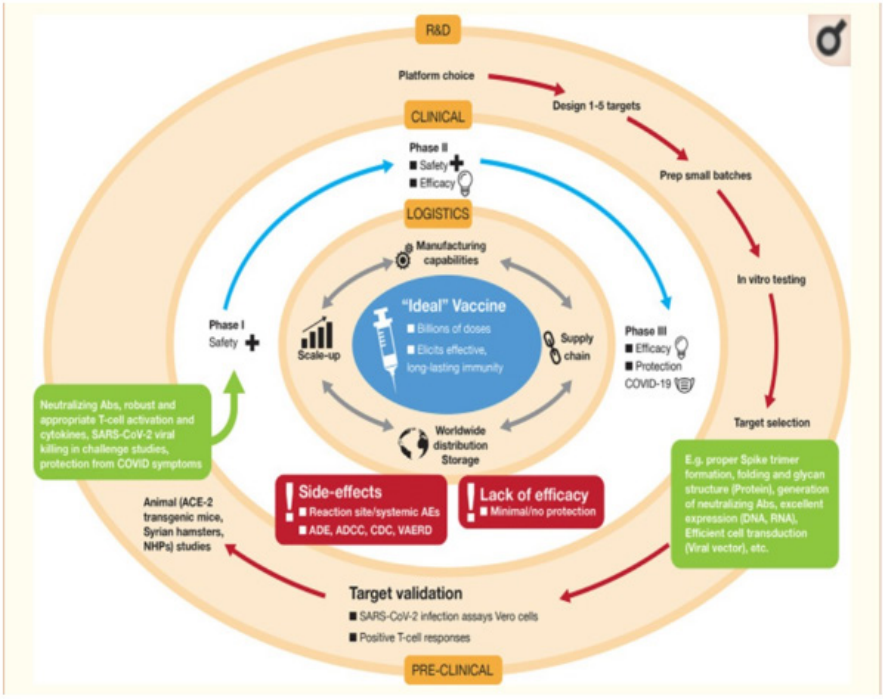


Figure 37: Development of the "ideal" vaccine for COVID-19 depicted by concentric circles converging to the target Colin D. Funk et al. [109].

Although as many as several million vaccine [111] doses may become available as a by-product of development in a pandemic situation once vaccine candidates are proved safe and effective doses must be manufactured in large quantities. Though some high-income countries may pay for development and manufacture with their own populations in mind there's no global entity responsible for financing or ordering vaccine manufacture. Discussions with global stakeholders about organizing and [111] financing large-scale vaccine manufacturing procurement and delivery are under way (Figure 38).

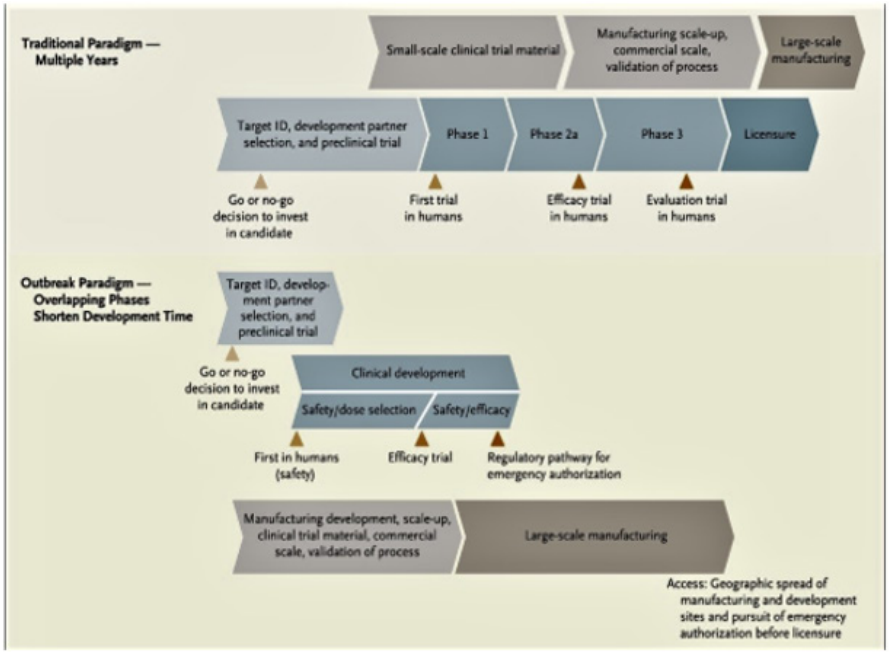


Figure 38: Difference between Traditional Vaccine Development and Development Using a Pandemic Paradigm. (Nicole Lurie, Melanie Saville, Richard Hatchett, Jane Halton, 2020).

The global vaccine R&D effort in response [111] to the COVID-19 pandemic is unprecedented in terms of scale and speed. Given the imperative for speed there is an indication that vaccines could be available under emergency use or similar protocols by early 2021. This would represent a fundamental step change from the traditional vaccine development pathway which takes on average over 10 years even compared with the accelerated 5-year timescale for development of the first Ebola vaccine. The approaches being applied for COVID-19 development which involve a new virus target and often novel vaccine technology platforms and novel development paradigms as well are likely to increase the risks associated with delivering a licensed vaccine [111] and will require careful evaluation of effectiveness and safety at each step (Figure 39).

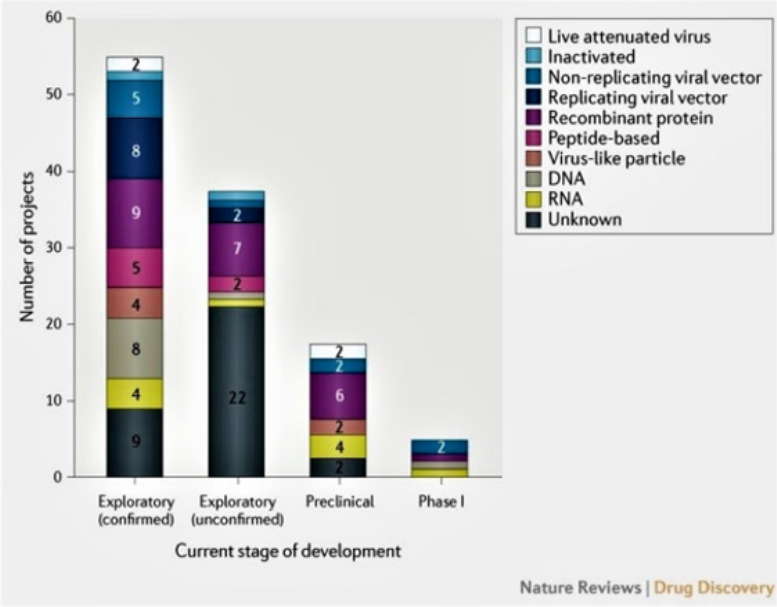


Figure 39: Pipeline of COVID-19 vaccine candidates by technology platform Nicole Lurie, et al. [111].

The great majority of licensed vaccines [112] are based in inactivation/attenuation pathogens which lengthen the development cost and production of the vaccine. Recombinant viral vectored DNA/RNA and protein technologies are setting the fastest records in vaccine development but just a selected few have been licensed so far for veterinary use only since for humans some vaccines have not met some regulatory requirements for approval and commercialization yet but international emergencies like the current COVID-19 could provide a final push towards obtaining licensure. This highlights the potential of vaccinology to make fast progress when [112] appropriate international support exists proving that when there is a will there is a way.

Treatment for COVID-19 Pandemic or the Supportive Treatment Available till August 2020

SARS-CoV-2 is the causative agent of [113] coronavirus disease-2019 (COVID-19) and is winning a proverbial chess match against all players simultaneous including physicians' clinicians' pathologists; doctors; scientists; economists; athletes and politicians. The COVID-19 outbreak has seriously threatened public health killing the most vulnerable persons and causing general panic. To stop this disease effective remedies [113] (i.e.; drugs; vaccines; personal protection elements; etc.) are urgently required. A number of anti-viral drugs such as [114] ribavirin; remdesivir; lopinavir/ritonavir; antibiotics such as azithromycin and doxycycline; and anti-parasite such as ivermectin have been recommended for COVID-19 treatment. In addition; sufficient pre-clinical rationale and evidence have been presented to use chloroquine for the treatment of COVID-19. Furthermore; Zn has the ability to enhance innate and [114] adaptive immunity in the course of a viral infection.

This Chlorpromazine-CPZ as [115] repositioning strategy also avoids numerous developmental and experimental steps and can save precious time to rapidly establish an anti-COVID-19 therapy with well-known limited and easy to manage side effects. Indeed; CPZ is an FDA-approved drug with an excellent tolerance profile prescribed for around 70 years in psychiatry but also in clinical routine in nausea and vomiting of pregnancy in advanced cancer and also to treat headaches in various neurological conditions. The broad spectrum of CPZ treatment including antipsychotic anxiolytic antiemetic; antiviral; immunomodulatory effects along with inhibition of clathrin-mediated endocytosis and modulation of blood-brain barrier is in line with the historical French commercial name for CPZ i.e. LARGACTIL; chosen as a reference to its "LARGe ACTion" properties. The discovery of those CPZ properties as for many [115] other molecules in psychiatry is both the result of serendipity and careful clinical observations.

Chinese medicine (CM) approaches including [116] oral administration of preventive herbal formulae wearing CM sachets and indoor herbal medicine fumigation were recommended for prevention and treatment and have shown pretty good effects. Currently *in vitro* studies have shown that lopinavir/ritonavir can inhibit the replication of Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV) to exert antiviral effects. Based on that lopinavir/ritonavir has been recommended for the clinical treatment of COVID-19 in China. Studies on the effect of ribavirin *in vitro* showed that ribavirin could reduce viral infection. However; the effectiveness and safety of ribavirin for COVID-19 still need further clinical trials to confirm. Arbidol exerts an antiviral effect by inhibiting the fusion of the viral lipid membrane with the host cell to block the replication of the virus. Remdesivir has shown good anti-MERS-CoV and anti-SARS-CoV activities *in vitro* and in animal models and has anti-SARS-CoV-2 activity *in vitro* indicating it could be used as a potential anti-SARS-CoV-2 drug. [116] Favipiravir became a potential drug for treatment of COVID-19 patients because studies have shown that favipiravir has inhibitory activity against almost all RNA viruses such as West Nile virus yellow fever virus; enterovirus; and Ebola virus.

Key evidence from *in vitro* research [117] animal models and clinical research in emerging coronaviruses is examined. The antiviral therapies remdesivir lopinavir/ritonavir and umifenovir; if considered should be initiated before the peak of viral replication for an optimal outcome. Ribavirin may be beneficial as an add-on therapy but is ineffective as monotherapy. [117] Corticosteroid use should be limited to specific co-morbidities. Although the Incidence; [118] Distribution; Illness; and mortality due to COVID-19 Pandemic is reducing day by day as compare to peak in March 2020 in the EU; the UK and the USA. But the Head of CDC USA warn the WHO and US Government that COVID-19 Pandemic has the tendency to become deadly as same as Spanish flu Pandemic in 1918 where approximately 60 to 100 million people died. In case of fever and shortness of breath take oxygen therapy; and paracetamol and ask the doctor for Antiviral; [118] Plasma therapy and dexamethasone others as soon as possible.

A large-scale study investigating [119] the clinical efficacy of remdesivir (200 mg on day 1; followed by 100 mg once daily) is on-going. The other excellent anti-influenza RdRp inhibitor favipiravir is also being clinically evaluated for its efficacy in COVID-19 patients. The protease inhibitor lopinavir/ritonavir (LPV/RTV) alone is not shown to provide better antiviral efficacy than standard care. However; the regimen of LPV/RTV plus ribavirin was shown to be effective against SARS-CoV *in vitro*. Another promising alternative is hydroxychloroquine (200 mg thrice daily) plus azithromycin (500 mg on day 1 followed by 250 mg once daily on day 2-5) which showed excellent clinical efficacy on Chinese COVID-19 patients and anti-SARS-CoV-2 potency *in vitro*. The roles of teicoplanin (which inhibits the viral genome exposure in cytoplasm) and monoclonal and polyclonal antibodies in the treatment of SARS-CoV-2 are under investigation. Avoiding the prescription of non-steroidal anti-inflammatory drugs angiotensin [119] converting enzyme inhibitors or angiotensin II type I receptor blockers is advised for COVID-19 patients.

Unfortunately; the antiviral drugs commonly used in [120] clinical practice to treat viral infections are not applicable to SARS-Cov-2 and no vaccine is available. Thus; it is extremely necessary to identify new drugs suitable for the treatment of the 2019-nCoV outbreak. Different preclinical studies conducted on other coronaviruses suggested that promising clinical outcomes for 2019-nCoV should be obtained by using alpha-interferon chloroquine phosphate arabinol; remdesivir; lopinavir/ritonavir; and anti-inflammatory drugs. Moreover; clinical trials with these suitable drugs should be performed on patients affected by SARS-Cov-2 to prove their efficacy and safety. Finally; a very promising therapeutic drug tocilizumab is discussed it is currently [120] used to treat patients presenting COVID-19 pneumonia.

The virus severe acute respiratory [121] syndrome-coronavirus-2 (SARS-CoV-2) is currently affecting more than 200 countries and territories worldwide. It has been declared as pandemic by World Health Organization (WHO) and the whole world is suffering from corona virus disease 2019 (COVID-19). Currently; no treatment for SARS-CoV-2 are approved because of lack of evidence but a number of clinical trials are in process and we are expecting fruitful results very soon. This review focuses on various approaches of treatment and few of the most [121] recent clinical trials carried out in this field. COVID-19 spread rapidly around the world in a short time. Confronted with such a highly infectious respiratory disease the research and development of anti-COVID-19 drugs became an urgent work due to the lack of specific drugs for the treatment of COVID-19. Nevertheless; several existing drugs are available to [122] relieve the clinical symptoms of COVID-19.

Patients Re-Infected by COVID-19 After Some Time When they have Tested Positive and then Negative; Later Again Tested Positive after Few Months?

There is rising concern that patients [123] who recover from COVID-19 may be at risk of reinfection. In this preprint; Bao et al. investigated acquired immunity to SARS-CoV-2 in rhesus macaques. Four rhesus monkeys were infected with SARS-CoV-2 and two were reinfected after confirmed recovery. After primary infection viral replication was detected in the nose pharynx; lungs and gut; with histopathological evidence of lung damage. Sera collected from recovered monkeys before reinfection exhibited neutralizing activity against SARS-CoV-2. Upon reinfection viral replication was not detected in nasopharyngeal or anal swabs and reinfected monkeys did not show any signs of COVID-19 disease

recurrence. This suggests that immunity acquired following primary infection with SARS-CoV-2 [123] may protect upon subsequent exposure to the virus.

Due to the expansion of the COVID-19 [124] epidemy in different parts of the world more and more cases are getting infected and of course. Many people will be recovering from this viral infection as today April 22 in Taiwan only 6 deaths have been reported out of 426 cases and 236 patients with confirmed infection have been released from the isolation. So; it is very important to be sure about the negative cases to be truly negative. Another concern is the reactivation of cases that got the infection recovered and left isolation. This issue has been brought to the public attention as on April 13 South Korea reported that 116 recovered cases of COVID-19 has been found positive again. As Korean approach to mark a patient as negative is two negative samples in within 24 hrs more precautions seem to be needed to be sure a patient had truly [124] recovered from COVID-19 or may not reactivate again after recovery.

For the first 3 months of COVID-19 pandemic COVID-19 [125] was expected to be an immunizing non-relapsing disease. We report a national case series of 11 virologically-confirmed COVID-19 patients having experienced a second clinically- and virologically-confirmed acute COVID-19 episode. According to the clinical history we discuss either re-infection or reactivation hypothesis. Larger studies including further virological immunological and epidemiologic data [125] are needed to understand the mechanisms of these recurrences.

Recently some patients have tested positive [126] for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) using reverse transcription polymerase chain reaction despite earlier recovery from coronavirus disease 2019 (COVID-19). Among 111 recovered patients 5% in China and 10% in South Korea have tested positive again. Typically; after recovery from a viral infection the body produces antibodies that can resist reinfection from the same virus. There is evidence that COVID-19 reinfection is not possible within 7 to 10 days. There is currently no supporting evidence for COVID-19 reinfection after recovery. However; it is important to ensure that samples are collected correctly and test procedures are followed properly. In accordance with the advice of the World Health Organization patients with no clinical symptoms can be discharged from [126] the hospital if they test negative for SARS-CoV-2 infection at least twice after a 24-hour interval [127] (Figure 40).

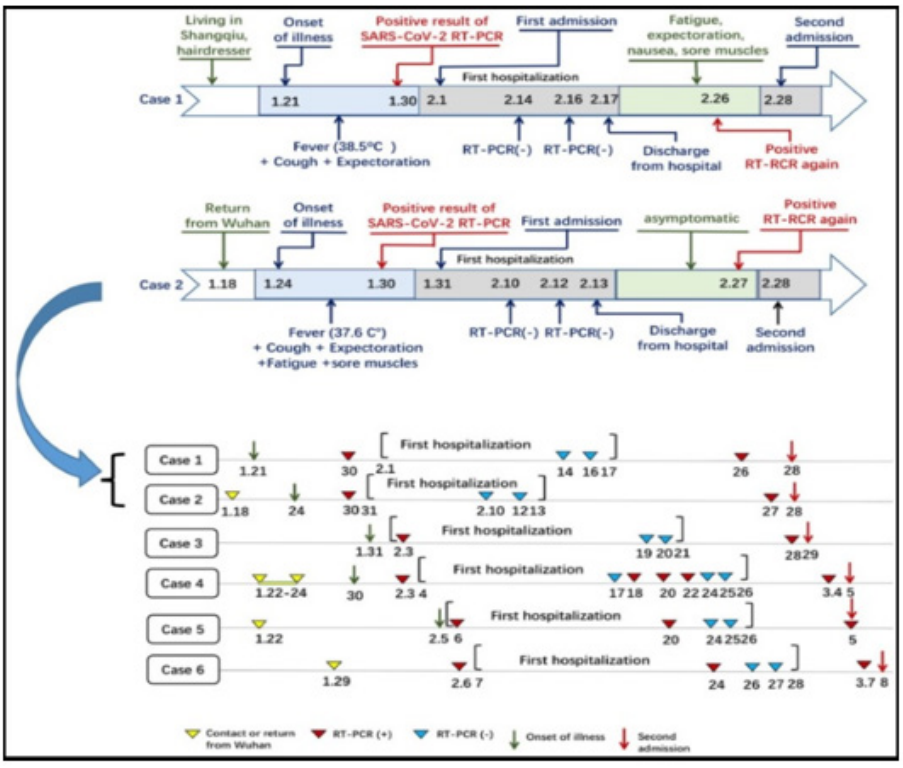


Figure 40: Timeline of six recurrence cases. Minlin Jiang, et al. [127].

The model differential equation was evaluated [128] for the disease-free equilibrium for the case of reinfection as well as the existence and stability criteria for the disease using the model proportions. This evaluation shows that the criteria for a local or worldwide asymptotic stability with a basic reproductive number (R0=0) were satisfied. Hence; there is a chance of no secondary reinfections from the recovered population as the rate of incidence of the recovered population vanishes (ie; B=0). With a total of about 900;000 infected cases worldwide numerical simulations for this study were carried out to complement the analytical results and investigate the effect that the implementation

of quarantine and observation procedures has on the projection of further virus spread. Most significant for this study is the rate of reinfection by the recovered population [128] which will decline to zero over time as the virus is cleared clinically from the system of the recovered class.

The COVID-19 pathophysiological mechanisms [129] resulting in minimal disease in this initial phase are not well known. In the remaining 20% of cases the disease may become severe and/or critical. In most patients of this latter group there is a phase characterized by the hyperresponsiveness of the immune system. A third phase corresponds to a state of hypercoagulability. Finally; in the fourth stage organ injury and failure occur. Antiphospholipid syndrome autoimmune cytopenia Guillain-Barré syndrome and Kawasaki disease have each been reported in patients with COVID-19. Here we present a scoping review of the relevant immunological findings in COVID-19 as well as the current [129] reports about autoinflammatory/autoimmune conditions associated with the disease. Recurrence of positive SARS CoV-2 PCR [130] has been described in patients discharged from hospital after 2 consecutive negative PCR. We discuss possible explanations including false negative reactivation and re-infection and propose different strategy to solve this issue. Prolonged SARS-CoV-2 RNA shedding and recurrence of viral RNA shedding in asymptomatic patients remain unknown. Transmission of SARS-CoV-2 by asymptomatic carriers had been documented. Considering the significance of this ongoing global public health emergency it is necessary to carry out large studies to [130] better understand the issue of potential SARS-CoV-2 recurrence in COVID-19 patients (Figure 41).

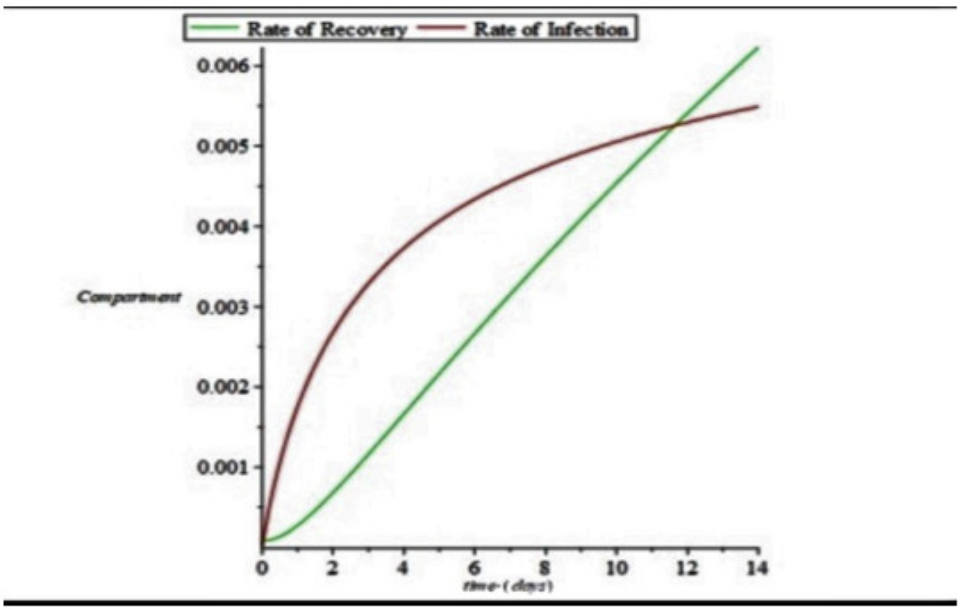


Figure 41: Chart of recovered and infectious compartments for coronavirus disease Alexander Victor Okhuese [128].

Epidemics of novel infection in humans are [131] inevitable and no single strategy alone can control an outbreak successfully. When facing a public health emergency with limited empirical evidence mechanistic and analogous evidence and professional judgement become important. In high-risk regions like China widespread proper use of facemasks when coupled with comprehensive health education campaigns and other personal and environmental hygiene measures may help to mitigate the COVID-19 epidemic. But may not be necessary nor cost-effective in low-risk areas where sustained human-to-human transmission is yet to occur. Instead of dismissing the potential value of facemasks based on the lack of [131] evidence further RCTs and cost-effectiveness studies should be conducted swiftly to clarify the controversy.

Retest Positive for severe acute [132] respiratory syndrome-related coronavirus-2 (SARS-CoV-2) from recoveredcoronavirus disease-19 (COVID-19) has been reported and raised several important questions for this novel coronavirus and COVID-19 disease. We are discussing several questions:

(a) Can SARS-CoV-2 re-infect the individuals who recovered from COVID-19? This question is also associated with other questions: whether or not SARS-CoV-2 infection induces protective reaction or neutralized antibody? Will SARS-CoV-2 vaccines work?

(b) Why could some recovered patients with COVID-19 be re-tested positive for SARS-CoV-2 RNA?

(c) Are some recovered COVID-19 patients with re-testing positive for SARS-CoV-2 RNA infectious? and

(d) How should the COVID-19 patients with retest positive [132] for SARS-CoV-2 be managed? (Figure 42)

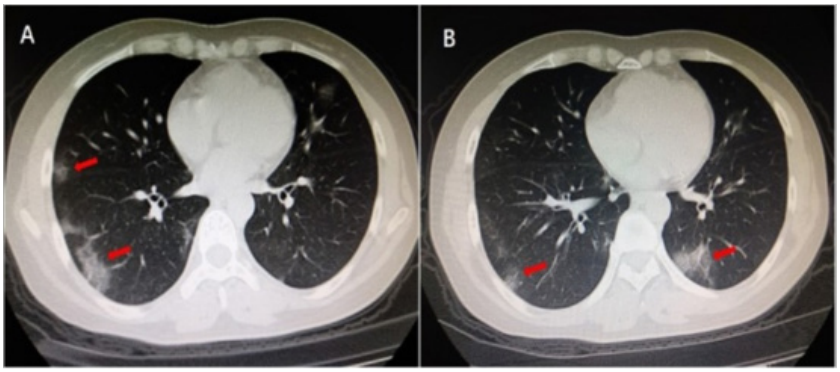


Figure 42: Chest HRCT images on 23 January 2020, showing multiple patchy ground glass opacities in bilateral subpleural areas (red arrows). HRCT, high-resolution computed tomography Dabiao Chen, et al. [401].

A novel coronavirus (COVID-19) pandemic [133] cause by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) threatens the world. We read with interest the recent report by Li et al. that included 610 patients with Coronavirus Disease 2019 (COVID-19). They reported a high false-negative rate of real-time reverse transcription polymerase chain reaction (RT-PCR) results for SARS-CoV-2 detection. In addition; recent report regarding SARS-CoV-2 "turn positive" in recovered cases with COVID-19 were published. Here; we studied the characteristics of nucleic acid conversion for SARS-CoV-2 from 70 COVID-19 patients [133]. We found that 15 (21.4%) patients experienced a "turn positive" of nucleic acid detection by RT-PCR test for SARS-CoV-2 after two consecutive negative results which may be related to the false negative of RT-PCR test and prolonged nucleic acid conversion.

We report the observation that 14.5% of COVID-19 patients [134] had positive RT-PCR testing again after discharge. We describe correlations between laboratory parameters and treatment duration (r= -0.637; p=0.002) and time to virus recrudescence (r= 0.52; p=0.008) respectively suggesting the need for additional measures to confirm illness resolution in COVID-19 patients.

How Long the COVID-19 Pandemic would Last? May be till 2030?

The WHO named the crisis as the sixth [135] PHEIC before its status was upgraded to a global pandemic. Case fatality rates remain high most notably among the elderly and those with comorbidities. Pandemic preparation and response take time; so healthcare and public health systems need to move forward quickly in their efforts to confront this disease around the globe actively anticipating new disease hotspots and allocating resources accordingly. The most important public health interventions to slow the spread include rapid identification and isolation of cases along with early implementations of physical distancing measures. A serious challenge in responding to COVID-19 is protecting HCWs and preventing nosocomial infection. Reliably sustainable supplies of PPE [135] and ventilators are urgently needed.

As far as we know our study presents [136] the first quantitative data for tropism replication kinetics and cell damage of SARS-CoV-2. These data provide novel insights into the lower incidence of diarrhoea decreased disease severity and reduced mortality in patients with COVID-19 with respect to the pathogenesis and high transmissibility of SARS-CoV-2 compared with SARS-CoV. SARS-CoV-2 infected and replicated to comparable levels in human Caco2 cells and Calu3 cells over a period of 120 h (p=0·52). By contrast; SARS-CoV infected and replicated more efficiently in Caco2 cells than in Calu3 cells under the same multiplicity of infection (p=0·0098). SARS-CoV-2; but not SARS-CoV; replicated modestly in U251 (neuronal) cells (p=0·036). SARS-CoV; but not SARS-CoV-2; infected and replicated in Rhinolophus sinicus bat kidney cells. SARS-CoV-2 consistently induced significantly delayed and milder levels of cell damage than did [136] SARS-CoV in non-human primate cells (VeroE6; p=0·016; FRhK4; p=0·0004).

Based on publicly available genomic data we analysed [137] the codon usage co-adaptation profiles of SARS-CoV-2 and other respiratory coronaviruses (CoVs). With their human host identified CoV-responsive human genes and their functional roles on the basis of both the relative synonymous codon usage-RSCU based correlation of viral genes with human genes and differential gene expression analysis and predicted potential drugs for COVID-19 treatment based on these genes. The ENc-GC3 plot indicated that SARS-CoV-2 genome was under strict selection pressure while SARS-CoV and MERS-CoV were under selection and mutational pressures. Using the drug-gene interaction database we screened a list of drugs [137] that could target these genes as potential COVID-19 therapeutics.

The major impact produced by the [138] severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) focused many researchers attention to find treatments that can suppress transmission or ameliorate the disease. Despite the very fast and large flow of scientific data on possible treatment solutions none have yet demonstrated unequivocal clinical utility against coronavirus disease 2019 (COVID-19). Drug

repurposing also known as drug repositioning and target-based methods are the most used strategies to advance therapeutic solutions into clinical practice. Current in silico; *in vitro* and *in vivo* [138] evidence regarding proposed treatments are summarized providing strong support for future research efforts.

First there is no unanimity [139] within the medical community for continuing the severe restrictions on activities of the vast majority of the total population that are mainly applicable to the most vulnerable very small minority of the total population. Second repurposed antiviral treatments can only be expected to have very limited results in controlling SARS-CoV-2 viral load of the most severely impacted based on trials conducted so far. Third it is difficult to see how safe COVID-19 vaccines can be developed and fully tested on time scales of one or two years as proposed presently. Fourth the only real protection against a future COVID-19 pandemic or any other viral pandemic is the one that was demonstrated to work in the SARS MERS COVID-19 and annual [139] influenza pandemics a healthy immune system capable of neutralizing incoming viruses as nature intended.

India implemented a complete shutdown [140] across the nation from March 25 2020 as lockdown I and went on to extend it by giving timely partial relaxations in the form of lockdown II; III & IV. The Group Method of Data Handling is a novel self-organized data mining technique with data driven adaptive learning capability which grasps the auto correlative relations between the samples and gives a high forecasting accuracy irrespective of the length and stochasticity of a time series. The GMDH model has been first validated and standardised by forecasting the number of active and confirmed [140] cases during lockdown III-IV with an accuracy of 2.58% and 2.00% respectively.

A common policy response to covid-19 outbreaks [141] has been the lockdown or quarantine. Designed to slow the spread of the disease lockdowns have unintended consequences for the environment. This article examines the impact of Colombia's lockdown on forest fires motivated by satellite data showing a particularly large upsurge of fires at around the time of lockdown implementation. To varying degrees across Colombia's regions the presence of armed groups is correlated with this fire upsurge. Mechanisms through which the lockdown might influence fire rates are discussed including the mobilisation of armed groups [141] and the reduction in the monitoring capacity of state and conservation organisations during the covid-19 outbreak.

Several new diseases have emerged in [142] different geographical areas with pathogens including Ebola virus Zika virus Nipah virus and coronaviruses (CoVs). Compared to other emerging viruses such as Ebola virus avian H7N9; SARS-CoV; and Middle East respiratory syndrome coronavirus (MERS-CoV) SARS-CoV-2 has shown relatively low pathogenicity and moderate transmissibility. Codon usage studies suggest that this novel virus has been transferred from an animal source such as bats. Early diagnosis by real-time PCR and next-generation sequencing has facilitated the identification of the pathogen at an early stage. Since no antiviral drug or vaccine exists to treat or prevent SARS-CoV-2 potential therapeutic strategies that are currently being evaluated [142] predominantly stem from previous experience with treating SARS-CoV; MERS-CoV; and other emerging viral diseases [143] (Figure 43).

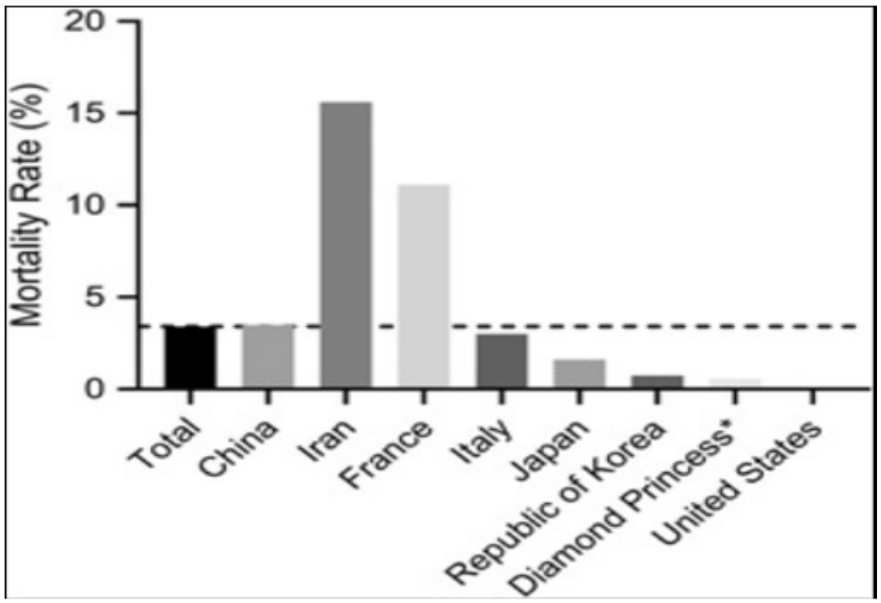


Figure 43: Mortality rates of different countries or regions, 27 February 2020. *A cruise ship currently in Japanese territorial waters Feng He, et al. [143].

The COVID-19 Pandemic has [144] progressed through the local outbreak stage and community transmission stage due to exposure at Wuhan's Huanan wholesale seafood market. The basic productive number (R0) at the beginning of the epidemic was 2.2 with an average incubation period of 5.2 days. The proportion of critically ill patients was 23.4%; the mortality rate was lower than those of SARS and Middle East respiratory syndrome and 96.5% of deaths occurred in Hubei Province where the outbreak occurred first. Among them elderly men with underlying diseases had a higher mortality rate. Chinese medical staff have summarized a set of effective strategies and methods in the diagnosis and treatment of this disease that are worthy of reference for their international counterparts. With powerful government intervention [144] and the efforts of Chinese medical staff China's outbreak has gradually improved.

Several efforts are currently made to find a [145] treatment for COVID-19 patients. In COVID-19 patients a pro-inflammatory status with high levels of interleukin (IL)-1B; IL-1 receptor (R)A and tumor necrosis factor (TNF)-α has been demonstrated. Moreover; high levels of IL-6 and TNF-α have been observed in patients requiring intensive care unit hospitalization. This provided rationale for the use of anti-rheumatic drugs as potential treatments for this severe viral infection. Other agents such as hydroxychloroquine and chloroquine might have a direct anti-viral effect. The anti-viral aspect of immunosuppressants towards a variety of viruses has been known since long time and it is [145] herein discussed in the view of searching for a potential treatment for SARS-CoV-2 infection.

Chest X RAYS; CT Scans; MRI of COVID-19 Patients

Chest CT examination plays an important role [146] in the initial diagnosis of the novel coronavirus pneumonia. Multiple patchy ground glass opacities in bilateral multiple lobular with periphery distribution are typical chest CT imaging features of the COVID-19 pneumonia. More than half of the patients presented bilateral multifocal lung lesions with peripheral distribution and 53 (59%) patients had more than two lobes involved. Of all included patients COVID-19 pneumonia presented with ground glass opacities in 65 (72%) consolidation in 12 (13%) crazy paving pattern in 11 (12%) interlobular thickening in 33 (37%) adjacent pleurae thickening in 50 (56%); and linear opacities combined in 55 (61%). Pleural effusion pericardial effusion and lymphadenopathy were uncommon findings. In addition; baseline chest CT [146] did not show any abnormalities in 21 patients (23%) but 3 patients presented bilateral ground glass opacities on the second CT after 3-4 days.

On CT imaging early stage patients (n = 53; 55.8%) showed [147] peripheral subpleural ground-glass opacities these were mainly local patches (22/53; 41.5%) while some lesions were accompanied by interlobular septal thickening. Thirty-four (35.8%) patients were classified in the progression stage based on CT imaging these patients typically showed lesions in multiple lung segments and lobes (21/34 61.8%) and an uneven increase in ground-glass opacity density accompanied by consolidation and grid-like or cord-like shadows (30.5%). Two patients (2.1%) showed a severe presentation on CT. These showed diffuse bilateral lung lesions mixed ground glass opacities and consolidation with cord-like interstitial thickening and air bronchograms entire lung involvement with a white lung presentation and mild pleural effusion. [147] Six patients in remission (6.3%); visible lesion absorption fibrotic lesions [148;149] (Figures 44 & 45).

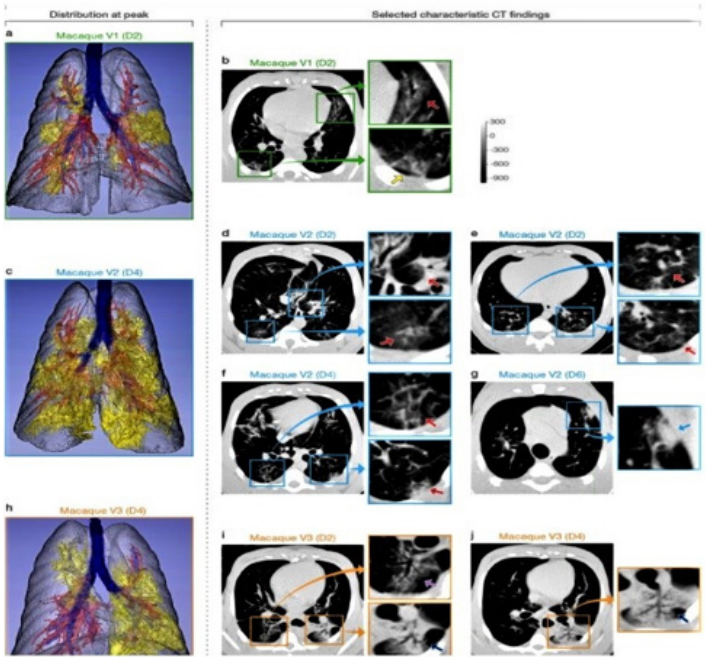


Figure 44: COVID-19-like CT abnormalities in the lungs of SARS-CoV-2 inoculated macaques V1 (a–b), V2 (c–g), and V3 (h–j) Courtney Finch, et al. [148].

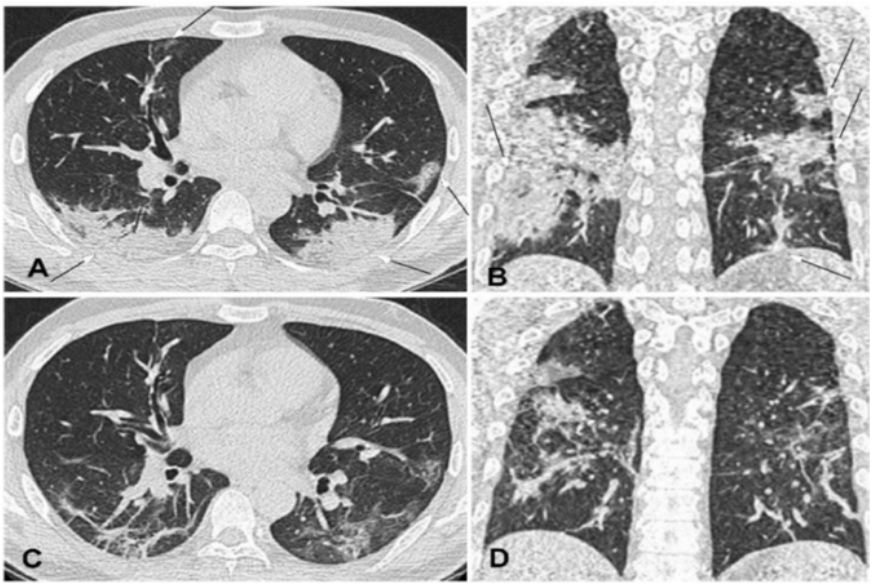


Figure 45: Severe novel coronavirus pneumonia in a 34-year-old man with fever and cough for ten days before admission. A&B. Computed tomography axial (A) and coronal (B) plane revealed multiple lesions of ground glass opacity, consolidation and fibrosis with symmetrical distribution in bilateral lungs, with the lesion extending towards the pulmonary hilum. Air bronchogram was observed within the lesion. C&D. Four days after treatment, the extent of lesion shrank with decreased density and formation of fibrosis Yu-Huan Xu, et al. [149].

By considering the growth rate [150] and inhibition constant of infectious diseases their propagation growth model is established. The parameters of the three coronavirus transmission growth models are obtained by nonlinear fitting. Parametric analysis shows that the growth rate of COVID-19 is about twice that of the SARS and MERS; and the COVID-19 doubling cycle is two to three days; suggesting that the number of COVID-19 patients would double in two to three days without human intervention. The infection inhibition constant in Hubei is two orders of magnitude lower than in other regions [150] which reasonably explains the situation of the COVID-19 outbreak in Hubei [150] (Figure 46).

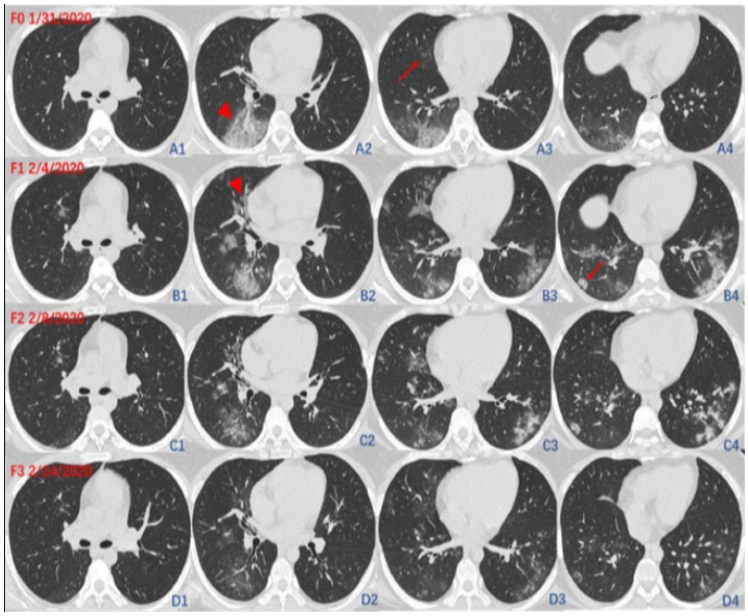


Figure 46: The initial CT images (F0) and three times of follow-up CT images (F1–F3) of P1. F0 showed patchy-like pure GGO located in the subpleural regions of the right middle lobe (F0, A3, arrow) and the right lower lobe, accompanied by crazy paving sign (F0, A2, arrowhead). Follow-up 1(F1, B1–B4): CT images showed diseases progression. The lesions manifested as coexisted nodular-like (F1, B4, arrow) and patchy-like lesions as well as peri bronchial (F1, B2, arrowhead), central and subpleural distribution. The lesions are migratory manifested as the absorption of the primary lesions and the emergence of new lesions. CT images of Follow-up 2 (F2, C1–C4) and Follow-up 3 (F3, D1–D4) showed lesion absorption. (Ying Zhu 1, Zhen-Hua Gao 2, Yang-Li Liu 3, Dan-Yang Xu et al, 2020).

The standard of reference for confirming COVID-19 relies on [151] microbiological tests such as real-time polymerase chain reaction (RT-PCR) or sequencing. However; these tests might not be available in an emergency setting. Computed tomography (CT) can be used as an important complement for the diagnosis of COVID-19 pneumonia in the current epidemic context (Figure 47).

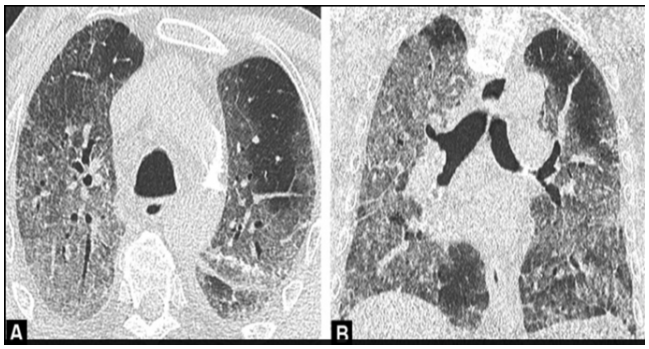


Figure 47: Unenhanced CT images of a "white lung" appearance in an 89-year-old man with respiratory distress due to COVID-19 pneumonia. Axial (A) and coronal (B) CT images, performed before admission in ICU demonstrate extensive ground glass opacities, with more than 75% of the lung involved. (C Hani, N H Trieu, I Saab, S Dangeard et al, 2020).

Of the 49 patients; 89.8% (44/49) patients [152] had a typical transition from early stage to advanced stage and then from advanced stage to dissipating stage. With the evidence of fibrosis for progression of CT results; 42.9% (21/49) patients developed fibrosis whereas 57.1% (28/49) patients demonstrated no definite fibrosis. Patients with fibrosis in follow CT were older (mean age; 45.4 vs. 33.8 years) with longer LOS (19.1 vs. 15.0 days) and higher rate of [152] ICU admission (19.0% (4/21) vs. 3.6% (1/28)) than that of those without fibrosis.

Knowledge of CT characteristics of COVID-19 pneumonia [153] might be helpful to the early diagnosis and treatment of patients and to control the spread of infection. The chest CT images of the patient were collected to describe the CT manifestations and characteristics and they were compared with the previous studies. Multiple patchy ground-glass opacities (GGOs) were seen in bilateral lung mostly in subpleural areas. They progressed within 3 days and nodular GGOs were also seen together with subpleural patchy GGOs. Our case of COVID-19 pneumonia showed multiple subpleural GGOs in bilateral lung rapid progression and it also accompanied nodular GGOs on chest CT. These findings were consistent with the previous reports and they might be [153] useful for early detection and evaluation of severity of COVID-19 pneumonia.

One of the challenges in managing [154] COVID-19 is the identification of a swift accessible and reliable diagnostic modality that could serve as an alternative to a reverse-transcriptase polymerase chain reaction (RT-PCR). As of the writing of this paper RT-PCR is still the recommended tool in diagnosing COVID-19 but the notion of a prompter and more accurate diagnostic tool is a possibility worth looking into. The objective of this case study is to investigate the importance and utility of chest computed tomography (CT) in the diagnosis of COVID-19 as increasing pieces of [154] evidence suggest that chest CT could prove useful in the clinical pathway in diagnosing COVID-19.

To date computed tomography (CT) findings [155] have been recommended as major evidence for the clinical diagnosis of COVID-19 in Hubei China. This review focuses on the imaging characteristics and changes throughout the disease course in patients with COVID-19 in order to provide some help for clinicians. Typical CT findings included bilateral ground-glass opacity pulmonary consolidation and prominent distribution in the posterior and peripheral parts of the lungs. This review also provides a comparison between COVID-19 and other diseases that have similar CT findings. Since most patients with COVID-19 infection share typical imaging features radiological [155] examinations have an irreplaceable role in screening diagnosis and monitoring treatment effects in clinical practice [156;157] (Figures 48-51).

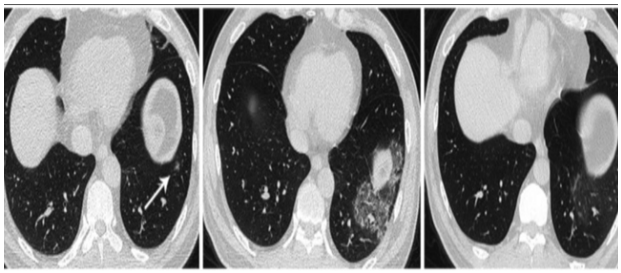


Figure 48: Chest CT images of 51-year-old man with COVID-19 pneumonia. A. Baseline chest CT image (7 days before onset of symptoms) shows solitary ill-defined ground-glass nodule 7 mm in size (arrow) in left lower lobe. Day 2, patient presented with fever and chest pain day earlier; follow-up CT image (B) shows confluent crazy-paving pattern and consolidation opacities appear in same location. Day 15 follow-up CT image (C) shows area of lesion has become smaller and density has begun to decrease Tianyi Xia, et al. [156].

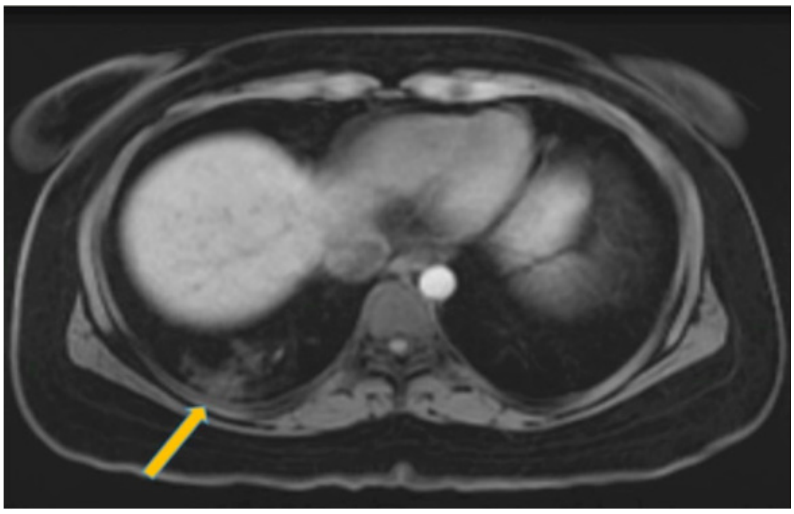


Figure 49: 26-year-old female with a recent history of sleeve gastrectomy complicated by splenic vein thrombosis presented to the emergency department with left lower quadrant abdominal pain. T1-weighted axial MRI with intravenous contrast of the abdomen and pelvis incidentally noted peripheral signal intensity abnormalities in the right lung base (arrow). The patient subsequently tested positive for COVID-19 with PCR testing. (Sayan Manna, Jill Wruble, Samuel Maron, Danielle T, 2020).

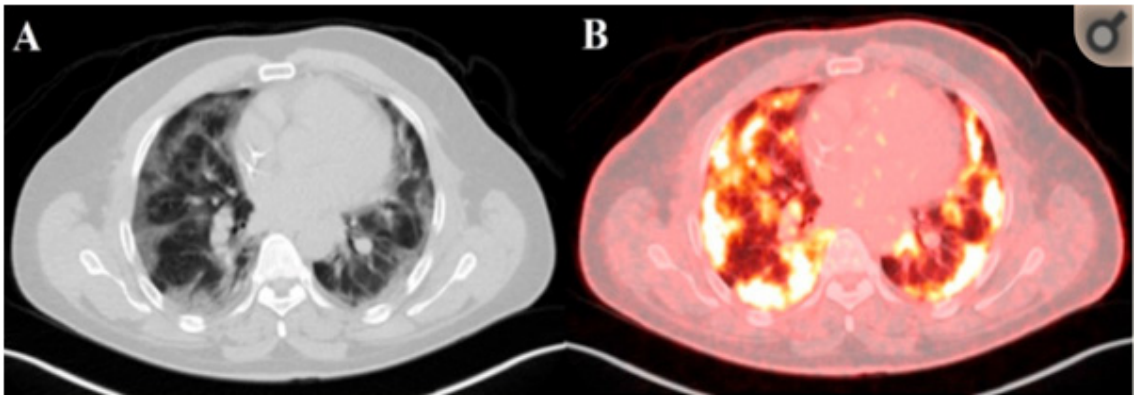


Figure 50: 33-year-old male with history of HIV and treated Hodgkin's lymphoma undergoing PET/CT, for oncologic restaging. Fused PET/CT imaging (B) shows bilateral peripheral predominant intense sites of FDG avidity that correspond to ground-glass and mixed attenuation opacities on CT (A). A maximum standardized uptake value of 9.98 was seen. The patient was asymptomatic at time of imaging but presented to the emergency department ten days later after developing hypoxia with 85% oxygen saturation on room air. The patient was confirmed to be positive for COVID-19 with PCR testing Sayan Manna, et al. [157].

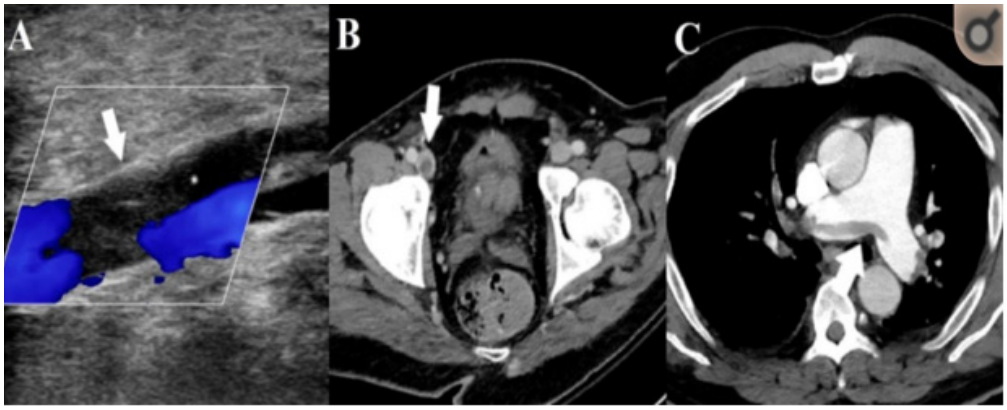


Figure 51: Venous thromboembolic disease in COVID-19. (A) Doppler ultrasound of the left lower extremity in a 57-year-old male with COVID-19 demonstrates non-occlusive thrombus in the popliteal vein (arrow). (B) CT Pelvis in a 33-year-old male demonstrates non-occlusive thrombus in the right common femoral vein (arrow). (C) CT Chest Angiography in a 69-year-old male demonstrates saddle pulmonary embolus (arrow) Sayan Manna, et al. [157].

The SARS-CoV-2 outbreak has rapidly reached [158] pandemic proportions and has become a major threat to global health. Although the predominant clinical feature of COVID-19 is an acute respiratory syndrome of varying severity; the cardiovascular system can be involved in several ways. Heart and lung multimodality imaging plays a central role in different clinical settings and is essential in diagnosis; risk stratification; and management of patients with COVID-19. To prevent and mitigate transmission; key preventive measures must be adopted; encompassing equipment; facilities; health care personnel; and disinfection procedures [158;159] (Figure 52).

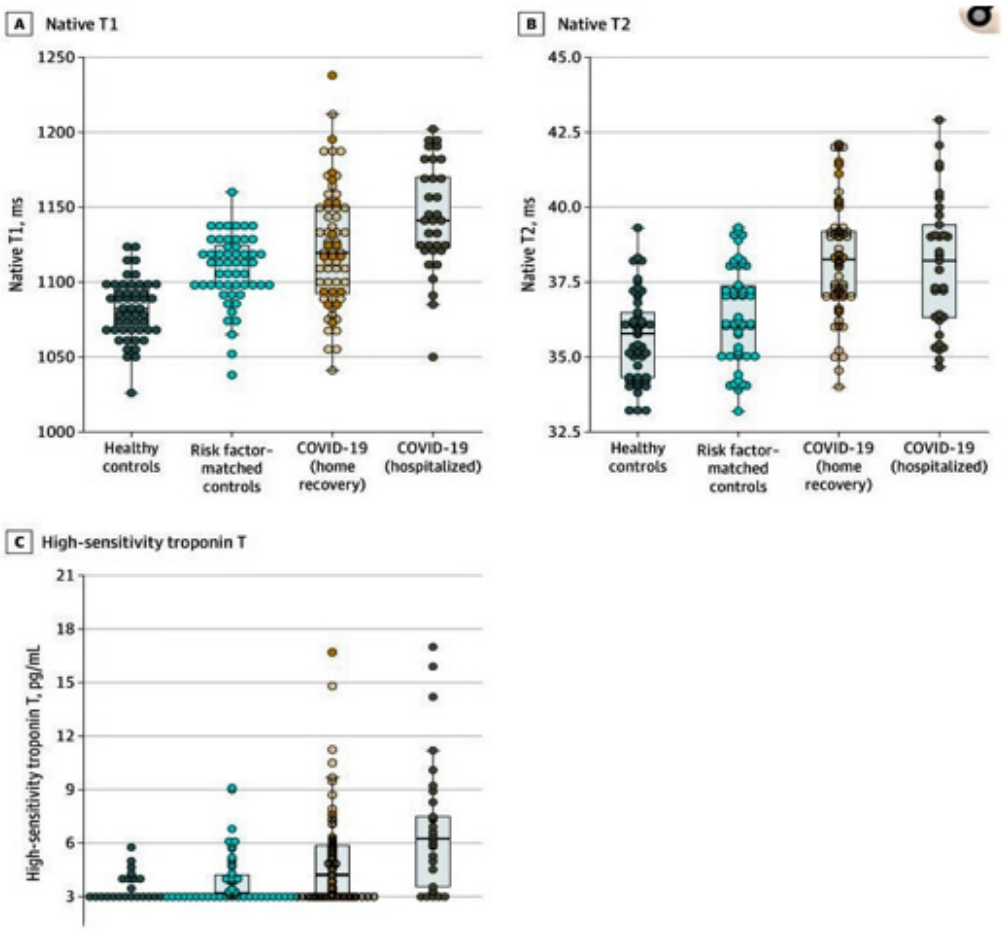


Figure 52: Scatterplots of Native T1, Native T2, and High-Sensitivity Troponin T Measures by Group. There was a small but significant difference between patients who recovered at home vs in the hospital for native T1 (median [interquartile range], 1122 [1113-1132] ms vs 1143 [1131-1156] ms; P = .02) but not for native T2, high-sensitivity troponin T, or N-terminal pro–b-type natriuretic peptide. For the coronavirus disease 2019 (COVID-19) home recovery group, dark circles indicate symptomatic illness and light circles indicate asymptomatic illness. Boxes indicate overlays of box-whisker plots, midlines indicate medians, and whiskers indicate interquartile ranges Valentina Puntmann, et al. [159].

During the peak phase of the COVID-19 pandemic [160] alterations of standard operating procedures were necessary for health systems to protect patients and healthcare workers and ensure access to vital hospital resources. As the peak phase passes re-activation plans are required to safely manage increasing clinical volumes. In the context of cardiovascular magnetic resonance (CMR) re-activation objectives include continued performance of urgent CMR studies and resumption of CMR in patients with semi-urgent and elective indications [160] in an environment that is safe for both patients and health care workers.

Lung/ Organs Transplant in Severely Ill COVID-19 Patients and Pictures

SARS-CoV-2 primarily invades the [161] respiratory tract and lungs leading to pneumonia and other systemic disorders. The effect of SARS-CoV-2 in transplant recipients has raised significant concerns especially because there is a large population of transplant recipients in China. Based on the current epidemic situation this study reviewed publications on this virus and coronavirus disease 2019 (COVID-19) analysed common features of respiratory viral pneumonias and presented the currently reported clinical characteristics of COVID-19 in transplant recipients [161] to improve strategies regarding the diagnosis and treatment of COVID-19 in this special population.

Despite the majority of the general population [162] displaying symptoms similar to the common cold COVID-19 has also induced alveolar damage resulting in progressive respiratory failure with fatalities noted in 6.4% of cases. Direct viral injury uncontrolled inflammation activation of coagulation and complement cascades are thought to participate in disease pathogenesis. Patients with COVID-19 have displayed kidney damage through acute kidney injury; mild proteinuria; haematuria; or slight elevation in creatinine possibly as consequence of kidney tropism of the virus and multiorgan failure. The impact of COVID-19 on patients with pre-existing kidney impairment including those with chronic kidney disease; kidney transplant recipients; and individuals on haemodialysis (HD) has not yet been clearly established. [162] No specific treatments for COVID-19 have been found yet.

Solid organ transplantation represents a field with a [163] high demand on staff intensive care units and follow-up facilities. The great therapeutic value of organ transplantation has to be weighed against mandatory constraints of health care capacities. In addressing these crucial questions transplant physicians are facing a total lack of scientific evidence. A high degree of consensus was found for temporarily suspending nonurgent transplant procedures and living donation programs. Systematic polymerase chain reaction-based testing of donors and recipients was broadly recommended. Additionally; more specific aspects (eg; screening of surgical explant [163] teams and restricted use of marginal donor organs) were included in our analysis.

In order to ensure transplantation safety donor [164] and recipient screening is necessary in COVID-19 spreading areas. The SOT recipients are an immunologically vulnerable group; and it is crucial to prevent viral infection in such patients. Both online education to spread awareness about COVID-19 and online follow-up could minimize the risk of infection in SOT patients. The long-lasting controversy over immunoregulation to balance infection and rejection continues during this battle with COVID-19. Antiviral drugs and methylprednisolone pulse therapy should be administered with great caution. Current antiviral therapy needs more evidence to prove that its efficacy can outweigh its potential adverse effects and drug-drug interactions. Lung transplant could be a possible way out for [164] end stage COVID-19 patients but great caution should be taken before COVID-19 lung injury is proven irreversible [165] (Figure 53).

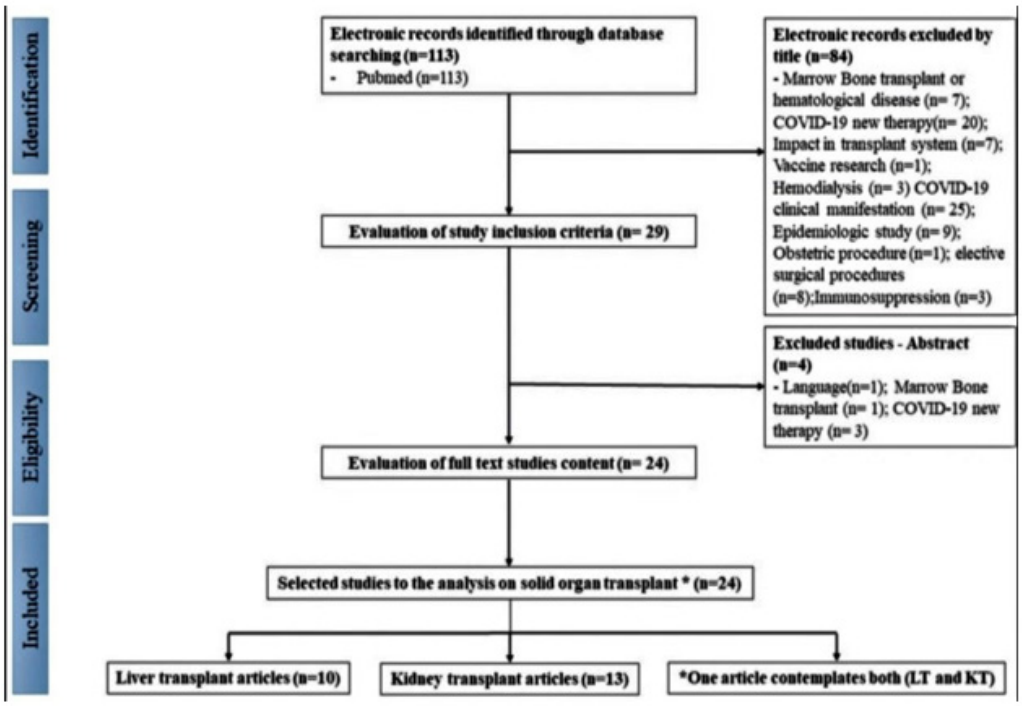


Figure 53: Flow diagram of the systematic literature search according to the PRISMA statement. *Kidney transplant (KT) and liver transplant (LT). (Lucas Nacif, Leonardo Zanini, Daniel Waisberg, Rafael P et al, 2020).

The WHO has declared the outbreak [166] of SARS-CoV-2 infection an international public health emergency. Lung lesions have been considered as the major damage caused by SARS-CoV-2 infection. However; liver injury has also been reported to occur during the course of the disease in severe cases. Similarly; previous studies have shown that liver damage was common in the patients infected by the other two highly pathogenic coronavirus severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus [166] (MERS-CoV) and associated with the severity of diseases [167] (Figure 54).

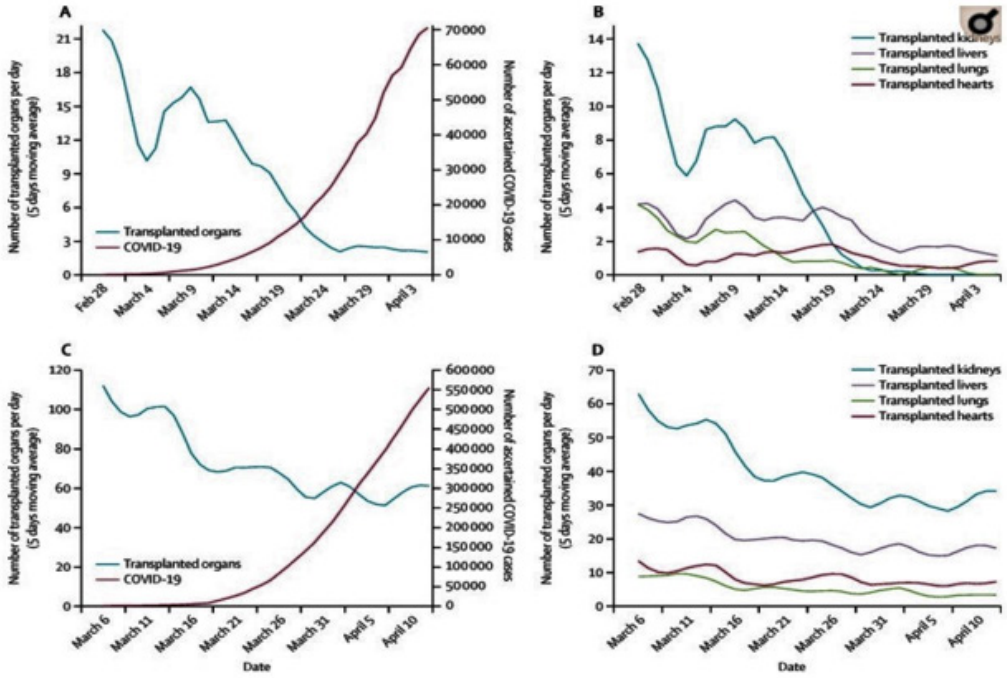


Figure 54:

1. Trends in COVID-19 spread over time in France and the USA and recovery of organs and solid-organ transplantation procedures from deceased donors (A, C).

2. Number of COVID-19 diagnoses and number of solid organs recovered for transplantation over time in France (A).

3. and the USA (C).

4. (B, D) Total number of transplants from deceased donors, with separate trend lines for kidney, liver, heart, and lung, over time in France (B).

5. and the USA (D).

6. Data were obtained from Public Health France (A),

7. the National Organ Procurement Agency (B),

8. Xu et al. (C),

9. and the United Network for Organ Sharing (D). Data accessed April 11, 2020. COVID-19=coronavirus disease 2019 Alexandre Loupy, et al. [167].

We report our preliminary experience with [168]18 SOT (kidney (44.4%) liver (33.3%) and heart (22.2%)) recipients diagnosed with COVID-19 by March 23; 2020 at a tertiary-care centre at Madrid. Median age at diagnosis was 71.0 ± 12.8 years and the median interval since transplantation was 9.3 years. Fever (83.3%) and radiographic abnormalities in form of unilateral or bilateral/multifocal consolidations (72.2%) were the most common presentations. Lopinavir/ritonavir (usually associated with hydroxychloroquine) was used in 50.0% of patients and had to be prematurely discontinued in 2 of them. Other antiviral regimens included hydroxychloroquine monotherapy (27.8%) and interferon-β (16.7%). As of April4 the case-fatality rate was 27.8% (5/18). After a median follow-up of 18 days from symptom onset 30.8% (4/13) of survivors [168] developed progressive respiratory failure 7.7% (1/13) showed stable clinical condition or improvement and 61.5% (8/13) had been discharged home.

The maintenance of the transplanted graft and its proper [169] function is of great importance in patients with COVID-19. With regard to receiving immunosuppressants and polypharmacy treatment options should be chosen with prudence in these patients. It is suggested that mTOR inhibitors be stopped throughout the course of COVID-19 and substituted with CNIs. Considering drug-drug interactions and adverse effects of medications used for the treatment of COVID-19 such as QT prolongation the dose reduction of some immunosuppressants

or avoidance of their administration should be considered in transplant recipients with COVID-19. QT prolongation should be considered when using hydroxychloroquine or lopinavir/ritonavir in combination with other QTc-prolonging drugs such as antipsychotics and cardiac medications. We should wait for further clinical trials and multicentre studies to [169] evaluate the safety and efficacy of treatment options for COVID-19 in transplant patients.

The transplant community is faced with [170] choosing a lesser of two evils initiating immunosuppression and potentially accepting detrimental outcome when transplant recipients develop COVID-19 versus postponing transplantation and accepting associated waitlist mortality. Notably prioritization of health care services for COVID-19 care raises concerns about allocation of resources to deliver care for transplant patients who might otherwise have excellent 1-year and 10-year survival rates. Children and young adults with end-stage organ disease in particular seem more disadvantaged by withholding transplantation because of capacity issues than from medical consequences of SARS-CoV-2. Worrisome there was a significant decrease in organ donation numbers affecting all organ transplant services. In addition; [170] there was a detrimental effect on transplantation numbers in children with end-organ failure.

Despite the COVID-19 Pandemic organ failure [171] and the need for transplant continues throughout the United States. Considering the perpetual scarcity of deceased donor organs; Kates et al present a viewpoint that advocates for the utilization of coronavirus disease 2019 (COVID-19)-positive donors in selected cases. We present a review of the current literature that details the potential negative consequences of COVID-19-positive donors. The factors we consider include

(1) The risk of blood transmission of SARS-CoV-2;

(2) Involvement of donor organs

(3) Lack of effective therapies

(4) Exposure of health care and recovery teams

(5) Disease transmission and propagation; and

(6) Hospital resource utilization.

For these reasons we believe the evidence and risks show that COVID-19 infection should continue [171] to remain a contraindication for donation as has been the initial response of donation and transplant societies.

Transplantation is one of the most affected [172] sectors as it relies on a variety of services that have been drastically occupied to treat patients affected by COVID-19. With this report from two transplant centres in Italy we aim to reflect on resource organization organ allocation virus testing and transplant service provision during the course of the pandemic and to provide actionable information highlighting advantages and drawbacks. To what extent can we preserve the noble purpose of transplantation in times of increased danger? Strategies to minimize risk exposure to the transplant population and health- workers include systematic virus screening protection devices social distancing and reduction of patients visits to the transplant centre. While resources for the transplant activity are inevitably reduced new dilemmas arise to the transplant community further optimization of time constraints during organ retrievals and implantation less organs and blood products donated limited space in the [172] intensive care unit and the duty to maintain safety and outcomes.


3
Chapter

Methodology

Definition of Methodology

The author has used Critical Literature review as a methodology for this book on epidemiology of COVID-19. The Author has reviewed approximately more than 450 Published article and essays published on PubMed Central; Newspapers and or on internet websites. The Author of this book has reviewed and critically analyzed published articles on epidemiology; Distribution and preventions of covid-19 and presented the graphs and diagrams on crucial data. Methodology is the systematic theoretical analysis [173] of the methods applied to a field of study. It comprises the theoretical analysis of the body of methods and principles associated with a branch of knowledge. Typically; it encompasses concepts such as paradigm theoretical model phases and [173] quantitative or qualitative techniques. A methodology offers the [173] theoretical underpinning for understanding which method; set of methods; or best practices can be applied to a specific case for example to calculate a specific result. Definition of methodology: (A body [174] of methods rules and postulates employed by a discipline; a particular procedure or set of procedures demonstrating library research methodology) (The analysis [174] of the principles or procedures of inquiry in a particular field).

Suitability of the Literature Review

Definition of Literature Review: A literature review is a survey of scholarly sources [175] on a specific topic. It provides an overview of current knowledge allowing you to identify relevant theories methods and gaps in the existing research. Writing a literature review involves finding relevant publications (such as books and journal articles) critically analysing them and explaining what you found. There are five key steps: 1: Search for relevant literature 2: Evaluate sources 3: Identify themes debates and gaps 4: Outline the structure 5: Write your literature review. A good literature review does not just summarize sources it analyses synthesizes and [175] critically evaluates to give a clear picture of the state of knowledge on the subject.

A literature review discusses published information in a [176] subject area and sometimes information in a particular subject area within a certain time. A literature review can be just a simple summary of the sources; but it usually has an organizational pattern and combines both summary and synthesis. A summary is a recap of the important information of the source; but a synthesis is a re-organization or a reshuffling of that information. It might give a new interpretation of old material or combine new with old interpretations. Or it might trace the intellectual progression of the field including major debates. And depending on the situation the literature [176] review may evaluate the sources and advise the reader on the most pertinent or relevant.

The purpose of a literature review is to [177] provide a review of writings on the given topic to establish the reviewer's own position in the existing field of scholarship on that topic. A literature review provides a reader with a comprehensive look at previous discussions prior to the one the reviewer will be making in his/her own research paper thesis or dissertation. In short; a literature review shows readers where the reviewer is entering the academic conversation on a particular topic in the context of existing scholarship. An annotated bibliography is a list of your references with a summary of the content and the publication's relationship to your research question. A literature review is an overview of the topic an explanation of how publications differ from one another and an [177] examination of how each publication contributes to the discussion and understanding of the topic.

The main types of literature reviews are evaluative exploratory [178] and instrumental. A fourth type the systematic review is often classified separately but is essentially a literature review focused on a research question trying to identify appraise select and synthesize all high-quality research evidence and arguments relevant to that question. A meta-analysis is typically a systematic review using statistical methods to effectively combine the data used on all selected studies to produce a more reliable result. Torraco (2016) describes an integrative literature review. The purpose of an integrative literature review is to generate new knowledge on a topic through the process [178] of review critique and then synthesis of the literature under investigation.

Systematic reviews are a type of literature review [179] that uses systematic methods to collect secondary data critically appraise research studies and synthesize findings qualitatively or quantitatively. Systematic reviews formulate research questions that are broad or narrow in scope and identify and synthesize studies that directly relate to the systematic review question. They are designed to provide a complete exhaustive summary of current evidence published and unpublished; that is "methodical; comprehensive; transparent; and replicable." An understanding of systematic reviews and how to implement them in practice is highly recommended for professionals involved in the delivery

of health care public health; and public policy. Systematic reviews of randomized controlled trials are key to the practice of evidence-based medicine and a review of existing studies is often quicker and cheaper than embarking on a new study. [179] Contrastingly systematic reviews of observational studies rank lower in the evidence-based hierarchy.

Not to be confused with a book review a literature review [180] surveys scholarly articles books and other sources (e.g. dissertations; conference proceedings) relevant to a particular issue area of research or theory providing a description summary and critical evaluation of each work. The purpose is to offer an overview of significant literature published on a topic. Like primary research development of the literature review requires four stages. 1: Problem formulation-which topic or field is being examined and what are its component issues? 2: Literature search-finding materials relevant to the subject being explored. 3: Data evaluation-determining which literature makes a significant contribution to the understanding of the topic. 4: Analysis and interpretation-discussing the findings and conclusions of pertinent literature. Literature reviews should comprise an overview of the [180] subject issue or theory under consideration along with the objectives of the literature review.

What and How to Search for Literature

Aim to be as comprehensive as possible when conducting [181] a literature review. Knowing exactly where to search for information is important. Scopus and Web of Science are good databases to start with for any research topic and literature review. Scopus: Scopus is a large multidisciplinary database covering published material in the humanities and sciences. It also provides citation analysis of authors and subject areas. Web of Science Core Collection: The leading citation index' of scholarly literature; chemical reactions and author information. Includes citation databases: Sciences Expanded (1965+); Social Sciences (1965+); Arts & Humanities (1975+). [181] Conference Proceedings (1991+) and Emerging Sources Citation (2005+).

Make a list of the databases you will search and remember [182] to include comprehensive databases such as World Cat and Dissertations & Theses if you need to. To find databases. 1: Find Databases by Subject and UWF Databases categorized by discipline. 2: Find Databases via Research Guides by librarians create research guides for all the disciplines on campus! Take advantage of their expertise and see what discipline specific search strategies they recommend. Review the abstracts of research studies carefully this will save you time. Write down the searches you conduct in each database so that you may duplicate them if you need to later or [182] avoid dead-end searches that you'd forgotten you'd already tried.

Resources Used

The Author of this book has used mostly articles published in the Pub Med Central and reliable sources and reputable scientific journals. The articles are searched on the Pub Med Central by using different words searches for example "Covid-19 Epidemiology; Covid19 preventions; Covid-19; Covid19 vaccination; Covid-19 treatment; mortality covid19; death rate covid-19; CT Scans covid19; data covid19; covid19 pathophysiology; pathogenesis covid19; economic impact covid19; dash board covid19; body temperature covid19; critical care covid-19; covid19 affected countries; covid19 free countries; covid19 test kit; covid19 guidelines; covid19 second wave; covid19 vs zip code USA; covid19 distribution; covid19 test kit; covid19 control; others". Author of this book has tried to select the valuable articles and data analysis for literature review and analysis. The book also includes the diagrams and graphs to show the analysis of the study.

There are many of databases available on internet or on websites; but researcher could not trust on the information available on every website or databases because some of the websites are not quality checked. Some of the web sites for example google search engine and Medent's and Trip database are very useful databases and search engines having much of quality information a researcher can use for references or for critical analysis. They include quality internet journals for example British Medical Journal; American Journal of Public Health; Lancet Journal; and Independent Journal.

Search Terms

A search term otherwise known as a search query is [183] the word or phrase someone enters a search engine such as Google. A search term often contains or is itself a keyword a word or phrase search marketers bid on in their search campaigns and try to rank for in the organic search results. During searching the literature; the researcher should widely search the literature to find out his/her material of interest about the focused research question the researcher should search the electronic databases and websites to find the literature of his/her interest or read books of different authors and search various journals to find the literature regarding the focused research question.

A search term is anything that users type in the search box [184] while keywords is what search engines have in their index. During the crawling and indexing phase search engines crawl a page and extract the keywords it is associated with and this is how it is stored in their

index. In many cases search terms and keywords are a perfect match while in some cases search engine algorithms using the help of machine learning will try and figure out what the user is looking for. In both cases Google will answer the search query using the best possible results because they have sophisticated [184] ranking algorithms that can extract the user intent from whatever the user types in the search box.

Boolean search is a type of search allowing users [185] to combine keywords with operators or modifiers such as AND; NOT and OR to further produce more relevant results. For example; a Boolean search could be "hotel" AND "New York". This would limit the search results to only those documents containing the two keywords. The following example describe the different Boolean search operators. Note that AND NOT and OR will generally need to be in capital letters when used as a search operator. Basic Boolean search commands quotes; [185] AND and OR are supported in Google search however Google defaults to AND searches automatically [186] (Figures 55 & 56).

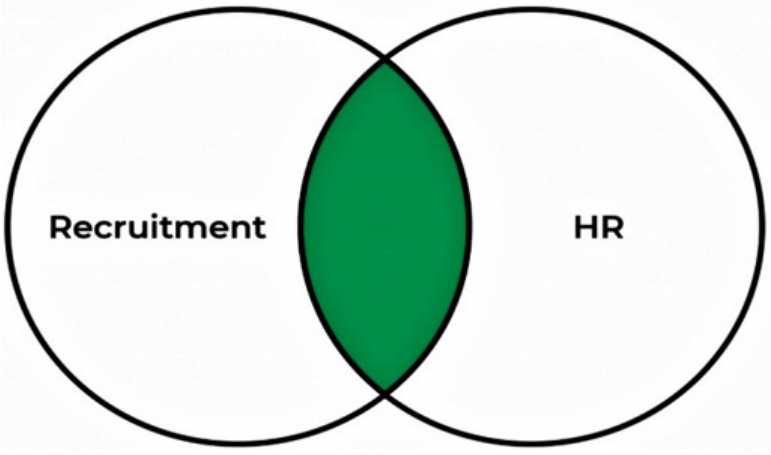


Figure 55: What is Boolean Search? Recruitment AND HR [186].

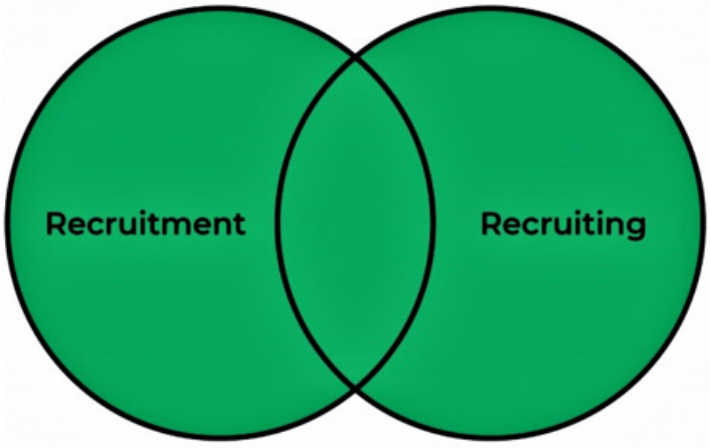


Figure 56: What is Boolean Search? Recrui

Boolean Search is a search process that allows [187] you to broaden limit and define your search options by adding Boolean Search Operators or Modifiers. With Boolean Search Operators you will be able to find profiles and candidates that more closely match your requirements. The author of this book has used Boolean search methods various times to find the appropriate article for the topics discussed in the book.

Selection Criteria and Comparison between Bray and Rees (1995) Critiquing Framework and Critical Appraisal Skills Programme (CASP)

There are several frameworks for critiquing research [188] some of which have been constructed to critique or evaluate both qualitative and quantitative studies. Others however have been constructed to critique only one of these. This series outlines the two main approaches to research (recognising that there are other more specialised approaches) and explains how to read and critique qualitative and quantitative research. The development of such skills should assist preregistration students with relevant assignments. They should also help practitioners to determine if a piece of research is relevant and suitable to be implemented in their practice. As practitioners gain a deeper understanding of

critiquing a single piece of research; they should [188] consider critiquing several research studies on a particular topic searching for common themes.

Critical appraisal skills enable you to [189] systematically assess the trustworthiness relevance and results of published papers. The Critical Appraisals Skills Programme- CASP has over 25 years of significant and unrivalled expertise in the delivery of training to healthcare professionals. The philosophy of CASP has always been about sharing knowledge and understanding working in ways that are non-hierarchical multidisciplinary and using problem-based approaches. This ensures that it is accessible and has practical day to day application. CASP offers critical appraisal skills training workshops and tools. These help you read and check [189] health research for trustworthiness results and relevance.

The Critical Appraisal Skills Programme- CASP helped to develop an [190] evidence-based approach in health and social care; working with local national and international groups. CASP aims to help individuals develop skills to find and make sense of research evidence helping them to apply evidence in practice. The Critical Appraisal Skills Programme- CASP tools were developed to teach people how to critically appraise different types of evidence. [190] There are seven checklists specifically designed to appraise;

1. Systematic Reviews
2. Randomized Controlled Trials (RCTs)
3. Qualitative Research
4. Economic Evaluation Studies
5. Cohort Studies
6. Case Control Studies
7. Diagnostic Test Studies

All critical appraisal tools consist of three sections to assess internal validity the results and the [190] relevance to practice.

Inclusion and Exclusion Criteria

The author of this book has used Boolean operators/keyword searches to find the focused literature and to precise the research. Author has found keyword search as a most important tool to collect the information required for the references. Author has used all the information and the article journals available in English language and excluded all the information available in other languages. Author has included all the studies in this book which was latest for example for critical literature review post 99 studies was included in this book. All the old; outdated research was excluded from this research. Studies for example Meta-analysis were also not included in the critical literature review. Boolean operators/keyword search is the most useful tool to find the latest and appropriate information and journal articles for this book.

Above all are the inclusion criteria for the researcher to follow to write up this book. The author has also considered some exclusion criteria for the research to avoid the weak written texts. Books and internet journal articles which are not available in English are not included because it is very time consuming to translate the literature and data from other languages. Also; studies with poor methodology are excluded following critical review. The author had used the Boolean operators/key word searchers to find out the most suitable and focused journal articles and information regarding the research question (Epidemiology of COVID-19 in incidence distribution and prevention; availability of possible vaccination and treatment. A Battle against the Pandemic while whole world is fighting the COVID 19 novel corona Virus possibly originated from Wuhan; Hubei Province China). The researcher had excluded all the articles and information which was not related to the research question.

Ethical Consideration

Research ethics is a complex construct; essentially concerned with the principles of right and wrong conduct [191]; that reflect various epistemological paradigms and methodological practices within particular social and cultural contexts [192]. Increasingly researchers question the assumptions that ethics can be reduced to codified sets of principles and that following these systematically will make research more ethically sound. Consequently; a key theme in the literature is using ethics to promote exploration and examination of dilemmas rather than purely as a basis for rules of research conduct [193].

Apart from plagiarism falsification and fabrication of data also [194] constitute serious offense. Falsification and fabrication call into question the integrity of data and the data record. Practice of omitting or altering research materials equipment data; or processes in such a way that the results of the research are no longer accurately reflected in the research result is called falsification whereas the practice of inventing data or results and recording them in the research record is called fabrication. Both of these affect the credential of the research. Double publication is a practice which involves repeat publication or attempts at publication of text; figures; or data in any form of publicly available media without citation in the later manuscript. All these things including plagiarism falsification and fabrication double [194] publications are serious transgression of academic ethics.

In the United States plagiarism is taken very seriously [195] both legally and ethically. It can lead to disciplinary action such as expulsion from the University. Additionally; plagiarizing will damage your reputation and credibility as a scholar in Western academia. Plagiarism can be intentional- purchasing a research paper online or sharing a test with a friend or unintentional- improperly citing a source in a paper or using an author's words without giving her/him credit. It might seem like using the ideas of others is a problem. However; this is not the case. Scholarship is a conversation that is you will be expected to read analyze and respond to the ideas of others when writing your papers. The key to doing this without [195] plagiarizing is to cite your sources.

The understanding of ethical consideration is the author have taken the written consents from the participants or samples of the study. The participants or samples are well informed that their answers and data for example laboratory findings of medical tests will be used for research purposes. In the case of using literature for references in Dissertation or books the researcher must use appropriate recognised referencing method for example Harvard referencing method to avoid case of plagiarism.


4
Chapter

Methods: Search Strategy

Data Collection

This chapter is about that how the author has conducted the research to collect the information and data to use it for references and for critical analysis. For this book; the author has performed a wide range of search for the literature and data of focused research question (Epidemiology of COVID-19 in incidence distribution and prevention; availability of possible vaccination and treatment. A Battle against the Pandemic while whole world is fighting the COVID 19 novel corona Virus possibly originated from Wuhan; Hubei Province China) from different books; journals articles; medical websites; and some pamphlets. Information from databases; books and journals for this book is taken from PubMed Central; WHO published literature; Athens Databases; Reputable Journals; and recommended internet websites.

Total 3300 studies were retrieved of which approximately 444 met the inclusion criteria and then included in the book for the critical literature review and the discussion. The author has chosen the latest articles of 2020 and 2019 for the referencing and to discuss and critically reviewed in the article. Some of the studies and articles did not focus on the research question but they are included because data was needed to support the argument about the Importance of using personal protective equipment; social distancing; hand hygiene and using hand sanitizers frequently. The author has included those journal articles which provide data and information regarding (Epidemiology of COVID-19 in incidence distribution and prevention; availability of possible vaccination and treatment. A Battle against the Pandemic while whole world is fighting the COVID 19 novel corona Virus possibly originated from Wuhan; Hubei Province China) (Table 1).

Table 1.

Included studies	Excluded studies
• Studies focusing on research question (Epidemiology of COVID-19 in incidence distribution and prevention, availability of possible vaccination and treatment. A Battle against the Pandemic while whole world is fighting the COVID 19 novel corona Virus possibly originated from Wuhan, Hubei Province China). • Research related to Epidemiology and preventions including use of PPE, Hand hygiene and use of hand sanitizers frequently all the time to avoid COVID19 Virus. • Research including Treatment available for covid19 Pandemic patients such as Antivirals Remdesivir, Ceftriaxone, Moxifloxacin, Azithromycin, Clarithromycin, Dexamethasone, Convalescent plasma, Oxygen therapy for covid19 patients' others. • Research published giving statistics about morbidity and mortality related to COVID19 Pandemic across worldwide including EU, the UK and the USA.	• Studies did not focus on research question (Epidemiology of COVID-19 in incidence distribution and prevention, availability of possible vaccination and treatment. A Battle against the Pandemic while whole world is fighting the COVID 19 novel corona Virus possibly originated from Wuhan, Hubei Province China). • Old research about PPE use and prevention about other communicable diseases. • Studies those are not published and did not have clear methodology. • Studies not published in English language
Total included studies for CLR = 444	Total excluded studies = 2856

The author used the academic journal articles for references which are more focused on (Epidemiology and preventions including use of PPE; Hand hygiene and use of hand sanitizers frequently all the time to avoid COVID19 Virus and research including Treatment available for covid19 Pandemic patients such as Antivirals Remdesivir; Ceftriaxone; Moxifloxacin; Azithromycin; Clarithromycin; Dexamethasone; Convalescent plasma; Oxygen therapy for covid19 patients' others) The computer and the internet is the most valuable tool to access electronic databases. Key words are used with concentration to get the relevant literature with the help of Boolean operators. Boolean operators such as PubMed central; Elsevier; Google scholar articles; Scopus; Clavirate analytics Journals; Research Gate Articles and authentic websites help to find the relevant literature on Epidemiology; Prevention; and treatment available for COVID19 Pandemic patients. The table for Boolean operators/databases; Electronic journals and Boolean search terms/ Key words used are provided here as: (Table 2)

Table 2.

Boolean operators/ Databases.	Health Journals for information.	Boolean search terms/ Key words/ Search Terms.
PubMed central.	American Journal of Public health, American Journal of internal Medicine, British Medical Journal, European journal of internal medicine.	Epidemiology of COVID-19 in incidence distribution and prevention, availability of possible vaccination and treatment. A Battle against the Pandemic while whole world is fighting the COVID 19 novel corona Virus possibly originated from Wuhan, Hubei Province China.
Elsevier Journals.	Infection disease and health, Journal of Infection and Public Health, Advances in Integrative medicine.	Availability and the use of Personal Protective equipment, Frequently Hand washing during the day, Use of Hand sanitizers all the time during the day.
Google Scholar articles	The New England Journal of Medicine, The Lancet, Journal of Clinical Oncology, Natural Medicine.	Mortality data about COVID-19, Death rate of COVID19 among male and female, Children mortality.
Research Gate Articles.	The new England journal of medicine, American journal of infectious diseases, Journal of Adolescent Research.	COVID19 Preventions recommendations by WHO, COVID19 Intervention programs, Safety procedures for COVID-19.
Scopus	Nature Reviews Immunology, The Lancet Oncology, Epidemiology Journal, Infectious disease journal.	Legislations to prevent COVID-19, Rules and Laws for COVID19 preventions, Strategies to prevent covid19, PPE rules and regulations.
Clavirate Analytics Journals.	AMERICAN JOURNAL OF EPIDEMIOLOGY, CLINICAL EPIDEMIOLOGY, EPIDEMIOLOGY AND INFECTION.	Epidemiology of COVID-19, Preventive methods for covid19, legislations and laws for covid19, The importance of PPE in covid19 preventions.
Web of Science Master Journal List.	EPIDEMIOLOGY, Journal of Epidemiology and community health, THE OPEN EPIDEMIOLOGY JOURNAL.	Epidemiology of COVID-19 in incidence distribution and prevention, availability of possible vaccination and treatment. A Battle against the Pandemic while whole world is fighting the COVID 19 novel corona Virus possibly originated from Wuhan, Hubei Province China.

In part of the literature review of this book the data and results are used mainly from the countries mostly affected from the covid19. The data included from the countries such as the USA; the UK; European Union; and the part of Asia including China; India; Pakistan; and Japan. The Epidemiology including the COVID-19 Incidence; Distribution; Preventions; and the treatment is mainly discussed in the literature review with both Proactive and the reactive approach. As of today 9 September 2020; there is no approved Vaccine and proven treatment available for COVID-19 Pandemic still research and analysis are needed to find out the accurate cure for covid19 to save the suffering mankind.

Research nowadays shows that there are 181 different critiquing frame works available to critique a research article. In this Dissertation the researcher has used critique framework of Bray and Rees (1995) to answer all the questions of the article. Bray and Rees (1995) is a critical framework which offers 12 sets of different questions which are more focused on different parts of the articles. Bray and Rees (1995) critique framework is descriptive; but it contains all the help to analyse the research article completely and in detail. It also offers same sets of 12 questions to critique for both qualitative and quantitative studies selected for critiquing. So; Bray and Rees (1995) critique framework is more helpful than other frame works for example Critical Appraisal Framework (CASP) framework which offers different sets of questions for qualitative and quantitative studies.

It takes more time of researcher to follow different sets of questions for different type of studies. The author of this book has used different thematic analysis techniques to interrelate the articles. It is important to find similar themes in all 444 selected articles for critical literature review by Bray and Rees (1995) critique framework. The researcher has used different thematic analysis techniques for example the author has presented tables of common themes across articles selected for CLR. The author has presented mind maps figures which show the problems discuss in all papers and what are the solutions of those problems. The Author has presented the table of characteristics across all 444 articles. These were the thematic analysis techniques the author has used to present 444 articles selected for CLR.


5 Chapter

Results

This chapter presents the findings of the reviewed published articles and critical appraisal of these studies by the use of appropriate tools.

Included and Excluded Studies

Table 3: below shows the results of the included and excluded studies; Boolean search/keywords used and the Boolean searchers/databases used. Researcher has used the inclusion and exclusion criterion which is explained in Chapter 3 Methodology part of the Dissertation (Table 3).

Table 3.

Boolean search/ Keywords/ Search Terms.	Boolean operators/ Databases	Total of studies Retrieved	Included studies	Excluded studies
Epidemiology of COVID-19 in incidence distribution and prevention, availability of possible vaccination and treatment. A Battle against the Pandemic while whole world is fighting the COVID 19 novel corona Virus possibly originated from Wuhan, Hubei Province China.	PubMed central.	700	70	630
Availability and the use of Personal Protective equipment, Frequently Hand washing during the day, Use of Hand sanitizers all the time during the day.	Elsevier Journals.	500	80	420
Mortality data about COVID-19, Death rate of COVID19 among male and female, Children mortality.	Google Scholar.	350	85	265
COVID19 Preventions recommendations by WHO, COVID19 Intervention programs, Safety procedures for COVID-19.	Research Gate.	370	60	310
Legislations to prevent COVID-19, Rules and Laws for COVID19 preventions, Strategies to prevent covid19, PPE rules and regulations.	SCOPUS.	250	75	175
Epidemiology of COVID-19, Preventive methods for covid19, legislations and laws for covid19, The importance of PPE in covid19 preventions.	Clavirate Analytics Journals.	600	25	575
Epidemiology of COVID-19 in incidence distribution and prevention, availability of possible vaccination and treatment.	Web of Science Master Journal List.	530	49	481
TOTAL		3300	444	2856

Above table shows that author have found 3300 articles from different journals. The author has included 444 journal articles as they are focusing the research question and excluded the 2856 journal articles. The next table shows the study designs of the 10 articles used for critical literature review (CLR).

Critical Appraisals

Following are given below 10 journal articles which were finally selected went through a critical appraisal. The studies were critically appraised by the use of appropriate tool (questionnaire and answer) using the critiquing framework of Bray and Rees (1995). The critiquing framework of Bray and Rees (1995) offers author the 12 different questions for each paper for critical analysis. The author of this book has followed the critiquing framework of Bray and Rees (1995) to critically analyse each paper included for critical literature review.

Article no 1. Showing analysis of cohort study by Pan Zhai; Yanbing Ding; Xia Wu; Junke Long et al. (2020) The epidemiology; diagnosis and treatment of COVID-19. Int J Antimicrob Agents. 2020 May;55(5):105955. doi: 10.1016/j.ijantimicag.2020.105955.

1. Focus:

The title of the article is to discuss the **epidemiology; diagnosis and treatment of COVID-19**. The title of the article is good indicator of the focus.

2. Background:

The author has clearly written down the background of the article that what is the extent of frequency; distribution and preventions of covid19 pandemic in china and other effected countries.

3. Terms of references:

COVID19 treatments including antiviral agents; chloroquine and hydroxychloroquine; corticosteroids; antibodies; convalescent plasma transfusion and vaccines are discussed in this article. In addition; in China registered trials investigating treatment options for COVID-19 infection are listed.

4. Study design:

This paper reviews the literature (Systematic literature review) on all available information about the epidemiology; diagnosis; isolation and treatments of COVID-19. Treatments including antiviral agents; chloroquine and hydroxychloroquine; corticosteroids; antibodies; convalescent plasma transfusion and vaccines; are discussed in this article. In addition; registered trials investigating treatment options for COVID-19 infection are listed.

5. Tool of data collection:

The authors of this article performed the Systematic literature review with Meta-analysis where they have evaluated the articles and combined their data by statistical method to produce a more reliable result.

6. Ethical consideration:

The ethical approval is not needed to conduct this study as this paper is Systematic literature review and meta-analysis of other recently published studies.

7. Sample:

The authors of this article performed the Systematic literature review with Meta-analysis where they have evaluated the articles and combined their data by statistical method to produce a more reliable result. The authors have presented the case studies about the clinical trials of antiviral agents in patients with COVID-19. The clinical trials of chloroquine and hydroxychloroquine in patients with COVID-19; clinical trials of corticosteroids in patients with COVID-19 and clinical trials of convalescent plasma transfusion in patients with COVID-19.

8. Data presentation:

The author of the article has presented the data in the tables of four different topics including topics such as. The authors have presented the case studies about the clinical trials of antiviral agents in patients with COVID-19. The clinical trials of chloroquine and hydroxychloroquine in patients with COVID-19; clinical trials of corticosteroids in patients with COVID-19 and clinical trials of convalescent plasma transfusion in patients with COVID-19.

9. Main findings:

All patients with COVID-19-infected pneumonia received antibacterial agents 90% received antiviral therapy; and 45% received methylprednisolone. Clinical trials are underway to investigate the efficacy of new antiviral drugs convalescent plasma transfusion; and vaccines. Most of the trials were initiated by investigators and the study period is 1 to 11 months. In the absence of vaccines and antivirals; isolation and quarantine are achieving remarkable results. It is necessary to strengthen the monitoring of COVID-19 and to develop drugs and vaccines against the COVID-19 infection as soon as possible.

10. Conclusions and recommendations:

The COVID-19 pandemic is a public health emergency of international concern and all countries need a coordinated international effort to fight COVID-19. The transmission of pneumonia associated with SARS-CoV-2 has not yet been eliminated. In the absence of vaccines and antivirals isolation and quarantine are achieving remarkable results. It is necessary to strengthen the monitoring of COVID-19 and to develop drugs and vaccines against the COVID-19 infection as soon as possible.

11. Readability:

The authors of this article have used simple text with systematic literature review of currently published articles. The reader could find easy to read and understand the meta-analysis to conclude the authentic results. The article is published in Pub med central with open free readable access to public and to referenced so it is extremely reader friendly for public.

12. Implication for practice: The authors have published the article with recommendation about prevention of covid19 pandemic. They have recommended that in absence of proven covid19 antivirals and vaccine; social distancing and quarantine plays successful preventive role to control covid19 Pandemic.

Article no 2. Kamal Sahu; Ajay Mishra; Amos Lal (2020) COVID-2019: update on epidemiology; disease spread and management. Monaldi Arch Chest Dis. 2020 Apr 16;90(1). doi: 10.4081/monaldi.2020.1292.

1. Focus: The article discusses about the covid19 epidemiology; its incidence and transmission; available treatment; preventions available and mortality rate in different age group.
2. Background: In addition to china this pandemic has involved more than 150 countries with a predominant disease load in Italy South Korea; Iran; Hong Kong; Macau; and Vietnam. A significant number of deaths have been reported in old individuals and in patients with multiple comorbidities. With so much concern and attention surrounding SARS-CoV-2 knowledge of key clinical information and recent developments is of extreme importance both as a patient and as health care provider.
3. Terms of references: The main aim and objective of the article is to find the cure and treatment; vaccine of the covid19 novel corona virus to save more lives of the mankind.
4. Study design: The title of this article is "COVID-2019: update on epidemiology; disease spread and management" and it mainly focus on covid19 epidemiology including the incidence distribution; spread; treatment; vaccine development; preventions and mortality against the disease covid19 novel corona virus. The study design is systematic literature review of various articles discussing the treatment methods and preventions of the covid19 pandemic. The author has done critical literature review in his article to analyse the disease treatment methods and to discuss the mortality with comorbidities and in different ages.
5. Tool of data collection: The authors of this article performed the Systematic literature review to collect and present the information about Epidemiology of covid19. The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study.
6. Ethical consideration: The ethical approval is not needed to conduct this study as this paper is Systematic literature review of other recently published studies. The issues about confidentiality; privacy; and handling study data during and after study were addressed in this study.
7. Sample: The authors have collected the information by systematic literature review about the epidemiology of covid19; its preventions; current affective treatment available and the covid19 vaccine development.
8. Data presentation: The authors have collected the information by systematic literature review about the epidemiology of covid19; its preventions; current affective treatment available and the covid19 vaccine development. The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study.

9. Main findings:

1. There are supportive treatment available to treat covid19 patients.

2. Remdesivir and Plasma therapy have 80 percent treatment success rate in covid19 patients.

3. CT Scan chest and other radiographic evidence helps to get correct diagnosis of covid19 illness.

3. Social distancing; PPE usage and hand washing/ hand sanitizing helps to reduce the spread of covid19 novel corona virus.

4. People with comorbidities such as Cardiac diseases; Hypertension; Asthma and respiratory illness; Diabetes mellitus; Tuberculosis; Hepatitis; HIV are more vulnerable to covid19 infection as compare to healthy individuals.

10. Conclusions and recommendations:

COVID-19 disease burden has put a lot of pressure on health resources and patient care. Elimination of COVID-19 is an international priority because without control of viral spread the disease burden is going to increase every day with increased mortality. Till now; the best proven measures are infection control policies of rigorous contact tracing stringent quarantine of symptomatic contacts and hospital isolation and screening of symptomatic cases.

11. Readability:

The article is easy to read and to understand. The authors have used the plain and easy language for reader to understand the article. The authors have explained the results in texts and tables which are understandable.

12. Implication for practice:

Social distancing; PPE used; Mask used on public places; hand washing/ hand sanitizing staying away from crowded places help to reduce the spread of covid19 novel corona virus.

Article no 3. H Yashavantha Rao; Chelliah Jayabaskaran (2020) The emergence of a novel coronavirus (SARS-CoV-2) disease and their neuro invasive propensity may affect in COVID-19 patients. J Med Virol. 2020 Jul;92(7):786-790. doi: 10.1002/jmv.25918.

1.Focus:

The article focusses on studies which are reporting that coronaviruses are not only causing respiratory illness but also invade the central nervous system through a synapse-connected route. SARS-CoV infections are reported in both patients and experimental animals' brains.

2. Background:

World Health Organization (WHO) has declared coronavirus disease-2019 (COVID-19) a Public Health Emergency of International Concern. Various changes in environmental factors and human behaviours have led towards the emergence of more than 30 new infectious diseases in the last 3 decades ranging from rotavirus to Middle East respiratory syndrome coronavirus. The increasing human population people movement across diverse borders rapid expansion of air traffic changes in the climate have modified the ecosystem has made these novel pathogens can easily spread across the world.

The literature review is current and clearly justifies the research.

3. Terms of references:

In the abstract of the article the aim and objective are clear that the study explains some COVID-19 patients also expressed neurologic signs like nausea; headache; and vomiting. Several studies have reported that coronaviruses are not only causing respiratory illness but also invade the central nervous system through a synapse-connected route.

4. Study design:

The article focusses on studies which are reporting that coronaviruses are not only causing respiratory illness but also invade the central nervous system through a synapse-connected route. SARS-CoV infections are reported in both patients and experimental animals' brains. The article discusses about the covid19 epidemiology its incidence and transmission available treatment; preventions available and mortality rate in different age group.

5. Tool of data collection:

The authors of this article performed the Systematic literature review to collect and present the information about Epidemiology of covid19 and its effect on central nervous system. The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study.

6. Ethical consideration:

The ethical approval is not needed to conduct this study as this paper is Systematic literature review of other recently published studies.

The issues about confidentiality; privacy; and handling study data during and after study were addressed in this study.

7. Sample:

The authors of this article performed the Systematic literature review with Meta-analysis where they have evaluated the articles and combined their data by statistical method to produce a more reliable result. Recently a study carried out by Mao et al on COVID-19 infected 214 patients found that around 88% of severe patients showed neurological manifestations like acute cerebrovascular disease (impaired consciousness). It is very important to note the fact that previous reports discussed above has documented few SARS-CoV-2 infected patients showed neurologic symptoms like nausea; headache; and vomiting. However more convincing evidence for brain illness caused by COVID-19 would include type 2 respiratory failure or specific focal neurological defects. This should be established by virus detection in cerebrospinal fluid by polymerase chain reaction PCR or viral culture.

8. Data presentation:

The authors have collected the information by systematic literature review about the epidemiology of covid19; its preventions; current affective treatment available and the covid19 vaccine development. The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study

9. Main findings: Patients with acute SARS-CoVs infection have shown the presence of the virus in cerebrospinal fluid. Baig et al have recently published an article where they suggested a putative transcrbrial SARS-CoV-2 route to the brain and emphasized that SARS-CoV-2 RNA isolation in the cerebrospinal fluid would be the conclusive evidence to report the COVID-19 neurovirulence. In SARS patients the neuromuscular disorder has considered as a critical illness neuropathy and myopathy. Besides more direct evidence has been reported in few countries. A COVID-19 case with encephalitis was reported in a male patient (age 56 years) on 16th March 2020 in Beijing Ditan Hospital Capital Medical University China. It is very important to note that the PCR amplification showed that the cerebrospinal fluid sample from the patient turned positive for SARS-CoV-2.

10. Conclusions and recommendations:

The SARS-CoV-2 outbreak has once again spotlighted the need to discover new vaccines rapid development and implementation of diagnostic tests against infectious diseases of the global health crisis. Indeed; further studies on COVID-19 and its pathogenesis will provide some guidance to deal with this rapidly spreading pandemic infectious disease. Several challenges remain as key areas including the recent people who have tested COVID-19 positive. Can the cured patient be transmitted to others? All these indicate that more detailed criteria are needed for the prevention and control of SARS-CoV-2 virus and strong rigorous criteria to discharge patients after treatment.

11. Readability: The article is easy to read and to understand although some parts were boring. The authors have used the plain and easy language for reader to understand the article. The authors have explained the results in texts and tables which are understandable.

12**. Implication for practice:**

It is expected that the differences in the sequence of spike proteins between COVID-19 virus and SARS-CoV will enable scientists to identify epitopes in COVID-19 virus for the development of monoclonal antibodies against this virus. Basic research studies on SARS-CoV-2-host interactions is the key to several unanswered questions in the prevention and control of the disease. Many important questions about the identification and mechanism of interferon antagonists encoded by COVID-19 yet to be answered.

Article no 4. Kangpeng Xiao; Junqiong Zhai; Yaoyu Feng; Niu Zhou et al (2020) Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins. Nature. 2020 Jul;583(7815):286-289. doi: 10.1038/s41586-020-2313-x.

1.Focus: The article focuses on the investigating that although bats may be the reservoir host for a variety of coronaviruses it remains unknown whether SARS-CoV-2 has additional host species. Here we show that a coronavirus which we name pangolin-CoV isolated from a Malayan pangolin has 100%; 98.6%; 97.8% and 90.7% amino acid identity with SARS-CoV-2 in the E; M; N and S proteins respectively.

2. Background:

The SARS-related coronavirus identified in the present study and the metagenomic assemblies of viral sequences from Malayan pangolins is genetically related to SARS-CoV-2 but is unlikely to be directly linked to the current outbreak because of its substantial sequence differences from SARS-CoV-2. However; a virus related to pangolin-CoV appears to have donated the RBD to SARS-CoV-2. SARS-related coronavirus sequences have previously been detected in dead Malayan pangolins. These sequences appear to be from the same virus (pangolin-CoV) that we identified in the present study as judged from their sequence similarity. Here we provide evidence for the potential for pangolins to act as the zoonotic reservoir of SARS-CoV-2-like coronaviruses. However; the pangolins we studied here showed clinical signs of disease. In general; a natural reservoir host does not show severe disease whereas an intermediate host may have clinical signs of infection.

3. Terms of references:

In the abstract of the article the aim and objective are clear that the study is to investigate that although bats may be the reservoir host for a variety of coronaviruses it remains unknown whether SARS-CoV-2 has additional host species. Here we show that a coronavirus which we name pangolin-CoV isolated from a Malayan pangolin has 100%; 98.6%; 97.8% and 90.7% amino acid identity with SARS-CoV-2 in the E; M; N and S proteins respectively.

4. Study design:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. Data availability or Sequence reads generated in this study are available in the NCBI SRA database under the Bio Project accession PRJNA607174. The complete genome sequence of pangolin-CoV has been deposited in GISAID with the accession number EPI_ISL_410721.

5. Tool of data collection:

The authors of this article performed the Systematic literature review to collect and present the information about Epidemiology of covid19 and its effect on central nervous system. The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study. The tools of data collection include Tables Diagrams and Graphs collected from NCBI Pubmed database and available studies providing information about:

1. Pathological changes in the lungs of pangolins that are potentially induced by pangolin-CoV.
2. Genomic comparison of pangolin-CoV with SARS-CoV-2; SARS-CoV and bat SARS-related coronaviruses.
3. Genome characterization of pangolin-CoV.

6. Ethical consideration:

The ethical approval is not needed to conduct this study as this paper is Systematic literature review of other recently published studies.

The issues about confidentiality; privacy; and handling study data during and after study were addressed in this study.

7. Sample: The authors of this article performed the Systematic literature review with Meta-analysis where they have evaluated the articles and combined their data by statistical method to produce a more reliable result. Pangolins used in the study were confiscated by Customs and Department of Forestry of Guangdong Province in March and August 2019. They included four Chinese pangolins (M. pentadactyla) and 25 Malayan pangolins (M. javanica). The first transport confiscated contained 21 Malayan pangolins and the second transport contained 4 Malayan pangolins and 4 Chinese pangolins. These pangolins were sent to the wildlife rescue centre and were mostly inactive and crying and eventually died in custody despite exhaustive rescue efforts. Tissue samples were taken from the lung of pangolins that had just died for histological and virologic examinations.

8. Data presentation: The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study. The tools of data collection include Tables Diagrams and Graphs collected from NCBI Pubmed database and available studies providing information about:

1. Pathological changes in the lungs of pangolins that are potentially induced by pangolin-CoV.
2. Genomic comparison of pangolin-CoV with SARS-CoV-2; SARS-CoV and bat SARS-related coronaviruses.
3. Genome characterization of pangolin-CoV.

The results and data were presented in tables and texts in easy way so reader can understand them easily.

9. Main findings: As coronaviruses are common in mammals and birds; we used the whole-genome sequence of SARS-CoV-2 (strain WHCV; GenBank accession number MN908947) in a Blast search of SARS-related coronavirus sequences in available mammalian and avian viromic metagenomic and transcriptomic data. We identified 34 closely related contigs in a set of viral metagenomes from pangolins and therefore focused our subsequent search on SARS-related coronaviruses in pangolins.
10. Conclusions and recommendations: In particular the receptor-binding domain of the S protein of pangolin-CoV is almost identical to that of SARS-CoV-2 with one difference in a noncritical amino acid. Our comparative genomic analysis suggests that SARS-CoV-2 may have originated in the recombination of a virus similar to pangolin-CoV with one similar to RaTG13. Pangolin-CoV was detected in 17 out of the 25 Malayan pangolins that we analysed. Infected pangolins showed clinical signs and histological changes and circulating antibodies against pangolin-CoV reacted with the S protein of SARS-CoV-2. The isolation of a coronavirus from pangolins that is closely related to SARS-CoV-2 suggests that these animals have the potential to act as an intermediate host of SARS-CoV-2. This newly identified coronavirus from pangolins the most-trafficked mammal in the illegal wildlife trade could represent a future threat to public health if wildlife trade is not effectively controlled.
11. Readability: The article is easy to read and to understand and the figure and tables about data and results were easy. The authors have used the plain and easy language for reader to understand the article. The authors have explained the results in texts; figures and tables which are understandable.
12. Implication for practice: The isolation of a coronavirus from pangolins that is closely related to SARS-CoV-2 suggests that these animals have the potential to act as an intermediate host of SARS-CoV-2. This newly identified coronavirus from pangolins the most-trafficked mammal in the illegal wildlife trade could represent a future threat to public health if wildlife trade is not effectively controlled. The consumption of wild pangolins or other animals such as wild bats pigs are not recommended to eat as they could infect the humans with different viruses rather then protein them energy and protein so better to avoid and not eat them.

Article no 5: Rong-Sheng Luan; Xin Wang; Xin Sun; Xing-Shu Chen et al. (2020) Epidemiology; Treatment; and Epidemic Prevention and Control of the Coronavirus Disease 2019: a Review. Sichuan Da Xue Xue Bao Yi Xue Ban. 2020 Mar;51(2):131-138. doi: 10.12182/20200360505.

1. Focus: The article focuses on the review which includes the Epidemiology; Treatment; and Epidemic Prevention and Control of the Coronavirus Disease 2019.
2. Background: This review summarizes the ongoing researches regarding aetiology epidemiology transmission dynamics treatment and prevention and control strategies of the coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with comparison to severe acute respiratory syndrome; coronavirus (SARS-CoV); Middle East respiratory syndrome coronavirus (MERS-CoV) and pandemic H1N1 virus. SARS-CoV-2 may be originated from bats and the patients and asymptomatic carriers are the source of epidemic infection. The virus can be transmitted human-to-human through droplets and close contact and people at all ages are susceptible to this virus. The main clinical symptoms of the patients are fever and cough accompanied with leukocytopenia and lymphocytopenia.
3. Terms of references: This article systematically introduces the latest research progress in multiple fields such as the aetiology; epidemiology; transmission dynamics; clinical characteristics; treatment; and prevention of the new coronavirus pneumonia; and compares the new coronavirus with the severe acute respiratory syndrome coronavirus. The similarities and differences of the epidemic characteristics caused by the Middle East Respiratory Syndrome coronavirus and H1N1 influenza virus. The original host of the new coronavirus may be bats and patients and asymptomatic infections are the source of infection. It can be spread from person to person by means of droplets and contact and the population is generally susceptible.

4. Study design:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. This review summarizes the ongoing researches regarding aetiology; epidemiology; transmission dynamics; treatment; and prevention and control strategies of the coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); with comparison to severe acute respiratory syndrome coronavirus (SARS-CoV); Middle East respiratory syndrome coronavirus (MERS-CoV) and pandemic H1N1 virus. SARS-CoV-2 may be originated from bats; and the patients and asymptomatic carriers are the source of epidemic infection.

5. Tool of data collection:

The author has performed the systematic literature review to collect the data about Epidemiology; Treatment; and Epidemic Prevention and Control of the Coronavirus Disease 2019. The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study. The tools of data collection include Tables Diagrams and Graphs collected from NCBI Pubmed database and available studies providing information about Epidemiology; Treatment; and Epidemic Prevention and Control of the Coronavirus Disease 2019.

6. Ethical consideration: The ethical approval is not needed to conduct this study as this paper is Systematic literature review of other recently published studies.

The issues about confidentiality; privacy; and handling study data during and after study were addressed in this study.

7. Sample:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. This review summarizes the ongoing researches regarding etiology; epidemiology; transmission dynamics; treatment; and prevention and control strategies of the coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); with comparison to severe acute respiratory syndrome coronavirus (SARS-CoV); Middle East respiratory syndrome coronavirus (MERS-CoV) and pandemic H1N1 virus. SARS-CoV-2 may be originated from bats and the patients and asymptomatic carriers are the source of epidemic infection.

8. Data presentation:

The authors have collected the information by systematic literature review about the Epidemiology; Treatment; and Epidemic Prevention and Control of the Coronavirus Disease 2019. The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study.

9. Main findings:

In the prevention and control strategy; on the one hand efforts should be made to develop vaccines to carry out primary prevention. on the other hand; to continue to implement the isolation of patients and close contacts; wear masks; and timely disinfect public places. At the same time vigorously develop rapid detection kits to achieve disease prevention. To carry out the secondary prevention and control strategy of early detection; early diagnosis; early isolation; and early treatment. In addition; efforts should be made to reduce the population's panic about the disease strengthen epidemic prevention publicity and health education and jointly prevent and control the spread of the epidemic.

10. Conclusions and recommendations: Public health education on this disease and prevention should be enhanced so as to mitigate panic and mobilize the public to jointly combat the epidemic. Ongoing efforts of the infected patients and close contacts quarantine; mask wearing promotion; regular disinfection in public places should be continued. Meanwhile; rapid detection kit for serological monitoring of the virus in general population is expected so as to achieve early detection; early diagnosis; early isolation and early treatment. In addition; public health education on this disease and prevention should be enhanced so as to mitigate panic and mobilize the public to jointly combat the epidemic. Ongoing efforts of the infected patients and close contacts quarantine; mask wearing promotion; regular disinfection in public places should be continued. Meanwhile; rapid detection kit for serological monitoring of the virus in general population is expected so as to achieve early detection; early diagnosis; early isolation and early treatment. In addition; public health education on this disease and prevention should be enhanced so as to mitigate panic and mobilize the public to jointly combat the epidemic. Public health education on this disease and prevention should be enhanced so as to mitigate panic and mobilize the public to jointly combat the epidemic. Public health education on this disease and prevention should be enhanced so as to mitigate panic and mobilize the public to jointly combat the epidemic.

11. Readability:

The article is easy to read and to understand and the tables and texts about data and results were easy for reader. The authors have used the plain and easy language for reader to understand the article. The authors have explained the results in texts and tables which are understandable.

12. Implication for practice:

In terms of the prevention and control strategies vaccine development as the primary prevention should be accelerated. Regarding the secondary prevention ongoing efforts of the infected patients and close contacts quarantine; mask wearing promotion; regular disinfection in public places should be continued. Meanwhile; rapid detection kit for serological monitoring of the virus in general population is expected so as to achieve early detection early diagnosis; early isolation and early treatment. In addition; public health education on this disease and prevention should be enhanced so as to mitigate panic and mobilize the public to jointly combat the epidemic. Ongoing efforts of the infected patients and close contacts quarantine mask wearing promotion; regular disinfection in public places should be continued. Meanwhile; rapid detection kit for serological monitoring of the virus in general population is expected so as to achieve early detection; early diagnosis; early isolation and early treatment.

Article no 6. Carla Prezioso; Maria Marcocci; Anna Palamara; Giovanna C et al (2020) The "Three Italy" of the COVID-19 epidemic and the possible involvement of SARS-CoV-2 in triggering complications other than pneumonia. J Neurovirol. 2020 Jun;26(3):311-323. doi: 10.1007/s13365-020-00862-z.

1. Focus:

This article gives a bird's eye view about the origin; spread; features; and related emerging complications of COVID-19 disease focusing on the situation in Italy.

2. Background:

The first cases of COVID-19 had been reported in Central Italy in Rome. The subjects were tourists from Wuhan who had travelled in Lombardy a Northern region of Italy. The first autochthonous diagnosed case in the Italian territory; was reported on the February 20; 2020 in a 38-year-old man from the city of Codogno (Lombardy) with no travel history to known areas of viral infection or relation to a probable or confirmed COVID-19 case. After the case in Codogno other people in Lombardy with flu-like symptoms were found positive for SARS-CoV-2 including medical staff. Thereafter; the Italian COVID-19 epidemic has been mainly characterized by a local transmission. Since the beginning of the epidemic several preventive measures to favour "social distancing" were undertaken initially at the local level and finally at the national level with a lockdown of the entire territory on March 11; 2020 (Italian Ministry of Health Covid-19 2020). Geographical spread of the COVID-19 has been heterogeneous with a substantial gradient at the latitude levels with the highest spread in the Northern regions and the lowest in the Southern regions and in the main Islands. The region of Lombardy has the highest number of cases of SARS-CoV-2 and appears to be the epicentre of the Italian outbreak unlike regions like Molise; Basilicata; and Sardinia; where the SARS-CoV-2 circulation has been encompassed (Italian National Institute of Health (ISS).

3. Terms of references:

The author of this article performed a review to describe in particular the origin and the diffusion of COVID-19 in Italy. Underlying how the geographical circulation has been heterogeneous and the importance of pathophysiology in the involvement of cardiovascular and neurological clinical manifestations.

4. Study design:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. This article gives a bird's eye view about the origin; spread; features; and related emerging complications of COVID-19 disease; focusing on the situation in Italy.

5. Tool of data collection:

The author has performed the systematic literature review to collect the data about "The "Three Italy" of the COVID-19 epidemic and the possible involvement of SARS-CoV-2 in triggering complications other than pneumonia". The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study. The tools of data collection include Tables Diagrams and Graphs collected from NCBI Pubmed database and available studies providing information about Epidemiology; Treatment; and Epidemic Prevention and Control of the Coronavirus Disease 2019.

6. Ethical consideration:

The ethical approval is not needed to conduct this study as this paper is Systematic literature review of other recently published studies.

The issues about confidentiality; privacy; and handling study data during and after study were addressed in this study.

7. Sample: The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. The author mainly focuses on following 7 points:

1: COVID19 Origin and spread of COVID-19 in Italy.

2: COVID19 Transmission; symptoms; and diagnosis.

3: COVID19 Virus and pathophysiology.

4: The role of angiotensin-converting enzyme 2 (ACE2).

5: COVID-19 and cardiovascular manifestations.

6. COVID19 Neurological implications.

7. Kawasaki outbreaks during COVID-19.

8. Data presentation:

The authors have collected the information by systematic literature review about the COVID-19 epidemic and the possible involvement of SARS-CoV-2 in triggering complications other than pneumonia in Italy. The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study.

9. Main findings:

The results and considerations support the hypothesis that the immune response to SARS-CoV-2 is responsible for a Kawasaki-like disease in susceptible patients. Since patients diagnosed with Kawasaki-like disease after the viral spreading revealed a severe course including KDSS and MAS; requiring adjunctive steroid treatment. Genetic studies in larger groups should be done in order to investigate the susceptibility of patients developing this disease to the triggering effect of SARS-CoV-2.

Several COVID-19 patients showed secondary mild neurological symptoms including headache; dizziness; and neuralgia; whereas some severe cases showed neurological complications such as encephalopathy and acute cerebrovascular diseases. Along this context besides other primary neurological manifestations such as seizures; increasing evidence indicate that SARS-CoV-2 can cause meningitis and encephalitis.

10. Conclusions and recommendations: Coronavirus disease 2019 (COVID-19) first reported in Wuhan; the capital of Hubei; China; has been associated to a novel coronavirus; the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In March 2020; the World Health Organization declared the SARS-CoV-2 infection a global pandemic. Soon after; the number of cases soared dramatically spreading across China and worldwide. Italy has had 12;462 confirmed cases according to the Italian National Institute of Health (ISS) as of March 11; and after the "lockdown" of the entire territory; by May 4; 209;254 cases of COVID-19 and 26;892 associated deaths have been reported. Here the author performed a review to describe in particular; the origin and the diffusion of COVID-19 in Italy underlying how the geographical circulation has been heterogeneous and the importance of pathophysiology in the involvement of cardiovascular and neurological clinical manifestations.

11. Readability:

The article is easy to read and to understand and the tables and texts about data and results were easy for reader. The authors have used the plain and easy language for reader to understand the article. The authors have presented the true facts and figures recorded by trained health professionals. The authors have explained the results in texts and tables which are understandable.

12. Implication for practice: This research mainly focuses on following 7 points:

1: COVID19 Origin and spread of COVID-19 in Italy.

2: COVID19 Transmission; symptoms; and diagnosis.

3: COVID19 Virus and pathophysiology.

4: The role of angiotensin-converting enzyme 2 (ACE2).

5: COVID-19 and cardiovascular manifestations.

6. COVID19 Neurological implications.

7. Kawasaki outbreaks during COVID-19.

By addressing above topics; it is easy to understand the Epidemiology; Treatment and prevention of COVID19 Virus. The use of PPE and the early availability of covid19 vaccination and treatment; social distancing would help to control the spread of covid19 to save the people.

Article no 7. Esteban Prado; Katherine Rivera; Lenin Barreno; Mario N et al. (2020) Clinical; molecular; and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019 (COVID-19); a comprehensive literature review. Diagn Microbiol Infect Dis. 2020 Sep; 98(1): 115094. doi: 10.1016/j.diagmicrobio.2020.115094.

1. Focus: The title of the article is to discuss Clinical; molecular and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019 (COVID-19).

2. Background:

The specific origin of this new pandemic is not totally understood. At the beginning of the outbreak it was believed that a viral jump occurred between a wild animal and a human being in one of the most populated wet market in Wuhan; China during the November 2019. Further investigations were focused around identifying which animals were responsible for these new zoonotic diseases Although it still remains unclear which animal is the intermediary host; it is well-known that bats are the main reservoirs for these types of virus and they probably emerged in one of the local wild-animal farms.

3. Terms of references:

The author did research and presented a comprehensive literature review on Clinical; molecular; and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019 (COVID-19).

4. Study design:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. The current classification of coronaviruses recognizes 39 species in 27 subgenera that belong to the family Coronaviridae. From those at least 7 coronaviruses are known to cause respiratory infections in humans. Four of these viruses can cause common cold-like symptoms. Those that infect animals can evolve and become infectious to humans. Three recent examples of these viral jumps include SARS CoV; MERS-CoV and SARS CoV-2 virus. They are responsible for causing severe acute respiratory syndrome (SARS) Middle East respiratory syndrome (MERS) and the most recently discovered coronavirus disease during 2019 (COVID-19).

5. Tool of data collection:

The author has performed the systematic literature review to collect the data about "Clinical; molecular; and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019 (COVID-19); a comprehensive literature review". The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study. The tools of data collection include Tables Diagrams and Graphs collected from NCBI Pubmed database and available studies providing information about Clinical; molecular; and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019.

6. Ethical consideration:

The ethical approval is not needed to conduct this study as this paper is Systematic literature review of other recently published studies.

The issues about confidentiality; privacy; and handling study data during and after study were addressed in this study.

7. Sample:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. The author mainly focuses on following 12 points:

1. Chronology of the pandemic.
2. Epidemiology trends for COVID-19.
3. SARS-CoV-2 replication cycle.
4. SARS CoV-2 and human immune responses.
5. Innate immunity and Adaptive immunity.
6. RT-qPCR and Clinical features of COVID-19; Asymptomatic infection.
7. Evolution of the disease: spectrum of clinical manifestations.
8. Acute infection: mild and moderate; Severe infection and critical state.
9. Clinical diagnosis and screening; Laboratory findings.
10. Imaging findings; Diagnosis methods to detect COVID-19.
11. HIV and COVID-19 risk; Antiretroviral therapy and protection/action against SARS-CoV-2.
12. COVID-19 in pregnant women; COVID-19 in children; SARS-COV-2 infection and cancer.

8. Data presentation:

Researchers presented the data and the results; most appropriately; in table form and also in text. The authors have collected the information by systematic literature review about the Clinical; molecular and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019 (COVID-19). The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study.

9. Main findings:

Patients with cancer are generally more susceptible to infections than healthy people; because they have a state of systemic immunosuppression that is exacerbated during chemotherapy or radiotherapy.

Reported complications derived from COVID-19 describe a severe disease that requires management in an intensive care unit (ICU) in approximately 5% of proven infections. Common complications include respiratory failure; cardiovascular dysfunction; cardiomyopathy and acute kidney injury.

According to the investigative mission of the WHO in China; the case-fatality rate ranged from 5.8% in Wuhan to 0.7 % in the rest of China. Of these cases; the deaths were mostly in patients with chronic diseases (cardiovascular disease; diabetes mellitus; chronic lung disease; hypertension and cancer) and the elderly.

According to WHO; the recovery time is estimated to be 2 weeks for patients with mild infections and 3 to 6 weeks for those with serious illnesses.

Currently; Remdesivir has been ranked as first potential drug in treatment for COVID-19; by the last publications. Remdesivir is a nucleotide analog; antiviral drug developed by Gilead Sciences.

The convalescent plasma is extracted from recovered individuals from an infection; being an antibody transfer medium to provide passive immunity (neutralizing antibodies and globulin). The goal is to provide a rapid immune response until the patient can develop their own active immune response in the hope that there will be clinical improvement.

10. Conclusions and recommendations:

The authors of this study examined the most important literature available in terms of the genetic; virology; clinical and therapeutic evidence on the SARS-CoV-2 virus and the novel Coronavirus diseases 2019 (COVID-19). This extensive and comprehensive literature review tries to offer a good insight of the most recent information available. This review was designed to offer a good insight of the virus and the diseases to the entire medical community. This document although summarized; tries to bring well-supported information on this new disease. A disease that has been keeping us on a partial or total lockdown all over the planet.

11. Readability:

The article is easy to read and to understand and the article is very short in length. The tables and texts about data and results were easy for reader. The authors have used the plain and easy language for reader to understand the article. The authors have presented the true facts and figures recorded by trained health professionals. The authors have explained the results in texts and tables which are understandable.

12. Implication for practice:

The authors of this study examined the most important literature available in terms of the genetic; virology; clinical and therapeutic evidence on the SARS-CoV-2 virus and the novel Coronavirus diseases 2019 (COVID-19). This extensive and comprehensive literature review tries to offer a good insight of the most recent information available. This review was designed to offer a good insight of the virus and the diseases to the entire medical community.

Article no 8. Jin Wang; Mengmeng Jiang; Xin Chen; Luis M (2020) Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection: Review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts. J Leukoc Biol. 2020 Jun 13: 10.1002/JLB.3COVR0520-272R. doi: 10.1002/JLB.3COVR0520-272R.

1. Focus:

The title of the article is to discuss Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection. A review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts.

2. Background:

Considering COVID19 worldwide reach and severity WHO declared the COVID-19 outbreak a global pandemic the first pandemic sparked by a coronavirus. In contrast to the global infection rate reached by SARS-CoV-2; severe acute respiratory syndrome-coronavirus (SARS-CoV; 2002–2003) and Middle East respiratory syndrome coronavirus (MERS-CoV; 2012) were largely localized to China and Saudi Arabia respectively. Like SARS-CoV-2 the outbreak of SARS-CoV and MERS-CoV were also caused by the zoonotic coronavirus crossing the species barrier. The diseases caused by these three coronaviruses share similarities in clinical presentations such as progression toward severe acute respiratory syndrome yet COVID-19′s clinical features remain distinct including unique pulmonary presentation on CT. Specifically; with the SARS epidemic dysregulation of the immune system resulted in acute fevers and decreased CD4+ and CD8+ T cell counts; yet lacked any evidence of pulmonary changes upon imaging.

3. Terms of references:

The aim of the study is clear that to prove the research "severe acute respiratory syndrome-coronavirus-2 infection often results from alveolar injury that impedes airway capacity and multi-organ failure both of which are associated with the hyperproduction of cytokines also known as a cytokine storm or cytokine release syndrome". The author has done critical literature review about cytokine storm in covid19 patients and death due to multi organ failure and presented in their article.

4. Study design:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites.

5. Tool of data collection:

The author has performed the systematic literature review to collect the data about "Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection. A review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts". The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study. The tools of data collection include Tables Diagrams and Graphs collected from NCBI Pubmed database and available studies providing information about Clinical; molecular; and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019.

6. Ethical consideration:

The ethical approval is not needed to conduct this study as this paper is Systematic literature review of other recently published studies.

The issues about confidentiality; privacy; and handling study data during and after study were addressed in this study.

7. Sample:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. The author mainly focuses on following 3 points:

1. CYTOKINE RELEASE WITH EMERGING CORONA VIRAL INFECTIONS: PROTECTIVE VERSUS PATHOGENIC CYTOKINE STORM RESPONSES.
2. CHARACTERISTICS OF LEUKOCYTE CHANGES AND CYTOKINE RELEASE DURING MILD AND SEVERE COVID-19 INFECTION.
3. TREATMENTS UNDER INVESTIGATION AGAINST THE CYTOKINE STORM IN COVID-19 INFECTION.

8. Data presentation:

Researchers presented the data and the results; most appropriately; in table form and also in text.

The authors have collected the information by systematic literature review about the "Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection. A review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts". The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study.

9. Main findings:

Clinical evidence indicates that the fatal outcome observed with severe acute respiratory syndrome-coronavirus-2 infection often results from alveolar injury that impedes airway capacity and multi-organ failure both of which are associated with the hyperproduction of cytokines; also known as a cytokine storm or cytokine release syndrome. Clinical reports show that both mild and severe forms of disease result in changes in circulating leukocyte subsets and cytokine secretion; particularly IL-6; IL-1β; IL-10; TNF; GM-CSF; IP-10 (IFN-induced protein 10); IL-17; MCP-3; and IL-1ra. Not surprising; therapies that target the immune response and curtail the cytokine storm in coronavirus 2019 (COVID-19) patients have become a focus of recent clinical trials.

10. Conclusions and recommendations:

It is generally believed that the cytokine storm triggered by SARS-CoV-2 infection is a central mediator for the lung injury and resulting ARDS found in cases of severe or critical COVID-19 patients. We present several leukocyte and cytokine changes that may help define the progression of COVID-19 from an initial to a late stage in both mild and severe cases. However; more needs to be learned regarding how elevations in specific cytokine(s) combinations (using standardized methods and defined ranges) could be used to describe each stage of the inflammatory response as the disease progresses. Apart from commonly used surrogates of disease progression (D-dimer; CRP; ferritin; and procalcitonin levels) with emphasis on D-dimer and ferritin; cytokine-based biomarkers still lack consensus on cut-off values for assessing disease progression (other than a pattern of a rise with severity). Disease staging with an integration of cellular (neutrophilia; decreases in lymphocytes; etc.); soluble plasma markers (D-dimer; etc.) together with cytokine changes also remains to be pursued. Based on currently reported clinical data to date priority could be placed on combining elevations of IL-6; TNF; IL-1β; IP-10; D-dimer; and ferritin with changes in circulating and activation states of myeloid; neutrophil; and T cell responses; which together could provide improved biomarkers for progression to CRS and severe COVID-19 patients.

11. Readability:

The article is easy to read and to understand. The tables and texts about data and results were easy for reader. The authors have used the plain and easy language for reader to understand the article. The authors have presented the true lab test results done by trained health professionals. The authors have explained the results in texts and tables which are understandable.

12. Implication for practice:

We also look at ongoing clinical studies aimed at blocking proinflammatory cytokines transfer of immunosuppressive mesenchymal stem cells use of convalescent plasma transfusion as well as immunoregulatory therapy and traditional Chinese medicine regimes. In examining leukocyte and cytokine activity in COVID-19; we focus in particular on how these levels are altered as the disease progresses (neutrophil NETosis; macrophage; T cell response; etc.) and proposed consequences to organ pathology (coagulopathy; etc.).

Viral and host interactions are described to gain further insight into leukocyte biology and how dysregulated cytokine responses lead to disease and/or organ damage. By better understanding the mechanisms that drive the intensity of a cytokine storm; we can tailor treatment strategies at specific disease stages and improve our response to this worldwide public health threat.

Article no 9. Xinjuan Sun; Tianyuan Wang; Dayong Cai; Zhiwei Hu et al (2020) Cytokine storm intervention in the early stages of COVID-19 pneumonia. Cytokine Growth Factor Rev. 2020 Jun;53: 38-42. doi: 10.1016/j.cytogfr.2020.04.002.

1. Focus:

The title of the article is to discuss "Cytokine storm intervention in the early stages of COVID-19 pneumonia. Cytokine Growth Factor Review". It indicates that the authors are focusing on strategies to avoid Cytokine storm in covid19 pandemic patients which could lead to mortality.

2. Background: In support of the authors observations a retrospective study of 41 patients with COVID-19 showed that most SARS-CoV-2 infected patients present clinically with mild symptoms; while a minority of patients progressively declined from the infection and eventually died of acute respiratory distress syndrome (ARDS) and multiple organ dysfunction syndrome (MOD). Guidelines for the diagnosis and treatment of SARS-CoV-2 infected pneumonia were first published on January 30th 2020; and recommended for the first time that cytokine monitoring be applied to improve the curative rate and reduce mortality. In view of the severe morbidity and mortality of COVID-19 pneumonia here we review the current understanding of treatment of human coronavirus infections from the perspective of a dysregulated immune response.

3. Terms of references:

In the abstract of the study; the aim is clear that this study examined the effect of maternal smoking during pregnancy on infant body proportion.

4. Study design:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. Clinical intervention in patients with corona virus disease 2019 (COVID-19) has demonstrated a strong upregulation of cytokine production in patients who are critically ill with SARS-CoV2-induced pneumonia. In a retrospective study of 41 patients with COVID-19 most patients with SARS-CoV-2 infection developed mild symptoms whereas some patients later developed aggravated disease symptoms; and eventually passed away because of multiple organ dysfunction syndrome (MODS); as a consequence of a severe cytokine storm. Guidelines for the diagnosis and treatment of SARS-CoV-2 infected pneumonia were first published January 30th 2020 these guidelines recommended for the first time that cytokine monitoring should be applied in severely ill patients to reduce pneumonia related mortality.

5. Tool of data collection:

The author has performed the systematic literature review to collect the data about "Cytokine storm intervention in the early stages of COVID-19 pneumonia. Cytokine Growth Factor Review". The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study. The tools of data collection include Tables Diagrams and Graphs collected from NCBI Pubmed database and available studies providing information about Clinical; molecular; and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019.

6. Ethical consideration:

The ethical approval is not needed to conduct this study as this paper is Systematic literature review of other recently published studies.

The issues about confidentiality; privacy; and handling study data during and after study were addressed in this study.

7. Sample:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. The author mainly focuses on following 3 points:

1. The role of cytokine storm in the pathogenesis and progression of COVID-19 pneumonia.
2. Treatment of the cytokine storm in COVID-19 pneumonia.

a. Current management strategies for COVID-19.

b. Immunotherapeutic strategies in COVID-19 pneumonia.

b.1: Neutralizing antibodies.

b.2: Interferons.

b.3: IFN-αβ inhibitors and IFN-λ.

b.4: Inhibition of oxidized phospholipids.

b.5: Sphingosine-1-phosphate receptor 1 agonist therapy.

b.6: Inhibitors of monocyte recruitment and function.

b.7: Continuous renal replacement therapy.

8. Data presentation: Researchers presented the data and the results; most appropriately; in table form and also in text. The authors have collected the information by systematic literature review about the "Cytokine storm intervention in the early stages of COVID-19 pneumonia. Cytokine Growth Factor Review". The authors have provided information in text form from various articles and there was special data collection tool or tables to be presented in the study.
9. Main findings: Further experimentation is required to understand the changes in the immune response of patients with COVID-19 infection and the mechanisms of abnormal cytokine expression in COVID-19 pneumonia. Accurate prediction and targeted intervention during the course of COVID-19 pneumonia will be essential to improve patient survival.
10. Conclusions and recommendations: After COVID-19 infection some patients develop systemic inflammatory response syndrome (SIRS) and MODS characterized by the uncontrolled release of inflammatory mediators; giving rise to a cytokine storm that contributes to increased mortality in ARDS. In summary; further experimentation is required to understand the changes in the immune response of patients with COVID-19 infection and the mechanisms of abnormal cytokine expression in COVID-19 pneumonia. Accurate prediction and targeted intervention during the course of COVID-19 pneumonia will be essential to improve patient survival.
11. Readability: The article is easy to read and to understand. The tables and texts about data and results were easy for reader and they explain all the data and results of the study. The authors have used the plain and easy language for reader to understand the article. The authors have explained the results in texts and tables which are understandable.
12. Implication for practice: Further experimentation is required to understand the changes in the immune response of patients with COVID-19 infection and the mechanisms of abnormal cytokine expression in COVID-19 pneumonia. Accurate prediction and targeted intervention during the course of COVID-19 pneumonia will be essential to improve patient survival

Article no 10. Souvik Dubey; Payel Biswas; Ritwik Ghosh; Subhankar C et al (2020) Psychosocial impact of COVID-19. Diabetes Metab Syndr. 2020 September-October; 14(5): 779–788. doi: 10.1016/j.dsx.2020.05.035.

1. Focus: The title of the article is to discuss "Psychosocial impact of COVID-19" which clearly indicates the fear and hysteria among of COVID19 Pandemic among the community.
2. Background: Along with its high infectivity and fatality rates; the 2019 Corona Virus Disease (COVID-19) has caused universal psychosocial impact by causing mass hysteria; economic burden and financial losses. Mass fear of COVID-19 termed as "corona phobia"; has generated a plethora of psychiatric manifestations across the different strata of the society. So; this review has been undertaken to define psychosocial impact of COVID-19.
3. Terms of references: In the abstract of the study the aim is clear to present and discuss the study "Psychosocial impact of COVID-19" which clearly indicates the fear and hysteria among of COVID19 Pandemic among the community.
4. Study design: The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. For better dealing with these psychosocial issues of different strata of the society psychosocial crisis prevention and intervention models should be urgently developed by the government; health care personnel and other stakeholders. Apt application of internet services technology and social media to curb both pandemic and infodemic needs to be instigated. Psychosocial preparedness by setting up mental organizations specific for future pandemics is certainly necessary.

5. Tool of data collection:

The author has chosen the systematic literature review as the methodology to complete this article. Pubmed and Google Scholar are searched with the following key terms- "COVID-19"; "SARS-CoV2"; "Pandemic"; "Psychology"; "Psychosocial"; "Psychiatry"; "marginalized"; "telemedicine"; "mental health"; "quarantine"; "infodemic"; "social media" and" "internet". Few newspaper reports related to COVID-19 and psychosocial impacts have also been added as per context.

6. Ethical consideration:

The ethical approval is not needed to conduct this study as this paper is Systematic literature review of other recently published studies.

The issues about confidentiality; privacy; and handling study data during and after study were addressed in this study.

7. Sample:

The author has conducted systematic literature review of various articles available on NCBI Pubmed and other reputable websites. The author mainly focuses on following 6 points:

1. "Corona positive"- a Stigma?
2. Psychosocial burden of quarantine and isolation.
3. Netizens; social media and COVID-19.
4. Psychosocial impact on health-care providers and other frontline workers- heal the healers.
5. Effects on different sections of society.
6. Home-quarantine for "Homeless" populace- A paradoxical irony.
7. Effects on people with pre-existing psychiatric illness.
8. Role of mental health-care workers.

8. Data presentation:

Researchers presented the data and the results; most appropriately; in table form and also in text. The researchers have used different tables and chart for example flow of participants through trial shows the participants involved in the study divided into control and intervention group the women attended the counselling sessions and women withdrawn from study. The results and data were presented in tables and texts in easy way so reader can understand them easily.

9. Main findings: Disease itself multiplied by forced quarantine to combat COVID-19 applied by nationwide lockdowns can produce acute panic anxiety; obsessive behaviours; hoarding; paranoia; and depression; and post-traumatic stress disorder (PTSD) in the long run. These have been fuelled by an "infodemic" spread via different platforms of social media. Outbursts of racism; stigmatization; and xenophobia against particular communities are also being widely reported. Nevertheless; frontline healthcare workers are at higher-risk of contracting the disease as well as experiencing adverse psychological outcomes in form of burnout; anxiety; fear of transmitting infection; feeling of incompatibility; depression; increased substance-dependence; and PTSD. Community based mitigation programs to combat COVID-19 will disrupt children's usual lifestyle and may cause florid mental distress. The psychosocial aspects of older people their caregivers; psychiatric patients and marginalized communities are affected by this pandemic in different ways and need special attention.

10. Conclusions and recommendations:

Setting up mental health organizations specific for future pandemics with branches in many nations and in individual healthcare institutions for research; mental healthcare delivery and arranging awareness program at both personal and community levels is desperately needed. Structured websites and toll-free helpline numbers may be launched for alleviating psychological distress among the general public regarding this ongoing pandemic. Social media is to be used in good sense; to educate people on transmission dynamics; symptoms of disease and time when exact medical consultations are needed. To protect social media from devaluations; strict government laws and legislation regarding fake news social media rumours disinformation and misinformation are to be implemented. The COVID-19 pandemic has clearly shown us

how a "virus" can negatively impact our lives even in the 21st century and simultaneously made us realize that the greatest assets of mankind are health; peace; love; solidarity; ingenuity; and knowledge.

11. Readability:
The article is easy to read and to understand. The tables and texts about data and results were easy for reader and they explain all the data and results of the study. The authors have used the plain and easy language for reader to understand the article. The authors have explained the results in texts and tables which are understandable.
12. Implication for practice: The government and stakeholders must appreciate the psychosocial morbidities of this pandemic and assess the burden; fatalities and associated consequences. Stigma and blame targeted at communities affected by the outbreak may hinder international trade; finance and relationships; instigating further unrest.

Here are 50 articles selected randomly for critical literature review and meta-analysis via SPSS Software for the presentation of findings. Three major points to be checked for comparison which discusses the preventions of covid19; availability of PPE for health staff and early development of covid19 vaccine (Table 4).

Table 4: 50 Selected studies for comparison which discusses the preventions of covid19, Availability of PPE for health staff and early development of covid19 vaccine.

S No:	Article Reference	Discuss Preventions of covid19	Availability of PPE for health staff	Discuss Development of covid19 vaccine
1	Shigeru Shibata, Hisatomi Arima, Kei Asayama, Satoshi H (2020) Hypertension and related diseases in the era of COVID-19: a report from the Japanese Society of Hypertension Task Force on COVID-19. Hypertens Res. 2020 Jul 31: 1–19. doi: 10.1038/s41440-020-0515-0.	YES	YES	NO
2	Celestino Sardu, Jessica Gambardella, Marco Morelli, Xujun Wang et al (2020) Hypertension, Thrombosis, Kidney Failure, and Diabetes: Is COVID-19 an Endothelial Disease? A Comprehensive Evaluation of Clinical and Basic Evidence. J Clin Med. 2020 May; 9(5): 1417. doi: 10.3390/jcm9051417.	YES	YES	NO
3	Zijun Wang, Qi Zhou, Chenglin Wang, Qianling Shi et al (2020) Clinical characteristics of children with COVID-19: a rapid review and meta-analysis. Ann Transl Med. 2020 May; 8(10): 620. doi: 10.21037/atm-20-3302.	YES	NO	NO
4	Hui Du, Xiang Dong, Jin-Jin Zhang, Yi-Yuan Cao et al. (2020) Clinical characteristics of 182 pediatric COVID-19 patients with different severities and allergic status. Allergy. 2020 Jun 10;10.1111/all.14452. doi: 10.1111/all.14452.	YES	NO	NO
5	Linjie Zhang, Tyele G Peres, Marcus Silva, Paulo C et al. (2020) What we know so far about Coronavirus Disease 2019 in children: A meta-analysis of 551 laboratory-confirmed cases. Pediatr Pulmonol. 2020 Aug;55(8):2115-2127. doi: 10.1002/ppul.24869. Epub 2020 Jun 10.	YES	YES	NO
6	Suriya Rehman, Tariq Majeed, Mohammad Ansari, Uzma Ali et al (2020) Current scenario of COVID-19 in pediatric age group and physiology of immune and thymus response. Saudi J Biol Sci. 2020 May 15. doi: 10.1016/j.sjbs.2020.05.024.	YES	NO	NO
7	Sarah Moore, Guy Faulkner, Ryan Rhodes, Mariana B et al (2020) Impact of the COVID-19 virus outbreak on movement and play behaviours of Canadian children and youth: a national survey. Int J Behav Nutr Phys Act. 2020; 17: 85. doi: 10.1186/s12966-020-00987-8.	YES	YES	NO
8	Nipunie Rajapakse, Devika Dixit (2020) Human and novel coronavirus infections in children: a review. Paediatr Int Child Health. 2020 Jun 25;1-20. doi: 10.1080/20469047.2020.1781356.	YES	YES	NO
9	Brandon Henry, Stefanie Benoit, Maria de Oliveira, Wan Hsieh et al (2020) Laboratory abnormalities in children with mild and severe coronavirus disease 2019 (COVID-19): A pooled analysis and review. Clin Biochem. 2020 Jul; 81: 1–8. doi: 10.1016/j.clinbiochem.2020.05.012.	YES	NO	NO
10	Yuanqiang Yu, Pingyang Chen (2020) Coronavirus Disease 2019 (COVID-19) in Neonates and Children from China: A Review. Front Pediatr. 2020; 8: 287. doi: 10.3389/fped.2020.00287.	YES	YES	YES
11	Maria Raissaki, Susan Shelmerdine, Maria Damasio, Seema T et al. (2020) Management strategies for children with COVID-19: ESPR practical recommendations. Pediatr Radiol. 2020 Jul 3: 1–11.doi: 10.1007/s00247-020-04749-3.	YES	YES	YES

12	Derek Chu, Elie Akl, Stephanie Duda, Karla Solo et al (2020) Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. Lancet. 2020 27 June-3 July; 395(10242): 1973–1987. doi: 10.1016/S0140-6736(20)31142-9.	YES	YES	YES
13	Alberto Berardi, Diego Perinelli, Hamid Merchant, Lorina B et al. (2020) Hand sanitizers amid CoViD-19: A critical review of alcohol-based products on the market and formulation approaches to respond to increasing demand. Int J Pharm. 2020 Jun 30; 584: 119431. doi: 10.1016/j.ijpharm.2020.119431.	YES	YES	NO
14	Q Ian Freckelton (2020) COVID-19: Fear, quackery, false representations and the law. Int J Law Psychiatry. 2020 Jul 10: 101611.doi: 10.1016/j.ijlp.2020.101611.	YES	YES	NO
15	NCBI Alcohol Sanitizer (2020) Introduction- Maintaining hand hygiene. Available at: https://www.ncbi.nlm.nih.gov/books/NBK513254/. (Accessed on: 03/08/2020).	YES	YES	NO
16	Jane Jing, Thong Yi, Rajendran Bose, Jason M et al. (2020) Hand Sanitizers: A Review on Formulation Aspects, Adverse Effects, and Regulations. Int J Environ Res Public Health. 2020 May 11;17(9):3326. doi: 10.3390/ijerph17093326.	YES	YES	NO
17	Dane Jensen, Michelle Danyluk, Linda Harris, Donald S (2015) Quantifying the effect of hand wash duration, soap use, ground beef debris, and drying methods on the removal of Enterobacter aerogenes on hands. J Food Prot. 2015 Apr;78(4):685-90. doi: 10.4315/0362-028X.JFP-14-245.	YES	YES	NO
18	Rebecca Montville, Yuhuan Chen, Donald S (2002) Risk assessment of hand washing efficacy using literature and experimental data. Int J Food Microbiol. 2002 Mar;73(2-3):305-13. doi: 10.1016/s0168-1605(01)00666-3.	YES	YES	NO
19	Alexandra Teslya, Thi Mui Pham, Noortje Godijk, Mirjam K et al (2020) Impact of self-imposed prevention measures and short-term government-imposed social distancing on mitigating and delaying a COVID-19 epidemic: A modelling study. PLoS Med. 2020 Jul 21;17(7): e1003166. doi: 10.1371/journal.pmed.1003166. eCollection 2020 Jul.	YES	YES	NO
20	Farnaz Araghi, Mohammadreza Tabary, Mehdi Gheisari, Fahimeh A et al. (2020) Hand Hygiene Among Health Care Workers During COVID-19 Pandemic: Challenges and Recommendations. Dermatitis. Jul/Aug 2020; 31(4):233-237. doi: 10.1097/DER.0000000000000639.	YES	YES	NO
21	Antonio Foddai, Irene Grant, Moira Dean (2020) Efficacy of Instant Hand Sanitizers against Foodborne Pathogens Compared with Hand Washing with Soap and Water in Food Preparation Settings: A Systematic Review. J Food Prot. 2016 Jun;79(6):1040-54. doi: 10.4315/0362-028X.JFP-15-492.	YES	YES	NO
22	Andrew Golin, Dexter Choi, Aziz Ghahary (2020) Hand sanitizers: A review of ingredients, mechanisms of action, modes of delivery, and efficacy against coronaviruses. Am J Infect Control. 2020 Jun 18. doi: 10.1016/j.ajic.2020.06.182.	YES	YES	NO
23	Huaiyu Tian, Yonghong Liu, Yidan Li, Chieh Wu et al (2020) An investigation of transmission control measures during the first 50 days of the COVID-19 epidemic in China. Science. 2020 May 8;368(6491):638-642. doi: 10.1126/science.abb 6105. Epub 2020 Mar 31.	YES	YES	YES
24	Qian Shen, Mo Wang, Ruochen Che, Qiu Li et al (2020) Consensus recommendations for the care of children receiving chronic dialysis in association with the COVID-19 epidemic. Pediatr Nephrol. 2020 Jul;35(7):1351-1357. doi: 10.1007/s00467-020-04555-x. Epub 2020 Apr 24.	YES	YES	YES
25	Deepak Pradhan, Prativa Biswasroy, Pradeep Naik, Goutam G et al. (2020) A Review of Current Interventions for COVID-19 Prevention. Arch Med Res. 2020 Jul;51(5):363-374. doi: 10.1016/j.arcmed.2020.04.020. Epub 2020 Apr 30.	YES	YES	YES
26	Yasemin Demirbilek, Gülen Pehlivantürk, Zeynep Özgüler, Emine M (2020) COVID-19 outbreak control, example of ministry of health of Turkey. Turk J Med Sci. 2020 Apr 21;50(SI-1):489-494. doi: 10.3906/sag-2004-187.	YES	YES	YES
27	Barbara Streit, Verena Mayr, Andreea Dobrescu, Andrea C et al. (2020) Quarantine alone or in combination with other public health measures to control COVID-19: a rapid review. Cochrane Database Syst Rev. 2020 Apr 8;4(4):CD013574. doi: 10.1002/14651858.CD013574.	YES	YES	YES

28	Rahmet GÜNER, İmran HASANOĞLU, Firdevs AKTAŞ (2020) COVID-19: Prevention and control measures in community. Turk J Med Sci. 2020; 50(3): 571–577. doi: 10.3906/sag-2004-146.	YES	YES	YES
29	Jia-Jung Lee, Shang-Jyh Hwang, Jee-Fu Huang (2020) Review of the present features and the infection control challenges of COVID-19 pandemic in dialysis facilities. Kaohsiung J Med Sci. 2020 Jun;36(6):393-398. doi: 10.1002/kjm2.12239.	YES	YES	NO
30	Daniele Veritti, Valentina Sarao, Francesco Bandello, Paolo L (2020) Infection control measures in ophthalmology during the COVID-19 outbreak: A narrative review from an early experience in Italy Eur J Ophthalmol. 2020 Jul;30(4):621-628. doi: 10.1177/1120672120927865. Epub 2020 May 17.	YES	YES	YES
31	Francis Kobia, Jesse Gitaka (2020) COVID-19: Are Africa's diagnostic challenges blunting response effectiveness? Version 1. AAS Open Res. 2020; 3: 4.doi: 10.12688/aasopenres.13061.1.	YES	YES	YES
32	Lauren Ching, Sandra Chang, Vivek N (2020) COVID-19 Special Column: Principles Behind the Technology for Detecting SARS-CoV-2, the Cause of COVID-19. Hawaii J Health Soc Welf. 2020 May 1; 79(5): 136–142.	YES	YES	YES
33	Waldemar Rastawicki, Natalia Rokosz-Chudziak (2020) Characteristics and assessment of the usefulness of serological tests in the diagnostic of infections caused by coronavirus SARS-CoV-2 on the basis of available manufacturer's data and literature review. Przegl Epidemiol. 2020;74(1):49-68. doi: 10.32394/pe.74.11.	YES	YES	YES
34	Alana Flexman, Arnoley Abcejo, Rafi Avitsian, Veerle S (2020) Neuroanesthesia Practice During the COVID-19 Pandemic: Recommendations from Society for Neuroscience in Anesthesiology and Critical Care (SNACC). J Neurosurg Anesthesiol. 2020 Apr 15; 32:doi: 10.1097/ANA.0000000000000691.	YES	YES	YES
35	Nicole Lurie, Melanie Saville, Richard Hatchett, Jane Halton (2020) Developing Covid-19 Vaccines at Pandemic Speed. N Engl J Med. 2020 May 21;382(21):1969-1973. doi: 10.1056/NEJMp2005630. Epub 2020 Mar 30.	YES	YES	YES
36	Sonia Pagliusi, Stephen Jarrett, Benoit Hayman, Ulrike K (2020) Emerging manufacturers engagements in the COVID −19 vaccine research, development and supply. Vaccine. 2020 Jul 22; 38(34): 5418–5423. doi: 10.1016/j.vaccine.2020.06.022.	YES	YES	YES
37	Colin D. Funk, Craig Laferrière, Ali Ardakani (2020) A Snapshot of the Global Race for Vaccines Targeting SARS-CoV-2 and the COVID-19 Pandemic. Front Pharmacol. 2020; 11: 937.doi: 10.3389/fphar.2020.00937.	YES	YES	YES
38	Eakachai Prompetchara, Chutitorn Ketloy, Tanapat P (2020) Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic. Asian Pac J Allergy Immunol. 2020 Mar;38(1):1-9. doi: 10.12932/AP-200220-0772.	YES	YES	YES
39	Julia Florez, Helena Campesino, Diego Artola, Rafaela M et al. (2020) Sensitivity of different RT-qPCR solutions for SARS-CoV-2 detection. Int J Infect Dis. 2020 Jul 31; S1201-9712(20)30603-2. doi: 10.1016/j.ijid.2020.07.058.	YES	YES	YES
40	Pandurangan Harikrishnan (2020) Saliva as a Potential Diagnostic Specimen for COVID-19 Testing. J Craniofac Surg. 2020 Jun 11: 10.1097/SCS.0000000000006724. doi: 10.1097/SCS.0000000000006724.	YES	YES	YES
41	Zhenhua Chen, Zhigao Zhang, Xiangming Zhai, Yongyin L (2020) Rapid and Sensitive Detection of anti-SARS-CoV-2 IgG, Using Lanthanide-Doped Nanoparticles-Based Lateral Flow Immunoassay. Anal Chem. 2020 May 19;92(10):7226-7231. doi: 10.1021/acs.analchem.0c00784. Epub 2020 May 5.	YES	YES	YES
42	Gajanan Sapkal, Anita Aich, Rajlaxmi Jain, Pragya Y (2020) Development of indigenous IgG ELISA for the detection of anti-SARS-CoV-2 IgG. Indian J Med Res. 2020 May;151(5):444-449. doi: 10.4103/ijmr.IJMR_2232_20.	YES	YES	YES
43	Jonathan Deeks, Jacqueline Dinnes, Yemisi Takwoingi, Clare D et al. (2020) Antibody tests for identification of current and past infection with SARS-CoV-2. Cochrane Database Syst Rev. 2020 Jun 25;6(6):CD013652. doi: 10.1002/14651858.CD013652.	YES	YES	YES
44	Marie Hardy, Alain Wilmet, Ingrid Beukinga, Jean-Michel D et al. (2020) Validation of a chemiluminescent assay for specific SARS-CoV-2 antibody. Clin Chem Lab Med. 2020 Jul 28;58(8):1357-1364. doi: 10.1515/cclm-2020-0594.	YES	YES	NO

45	Waquar Ahsan, Shamama Javed, Mohammed Bratty, Hassan A et al. (2020) Treatment of SARS-CoV-2: How far have we reached? Drug Discov Ther. 2020 May 6;14(2):67-72. doi: 10.5582/ddt.2020.03008.	YES	YES	YES
46	Yhojan Rodríguez, Lucia Novelli, Manuel Rojas, Maria S et al (2020) Auto-inflammatory and autoimmune conditions at the crossroad of COVID-19. J Autoimmun. 2020 Jun 16: 102506. doi: 10.1016/j.jaut.2020.102506.	YES	YES	YES
47	Alexander Victor Okhuese (2020) Estimation of the Probability of Reinfection With COVID-19 by the Susceptible-Exposed-Infectious-Removed-Undetectable-Susceptible Model. JMIR Public Health Surveill. 2020 May 13;6(2): e19097. doi: 10.2196/19097.	YES	YES	YES
48	S Law, A W Leung, C Xu (2020) Is reinfection possible after recovery from COVID-19? Hong Kong Med J. 2020 Jun;26(3):264-265. doi: 10.12809/hkmj208601.	YES	YES	YES
49	Dominique Batisse, Nicolas Benech, Elisabeth Nevers, Kevin B (2020) Clinical recurrences of COVID-19 symptoms after recovery: viral relapse, reinfection or inflammatory rebound? J Infect. 2020 Jun 30; S0163-4453(20)30454-0. doi: 10.1016/j.jinf.2020.06.073. Online ahead of print. 125. 126. 127.	YES	YES	YES
50	Javad Alizargar (2020) Risk of reactivation or reinfection of novel coronavirus (COVID-19) J Formos Med Assoc. 2020 Jun;119(6):1123. doi: 10.1016/j.jfma.2020.04.013.	YES	YES	YES

Summary of Findings

As the author has done Systematic literature review of approximately 460 articles and internet research on Epidemiology of COVID19; treatment and preventions. There is continued research going on currently with COVID19 Epidemiology Treatment Prevention and vaccination development. As we all know that still there is no approved treatment and vaccination available till 22 September 2020 and all covid19 vaccinations are in trial. There is more hard work and advanced research needed to prepare covid19 treatment medicines and covid19 vaccine to save the mankind. The authors of approximately 460 literature reviewed articles discusses various topics including covid19 incidence; frequency; transmission; treatment; preventions and covid19 vaccination availability. The 10 articles are criticized by Bray and Rees (1995) Questionnaires and provided answers. Also 50 other articles were presented in a table which identify the discussion of covid19 preventions; PPE availability and vaccination development. In each article provided questionnaire and answers followed by Bray and Rees (1995) gives variety of different answers from each article. At the end of every article result by Bray and Rees (1995) Implication for practice is given to follow in future studies.


6
Chapter

Analysis of the study & SPSS Diagrams

For critical reading and analysis; the author should focus on following steps for the purpose of the literature review [196].

1. Think about what you expect from the article or chapter; before reading it.
2. Skim the abstract; headings; conclusion; and the first sentence of each paragraph.
3. Focus on the arguments presented rather than facts [196].
4. Take notes as you read and start to organize your review around themes and ideas.
5. Consider using a table; matrix or concept map to identify how the different sources relate to each other.
6. Note four to six points for each study that summarizes the main points and conclusions.
7. Be as objective as possible.

Table 1: Characteristics of the 10 articles reviewed (Tables 1.1 & 1.2).

Table 1.1: (Articles 1 to 5).

Authors	Pan Zhai, Yanbing Ding, Xia Wu, Junke Long et al. (2020)	Kamal Sahu, Ajay Mishra, Amos Lal (2020)	H Yashavantha Rao, Chelliah Jayabaskaran (2020)	Kangpeng Xiao, Junqiong Zhai, Yaoyu Feng, Niu Zhou et al (2020)	Rong-Sheng Luan, Xin Wang, Xin Sun, Xing-Shu Chen et al. (2020)
Clear aim of research	+	+	+	+	+
Methodology	Literature Review	Literature Review	Literature Review	Literature Review	Literature Review
Recruitment Strategy	Randomly selected	Randomly selected	Randomly selected	Cluster sampling	Randomly selected
Tools for Collection of Data	Hospital records	Hospital records	Hospital records	Hospital records	Hospital records
Collection point of data	Hospitals.	Hospitals.	Hospitals.	Hospitals.	Hospitals.
Data analysis	NR	Rigorous	NR	Rigorous	Rigorous
Year of publication	2020	2020	2020	2020	2020
Subjects	COVID19 Patients.	COVID19 Patients.	COVID19 Patients.	COVID19 Patients.	COVID19 Patients.
Consideration of ethics	+	+	+	+	+
Clear conclusion of the study	+	+	+	+	+

Table 1.2: (Articles 6 to 10).

Authors	Carla Prezioso, Maria Marcocci, Anna Palamara, Giovanna C et al (2020)	Esteban Prado, Katherine Rivera, Lenin Barreno, Mario N et al. (2020)	Jin Wang, Mengmeng Jiang, Xin Chen, Luis M (2020)	Xinjuan Sun, Tianyuan Wang, Dayong Cai, Zhiwei Hu et al (2020)	Souvik Dubey, Payel Biswas, Ritwik Ghosh, Subhankar C et al (2020)
Clear aim of research	+	+	+	+	+
Methodology	Literature Review	Literature Review	Literature Review	Literature Review	Literature Review
Recruitment Strategy	Randomly Selected	Randomly Selected	Randomly Selected	Randomly Selected	Randomly Selected
Tools for Collection of data	Hospital records	Hospital records	Hospital records	Hospital records	Hospital records
Collection point of data	Hospitals.	Hospitals.	Hospitals.	Hospitals.	Hospitals.
Data analysis	Rigorous	Rigorous	Rigorous	NR	NR
Year of publication	2020	2020	2020	2020	2020
Subjects	COVID19 Patients.	COVID19 Patients.	COVID19 Patients.	COVID19 Patients.	COVID19 Patients.
Consideration of ethics	+	+	+	+	+
Clear conclusion of the study	+	+	+	+	+

Tables of themes/outcomes of 10 articles

The following tables will show the interrelationship between the main ideas and common themes across the articles selected for this Book. Table 2.1 shows themes/outcomes of the papers 1 to 6 and the relation of the ideas between them. Table 2.2 shows themes/outcomes of papers 6 to 10 and the relation of the ideas. All the papers selected for this book are interrelated and they have common ideas between them. Some of the papers provide intervention strategies and ideas for planning future strategies and almost all the papers discuss the Epidemiology; Incidence; distribution; Preventions; Treatment and vaccine development of COVID19 Novel corona virus (Tables 2.1 & 2.2).

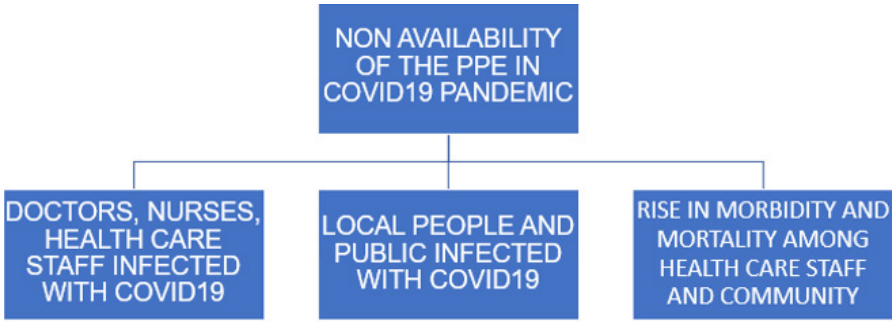
Table 2.1.

Authors	Themes	Authors	Themes
Paper 1 by Pan Zhai, Yanbing Ding, Xia Wu, Junke Long et al. (2020)	All patients with COVID-19-infected pneumonia received antibacterial agents 90% received antiviral therapy, and 45% received methylprednisolone. Clinical trials are underway to investigate the efficacy of new antiviral drugs convalescent plasma transfusion, and vaccines. Most of the trials were initiated by investigators and the study period is 1 to 11 months. In the absence of vaccines and antivirals, isolation and quarantine are achieving remarkable results. It is necessary to strengthen the monitoring of COVID-19 and to develop drugs and vaccines against the COVID-19 infection as soon as possible.	Paper 4 by Kangpeng Xiao, Junqiong Zhai, Yaoyu Feng, Niu Zhou et al (2020).	The article focuses on the investigating that although bats may be the reservoir host for a variety of coronaviruses it remains unknown whether SARS-CoV-2 has additional host species. Here we show that a coronavirus which we name pangolin-CoV isolated from a Malayan pangolin has 100%, 98.6%, 97.8% and 90.7% amino acid identity with SARS-CoV-2 in the E, M, N and S proteins respectively.
Paper 2 Kamal Sahu, Ajay Mishra, Amos Lal (2020).	The main aim and objective of the article is to find the cure and treatment, vaccine of the covid19 novel corona virus to save more lives of the mankind. The article discusses about the covid19 epidemiology, its incidence and transmission, available treatment, preventions available and mortality rate in different age group.	Paper 5 by Rong-Sheng Luan, Xin Wang, Xin Sun, Xing-Shu Chen et al. (2020).	This review summarizes the ongoing researches regarding aetiology epidemiology transmission dynamics treatment and prevention and control strategies of the coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with comparison to severe acute respiratory syndrome, coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV) and pandemic H1N1 virus. SARS-CoV-2 may be originated from bats and the patients and asymptomatic carriers are the source of epidemic infection.
Paper 3 by H Yashavantha Rao, Chelliah Jayabaskaran (2020).	The main theme of this paper is that it focusses on studies which are reporting that coronaviruses are not only causing respiratory illness but also invade the central nervous system through a synapse-connected route. SARS-CoV infections are reported in both patients and experimental animals' brains.	Paper 6 by Carla Prezioso, Maria Marcocci, Anna Palamara, Giovanna C et al (2020).	The author of this article performed a review to describe in particular the origin and the diffusion of COVID-19 in Italy. Underlying how the geographical circulation has been heterogeneous and the importance of pathophysiology in the involvement of cardiovascular and neurological clinical manifestations.

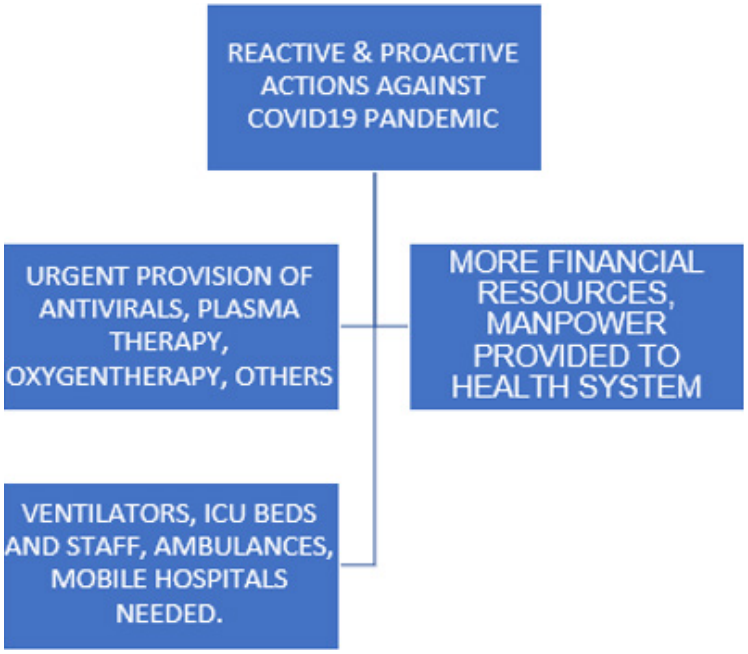
Table 2.2.

Authors	Themes	Authors	Themes
Paper 7 by Esteban Prado, Katherine Rivera, Lenin Barreno, Mario N et al. (2020).	The author has performed the systematic literature review to collect the data about "Clinical, molecular, and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019 (COVID-19), a comprehensive literature review".	Paper 9 by Xinjuan Sun, Tianyuan Wang, Dayong Cai, Zhiwei Hu et al (2020).	The Theme of the article is to discuss "Cytokine storm intervention in the early stages of COVID-19 pneumonia. Cytokine Growth Factor Review". It indicates that the authors are focusing on strategies to avoid Cytokine storm in covid19 pandemic patients which could lead to mortality.
Paper 8 by Jin Wang, Mengmeng Jiang, Xin Chen, Luis M (2020).	The aim of the study is clear that to prove the research "severe acute respiratory syndrome-coronavirus-2 infection often results from alveolar injury that impedes airway capacity and multi-organ failure both of which are associated with the hyperproduction of cytokines also known as a cytokine storm or cytokine release syndrome".	Paper 10 by Souvik Dubey, Payel Biswas, Ritwik Ghosh, Subhankar C et al (2020).	The Main Theme of the article is to discuss "Psychosocial impact of COVID-19" which clearly indicates the fear and hysteria among of COVID19 Pandemic among the community.

Mind maps for the common themes and factors identified across 10 papers contributing to affect the health of children in contact with passive smoking: (Mind map 1-3):



Mind map 1



Mind map 2

Mind map 3

COVID19 Pandemic has taught us the lesson that WHO; UN; UNICEF; UNESCO and all the Governments of G8; G20 and the rest of world were not prepared for the COVID19 Prevention and Treatment. As we all know that there is no Approved Vaccine or Antiviral affective Treatment of COVID19 Virus available till date 26 September 2020. It is very easy to talk more about the preparation in Medical Emergency Epidemic or Pandemic. But when the time comes people come to know that there is no treatment available for most of the dangerous deadly diseases. More funding's; Genuine research is needed to find the treatment and vaccines for deadly viruses and Bacteria's. WHO Guidelines recommended Social distancing; Use of PPE; Hand washing for 40 seconds from soap; Use of Alcohol based hand sanitizers; avoid public gatherings; Unnecessary Travelling; symptomatic medical treatment to control the spread of COVID19 Virus.

Mind map for the intervention recommendations derived from 10 papers (Figure 57)

Above Mind maps shows the methods and preventive strategies against COVID19 Virus recommended by WHO and other Health agencies. More stricter policies and rules are needed to control the COVID19 spread.

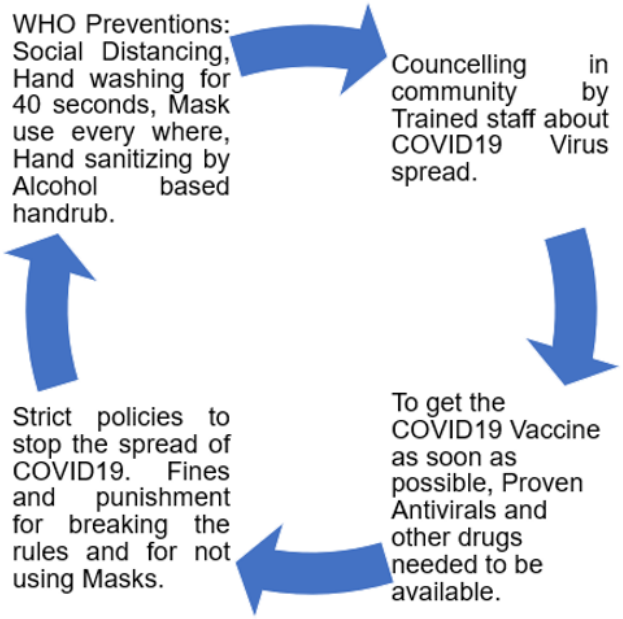


Figure 57.

SPSS Diagrams and Data Analysis

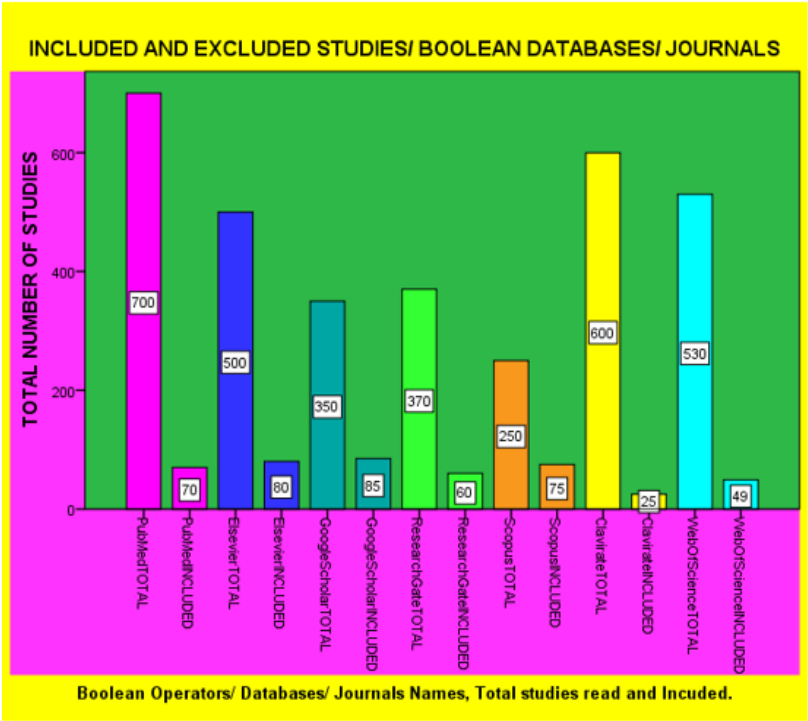


Diagram 1: Included and Excluded Studies.

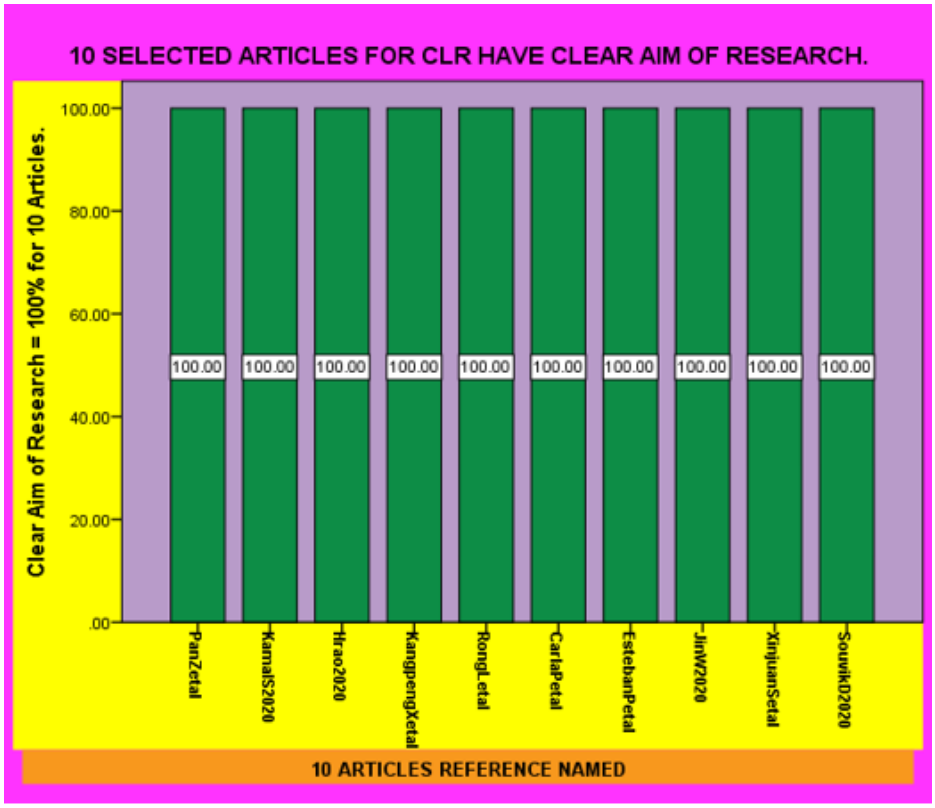


Diagram 2: 10 selected articles for CLR have Clear aim of research.

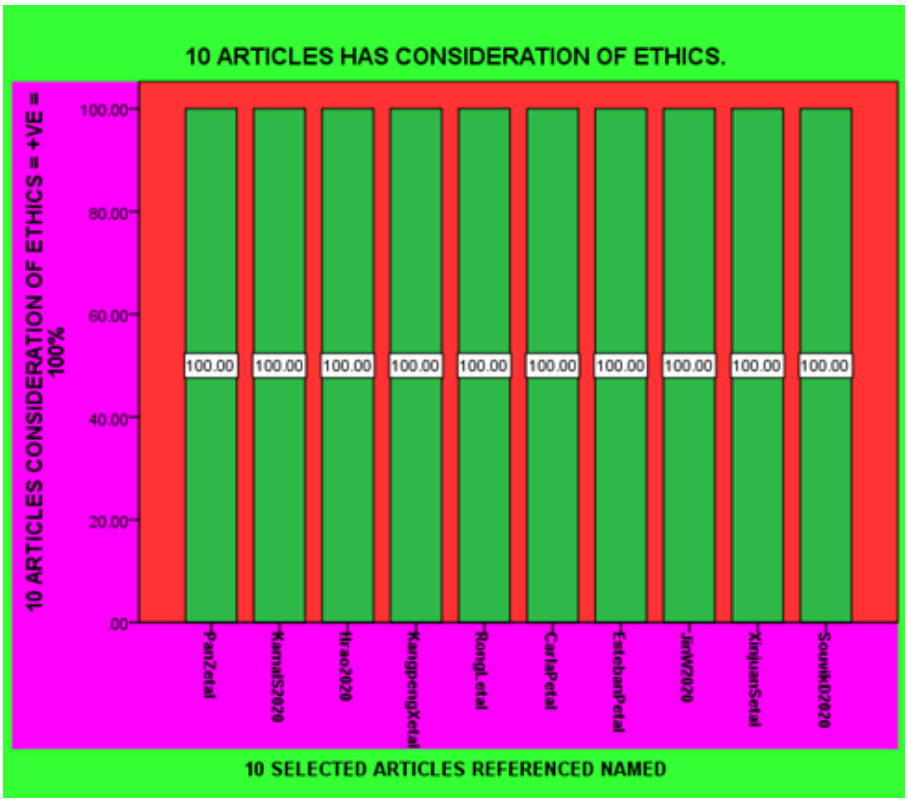


Diagram 3: 10 articles for CLR have consideration of ETHICS.

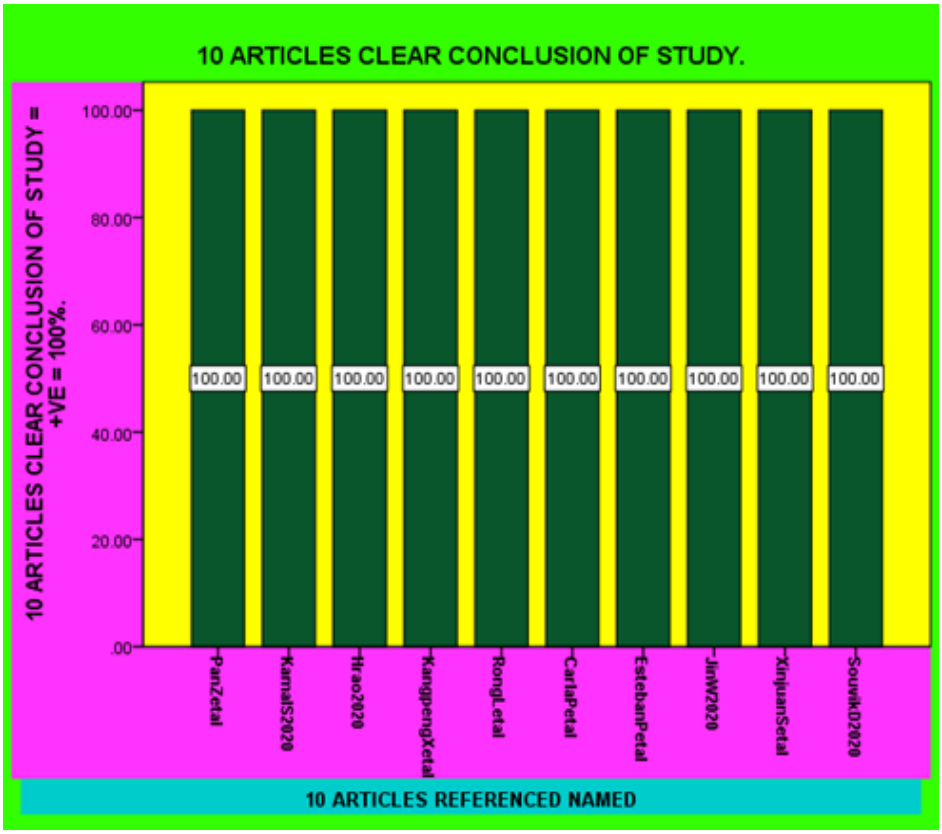


Diagram 4: 10 articles for CLR has clear conclusion of the study.

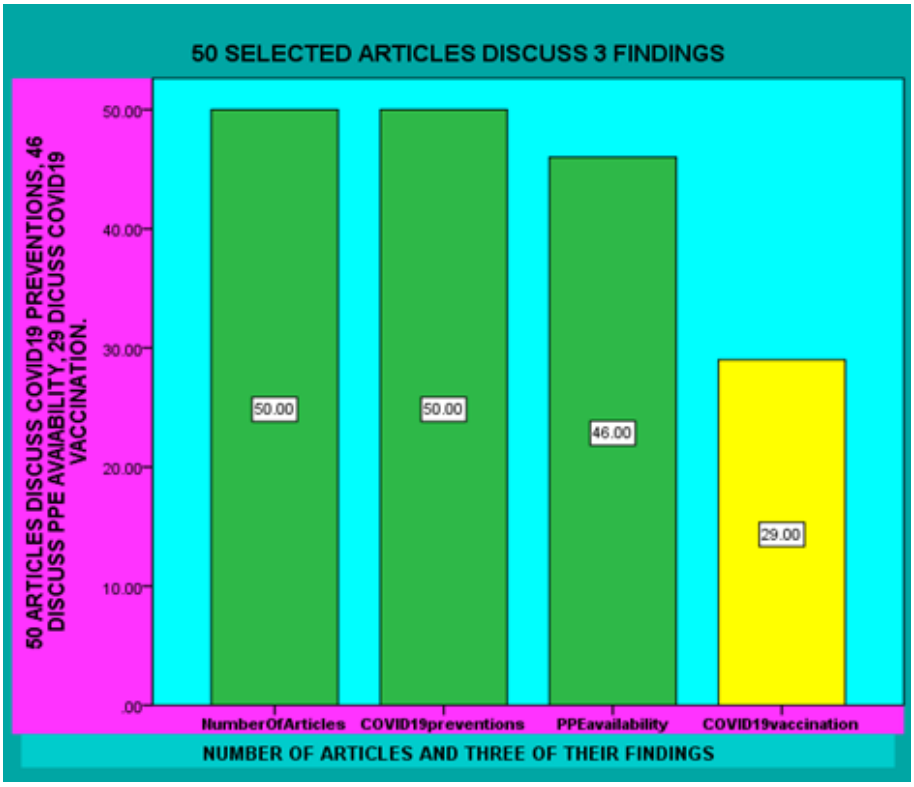


Diagram 5: 50 selected articles discuss 3 different findings.


7
Chapter

Discussion

COVID-19 in Context of 5 W's of Epidemiology (Diagnosis or Health Event (what); Person (Who); Place (Where); Time (When); and Causes; Risk Factors; and Modes of Transmission (Why/How)

The difference is that epidemiologists tend [197] to use synonyms for the 5 W's diagnosis or health event (what); person (who); place (where); time (when); and causes; risk factors; and modes of transmission (why/how). Descriptive epidemiology searches for patterns by examining characteristics of person place & time. These characteristics are carefully considered when a disease outbreak occurs because they provide important clues regarding the source of the outbreak. Epidemiology is the study of how often diseases occur in different groups of people and why. Epidemiological information is used to plan and evaluate strategies to prevent illness and as a guide to the [197] management of patients in whom disease has already developed.

The COVID-19 pandemic is largely and [198] rapidly affecting daily clinical practice and cardiologists and cardiovascular surgeons are not exempt. Being aware of and updated on how SARS-CoV-2 is transmitted how it can be prevented and who should be screened for infection is currently crucial for the exercise of professional duties. Also; all clinicians should be able to identify early clinical manifestations of COVID-19 including cardiovascular complications and therapeutic options as well as potential interactions with cardiovascular drugs should be well known. From a professional standpoint it seems wise to build a strong straightforward coordinated and anticipated response during the initial phase of disease locally. Early implementation of exponential preventive measures by means of universal use of masks minimization of personnel/patient and co-worker interaction along with rescheduling non-urgent consultations and surgeries may facilitate better institutional preparation for the peak caseload. Alignment of regulatory bodies healthcare institutions clinical services and individual professional initiatives in the right direction could allow avoidance of unnecessary mortality [198] and complications related to severe forms of COVID-19 in the general population and early after cardiovascular procedures.

The COVID-19 pandemic has greatly impacted [198] the daily clinical practice of cardiologists and cardiovascular surgeons. Preparedness of health workers and health services is crucial to tackle the enormous challenge posed by SARS-CoV-2 in wards; operating theatres; intensive care units; and interventionist laboratories. This Clinical Review provides an overview of COVID-19 and focuses on [198] relevant aspects on prevention and management for specialists within the cardiovascular field (Figure 58).

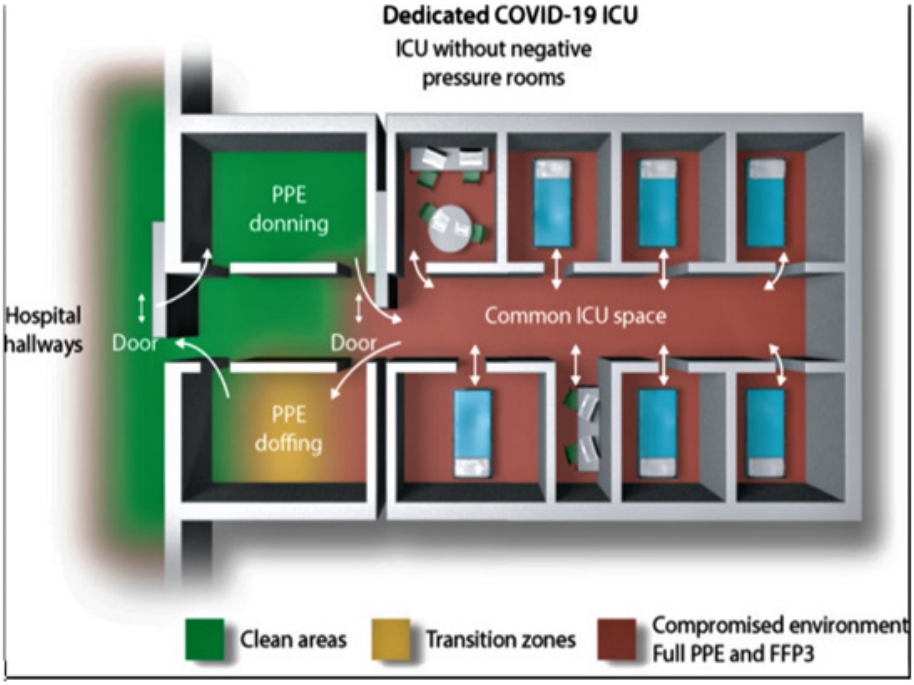


Figure 58: (J M Pericàs, M Meneses, T Sheahan, E Quintana, 2020) Proposed organization of an ICU during the COVID-19 pandemic - FFP3, filtering facepiece protection 3; PPE, personal protective equipment.

Due to the incomplete understanding of the [199] pathogenic mechanism of the COVID-19 virus it is difficult for humans to fight against the virus quickly and effectively once the outbreak occurs. In early 2020; a novel coronavirus was discovered in Wuhan China. Soon after similar cases were found in other countries around the world and the number of infected people increased rapidly. So far; the global cumulative number of infected people has exceeded 3 million and more than 200;000 people have died which has had a huge impact on global human health and economic development. Every outbreak of disease makes a deep impression on mankind. Herein; we summarize the virology epidemiology clinical manifestations diagnosis treatment and prevention of SARS-CoV-2 and [199] hope that countries can control the outbreak as soon as possible to minimize the loss.

To assess the diagnostic accuracy [200] of signs and symptoms to determine if a person presenting in primary care or to hospital outpatient settings such as the emergency department or dedicated COVID-19 clinics has COVID-19 disease or COVID-19 pneumonia. The individual signs and symptoms included in this review appear to have very poor diagnostic properties although this should be interpreted in the context of selection bias and heterogeneity between studies. Prospective studies in an unselected population presenting to primary care or hospital outpatient settings examining combinations of signs and symptoms to evaluate the syndromic presentation of COVID-19 disease are urgently needed. Results from such studies could inform subsequent management decisions such as self-isolation or selecting patients for [200] further diagnostic testing. We also need data on potentially more specific symptoms such as loss of sense of smell. Studies in older adults are especially important.

The zoonotic pathogen identified as an enveloped [201] positive-sense single-stranded RNA beta-coronavirus with 96.2% similarity to that of a bat coronavirus (termed BatCoV RaTG13) is believed to have originated from infected bats and is transmissible between animals and humans as well as between humans and humans with up to 24 days of incubation period. Although the current mortality rate of COVID-19 is relatively low at approximately 2% compared to SARS (9.6%) and MERS (35%) the SARS-CoV-2 is highly contagious and has infected more patients than both SARS and MERS combined over a shorter period of time. Strict containment measures have been effectively implemented throughout China particularly in infected areas preventing uncontrolled spreading. Promising medical interventions have been administered to COVID-19 patients with a total of 6271 patients discharged from hospitals in various countries (as of February 13; 2020). That being said there are no available vaccines [201] against the SARS-CoV-2 and little is still known about the post-effects of the COVID-19 [202] (Figure 59).

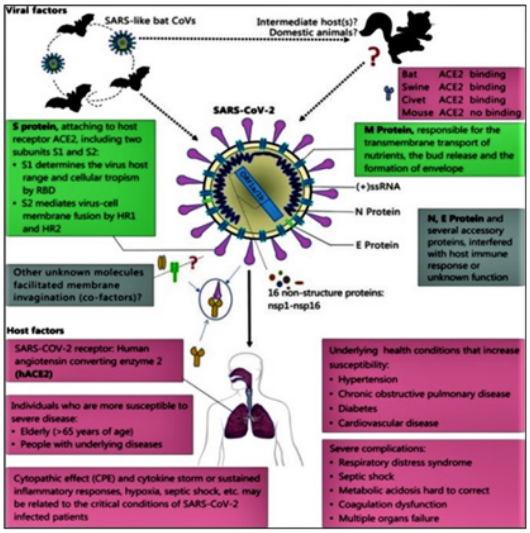


Figure 59: Viral and host factors that influence the (Yan-Rong Guo, Qing-Dong Cao, Zhong-Si Hong, Yuan T, 2020) pathogenesis of SARS-CoV-2. Bats are the reservoir of a wide variety of coronaviruses including severe acute respiratory syndrome coronavirus (SARS-CoV) -like viruses. SARS-CoV-2 may originate from bats or unknown intermediate hosts and cross the species barrier into humans. Virus-host interactions affect viral entry and replication. Upper panel viral factor. SARS-CoV-2 is an enveloped positive single-stranded RNA (ssRNA) coronavirus. Two-thirds of viral RNA mainly located in the first open reading frame (ORF 1a/b), encodes 16 non-structure proteins (NSPs). The rest part of the virus genome encodes four essential structural proteins, including spike (S) glycoprotein small envelope (E) protein matrix (M) protein and nucleocapsid (N) protein and also several accessory proteins. S glycoprotein of SARS-CoV-2 binds to host cell receptors angiotensin-converting enzyme 2 (ACE2) that is a critical step for virus entry. The possible molecules facilitated membrane invaginations for SARS-CoV-2 endocytosis are still unclear. Other virus proteins may contribute to pathogenesis. Host factors (Lower panel) can also influence susceptibility to infection and disease progression. The elderly and people with (Yan-Rong Guo, Qing-Dong Cao, Zhong-Si Hong, Yuan T, 2020) underlying disease are susceptible to SARS-CoV-2 and tend to develop into critical conditions. RBD receptor-binding domainHR1, heptad repeats 1; HR2, heptad repeats 2. (Yan-Rong Guo, Qing-Dong Cao, Zhong-Si Hong, Yuan T, 2020).

In evolutionary history these three [203] coronaviruses have some similar biological features as well as some different mutational characteristics. Their receptors and routes of transmission are not all the same which makes them different in clinical features and treatments. We discovered through the auto dock simulations that Met124 plays a key role in the efficiency of drugs targeting ACE2 such as remdesivir; chloroquine; ciclesonide and niclosamide; and may be a potential target in COVID-19. We searched for studies on each outbreak and their solutions and found that the main biological differences among SARS-CoV-2; SARS-CoV and MERS-CoV are in ORF1a and the sequence of gene spike coding protein-S. In addition to the common route of transmission including airborne transmission these three viruses have their own unique routes [203] of transmission such as fecal-oral route of transmission COVID-19.

COVID-19 How did it Start?

A cluster of pneumonia (COVID-19) cases have been [204] found in Wuhan China in late December 2019 and subsequently a novel coronavirus with a positive stranded RNA was identified to be the etiological virus (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) which has a phylogenetic similarity to severe acute respiratory syndrome coronavirus (SARS-CoV). SARS-CoV-2 transmits mainly through droplets and close contact and the elder or people with chronic diseases are high-risk population. People affected by SARS-CoV-2 can be asymptomatic which brings about more difficulties to control the transmission. COVID-19 has become pandemic rapidly after onset and so far; the infected people have been above 2 000 000 and more than 130 000 [204] died worldwide according to COVID-19 situation dashboard of World Health Organization (https://covid19.who.int).

An acute respiratory disease caused by a novel [14] coronavirus (SARS-CoV-2 previously known as 2019-nCoV) the coronavirus disease 2019 (COVID-19) has spread throughout China and received worldwide attention. On 30 January 2020; World Health Organization (WHO) officially declared the COVID-19 epidemic as a public health emergency of international concern. The emergence of SARS-CoV-2 since the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012 marked the third introduction of a highly pathogenic and large-scale epidemic coronavirus into the human population in the twenty-first century. As of 1 March 2020; a total of 87;137 confirmed cases globally 79;968 confirmed in China and 7169 outside of China with 2977 deaths (3.4%) had been reported by WHO. The novel coronavirus uses the same receptor angiotensin-converting enzyme 2 (ACE2) as that for SARS-CoV; and mainly spreads through the respiratory tract. Importantly increasingly evidence [14] showed sustained human-to-human transmission along with many exported cases across the globe [205] (Figure 60).

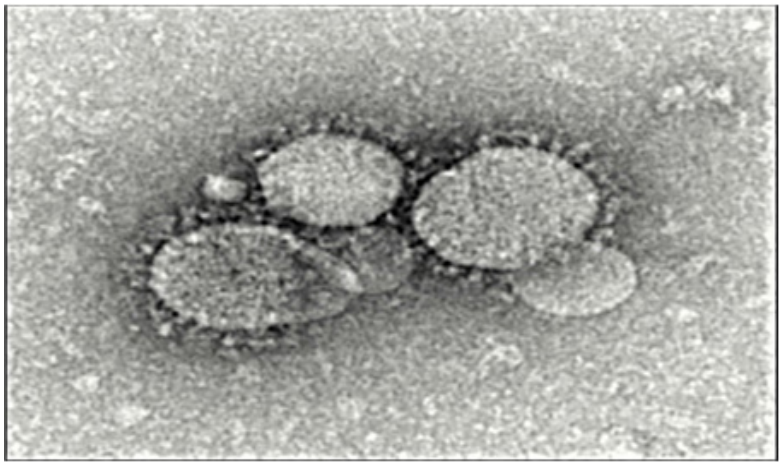


Figure 60: Electron microscopy photograph of negative stain of a corona virus (image from the Public Health Image Library) Jeannette Guarner [205].

Since December 2019 the emergence of the Severe [206] Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) infection has been reported unexpectedly in Wuhan; China; with staggering infection speed across China and around the world. To date; seven known strains of HCoVs belonging to four genera (i.e.; α?; β?; γ; and δ-CoV) have been recognized the latest one has been identified as the SARS-CoV-2. Although the common transmission routes of SARS-CoV-2 is the respiratory tract it seems that other routes such as the gastrointestinal tract may be effective for the entry of the virus in the body. Initial data revealed that males; pregnant women; elderly; and underlying conditions predispose patients to higher morbidity or mortality and also might be at risk for a severe infection of COVID-19. To date despite the whole world effort to review various aspects of SARS-CoV-2; including epidemiology; [206] clinical manifestations; diagnosis; and treatment options there are still gaps in the knowledge of this disease and many issues remain unclear [207] (Figure 61).

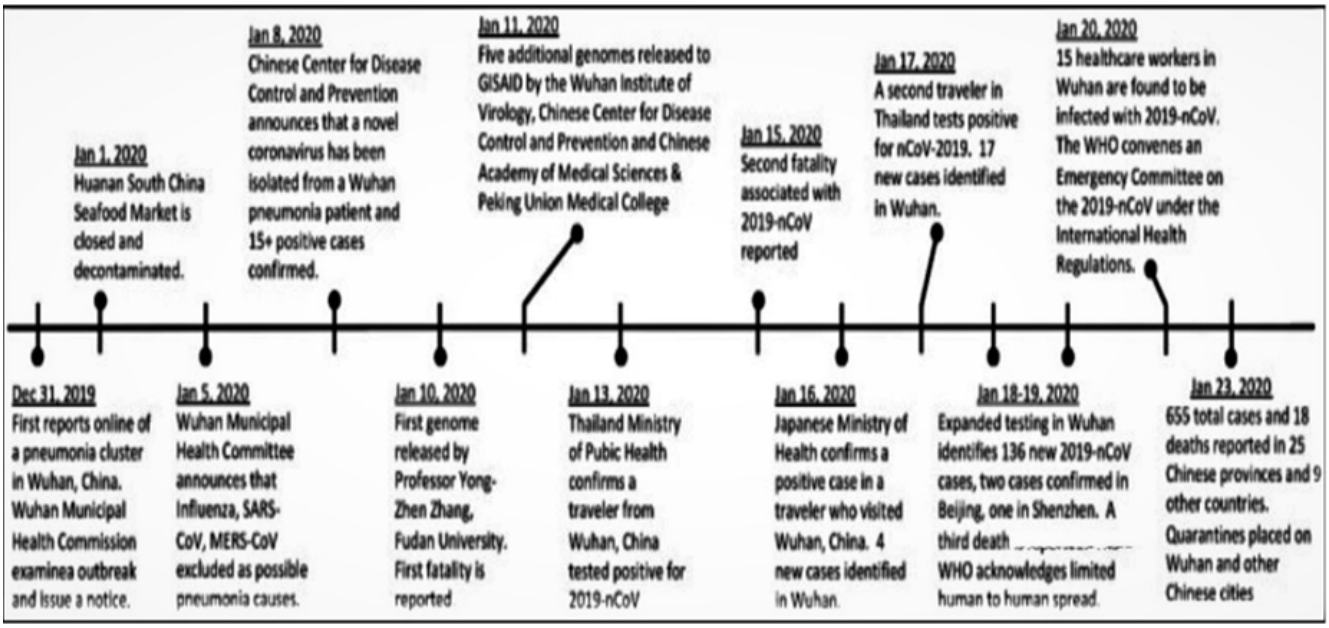


Figure 61: Timeline of the key 2019-nCoV events Lisa Gralinski, et al. [207].

The recent outbreak of SARS-CoV-2 that started [208] in Wuhan China has now spread to several other countries and is in its exponential phase of spread. Before this outbreak the most recent coronavirus outbreaks were the SARS-CoV and the MERS-CoV outbreaks that happened in China and Saudi Arabia respectively. Since the SARS-CoV-2 belongs to the same family as of SARS-CoV and MERS-CoV; they share several similarities. So this review aims at understanding the new scenario of SARS-CoV-2 outbreak and compares the epidemiology clinical presentations and the genetics of these coronaviruses. Studies reveal that SARS-CoV-2 is very similar in structure and pathogenicity with SARS-CoV; but the most important structural protein i.e.; the spike protein (S) is slightly different in these viruses. The presence of a furin-like cleavage site in SARS-CoV-2 facilitates the S protein priming and might increase the efficiency of the spread of SARS-CoV-2 as compared to other beta coronaviruses. So [208] furin inhibitors can be targeted as potential drug therapies for SARS-CoV.

Coronavirus infections of multiple origins [209] have spread to date worldwide causing severe respiratory diseases. Seven coronaviruses that infect humans have been identified HCoV-229E; HCoV-OC43; HCoV-NL63; HCoV-HKU1; SARS-CoV; MERS-CoV; and SARS-CoV-2. Among them SARS-CoV and MERS-CoV caused outbreaks in 2002 and 2012; respectively. SARS-CoV-2 (COVID-19) is the most recently discovered. It has created a severe worldwide outbreak beginning in late 2019 leading to date to over 4 million cases globally. Viruses are genetically simple yet highly diverse. However; the recent outbreaks of SARS-CoV and MERS-CoV; and the ongoing outbreak of SARS-CoV-2 indicate that there remains a long way to go to identify and develop specific therapeutic treatments [209]. Only after gaining a better understanding of their pathogenic mechanisms can we minimize viral pandemics.

The COVID-19 pandemic is spreading from [210] Asia to the West. We have qualified epidemiological and technical information through scientific reports from China and other countries that have been published in the main categorized scientific journals. There is an effort by the World Health Organization (WHO) and the scientific community in general to order and consolidate this information which is essential for the guidance of health professionals and managers in the construction of safe and effective strategies for coping with the pandemic. The responsibility of the Technicians and Managers is to ensure that all recommended personal protective equipment is available at all times. Our strength should not be exposed to additional risks. Whenever possible young people should be assigned to direct care. Older people can supervise and carry out rear tasks. Visits and the flow of people in the units must be restricted. The authorities announce the expansion of intensive care services in Brazil to face the pandemic. Qualified personnel may not be available in all locations. AMIB will support expansion and provide remote consultancy to doctors [210] involved in the care. Our goal is to reduce mortality and morbidity.

The year 2020 has started with a rapid [211] global epidemic of the virus SARS-CoV-2 causing the disease COVID-19. The virus appears to have transmitted to humans in a zoonotic event from bats. There are many questions to investigate regarding all aspects of SARS-CoV-2 virology and epidemiology. These questions range from how the virus emerged to how it spreads and how the disease manifests. But most pressingly as the global outbreak continues to grow can we develop effective vaccine and therapeutic strategies to treat not only this epidemic

but any future coronavirus spillover events? The recent emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from the Hubei province in China in late 2019 demonstrates the epidemic potential of coronaviruses. The rapid spread of this virus across the world in only 2 [211] months highlights the transmissibility of this family of viruses and the significant morbidity and mortality that they can cause.

An unprecedented outbreak of pneumonia [212] of unknown etiology in Wuhan City Hubei province in China emerged in December 2019. A novel coronavirus was identified as the causative agent and was subsequently termed COVID-19 by the World Health Organization (WHO). Considered a relative of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) COVID-19 is caused by a beta coronavirus named SARS-CoV-2 that affects the lower respiratory tract and manifests as pneumonia in humans. Despite rigorous global containment and quarantine efforts the incidence of COVID-19 continues to rise with 90;870 laboratory-confirmed cases and over 3;000 deaths worldwide. In response to this global outbreak we [212] summarize the current state of knowledge surrounding COVID-19.

At the end of 2019 a novel virus severe acute [213] respiratory syndrome coronavirus 2 (SARS-CoV-2) causing severe acute respiratory syndrome expanded globally from Wuhan China. In March 2020 the World Health Organization declared the SARS-Cov-2 virus a global pandemic. Although only when the pandemic ends it will be possible to assess the full health social and economic impact of this global disaster this review represents a picture of the current state of the art. In particular; we focus on public health impact pathophysiology and [213] clinical manifestations diagnosis case management emergency response and preparedness.

Policies; Programmes and their Implications – WHO; CDC and Other Government Action Plan against the COVID-19 Pandemic

The outbreak the SARS-CoV-2 (CoV-2) virus has [214] resulted in over 6.5 million cases of COVID19; greatly stressing global healthcare infrastructure. Lacking medical prophylactic measures to combat disease spread; many nations have adopted social distancing policies in order to mitigate transmission of CoV-2. While mathematical models have suggested the efficacy of social distancing to curb the spread of CoV-2; there is a lack of systematic studies to quantify the real-world efficacy of these approaches. Here; we first demonstrate that implementation of social distancing policies in US states corresponded with a reduction in COVID19 spread rates; and that the reduction in spread rate is proportional to the average change in mobility. We validate this observation on a worldwide scale by analyzing COVID19 spread rate in 134 nations with varying social distancing policies. Globally; we find that social distancing policies significantly reduced the COVID19 spread rate; with resulting in an estimated 65% reduction (95% CI = 39–80%) in new COVID19 cases over a two-week time period. [214] These data suggest that social distancing policies may be a powerful tool to prevent spread of COVID19 in real-world scenarios.

The purpose of the legislation [215] Coronavirus Act 2020 was to respond to the emergency situation created by the COVID-19 pandemic in particular the increase pressure placed on health services in the United Kingdom. An overview is provided of the government's rationale for the changes to Northern Ireland mental health and capacity laws as well as exploring how they are likely to be operationalized in practice. Consideration is also given as to how such changes may impact upon existing human rights protections for persons assessed as lacking mental capacity. It is argued that it is important that regular parliamentary oversight is maintained in relation to the potential impact and consequences of such changes during the period they are in force. This should be done in order to assess whether they remain a necessary proportionate and least restrictive response to the challenges faced in managing mental health [215] and capacity issues in Northern Ireland during this public health emergency.

The prevention policies and containment [216] measures implemented by the government and medical institutions are highly effective in controlling the spread of the epidemic and increasing the recovery rate of COVID-19 patients. As of March15 the cumulative incidence of COVID-19 in Chongqing was 1.84/100000 [216] (576 cases) and the infection fatality rate was 1.04% (6/576). COVID-19 Pandemic has taught the Global community A big lesson after losing [217] Approximately 370;000 innocent lives and approximately Half Million people being sick of COVID-19.

The lesson is that in this high-tech 21st century where countries claim to be super Developed and Civilized countries don't have enough PPE for their health care workers and for local people. The Governments has not done their Homework to fight the Battle against COVID-19 Pandemic and people are still losing the lives due to lack of PPE'S [217] Not development of VACCINE No confirmed TREATMENT available for COVID-19.

Organizations like WHO and UNESCO are extremely [218] important to keep the countries updated share different countries' measures and show the global aspect. They have to be clear and transparent in each step not to lost the trust of the populations. Besides their informative roles managing bridges between different countries and providing the important supplies like PPE and hygiene products to those countries in need are extremely important roles in a pandemic. Health protection agencies and CDC like institutions have leader roles guiding the

authorities about the virus' characteristics reading the outbreak curve measures to be taken etc. Health ministries of countries should guide the operational plans in different levels. Other ministries should follow the advices and proposals to manage their routine work in a pandemic era. Educational institutions; primary and secondary schools should continue to connect with their students not to lost even a year for a generation in a pandemic. Universities should not suspend their important researches especially those which can help for [218] prevention and control of the pandemic but try to continue as much as the outbreak allows.

As the world mobilizes to contain the COVID-19 scientists [219] and public health experts are increasingly alarmed about the potentially catastrophic effects of an outbreak in Africa. The establishment of Africa Centers for Disease Control and Prevention by the Africa Union in 2017 was an unprecedented move toward strengthening national responses so far enabling all fifty member states with confirmed cases of COVID-19 to adequately respond break chains of transmission and effectively contain the spread of SARS-CoV-2. We enter an uncertain and challenging period that may severely test the preparedness organizational resource and resilience of African states and the fabric of their societies. However; we speculate that the fear associated with COVID-19 may also lead to some of the long-standing messages about simple measures to reduce the spread such as hand washing finally becoming absorbed and more universally adopted by health workers and the public. Is it possible that regardless of the terrible threat posed by SARS-CoV-2 the increased adoption of these [219] health protection measures may result in a reduction in the spread of other infectious diseases?

Coronavirus disease (COVID-19) is a worldwide [220] epidemic and various countries have responded with different containment measures to reduce disease transmission including stay-at-home orders curfews and lockdowns. Comparative studies have not yet been conducted to investigate the impact of these containment measures these studies are needed to facilitate public health policy-making across countries. We included 122;366 patients with confirmed COVID-19 infection from 54 countries and 24;071 patients from 4 epicenters on the effective dates on which stay-at-home orders curfews or lockdowns were implemented between January 23 and April 11; 2020. Stay-at-home; curfew; and lockdown measures commonly commenced in countries with approximately 30%; 20%; or 10% increases in daily new cases. Different national containment measures were associated with a decrease in daily new cases of confirmed COVID-19 infection. Stay-at-home orders curfews and lockdowns [220] curbed the percent increase in daily new cases to <5 within a month. Resurgence in cases within one month was observed in some South American countries.

Decision modelling is not designed to predict the future [221] but rather to provide decision makers with a credible envelope of possible scenarios. As witnessed in other jurisdictions in a pandemic failure to make anticipatory decisions can have dire consequences. Balanced against the direct impacts of the pandemic delayed presentation and treatment of non–COVID-19 conditions such as cardiac disease; result in significant sequelae these spillover impacts are also critical consequences of the pandemic. The use of decision analytic modelling that is iterated on rapidly evolving data is a [221] tool to help inform health policy decisions to address these difficult trade-offs (Figure 62).

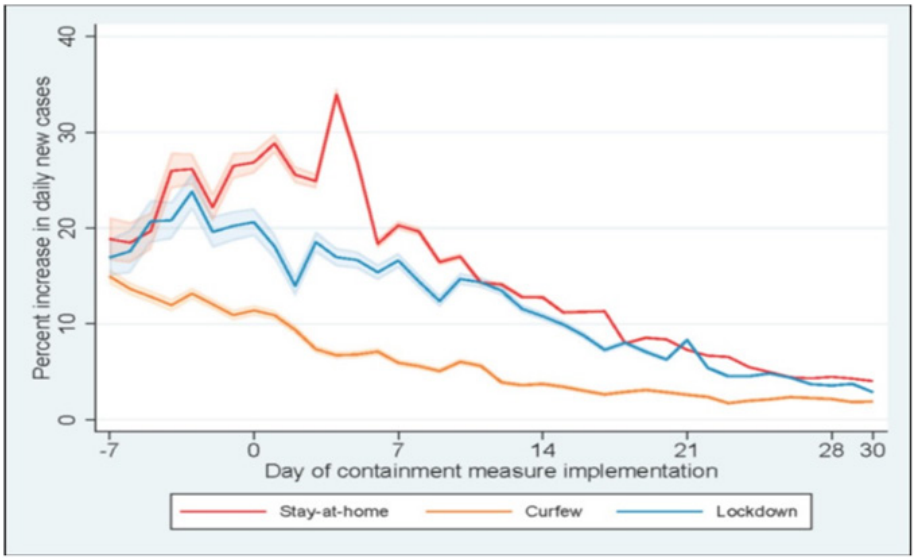


Figure 62: Percent increase in daily new cases vs days since containment measure by type of containment measure Carlos Wong, et al. [220].

Since the absence of medical [222] resources or targeted therapeutics systemic containment policies have been prioritized but some critics query what extent can they mitigate this pandemic. We construct a fine-grained transmission dynamics model to forecast the crucial

information of public concern therein using dynamical coefficients to quantify the impact of the implement schedule and intensity of the containment policies on the spread of epidemic. Statistical evidences show the comprehensive identification and quarantine policies eminently contributed to reduce casualties during the phase of a dramatic increase in diagnosed cases in Wuhan and postponing or weakening such policies would undoubtedly exacerbate the epidemic. Hence; we suggest that [222] governments should swiftly execute the forceful public health interventions in the initial stage until the pandemic is blocked (Figure 63).

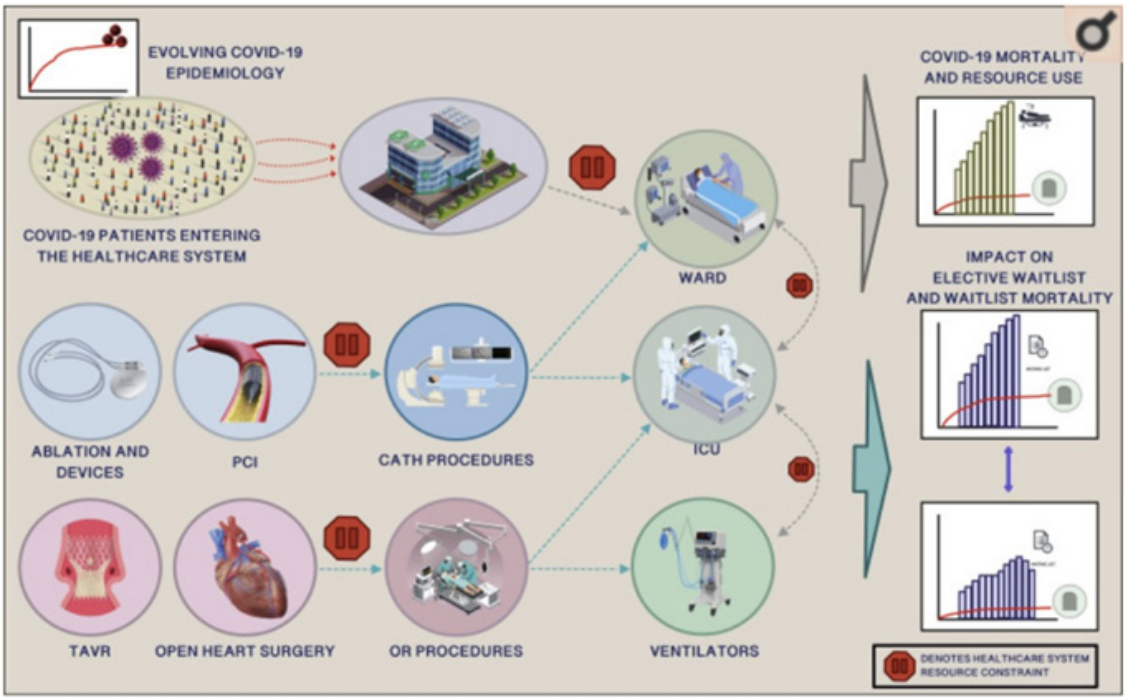


Figure 63: A schematic illustration of the COVID-19 Resource Estimator decision analytic model and the cardiac disease submodule that includes catheter-based procedures (electrophysiology procedures transcatheter aortic valve replacement (TAVR) percutaneous coronary interventions (PCIs)) and open surgical procedures (coronary artery bypass grafting, valve surgery) Derrick Tam, et al [221].

COVID-19 Surveillance and Tracking in the Community

Surveillance is the core function [223] of any public health system and a multi-component surveillance system for COVID-19 is essential to understand the burden across the different strata of any health system and the population. Many countries and public health bodies utilise 'syndromic surveillance' (using real-time; often non-specific symptom/preliminary diagnosis information collected during routine healthcare provision) to supplement public health surveillance programmes. The current COVID-19 pandemic has revealed a series of unprecedented challenges to syndromic surveillance including the impact of media reporting during early stages of the pandemic changes in healthcare-seeking behaviour resulting from government guidance on social distancing and accessing healthcare services and changes in clinical coding and patient management systems. These have impacted on the presentation of syndromic outputs with changes in denominators creating challenges for the interpretation of surveillance data. Monitoring changes in healthcare utilisation is [223] key to interpreting COVID-19 surveillance data which can then be used to better understand the impact of the pandemic on the population.

General practice clinical system providers have introduced an [224] emergency new set of clinical codes to support COVID-19 surveillance. Additionally; practices participating in current virology surveillance are now taking samples for COVID-19 surveillance from low-risk patients presenting with LRTIs. The RCGP RSC a network of over 500 general practices in England extract pseudonymized data weekly. This extended surveillance comprises of five components

1. Recording in medical records of anyone suspected to have or who has been exposed to COVID-19. Computerized medical records suppliers have within a week of request created new codes to support this.

2. Extension of current virologic surveillance and testing people with influenza-like illness or lower respiratory tract infections (LRTI) with the caveat that people suspected to have or who have been exposed to COVID-19 should be referred to the national containment pathway and not seen in primary care.

3. Serology sample collection across all age groups. The 100 general practices currently undertaking annual influenza virology surveillance will be involved in the extended (Simon Lusignan; Jamie Bernal; Maria Zambon; Oluwafunmi A et al; 2020) virologic and serological surveillance.

4. Collecting convalescent serum samples.

5. Data curation.

UK primary care coding of covid-19 is a mess [225] we need to stop the use of bad codes and migrate from the use of ugly to good codes but will only be able to do so when they are finally released. Key data computerised medical record (CMR) systems are recorded using codes to standardise recording and so attendances about a medical problem can be linked. At the start of the COVID-19 pandemic there was neither international agreement about nomenclature nor codes available [225] in primary care CMRs with which to record exposure testing or infection. Current Pandemic of COVID-19 [226] has taught all the Global Health authorities such as WHO; UN; UNESCO; UNICEF; UNHCR; EU Others and all Governments of 200 countries that we were not ready for COVID-19. Although Developed Countries such as USA; UK; France and countries of EU spends Billions of US Dollars on their Health System but it did not stop the Deaths of COVID-19 Pandemic in their [226] countries and they are actually affected the most in this world.

TA indicators tested here proved to be [227] reliable tools to identify in the short mid-term a subsequent change of direction of viral spread trend either downward upward or sideward. We found that the use of both fast/slow SMAs and MACD provided a reliable signal of trend inversion of SARS-Cov-2 spread. Results were consistent for all the 3 countries considered. The trend reversals signalled by the indicators were always followed by a sustained trend persistence until a new signal of reversal appeared. Analysis was performed on datasets from Italy Iran and Brazil. TA indicators tested were

1. The combined use of a faster (3-d) and a slower (20-d) simple moving averages (SMA)

2. The moving average converge/divergence (MACD) and

3. The [227] divergence in the direction of the number of new daily cases trend and the corresponding MACD histogram.

A coordinated system of disease surveillance will be critical to [228] effectively control the coronavirus disease 2019 (Covid-19) pandemic. Such systems enable rapid detection and mapping of epidemics and inform allocation of scarce prevention and intervention resources. The program involves telephone-based interviews with over 20;000 households every four months plus a sub-study calling 750 households every two weeks. Each call asks a household representative how the epidemic and NPI are affecting the household and conducts a Covid-19 risk screen for all resident members. Any individuals screening positive are invited to a clinical screen; potential test and referral to necessary care conducted in-person near their home following careful risk minimization procedures. In this protocol we report the details of our cohort design questionnaires data and reporting structures and standard operating [228] procedures in hopes that our project can inform similar efforts elsewhere.

An integrated surveillance strategy outbreak management [229] and encouraging individual responsibility were successful in early detection of clusters of COVID-19 among HCWs. With ongoing local transmission vigilance must be maintained for intrahospital spread in nonclinical areas where social mingling of HCWs occurs. Because most individuals with COVID-19 have mild symptoms addressing presenteeism is crucial to minimize potential staff and patient exposure. Over a 16-week surveillance period we detected 14 cases of COVID-19 among HCWs with ARI symptoms. Two of the cases were linked epidemiologically and thus constituted a COVID-19 cluster with intrahospital HCW–HCW transmission we also detected 1 family cluster and 2 clusters among HCWs who shared accommodation. No transmission to HCWs or patients was detected after containment measures were instituted. Early detection minimized the number of HCWs [229] requiring quarantine hence preserving continuity of service during an ongoing pandemic.

Triage screening by emergency physicians and surveillance [230] protocols with an externally located chest imaging facility were effective in the early isolation of COVID-19 patients. In future outbreaks of emerging infectious diseases efforts should be focused toward the provision of continued ED treatment with the implementation of revised triage and surveillance protocols. During the study period 6 level 1 or 2 emergency rooms included in the study were shut down 27 times for 769 hours. Thirty-one confirmed COVID-19 cases of whom 7 died were associated with the incidence of ED closure. Typical patient presentation with respiratory symptoms of COVID-19 was seen in less than 50% of patients whereas abnormal findings on chest imaging investigations were detected in 93.5% of the study population. The chest radiography facility resuscitation rooms and triage area were moved to locations outside the ED and a new surveillance protocol was applied to determine the factors warranting quarantine including symptoms chest radiographic findings and exposure to a source of infection. The incidence of [230] ED closures decreased after the implementation of the revised triage and surveillance protocols [231] (Figure 64).

Evaluation of available surveillance systems and datasets that could potentially be used for SARI surveillance in the Netherlands.

System or dataset	Data quality	Timeliness	Representativeness	Simplicity	Flexibility	Acceptability	Stability	*Sustain-ability*	*Score(% of maximum score)*[a]
Quality of care management system	Good	Poor	Moderate	Moderate	Good	Good	Good	Good	20 (83)
National register discharge diagnoses	Moderate	Poor	Moderate	Good	Moderate	Good	Moderate	Good	18 (75)
Mortality monitoring	Good	Good	Moderate	Good	Good	Good	Good	Good	23 (96)
SARI sentinel surveillance	Moderate	Good	Poor	Poor	Poor	Moderate	Poor	Moderate	13 (54)
Financial coding system	Moderate	Good	Poor	Good	Poor	Good	Moderate	Good	16 (67)
Ambulance dispatch calls data	Moderate	Good	Poor	Good	Good	Moderate	Poor	Poor	16 (67)
Virological laboratory surveillance	Good	Good	Poor	Moderate	Moderate	Good	Good	Good	20 (83)

Figure 64: A Score: per evaluation criterion the following scores were attributed: 3 points if rated ''good", 2 points if rated ''moderate", 1 point if rated "poor". The total evaluation score was expressed as the sum of all individual evaluation criteria and percentage of the total maximum score S. D Marbus, et al. [231].

ORCHID- Oxford Royal College of General Practitioners Clinical Informatics Digital Hub [232] will provide equitable and innovative use of big data through a professionally led national primary care network and the application of FAIR principles. The secure data hub will host routinely collected general practice data linked to other key health care repositories for clinical trials and support enhanced in situ surveillance without always requiring large volume data extracts. ORCHID will support rapid data extraction analysis and dissemination with the aim of improving future research and development in general practice to positively impact patient care. The hub will be a bottom-up professionally led network that will provide benefits for member practices our health service and the population served. Data will only be used for SQUIRE (surveillance; quality improvement; research; and education) purposes. COVID-19 surveillance has resulted in tripling of the number of virology sites to 293 (target 300) which has aided the collection of the largest ever weekly total of surveillance swabs in the United Kingdom as [232] well as over 3000 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serology samples.

COVID-19 Economic Impact on the Countries and Statistics

Various environmental factors influence the (Sorin Cheval; Cristian Adamescu; Teodoro Georgiadis; Mathew H et al; 2020) outbreak and spread of epidemic or even pandemic events which in turn may cause feedbacks on the environment. The novel coronavirus disease (COVID-19) was declared a pandemic on 13 March 2020 and its rapid onset spatial extent and complex consequences make it a once-in-a-century global disaster. Most countries responded by social distancing measures and severely diminished economic and other activities. Consequently; by the end of April 2020 the COVID-19 pandemic has led to numerous environmental impacts both positive such as enhanced air and water quality in urban areas and negative such as shoreline pollution due to the disposal of sanitary consumables. This study presents an early overview of the observed and potential impacts of the COVID-19 on the environment. We argue that the effects of COVID-19 are determined mainly by anthropogenic factors which are becoming obvious as human activity (Sorin Cheval; Cristian Adamescu; Teodoro Georgiadis; Mathew H et al; 2020) diminishes across the planet and the impacts on cities and public health will be continued in the coming years.

This chapter evaluates the short-term [233] impact of the coronavirus outbreak on 21 leading stock market indices in major affected countries including Japan; Korea; Singapore; the USA; Germany; Italy; and the UK etc. The consequences of infectious disease are considerable and have been directly affecting stock markets worldwide. Using an event study method; our results indicate that the stock markets in major affected countries and areas fell quickly after the virus outbreak. Countries in Asia experienced more negative abnormal returns as compared to other countries. Further panel fixed effect regressions also support the adverse effect of COVID-19 confirmed cases on stock indices abnormal returns through an effective channel by adding [233] up investor's pessimistic sentiment on future returns and fears of uncertainties.

The stock market provides a view of what investors [234] expect for the future. It is precisely in complex situations such as the COVID-19 outbreak that the prescience of the market is particularly valuable. COVID-19 represents a fearsome and novel risk. As such it stirred feverish behaviour by investors. Yet despite the volatility despite the panic reasonable economic expectations underlay movements in the stock prices of individual companies. Society can thus learn about the nature of the challenge we are facing in these trying times. The stock price reactions suggest that broad actions including fiscal policy interventions are required to avoid further negative outcomes and propagations of the

COVID-19 shock. The crystal ball of the market foretells a different economic landscape than the one we have gotten used to. Such changes bring potentially massive social and political upheavals. [234] Hopefully we can avoid the inherent dangers and benefit from the opportunities.

Covid-19 Pandemic has also sparked [235] fears of an impending economic crisis and recession. Social distancing; self-isolation and travel restrictions have led to a reduced workforce across all economic sectors and caused many jobs to be lost. Schools have closed down and the need for commodities and manufactured products has decreased. In contrast the need for medical supplies has significantly increased. The food sector is also facing increased demand due to panic-buying and stockpiling of food products. In response to this global outbreak we summarise the [235] socio-economic effects of COVID-19 on individual aspects of the world economy.

COVID-19 social isolation measures have [236] had a profound impact on the psychological and mental well-being of individuals across society. Many of the anticipated consequences of isolation measures are themselves key risk factors for mental health issues including suicide self-harm substance misuse; and domestic and child abuse. Social interaction has been widely interlinked with psychological well-being social opportunities and employment thereby restriction of these measures is suggested to be profoundly distressing to those experiencing strict isolation. Previous epidemics have induced widespread fear loneliness and psychological sequelae COVID-19 is inducing similar effects. It has been reported that over 4000 arrests for domestic abuse offences have been made in the United Kingdom since the 9th of March equating to roughly 100 a day highlighting the potentially fatal impact of social isolation policies. The rise in domestic abuse cases are alarming and bring to [236] light concerns surrounding the collateral psychological and mental health impacts of social isolation during the COVID-19 pandemic.

We examine the role of various [237] socioeconomic mediating factors including public health measures that encourage social distancing in local communities. Weather characteristics 2 weeks prior are used as instrumental variables for causal inference. Stringent quarantines city lockdowns and local public health measures imposed in late January significantly decreased the virus transmission rate. The virus spread was contained by the middle of February. Population outflow from the outbreak source region posed a higher risk to the destination regions than other factors including geographic proximity and similarity in economic conditions. We quantify the effects of different public health measures in reducing the number of infections through counterfactual analyses. Over 1.4 million infections and 56;000 deaths may have been avoided as a result [237] of the national and provincial public health measures imposed in late January in China.

We implement a machine learning approach [237] to select instrumental variables that strongly predict virus transmission among the rich exogenous weather characteristics. Our 2SLS estimates show that the stringent quarantine massive lockdown and other public health measures imposed in late January significantly reduced the transmission rate of COVID-19. By early February; the virus spread had been contained. While many socioeconomic factors mediate the virus spread; a robust government response since late January played a determinant role in the containment of the virus. We also demonstrate that the actual population flow from the outbreak source poses a higher risk to the destination than other factors such as geographic proximity and similarity in economic conditions. [237] The results have rich implications for ongoing global efforts in containment of COVID-19.

While isolation is a necessary measure [238] to protect public health results indicate that it alters physical activity and eating behaviours in a health compromising direction. A more detailed analysis of survey data will allow for a segregation of these responses in different age groups countries and other subgroups which will help develop interventions to mitigate the negative lifestyle behaviours that have manifested during the COVID-19 confinement. 1047 replies (54% women) from Asia (36%); Africa (40%); Europe (21%) and other (3%) were included in the analysis. The COVID-19 home confinement had a negative effect on all PA intensity levels (vigorous; moderate; walking and overall). Additionally; daily sitting time increased from 5 to 8 h per day. Food consumption and meal patterns (the type of food; eating out of control; snacks between meals; number of main meals) were unhealthier during [238] confinement with only alcohol binge drinking decreasing significantly.

In response to the COVID-19 health crisis [239] the French government has imposed drastic lockdown measures for a period of 55 days. This paper provides a quantitative assessment of the economic and environmental impacts of these measures in the short and long term. We find that the lockdown has led to a significant decrease in economic output of 5% of GDP but a positive environmental impact with a 6.6% reduction in CO2 emissions in 2020. Both decreases are temporary economic and environmental indicators return to their baseline trajectory after a few years. CO2 emissions even end up significantly higher after the COVID-19 crisis when we account for persistently low oil prices. We then investigate whether implementing carbon pricing can still yield positive macroeconomic dividends in the post-COVID recovery. We find that implementing ambitious carbon pricing speeds up economic recovery while significantly reducing CO2 emissions. By maintaining high fossil fuel prices carbon taxation reduces the imports of fossil energy and stimulates energy efficiency investments [239] while the full redistribution of tax proceeds does not hamper the recovery.

COVID-19 pandemic has affected nearly all aspects [240] of surgical procedures scheduling and staffing. Special precautions were taken before during or after surgeries. New treatment and teaching modalities emerged in response to the pandemic. Psychological support and training platforms are necessary for the surgical team. Sixty-six articles were reviewed in this article. A scoping search in PubMed and Google Scholar was done using the search terms "Coronavirus;" "COVID-19"; "SARS-CoV-2"; "nCoV-2019" and "surgery." They were either searched individually or in combination. Through these articles we provide guidance and recommendations on the preoperative preparation and safety precautions intraoperative precautions postoperative precautions; postoperative complications (related to COVID-19); surgical scheduling; emergency surgeries; elective surgeries; cancer surgery; [240] psychological impact on surgical teams; and surgical training during the COVID-19 pandemic.

We find the announcements regarding the implementation [241] of social distancing measures by governments have dual a direct negative and an indirect positive effect on stock market returns. Specifically; the announcements of social distancing measures result in negative stock market returns due to their expected adverse impact on economic activity. Government announcements regarding public awareness programs testing and quarantining policies and income support packages largely result in positive market returns. Using daily data from January 22 to April 17; 2020 from 77 countries; we find announcements of government social distancing measures have a direct negative effect on stock market returns due to their adverse effect on economic activity; while an indirect positive effect through the reduction in COVID-19 confirmed cases. Government announcements regarding public awareness programs; testing and quarantining policies; and income support packages largely result in positive market returns. Our findings have important policy implications; primarily by showing that government [241] social distancing measures have both positive and negative economic impact.

COVID-19 Awareness and Rise in Body Temperature?

Our results suggest that information dissemination [242] about COVID-19 which causes individual adoption of handwashing mask-wearing and social distancing can be an effective strategy to mitigate and delay the epidemic. Early initiated short-term government-imposed social distancing can buy time for healthcare systems to prepare for an increasing COVID-19 burden. We stress the importance of disease awareness in controlling the ongoing epidemic and recommend that; in addition to policies on social distancing governments and public health institutions mobilize people to adopt self-imposed measures with proven efficacy in order to successfully tackle COVID-19. Many countries have implemented social distancing as a measure to "flatten the curve" of the ongoing epidemics. Evaluation of the impact of government-imposed social distancing and of other measures to control further spread of [242] COVID-19 is urgent especially because of the large societal and economic impact of the former.

The world is currently impacted by [243] the novel coronavirus disease (COVID-19). The scale of the impacts is unprecedented and studies have suggested that it might take more than a decade for the world to recover; societally and economically and might significantly compromise the progress [243] of Sustainable Development Agenda (SDGs) 2030. The main theme [244] of this Article is to discuss the Preventions; training and control strategies against COVID-19 novel corona virus in China in initial first two months of Pandemic. In most of the cases they have found (TCM) Traditional Chinese medicines more effective than other medicines. The current positive statistics of Pandemics about China shows the complete control on COVID-19 with no spread and no Fatalities in May 2019. While the Pandemic of COVID-19 is on the rise all [244] around the world specially in the USA; Europe and the UK.

Most of the COVID-19 deceased were elderly males. [245] Fever dyspnoea dry cough fatigue hypertension; chronic cardiovascular and cerebrovascular disease; diabetes; and laboratory examinations showed low levels of platelet content increased CRP and LDH were associated with the risk of dying. ARDS and shock were risk factors for death in COVID-19 patients. A total of 2401 patients in 15 articles were included in this study. Meta-analysis showed that 66.6% of COVID-19 deceased were male with a median age of 69.9 years. Compared with the surviving COVID-19 patients the deceased had lower platelet levels (mean difference (MD) = - 39.35; 95% CI - 55.78 ~ - 22.93) and higher C-reactive protein (CRP) (MD = 80.85; 95% CI 62.53 ~ 99.18) and lactate dehydrogenase (LDH) (MD = 246.65; 95% CI 157.43 ~ 335.88) at admission. The most common [245] complications of the deceased were acute respiratory distress syndrome (ARDS) (OR = 100.36; 95% CI 64.44 ~ 156.32) and shock (OR = 96.60; 95% CI 23.80 ~ 392.14.

The present study successfully and systematically [246] evaluated the relationship between multiorgan dysfunction and COVID-19 severity. Patients with a history of organ dysfunction have a greater risk of developing severe COVID-19 and in turn COVID-19 can promote acute multiorgan injury. Clinicians should increase their awareness regarding the monitoring of multiorgan function in hospitalized COVID-19 patients. Early detection and effective intervention to prevent [246] multiorgan dysfunction may aid in reducing the number of deaths in these patients (Figure 65).

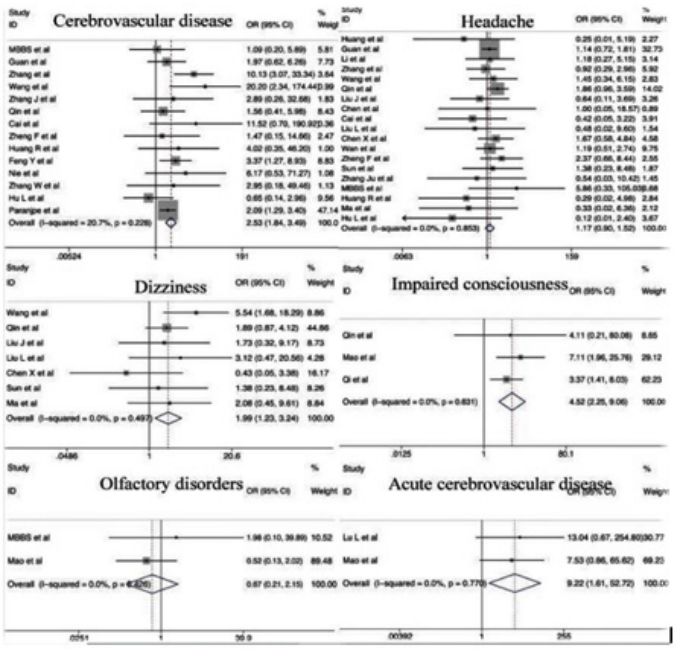


Figure 65: Relationship between neurologic dysfunction and COVID-19 severity Ting Wu, et al. [246].

The emergence of novel respiratory viruses such as [247] the SARS-CoV-2 creates dramatic challenges to the healthcare services including surgical pathology laboratories despite their extensive daily experience in dealing with biological and chemical hazards. Here we cover important aspects on the knowledge on COVID-19 gathered during the first six months of the pandemic and address relevant issues on human biological sample handling in the Anatomic Pathology laboratory in the context of COVID-19 global threat. In addition; we detail our strategy to minimize the risk of contamination upon exposure to the different biological products received in the laboratory which can be of general interest to other laboratories worldwide. Our approach has enabled a safe work environment for laboratory staff while ensuring the maintenance of high-quality standards of the work performed. In times of uncertainty and given the lack of specific guidelines directed at Anatomic Pathology services to better deal with the global COVID-19 public-health emergency it is essential to share with the community rigorous methodologies that will enable us to better cope with probable novel waves of [247] COVID-19 infection and other viruses that will possibly arise in the near future.

We have demonstrated that a preliminary clinical profiling [248] of COVID-19 from the Ayurvedic perspective is possible through literature review supported by discussions with Allopathic clinicians as well as examination of patient case records. The provisional diagnosis proposed can be further developed with continued review of literature; wider cooperation and teamwork with Allopathic physicians and access to clinical data as well as direct clinical assessment of COVID-19 patients. COVID-19 can be provisionally understood from the Ayurvedic perspective as vātakapha dominant sannipātajvara of āgantu origin with pittānubandha. The asymptomatic; pre symptomatic; mild; moderate; severe and critical stages of COVID-19 with varying clinical presentations have been analysed on the basis of nidāna; doṣa; dūṣya; nidānapañcaka and ṣaṭkriyākāla to [248] present a preliminary clinical profile of the disease [249] (Figures 66 & 67).

Multivariable logistic regression analysis of prognostic factors for severe COVID-19

Prognostic factors	Multivariable model 1[a]		Multivariable model 2[b]	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age, yr				
≥ 70			3.37 (0.26–43.58)	0.352
Male, sex			2.98 (0.23–38.81)	0.404
Diabetes mellitus	6.53 (2.26–18.87)	0.001	19.15 (1.90–193.42)	0.012
Hypertension	1.44 (0.49–4.26)	0.508	1.00 (0.09–10.78)	0.999
Body temperature ≥ 37.8°C	8.27 (2.62–26.09)	< 0.001	10.91 (1.35–88.36)	0.025
Peripheral oxygen saturation < 92%	15.39 (4.83–48.98)	< 0.001	33.31 (2.45–452.22)	0.008
Albumin < 3.5	27.21 (6.98–106.10)	< 0.001	5.36 (0.49–59.32)	0.171
Total bilirubin > 1.2	2.53 (0.92–6.97)	0.073	5.92 (0.69–51.01)	0.106
CK-MB > 6.3	13.00 (1.41–120.27)	0.024	56.84 (2.64–1,223.78)	0.010

COVID-19 = coronavirus disease 2019, OR = odds ratio, CI = confidence interval, CK-MB = creatine-kinase MB.
[a]Adjusted for age, sex; [b]Adjusted for age, sex, diabetes mellitus, hypertension, body temperature, peripheral oxygen saturation, albumin, total bilirubin, and CK-MB.

Figure 66: Jong Jang, et al. [249].

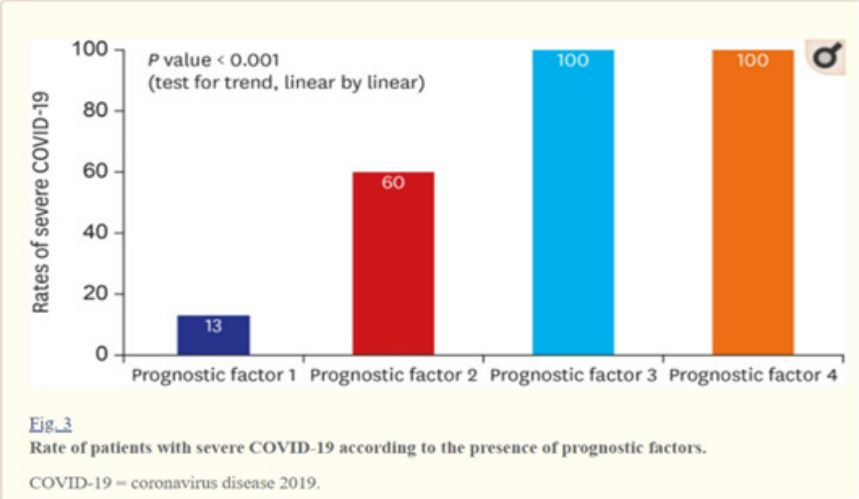


Fig. 3
Rate of patients with severe COVID-19 according to the presence of prognostic factors.
COVID-19 = coronavirus disease 2019.

Figure 67: Jong Jang, et al. [249].

To date more than 700 COVID-19 patients [250] have been admitted to our hospital and further more in-depth studies will follow. However; this picture of the first week of COVID-19 outbreak provides information regarding the disease outside China in a real life-setting of a country with very high case numbers. Although our study is limited by the small number of patients and by the short follow-up our findings suggest that in a Caucasian aged population with high prevalence of coexisting illnesses COVID-19 is characterised by notable morbidity. We describe clinical characteristics; treatments and outcomes of 44 Caucasian patients with coronavirus disease (COVID-19) at a single hospital in Pavia Italy; from 21–28 February 2020 at the beginning of the outbreak in Europe. Seventeen patients developed severe disease two died. After a median of 6 days 14 patients were discharged from hospital. Predictors of lower [250] odds of discharge were age > 65 years antiviral treatment and for severe disease lactate dehydrogenase > 300 mg/dL.

Through collection of 2132 questionnaire responses [251] in field research the present researchers analysed the data using descriptive statistics and various approaches. In conclusion; the public's high level of willingness to share information sufficient knowledge of and consensus on epidemic prevention between individuals and family's strict compliance with relevant regulations effective preventive measures and adequate public facilities have contributed to control of COVID-19. However; vigilance and awareness of the pandemic in some individual's epidemic-prevention campaigns and community-based preventive measures were insufficient. Some citizens subsequently suffered from headaches anxiety; and mood instability. Furthermore; demographic variables (place of residence; sex; age; and occupation) and physical and mental health status produced various effects on citizens awareness attitude and [251] behaviour regarding epidemic prevention as well as the perceived effect of COVID-19 on physical and mental health.

Critical Care for the COVID-19 Patients

COVID-19 has placed unprecedented pressure on [252] critical care services which is likely to stretch resources beyond capacity. The situation is exacerbated by increased staff absence from self-isolation and illness increased referral of patients with suspected or confirmed COVID-19 who develop respiratory failure and limited availability of Extra Corporeal Membrane Oxygenation (ECMO) services. In addition; there is the ongoing challenge of patients being transferred between departments and hospitals for ongoing care. In consequence as current needs continue to rise innovative approaches are needed to redress shortages and support the continuance of services. This article provides an overview of severe COVID-19 infection outlining treatment [252] strategies and nursing processes that will need to develop and extend in response to this evolving situation.

The Society for Neuroscience in Anaesthesiology [253] and Critical Care appointed a task force to provide timely; consensus based expert guidance for neuro anaesthesiologists during the COVID-19 pandemic. The aim of this document is to provide a focused overview of COVID-19 disease relevant to neuro anaesthesia practice. This consensus statement provides information on the neurological manifestations of COVID-19 advice for neuro anaesthesia clinical practice during emergent neurosurgery interventional radiology (excluding endovascular treatment of acute ischemic stroke) trans nasal neurosurgery awake craniotomy and electroconvulsive therapy as well as information about health care provider wellness. Institutions and health care providers are encouraged to adapt these recommendations to [253] best suit local needs considering existing practice standards and resource availability to ensure safety of patients and providers [254] (Figure 68).

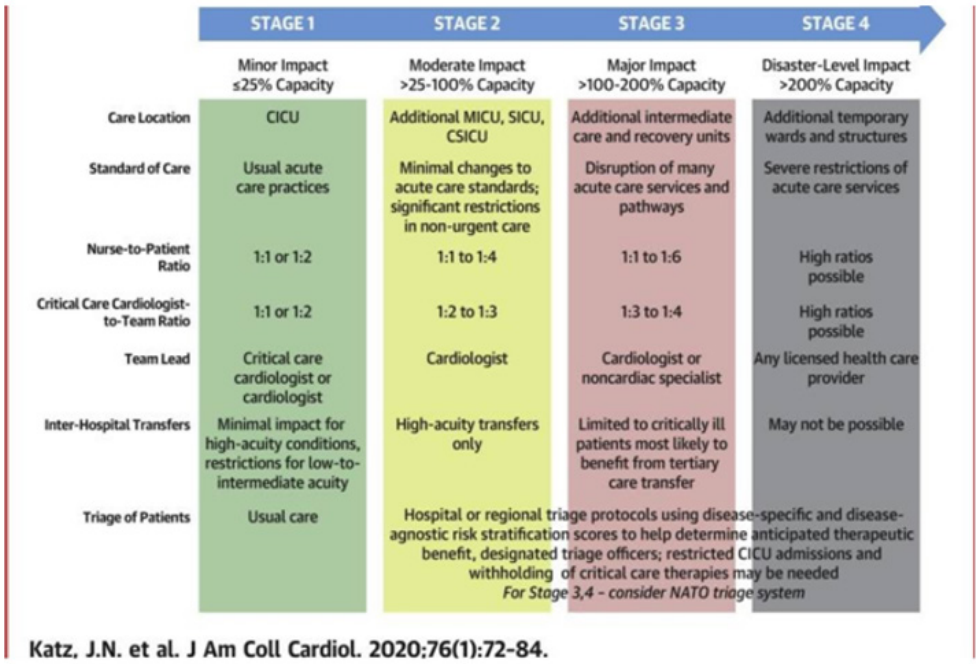


Figure 68: Jason Katz, et al. [254].

Healthcare systems worldwide are responding to [255] Coronavirus Disease 2019 (COVID-19) an emerging infectious syndrome caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus. Patients with COVID-19 can progress from asymptomatic or mild illness to hypoxemic respiratory failure or multisystem organ failure necessitating intubation and intensive care management. Healthcare providers; and particularly anaesthesiologists are at the frontline of this epidemic and they need to be aware of the best available evidence to guide therapeutic management of patients with COVID-19 and to keep themselves safe while doing so. Here; the authors review COVID-19 pathogenesis presentation diagnosis and potential therapeutics with a focus on management of COVID-19–associated respiratory failure. The authors draw on literature from other viral epidemics treatment of acute respiratory distress syndrome and recent publications [255] on COVID-19 as well as guidelines from major health organizations.

The Society of Neuroscience in Anaesthesiology and Critical Care (SNACC) [256] created a task force to provide expert consensus recommendations on aesthetic management of endovascular treatment of AIS. The task force conducted a systematic literature review (up to August 2012). Because of the limited number of research articles relating to this subject; the task force solicited opinions from experts in this area. The task force created a draft consensus statement based on the available data. Classes of recommendations and levels of evidence were assigned to articles specifically addressing anaesthetic management during endovascular treatment of stroke using the standard American Heart Association evidence rating scheme. The draft consensus statement was reviewed by the Task Force SNACC Executive Committee and representatives of Society of Neuro interventional Surgery (SNIS) and Neurocritical Care Society (NCS) reaching consensus on the final document. Each topic includes a summary of available data followed by recommendations. This consensus statement is intended for use by individuals involved in the care of patients with acute ischemic stroke such as anaesthesiologists interventional [256] neuroradiologists neurologist's neuro intensivists and neurosurgeons.

In response to the estimated potential impact of coronavirus [257] disease-COVID-19 on New York City hospitals our institution prepared for an influx of critically ill patients. Multiple areas of surge planning progressed simultaneously focused on infection control clinical operational challenges ICU surge capacity staffing; ethics; and maintenance of staff wellness. The protocols developed focused on clinical decisions regarding intubation the use of high-flow oxygen engagement with infectious disease consultants and cardiac arrest. Mechanisms to increase bed capacity and increase efficiency in ICUs by outsourcing procedures were implemented. Novel uses of technology to minimize staff exposure to COVID-19 as well as to facilitate family engagement and end-of-life discussions were encouraged. Education and communication remained key in our attempts to standardize care stay apprised on emerging data and review seminal literature on respiratory failure. Challenges were encountered and overcome through interdisciplinary collaboration and iterative surge planning as ICU admissions rose. [257] Support was provided for both clinical and nonclinical staff affected by the profound impact COVID-19 had on our city.

The COVID-19 pandemic will place extraordinary and [258] sustained demands on critical care services. Critical care providers must take the lead to initiate planning and rapidly implement measures to ensure that healthcare services are maintained. It is equally important to maintain critical care services for non-COVID-19 patients protect HCWs and consider the ethical and social implications of triaging during a crisis. The coronavirus disease 2019 (COVID-19) has rapidly evolved into a worldwide pandemic. Preparing intensive care units (ICU) is an integral part of any pandemic response. In this review; we discuss the key principles and strategies for ICU preparedness. We also describe our initial outbreak measures and share some of the challenges faced. To achieve sustainable ICU services we propose the need to

1. Prepare and implement rapid identification and isolation protocols and a surge in ICU bed capacity
2. Provide a sustainable workforce with a focus on infection control
3. Ensure adequate supplies to equip ICUs and protect healthcare workers and
4. Maintain [258] quality clinical management as well as effective communication.

Coronavirus disease 2019 (COVID-19) stands out as [259] the major pandemic that we have experienced in the last century. As it affects every social structure it brought the importance of intensive care support once again to the agenda of healthcare system after causing severe acute respiratory syndrome. The precautions to be taken against this virus; where our knowledge is extremely small intensive care units take an indispensable place in pandemic planning. In this review; we aimed to emphasize the crucial points regarding intensive care management of COVID-19 patients [259] which we have written not only for intensivists but also for all healthcare professionals.

The intensive care unit (ICU) community [260] must prepare for the challenges associated with this COVID-19 pandemic. Streamlining of workflows for rapid diagnosis and isolation clinical management and infection prevention will matter not only to patients with COVID-19 but also to health-care workers and other patients who are at risk from nosocomial transmission. Management of acute respiratory failure and haemodynamic is key. ICU practitioner's hospital administrators' governments; and policy makers must prepare for a substantial increase in critical care bed capacity with a focus not just on infrastructure and supplies but also on staff management. Critical care triage to allow the rationing of scarce ICU resources might be needed. Researchers must address unanswered questions including the role of repurposed and experimental therapies. Collaboration at the [260] local regional national and international level offers the best chance of survival for the critically ill.

Mortality due to COVID-19 pneumonia was concentrated [261] in patients above the age of 65 years especially those with major comorbidities. Patients who were admitted to the ICU lived longer than those who were not. Our findings should aid in the recognition and clinical management of such infections especially with regard to ICU resource allocation. The mean age of 109 decedents with COVID-19 pneumonia was 70.7 years; 35 patients (32.1%) were female; and 85 patients (78.0%) suffered from one or more underlying comorbidities. Multiple organ failure especially respiratory failure and heart failure appeared in all patients even at the early stage of disease. Overall; the mean time from onset of symptoms to death was 22.3 days. All 109 hospitalized patients needed admission to an intensive care unit (ICU) however because of limited availability only 51 (46.8%) could be admitted. The period from hospitalization to [261] death in the ICU group and non-ICU group was 15.9 days (standard deviation = 8.8 d) and 12.5 days (8.6 d; P = 0.044); respectively.

Defining the optimal approach for managing a critically ill COVID-19 [262] patient is rapidly changing. Goal-directed transoesophageal echocardiography (TEE) is frequently used by physicians caring for intubated critically ill patients as a reliable imaging modality that is well suited to answer questions at bedside. In the right clinical scenario TEE is a tool that can provide the information needed to deliver the best and safest possible care for the critically ill patients. Although transthoracic echocardiography can provide the information needed in most patients there are specific scenarios in which TEE represents the modality of choice. TEE provides acute care clinicians with a goal-directed framework to guide clinical care and represents an ideal modality to evaluate hemodynamic instability during prone ventilation perform serial [262] evaluations of the lungs support cardiac arrest resuscitation and guide veno venous ECMO cannulation.

In Thailand an upper middle-income country with a limited [263] healthcare infrastructure and restricted human resources nearly 3;000 confirmed COVID-19 cases have been reported as of early May 2020. Public health policies aimed at preventing new COVID-19 cases were very effective in halting the pandemic in Thailand. Case fatality in Thailand has been low (1.7%) at least in part due to early stratification according to risk of disease severity and timely initiation of supportive care with affordable measures. We present our initial experience with COVID-19 in Thailand focusing on several aspects that may have played a crucial role in curtailment of the pandemic and elements of care for severely ill COVID-19 patients including stratification [263] isolation and affordable diagnostic approaches and supportive care measures.

Mortality or Death Rate in COVID-19?

We report a new methodology the Patient Information [264] Based Algorithm (PIBA) for estimating the death rate of a disease in real-time using publicly available data collected during an outbreak. PIBA estimated the death rate based on data of the patients of COVID-19 in Wuhan and then in other cities throughout China. The estimated days from hospital admission to death was 13 standard deviation (SD) 6 days. The death rates based on PIBA were used to predict the daily numbers of deaths since the week of February 25 2020 in China overall; Hubei province Wuhan city and the rest of the country except Hubei province. The death rate of COVID-19 ranges from 0.75% to 3% and may decrease in the future. The results showed that the real death numbers had fallen into the predicted ranges. In addition; using the preliminary data from China the PIBA method was successfully used to estimate the death rate and predict the death numbers of the Korean population. In conclusion; PIBA can be used to efficiently [264] estimate the death rate of a new infectious disease in real-time and to predict future deaths.

The numbers of confirmed cases are increased [265] daily in different countries especially in Unites State America Spain; Italy; Germany; China; Iran; South Korea and others. The spread of the COVID-19 has many dangers and needs strict special plans and policies. Therefore; to consider the plans and policies the [265] predicting and forecasting the future confirmed cases are critical. While there is no vaccine currently [266] available for COVID-19 patients the treatment with Convalescent Plasma with other western medicines saves lives of hundreds of thousands of patients in COVID-19 Pandemic. Global health including public health preventive medicine has failed the world in this current COVID-19 Pandemic when more than Quarter million people died all [266] around the world and approximately 4.2 Million people suffered from this deadly COVID-19 Pandemic (Figure 69).

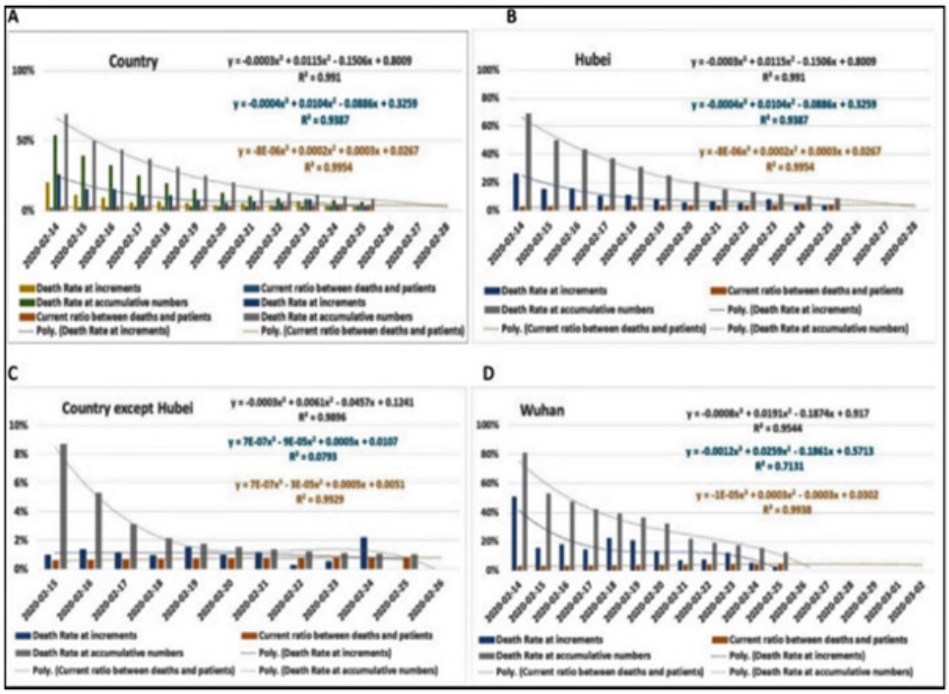


Figure 69: The estimated death rate in (Lishi Wang, Jing Li, Sumin Guo, Ning X et al, 2020)Mainland China and Hubei Province. The blue curve represents the mortality calculated by the actual increase in deaths per lagging day divided by the increase in actual patients on the previous corresponding day. The gray curve represents the total number of deaths per lagging day, divided by the total number of identified actual patients on the corresponding previous day. The orange curve shows the number of deaths per day divided by the total number of patients the same day. The number on the vertical bar represents the death rate; the number on the horizontal bar shows the date. A: Overall death rate in Mainland China. B: Death rate in Hubei province. C. The death rate in the rest of the country except Hubei province. D: Death rate in Wuhan city. Lishi Wang, et al. [264].

People <65 years old have very small risks of COVID-19 death [267] even in pandemic epi centres and deaths for people <65 years without underlying predisposing conditions are remarkably uncommon. Strategies focusing specifically on protecting high-risk elderly individuals should be considered in managing the pandemic. Individuals with age <65 account for 4.5–11.2% of all COVID-19 deaths in European countries and Canada 8.3–22.7% in the US locations and were the majority in India and Mexico. People <65 years old had 30- to 100-fold lower risk of COVID-19 death than those ≥65 years old in 11 European countries and Canada 16- to 52-fold lower risk in US locations and less than 10-fold in India and Mexico. The absolute risk of COVID-19 death as of June 17 2020 for people <65 years old in high-income countries ranged from

10 (Germany) to 349 per million (New Jersey) and it was 5 per million in India and 96 per million in Mexico. The absolute risk of COVID-19 death for people ≥80 years old ranged from 0.6 (Florida) to 17.5 per thousand (Connecticut). The COVID-19 mortality rate in people <65 years old during the period of fatalities from the epidemic was equivalent to the mortality rate from driving between 4 and 82 miles per day for 13 countries [267] and 5 states and was higher (equivalent to the mortality rate from driving 106–483 miles per day) for 8 other states and the UK.

The COVID-19 pandemic has devastated [268] the global population by hitting the health individuals. It is a highly contagious disease and has caused a high rate of mortality particularly in high risk individuals. The pattern of infection and mortality rates has varied significantly amongst the countries. Surprisingly; more affluent countries with greater healthcare resources have been more affected by it and have seen higher mortality rates compared to less affluent countries like India and other Southeast Asian nations. We have analysed and discussed several factors that may be responsible for such discrepancy. The mortality observed in Indian and south Asian subcontinent is lower than in the west. Multifactorial reasons indicated for this [268] differential mortality due to COVID-19 have been described in the current literature.

A major underlying cause of COVID-19 mortality is a [269] hyperinflammatory cytokine storm in severe/critically ill patients. Although many clinical trials are testing the efficacy of targeting inflammatory cytokines/chemokines in COVID-19 patients the critical inflammatory mediator initiating COVID-19 patient death is undefined. Here we suggest that the immunopathological pathway leading to COVID-19 mortality can be divided into three stages with distinct clinical features that can be used to guide therapeutic strategies. Our interpretation of the recently published clinical trials from COVID-19 patients suggests that the clinical efficacy in preventing COVID-19 mortality using IL-1 blockade is subjected to notable caveats while that for IL-6 blockade is suboptimal. We discuss critical factors in determining appropriate inflammatory [269] cytokine/chemokine targets timing and combination of treatments to prevent COVID-19 mortality [270] (Figure 70).

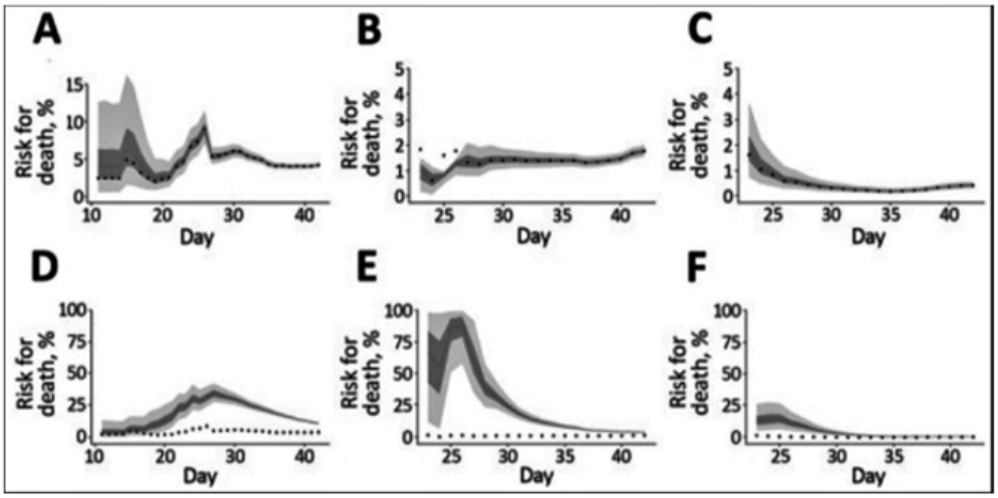


Figure 70: Temporal variation of risk for death (Kenji Mizumoto, Gerardo Chowell, 2020) associated with corona virus disease in 3 areas in China, January 1–February 11, 2020. Observed and posterior estimates of

A. crude case-fatality ratio in Wuhan,

B. Hubei Province excluding Wuhan, and

C. China excluding Hubei Province, and

D. time-delay adjusted case-fatality ratio in Wuhan,

E. Hubei Province excluding Wuhan, and

F. China excluding Hubei Province. Day 1 corresponds to January 1, 2020. Black dots show crude case-fatality ratio, light gray area shows 95% credibility interval for posterior estimates, and dark gray area shows 50% credibility intervals for posterior estimates.

The 30-day death rate of cancer patients with or without [271] documented SARS-COV-2 infection is poor but the majority of deaths occur in RT-PCR–negative patients. Fifty-five of the 302 (18.2%) patients with suspected COVID-19 had detectable SARS-COV-2 with RT-PCR in nasopharyngeal samples. RT-PCR–positive patients were older had more frequently haematological malignancies respiratory symptoms and suspected COVID-19 pneumonia of computed tomography (CT) scan. After seeing the Disaster [272] resulting from COVID-19 Pandemic in last five months all over the world; where almost 370;000 people died and approximately 6 Million people are sick due to COVID-19. There is urgent need of VACCINE of COVID-19 Pandemic and there is news that may be Vaccine could be available in December 2020 or later. The

lesson learned is that we in Twenty first century do not have capability to develop immediate Medicines or Vaccines for new disease. Medical Scientists need to study [272] more and Medical Science need more hard work to learn the diseases and their urgent treatment.

A new methodology Patient Information Based Algorithm (PIBA) [273] has been adapted to process the data and used to estimate the death rate of COVID-19 in real-time. Assumption is that the number of days from inpatients to death fall into a pattern of normal distribution and the scores in normal distribution can be obtained by observing 33 death cases and analysing the data. We selected 5 scores in normal distribution of these durations as lagging days which will be used in the following estimation of death rate. We calculated each death rate on accumulative confirmed cases with each lagging day from the current data and then weighted every death rate with its corresponding possibility to obtain the total death rate on each day. While the trendline of these death rate curves meet the curve of current ratio between accumulative death cases and confirmed cases at some points in the near future we [273] considered that these intersections are within the range of real death rates.

Many researchers have been exclusively asked whether high temperature during summer can slow down the spread of the COVID-19 as it has with other seasonal flues [274]. The machine learning algorithms employed in this work estimate the impact of weather variables such as temperature and humidity on the transmission of COVID-19 by extracting the [274] relationship between the number of confirmed cases and the weather variables on certain regions. Modern Medical science inventions and latest treatment [275] has helped the people to live longer and enjoy healthy life as compare to past decades. Although still there is no Vaccination or treatment available for COVID-19 Pandemic but due to Medical science and technology still supportive treatment is available. Currently Dexamethasone; Remdisivir; Favipiravir; Azithromycin and Plasma therapy has shown some promising results against COVID-19 Novel Cov. Preventions such as Hand washing for 40 seconds; Isolation wearing mask N95 [275] others in crowded places also help to reduce the numbers of COVID-19 Cases.

The impact of the COVID-19 pandemic on all-cause mortality [276] was considerably greater than that indicated by official counts of victims. Limited testing capacity and causes of death other than COVID-19 could have contributed to the increase in overall mortality rates. The nationwide number of excess deaths and COVID-19 deaths was 26;701 and 13;710 respectively with a difference of 12;991. The NCIEM in different regions showed a direct correlation with COVID-19 mortality ($r2 = 0.61$; $p < 0.001$) and total cases ($r2 = 0.30$; $p = 0.012$) and an inverse correlation with cases/total tests ratio ($r2 = 0.49$; $p = 0.001$). Direct correlations were also found with the proportion of institutionalised elderly whereas inverse correlations were observed with prevalence of [276] diabetes cardiovascular mortality and density of general practitioners.

COVID-19 is not deadly early in life but mortality [277] increases exponentially with age which is the strongest predictor of mortality. Mortality is higher in men than in women because men age faster and it is especially high in patients with age-related diseases such as diabetes and hypertension because these diseases are manifestations of aging and a measure of biological age. At its deepest level aging (a program-like continuation of developmental growth) is driven by inappropriately high cellular functioning. The hyperfunction theory of quasi-programmed aging explains why COVID-19 vulnerability (lethality) is an age-dependent syndrome linking it to other age-related diseases. It also explains inflammaging and immune senescence hyperinflammation; hyper thrombosis; and cytokine storms all of which are associated with COVID-19 vulnerability. Anti-aging interventions such as rapamycin may slow aging and [277] age-related diseases potentially decreasing COVID-19 vulnerability.

World Dashboard of COVID-19 and Global Statistics

Based on the results of the study it was concluded [278] that the SEIR model could be a reference model for the spread of COVID-19 in Indonesia. Analysis of the model provides an overview of global stability in the spread of COVID-19 and also provides information if Indonesia is in COVID-19 endemic status. Then the simulation results provide a predictive picture of the number of COVID-19 cases in Indonesia and also show that vaccines can accelerate COVID-19 healing and the isolation period can slow the spread of COVID-19 in Indonesia. The results obtained can be used as a reference for early prevention of the spread of COVID-19 in Indonesia. Numerical simulation models use secondary data on the number of COVID-19 cases in Indonesia. The results obtained are the SEIR model for COVID-19 model analysis yields global stability from the spread of COVID-19 The results of the analysis [278] also provide information if no vaccine Indonesia is endemic COVID-19.

Although governments imposing numerous containment [279] and social distancing measures the need for the healthcare systems has dramatically increased and the effective management of infected patients becomes a challenging problem for hospitals. Recently deep learning models demonstrated important improvements when handling time-series data in different applications. This paper presents a comparative study of five deep learning methods to forecast the number of new cases and recovered cases. Specifically; simple Recurrent Neural Network (RNN) Long short-term memory (LSTM) Bidirectional LSTM (BiLSTM) Gated recurrent units (GRUs) and Variational AutoEncoder (VAE) algorithms have been applied for global forecasting of COVID-19 cases based on a small volume of data. This study is based on daily confirmed

and recovered cases collected from six countries namely Italy; Spain; France; China; USA; and Australia. Results demonstrate the promising potential of [279] the deep learning model in forecasting COVID-19 cases and highlight the superior performance of the VAE compared to the other algorithms.

All programs promptly responded to the pandemic by making [280] appropriate changes to suspend elective surgery and to limit patient care to emergent and urgent services. OMFS training programs should give more consideration to provide residents with adequate stress reduction resources to maintain their wellbeing and training to minimize exposure risk during an evolving global epidemic. The survey response rate from OMFS program directors was 35% (33/95) with most responses from states with high incidence of COVID19. All OMFS programs (100%) implemented guidelines to suspend elective and non-urgent surgical procedures and limited ambulatory clinic visits by third week of March with an average date of March 16th; 2020 (Date range March 8th -23rd). Programs used telemedicine (40%) and modified in-person visit (51%) protocols for dental and maxillofacial emergency triage to minimize exposure risk of HCP to SARS CoV2. PPE shortage was experienced by 51% of the programs. Almost two-thirds (63%) of the respondents recommended the use of a filtered respirator (i.e.; N95 respirator) with full face shield as their preferred PPE while 21% recommended Powered Air Purifying Respirators (PAPRs) [280] during OMFS procedures. Only (73%) of the programs had resources for resident wellness and stress reduction [281] (Figure 71).

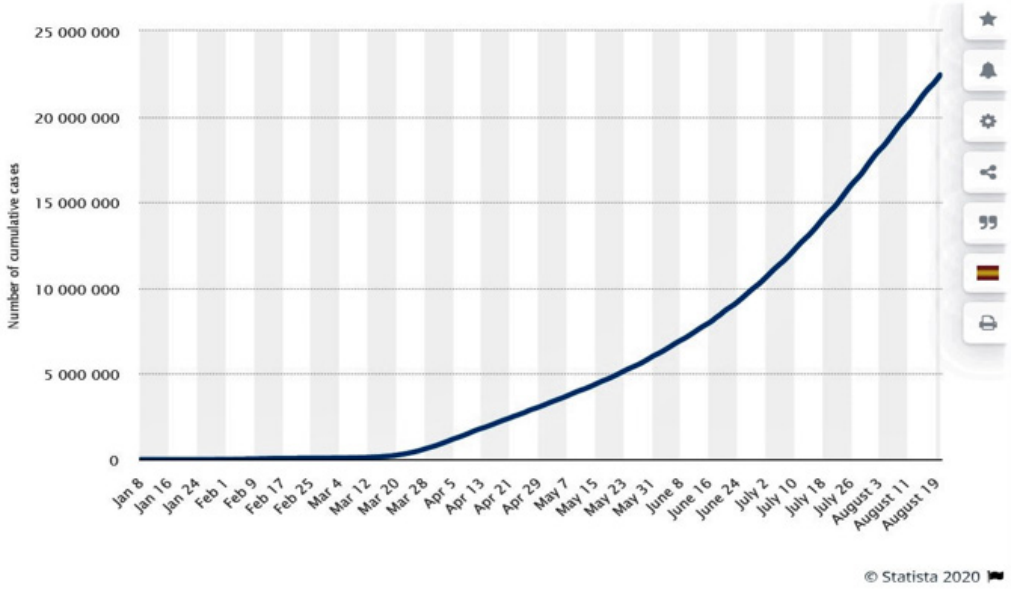


Figure 71: Number of Cumulative cases of COVID-19 worldwide from January 8 to August 20, 2020: (363) Statistica, 2020).

Pre-existing diabetes is significantly associated with [282] greater risk of severe/critical illness and in-hospital mortality in patients admitted to hospital with COVID-19. We systematically searched PubMed Scopus and Web of Science from 1st January 2020 to 15th May 2020 for observational studies of patients admitted to hospital with COVID-19. Meta-analysis was performed using random-effects modelling. A total of 83 eligible studies with 78;874 hospitalized patients with laboratory-confirmed COVID-19 were included. The pooled prevalence of established diabetes was 14.34% (95% CI 12.62–16.06%). However; the prevalence of diabetes was higher in non-Asian vs. Asian countries (23.34% [95% CI 16.40–30.28] vs. 11.06% [95% CI 9.73–12.39]); and in patients aged ≥60 years vs. those aged <60 years (23.30% [95% CI 19.65–26.94] vs. 8.79% (95% CI 7.56–10.02)). Pre-existing diabetes was associated with an approximate twofold higher risk of having severe/critical COVID-19 illness (n = 22 studies; random-effects odds ratio 2.10; 95% CI 1.71–2.57; I2 = 41.5%) and ~threefold increased risk of in-hospital mortality (n = 15 studies; random-effects odds ratio 2.68; 95% CI 2.09–3.44; I2 = 46.7%). [282] Funnel plots and Egger's tests did not reveal any significant publication bias.

Understanding the transmission dynamics of the infection [283] in each country which got affected on a daily basis and evaluating the effectiveness of control policies are critical for our further actions. To date the statistics of COVID-19 reported cases show that more than 80% of infected are mild cases of disease around 14% of infected have severe complications and about 5% are categorized as critical disease victims. Today's report (5th April 2020 daily updates in the prepared website) shows that the confirmed cases of COVID-19 in the United States Spain Italy; and Germany are 308850; 126168; 124632; and 96092; respectively. Calculating the total case fatality rate (CFR) of Italy (4th April 2020) about 13.3% of confirmed cases have passed away. Compared with South Korea's rate of 1.8% (seven times lower than Italy) and China's

4% (69% lower than Italy) the CFR of Italy is too high. Some effective policies that yielded significant changes in the trend of cases were the lockdown policy in China Italy; and Spain (the effect observed after some days); the shutdown of all [283] nonessential companies in Hubei (the effect observed after 5 days) combined policy in South Korea; and reducing working hours in Iran [284] (Figure 72).

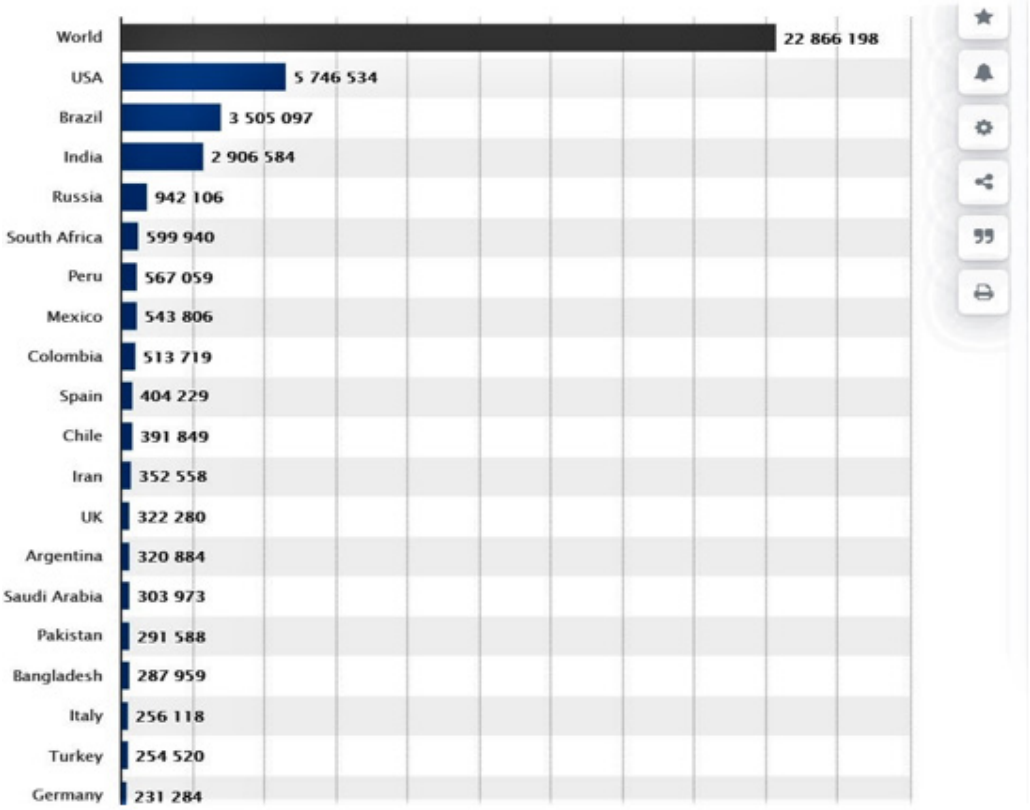


Figure 72: Number of coronavirus (COVID-19) cases worldwide as of August 21, 2020, by country. (364) Statistica, 2020).

The relationship between appraisal of medias positive and [285] negative facets vary with demographic differences in mental health resiliency. The media repertoire approach is an important tool in studies that focus on assessing the benefits and harms of screen overuse in different populations especially in the context of the COVID-19 pandemic. More than 90% of the survey respondents were in Canada and the east coast of the United States. From 685 completed responses 169 respondents were [285] very stressed and 452 were slightly worried about the pandemic. Current Pandemic of COVID-19 has [286] taught us that we in the twenty first century is not ready to provide health care to vulnerable community such as elders; children and sick people with chronic illness. Such vulnerable people with bad health and low socio-economic status are more prone to get effected by COVID-19 novel corona virus. More serious work needed to be done by Global health agencies and world organizations such as WHO; CDC; UN; UNESCO; UNHCR others. Governments and health departments has to make useful health [286] policies to implement in deadlines with serious accountability to fight against any Epidemic or Pandemic.

Pre-existing type II diabetes/kidney diseases and living in [287] high population density areas were associated with high risk for COVID-19 susceptibility and poor prognosis. Association of risk factors with COVID-19 outcomes differed by race. NHAA patients were disproportionately affected by obesity and kidney disease. We identified factors associated with testing and testing positive for COVID-19; being hospitalized; requiring intensive care unit (ICU) admission; and mortality (in/out-patient during the time frame). Factors included race/ethnicity; age; smoking; alcohol consumption; healthcare utilization; and residential-level socioeconomic characteristics (SES; i.e.; education; unemployment; population density; and poverty rate). Medical comorbidities [287] were defined from the International Classification of Diseases (ICD) codes; and were aggregated into a comorbidity score.

Adolescents poor dietary habits increase their [288] subsequent risk of degenerative diseases such as obesity diabetes cardiovascular pathologies; etc. Our aim was to study nutritional modifications during COVID-19 confinement in adolescents aged 10 to 19 years compare them with their usual diet and dietary guidelines and identify variables that may have influenced changes. Data were collected by an anonymous online questionnaire on food intake among 820 adolescents from Spain Italy Brazil Colombia; and Chile. The results show that

COVID-19 confinement did influence their dietary habits. In particular we recorded modified consumption of fried food sweet food legumes; vegetables; and fruits. Moreover; gender family members at home watching TV during mealtime country of residence and maternal education were diversely correlated with adequate nutrition during COVID-19 confinement. Understanding the adolescents' nutrition behaviour during COVID-19 lockdown will help [288] public health authorities reshape future policies on their nutritional recommendations in preparation for future pandemics [289] (Figure 73). Effectively designing and evaluating public health responses [290] to the ongoing COVID-19 pandemic requires accurate estimation of the prevalence of COVID-19 across the United States (US).

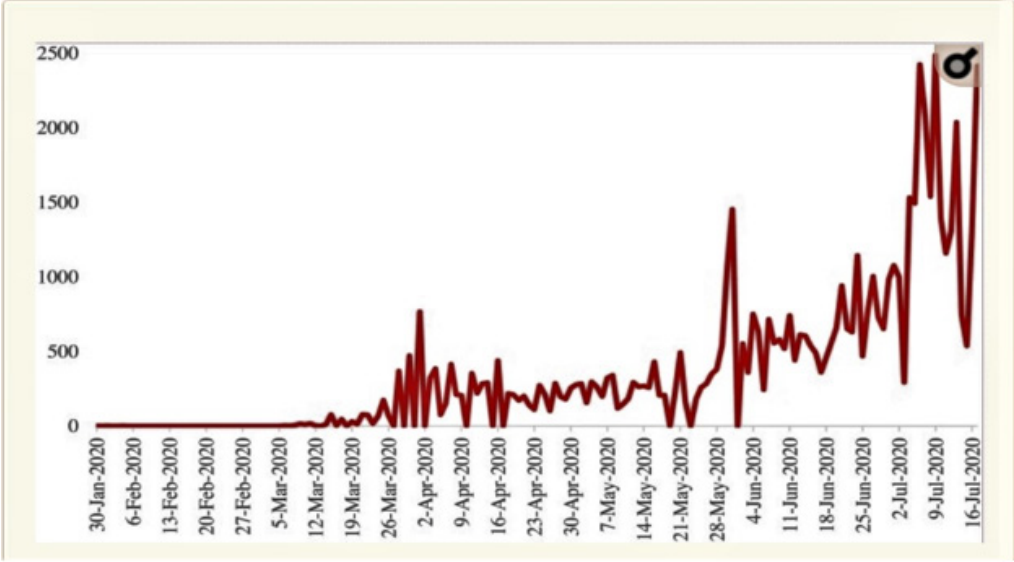


Figure 73: Confirmed COVID-19 cases in the Philippines as of July 17th, 2020 (https://covid19.who.int/) Yogi Tri Prasetyo, et al. [289].

Equipment shortages and varying testing capabilities have however hindered the useful-ness of the official reported positive COVID-19 case counts. We introduce four complementary approaches to estimate the cumulative incidence of symptomatic COVID-19 in each state in the US as well as Puerto Rico and the District of Columbia using a combination of excess influenza-like illness reports COVID-19 test statistics COVID-19 mortality reports and a spatially structured epidemic model. Across our four approaches emerges the consistent conclusion that on April 4; 2020; the estimated case count was 5 to 50 times higher than the official positive test counts across the different states. Nationally our estimates of COVID-19 symptomatic cases as of April 4 have a likely range of 2.2 to 4.9 million with possibly as many as 8.1 million cases up to 26 times greater than the cumulative confirmed cases of about 311;000. Extending our method to May 16; 2020 we estimate that [290] cumulative symptomatic incidence ranges from 6.0 to 10.3 million; as opposed to 1.5 million positive test counts.

Community pharmacists in the UK are facing considerable [291] challenges in terms of personal protection and the delivery of pharmacy services. Inappropriate behaviour from patients and carers towards community pharmacists require urgent attention to ensure a safe working place for all community pharmacists. A total of 206 pharmacists responded to the survey with representations from England Northern Ireland; Scotland; and Wales. The majority of pharmacists (>75% or above) reported an increase in customer traffic to their pharmacy and were asking relevant questions from patients with flu-like symptoms before signposting them to the appropriate care. Most pharmacists (>85%) were maintaining a safe distance of 2 m from customers and 72% were wearing an N95 protective mask and 28% were using protective gloves and apron in addition to safe distancing and protective masks. Ninety-nine percent of pharmacists reported drug shortages with 38% and 26% reported significant drug shortages and critical drug shortages causing disruptions beyond over the counter medicines. Eighty-nine percent pharmacists reported inappropriate behaviour from patients or [291] carers with 31% and 16% reported it to be a regular or frequent problem respectively.

In conclusion this meta-analysis indicated that chest CT scan [292] had a high sensitivity in diagnosis of patients with COVID-19. Therefore; CT can potentially be used to assist in the diagnosis of COVID-19. A total of 103 studies with 5;673 patients were included. Using reverse transcription polymerase chain reaction (RT-PCR) results as reference a meta-analysis based on 64 studies estimated [292] the sensitivity of chest CT imaging in COVID-19 was 99% (95% CI; 0.97–1.00). Technology in medical Sciences; inventions; Discovery of new Medicines [293] and Surgical Instruments are Blessings for Mankind. Latest technologies such as MRI Scans; CT Scans; Chemotherapy; Radiotherapy; Nuclear Technology; X rays/ Ultrasound; Latest Laparoscopic surgery; Endoscopy; Angioplasty others are treating more ill patients than ever before.

But more Medical research is needed to find the treatment for COVID-19 pandemic; Ebola; MERS; Avian Influenza; Swine Flu and other Viral diseases. Urgent research institutes [293] needed to build up for the discovery of new Vaccines when needed in times of COVID-19 Pandemic.

The clinical management of COVID-19 is challenging. Medical imaging [294] plays a critical role in the early detection clinical monitoring and outcomes assessment of this disease. Chest x-ray radiography and computed tomography are the standard imaging modalities used for the structural assessment of the disease status while functional imaging (namely; positron emission tomography) has had limited application. Artificial intelligence can enhance the predictive power and utilization of these imaging approaches and new approaches focusing on detection stratification and prognostication are showing encouraging results. We review the current landscape of these imaging modalities and artificial intelligence approaches as applied in COVID-19 management. The volume of evidence and experience with imaging for COVID-19 is growing exponentially. As we enter what might be the later stages of the pandemic; hopefully; we are becoming more adept [294] and nuanced in how we use imaging and AI to manage patients with COVID-19 better.

It has affected more than 40 million people in 216 countries. Almost [295] in all the affected countries the number of infected and deceased patients has been enhancing at a distressing rate. As the early prediction can reduce the spread of the virus it is highly desirable to have intelligent prediction and diagnosis tools. The inculcation of efficient forecasting and prediction models may assist the government in implementing better design strategies to prevent the spread of virus. In this paper a state-of-the-art analysis of the ongoing machine learning (ML) and deep learning (DL) methods in the diagnosis and prediction of COVID-19 has been done. Moreover; a comparative analysis on the impact of machine learning and other competitive approaches like mathematical and statistical models on COVID-19 problem has been conducted. Finally; some important research directions for further research on COVID-19 are highlighted which may facilitate the researchers and technocrats to develop competent intelligent [295] models for the prediction and forecasting of COVID-19 real time data.

COVID-19 Free Countries and Affected Countries

Autopsy studies have established that COVID-19 is a [296] systemic disease with major involvement of the cardiovascular and pulmonary systems and with the expected accompaniment of major activation of the inflammatory and immune systems. The autopsy studies also provide evidence that SARS-COV-2 patients have a baseline hypercoagulable state and are at increased risk for pulmonary thrombotic microangiopathy as well as the development of deep vein thromboses and major pulmonary thromboembolism. The initial approach to acute therapy for COVID-19 patients with life-threatening respiratory failure has involved administration of supplemental oxygen artificial ventilation and use of the extracorporeal membrane oxygenator when necessary. [296] Additional approaches and strategies for treatment of COVID-19 patients are actively being pursued and they are clearly needed.

The coronavirus disease 2019 (COVID-2019) that emerged in Wuhan China [297] has rapidly spread to many countries across all six WHO regions. However; its pathobiology remains incompletely understood and many efforts are underway to study it worldwide. Current Pandemic of COVID-19 novel corona virus has taught us a lesson that [298] Global Health Agencies and Governments of the countries are not prepare for such Pandemic. The Governments has acted slowly or irresponsibly for the fight against COVID-19 Pandemic. Due to slow action to implement Preventive actions against COVID-19 approximately 300;000 people have lost their lives and more than four million people are Infected across the world. Better preparations [298] are needed in the future to fight against such a cruel Pandemic disease [299] (Figure 74).

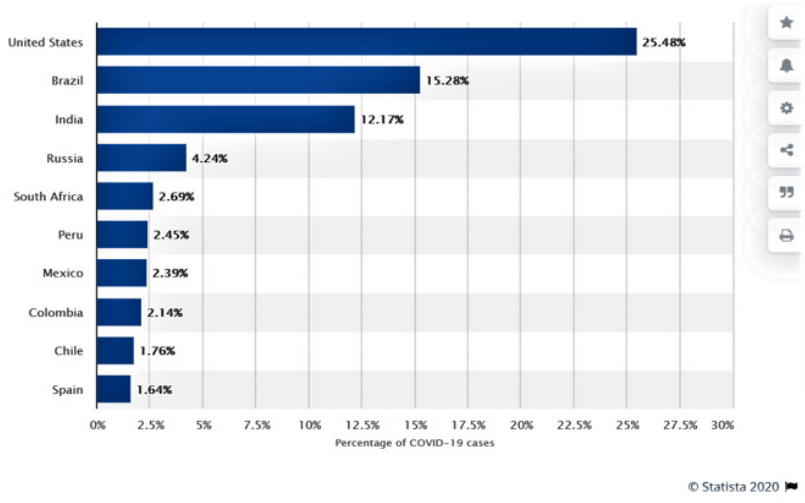


Figure 74: Distribution of coronavirus (COVID-19) cases worldwide as of August 17, 2020. (365) Statistica, 2020).

In the northern German Federal State of Hamburg all deaths [300] of Hamburg citizens with ante- or post-mortem PCR-confirmed SARS-CoV-2 infection have been autopsied since the outbreak of the pandemic in Germany. Our evaluation provides a systematic overview of the first 80 consecutive full autopsies. A proposal for the categorisation of deaths with SARS-CoV-2 infection is presented (category 1 definite COVID-19 death category 2: probable COVID-19 death category 3 possible COVID-19 death with an equal alternative cause of death category 4 SARS-CoV-2 detection with cause of death not associated to COVID-19). In six cases SARS-CoV-2 infection was diagnosed post-mortem by a positive PCR test in a nasopharyngeal or lung tissue swab. In the other 74 cases SARS-CoV-2 infection had already been known antemortem. The deceased were aged between 52 and 96 years (average 79.2 years; median 82.4 years). In the study cohort 34 deceased were female (38%) and 46 males (62%). Overall; 38% of the deceased were overweight or obese. All deceased except for two women in whom no significant pre-existing conditions were found autoptically had relevant comorbidities (in descending order of frequency)

1. Diseases of the cardiovascular system
2. Lung diseases
3. Central nervous system diseases
4. Kidney diseases and
5. Diabetes mellitus.

A total of 76 cases (95%) were classified as COVID-19 deaths [300] corresponding to categories 1–3. Four deaths (5%) were defined as non-COVID-19 deaths with virus-independent causes of death [301] (Figure 75).

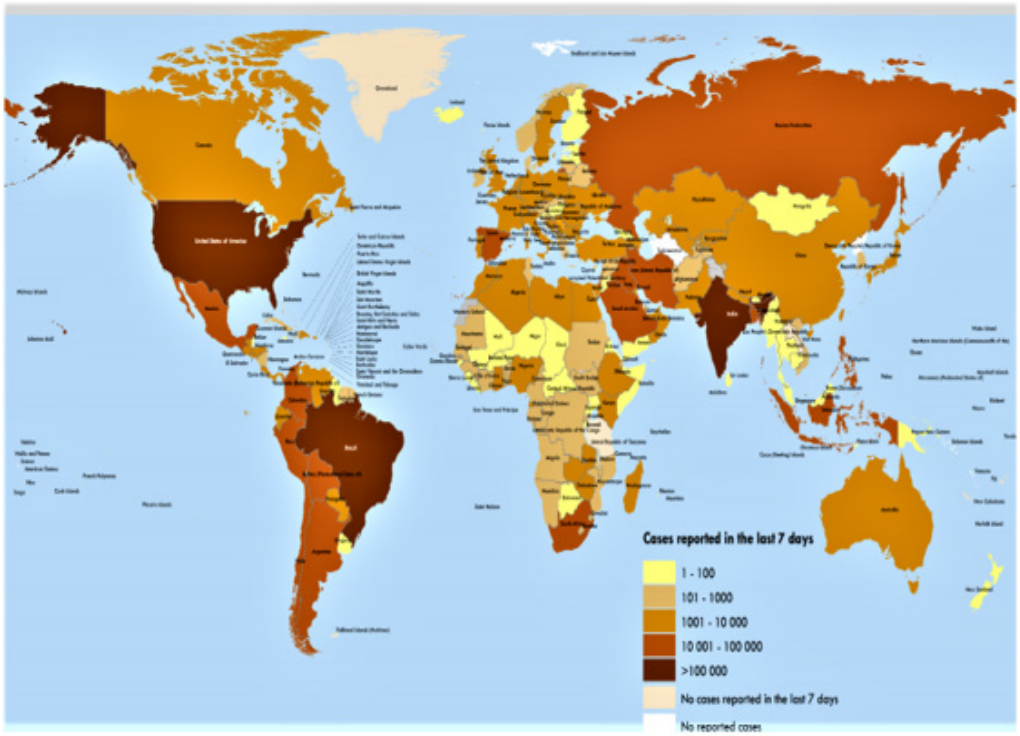


Figure 75: Surveillance: Number of confirmed COVID-19 cases reported in the last seven days by country, territory or area, 30 July to 5 August. (WHO Corona Virus situation report, 2020).

The COVID-19 pandemic which started around December 2019 has at present resulted in over 450;000 deaths globally and approximately 1% of these deaths have been reported in Africa [302]. Despite the high prevalence of COVID-19 risk factors namely hypertension diabetes chronic pulmonary disease cardiovascular diseases (CVDs) such as rheumatic heart disease; compromised immunity and obesity; low case fatality rates have been recorded in many parts of Africa so far. COVID-19 severity has previously been shown to be worse in patients with CVD and hypertension. We observed the severity of COVID-19 and mortality rates in Africa and compared outcomes with prevalence of established risk factors (hypertension and CVD). We stratified data as per the United Nations 5 African subregions. North African countries show a positive association between the risk factors and the mortality rates from COVID-19. However; we observed discordant patterns in the relationship

between COVID-19 and either CVD or hypertension in sub-Saharan African countries. Here we also review the pathogenesis of SARS-CoV-2 infection and how it worsens CVD and postulate that the differences in modulation of the renin–angiotensin–aldosterone system (RAAS) axis which controls angiotensin [302] converting enzyme (ACE)/ACE2 balance may be an important determinant of COVID-19 outcomes in Africa.

We reached a consensus on a core data set [303] and established data sharing processes with multiple partners to address an urgent need for information to guide clinical practice. First results show that partners are motivated to share data to attain the ultimate joint goal better understand the effect of COVID-19 in PwMS. Numerous stakeholders were brought together. Small dedicated interdisciplinary task forces were created to speed-up the formulation of the study design and work plan. First step was to agree upon a COVID-19 MS core data set. Second; we worked on providing a user-friendly and rapid pipeline to share COVID-19 data at a global scale. The COVID-19 MS core data set was agreed within 48 hours. To date 23 data collection [303] partners are involved and the first data imports have been performed successfully. Data processing and analysis is an on-going process.

In particular individuals belonging to racial/ethnic [304] minorities in the U.S. and other countries have been significantly and disproportionately impacted. Multiple and complex socioeconomic factors have long played a role in increasing the risk for diabetes and now for COVID-19. Since the pandemic began the global healthcare community has accumulated invaluable clinical experience on providing diabetes care in the setting of COVID-19. In addition; understanding of the pathophysiological mechanisms that link these two diseases is being developed. The current clinical management of diabetes is a work in progress requiring a shift in patient-provider interaction beyond the walls of clinics and hospitals the use of tele-medicine when feasible innovative patient education programs; strategies to ensure medication and glucose testing availability and affordability as well as numerous ideas on how to improve meal plans and physical activity. Notably this worldwide experience offers us the possibility to not [304] only prepare better for future disasters but also transform diabetes care beyond the COVID-19 era.

Here this study provides an alarming overview of the unpreparedness [305] of Libyan hospitals for detecting and treating patients with COVID-19 and limiting the spread of the pandemic. A cross-sectional survey evaluating hospital and intensive care unit's capacity and readiness was performed from 16 leading Libyan hospitals in March 2020. Out of 16 hospitals; the highest hospital capacity was 1000 in-patient beds while the lowest was 25 beds with a median of 200 (IQR 52–417; range 25–1000) hospital beds. However; a median of only eight (IQR 6–14; range 3–37) available functioning ICU beds were reported in these hospitals. Only 9 (IQR 4.5–14; range 2–20) mechanical ventilators were reported and none of the hospitals had a reverse transcription-polymerase chain reaction machine for COVID-19 testing. Moreover; they relied on one of two central laboratories located in major cities. Our PPE survey revealed that 56.7% hospitals lacked PPE and 53% of [305] healthcare workers reported that they did not receive proper PPE training.

There is a lack of different forms of PPE in the US and Pakistan [306]. Doctors from both countries reported that they had been forced to work without PPE. Compared to the US more doctors from Pakistan reported having faced discrimination in receiving PPE. After informed consent 574 doctors (60.6% from Pakistan and 39.4% from the US) were included in the analysis. The majority of the participants were females (53.3%); and the mean age of the participants was 35.3 ± 10.3 years. Most doctors (47.7%) were from medicine and allied fields. Among the participants; 87.6% of doctors from the US reported having access to masks/N95 respirators; 79.6% to gloves 77.9% to face-shields or goggles; and 50.4% to full-suit/gown. Whereas doctors in Pakistan reported to have poor availability of PPE with only 37.4% having access to masks/N95 respirator 34.5% to gloves; 13.8% to face-shields or goggles; and 12.9% to full-suit/gown. The reuse of PPE was reported by 80.5% and 60.3% physicians from the US and Pakistan respectively. More doctors from Pakistan (50.6%) reported [306] that they had been forced to work without PPE compared to doctors in the US (7.1%).

As a southern hemisphere country like South Africa [307] stands now as the most COVID-19 and HIV affected country in Africa we use in this paper recent COVID-19 data to provide a statistical and comparative analysis that may alert southern hemisphere countries entering the winter season. After that we use a generalized simple mathematical model of HIV-COVID-19 together with graphs curves and tables to compare the pandemic situation in countries that were once the epicentre of the disease such as China Italy; Spain; United Kingdom (UK) and United States of America (USA). We perform stability and bifurcation analysis and show that the model contains a forward and a backward bifurcation under certain conditions. We also study different scenarios of stability/instability equilibria for the model. The fractional (generalized) COVID-19 model is solved numerically and a predicted prevalence for the COVID-19 is provided. Recall that Brazil and South Africa share number of similar social features like Favellas (Brazil) and Townships (South Africa) with issues like promiscuity poverty [307] and where social distancing is almost impossible to observe.

It is observed that the countries having routine BCG vaccination [308] programme had shown to have lower incidence of COVID-19 suggesting some protective mechanisms of BCG against COVID-19 in such countries. Countries like India despite vast population density and

other adversities and growing numbers of COVID19 infections the mortality rate and severity of COVID has been low in comparison to TB non-endemic countries (like Europe and USA). In addition; there are evidences that BCG vaccination offers partial protection and survival in low-income countries where tuberculosis is prevalent. The nonspecific effects (NSEs) of immune responses induced by BCG vaccination protect against other infections are seems to be due to its immunological memory eliciting lymphocytes response and trained immunity. The protective effect on other viral infection in humans are believed to be mediated by heterologous lymphocyte activation and the initiation of innate immune memory may be applicable to SARS CoV2. The BCG vaccination at birth does not have protective effect beyond [308] childhood against COVID-19. In adult; there might be some other factors dampening the virulence and pathogenicity of COVID-19.

The COVID-19 pandemic is exceptional. [309] Its effect will likely be imprinted on each individual involved. Extensive stressors will emerge or become worsened. Many medical staff workers will be harmfully psychologically affected. In this general review we examined the literature about the psychological effects of COVID-19 pandemic. In total 65 papers were reviewed using the Medline computer database. Only publications in English were selected. Children are likely to be experiencing worry anxiety and fear and older people are also those with underlying health conditions having been identified as more vulnerable to COVID-19 can be extremely frightening and very fear-inducing. China and several other countries took strict isolation measures. Medical staff and affiliated healthcare workers [309] are under both physical and psychological pressure.

COVID-19 Guidelines and the Significant use of covid-19 Test Kit

At this moment the world lives under the [310] SARS-CoV-2 outbreak pandemic. As Otolaryngologists Head & Neck Surgeons we need to perform and participate in examinations and procedures within the head and neck region and airway that carry a particularly high risk of exposure and infection because of aerosol and droplet contamination. One of those surgical procedures in demand at this moment is tracheostomy due the increasing ICU admissions. This review of international guidelines for tracheostomy in COVID-19 infected patients aims to summarize in a systematic way the available recommendations indications timing [310] technique and safety measures for tracheostomy; from all over the world.

Through contact with Taiwan No 19-case patient [311] on 27th January COVID-19 patients A and B were infected. Both patients had no identified comorbidities and developed mild illness with temporal fever persistent cough and lung interstitial infiltrates. Owing to the persistence of positive SARS-CoV-2 in respiratory specimen the two COVID-19 patients are still in the isolation rooms despite recovery until 10th of March. The results of Film ArrayTM Respiratory Panel revealed 22 of the 41 non-COVID-19 patients were infected by particular pathogens. In general; seasonal respiratory pathogens are more prevalent than SARS-CoV-2 in symptomatic patients in non- COVID-19 endemic area during the flu season. Since all patients shared similar clinical and laboratory findings expanded surveillance of detailed exposure history for [311] suspected patients and application of rapid detection tools are highly recommended.

We present suggestions for how the risk of transmission [312] by and to anaesthetists can be minimised and how personal protective equipment policies relate to COVID-19 pandemic context. The group has endeavoured to produce a minimum number of recommendations to highlight the strengths to be retained in the 7 predefined areas;

1. Protection of staff and patients;
2. Benefit/risk and patient information;
3. Preoperative assessment and decision on intervention;
4. Modalities of the pre anaesthesia consultation;
5. Specificity of anaesthesia and analgesia;
6. Dedicated circuits and;
7. Containment exit type of interventions.

The SFAR Guideline panel provides 51 statements on anaesthesia management in the context of COVID-19 pandemic. After one round of discussion and various amendments a [312] strong agreement was reached for 100% of the recommendations and algorithms.

The time required to perform the necessary randomized controlled trials [313] a systematic literature review and meta-analysis of these trials to then create; accept; promulgate; and educate the practicing clinicians to use the evidence-based clinical guidelines is typically measured in years. When the severe acute respiratory syndrome novel coronavirus-2 (SARS-nCoV-2) pandemic commenced in Wuhan China at

the end of 2019 there were few available clinical guidelines to deploy; let alone adapt and adopt to treat the surge of coronavirus disease 2019 (COVID-19) patients. The aim is to first explain how clinical guidelines on which bedside clinicians have grown accustomed can be created in the midst of a pandemic with an evolving scientific understanding of the pathophysiology of the hypercoagulable state. The second is to adapt and adopt current venous thromboembolism diagnostic and treatment guidelines while relying on the limited available observational [313] reporting of COVID-19 patients to create a comprehensive clinical guideline to treat COVID-19 patients.

So far; no pharmacological intervention was proven effective [314] and safe to warrant its use in the routine treatment of COVID-19 patients therefore such patients should ideally be treated in the context of clinical trials. The recommendations herein provided will be revised continuously aiming to capture newly generated evidence. Eleven recommendations were issued based on low or very-low level evidence. We do not recommend the routine use of hydroxychloroquine chloroquine azithromycin; lopinavir/ritonavir; corticosteroids; or tocilizumab for the treatment of COVID-19. Prophylactic heparin should be used in hospitalized patients however no anticoagulation should be provided for patients without a specific clinical indication. Antibiotics and oseltamivir should only be considered for patients [314] with suspected bacterial or influenza coinfection respectively.

Since the first case was reported in Wuhan Hubei Province China [315] on December 12; 2019; Coronavirus disease 2019 (COVID-19) has spread widely to other countries since January 2020. As of April 16; 2020; 10635 confirmed cases have been reported; with 230 deaths in Korea. COVID-19 patients may be asymptomatic or show various clinical manifestations including acute symptoms such as fever fatigue sore throat; pneumonia presenting as acute respiratory distress syndrome; and multiple organ failure. As COVID-19 has such varied clinical manifestations and case fatality rates no standard antiviral therapy regimen has been established other than supportive therapy. In the present guideline we aim to introduce potentially helpful antiviral and other drug therapies based on in vivo and in vitro research and [315] clinical experiences from many countries.

Numerous preventative strategies and non-pharmaceutical [316] interventions have been employed to mitigate the spread of disease including careful infection control the isolation of patients and social distancing. Management is predominantly focused on the provision of supportive care with oxygen therapy representing the major treatment intervention. Medical therapy involving corticosteroids and antivirals have also been encouraged as part of critical management schemes. However; there is at present no specific antiviral recommended for the treatment of COVID-19 and no vaccine is currently available. Despite the strategic implementation of these measures the number of new reported cases continues to rise at a profoundly alarming rate. As new findings emerge there is an urgent need for up-to-date management guidelines. In response to this call we review what is currently known regarding the [316] management of COVID-19 and offer an evidence-based review of current practice.

Guidelines available early in the covid-19 pandemic had methodological [317] weaknesses and neglected vulnerable groups such as older people. A framework for development of clinical guidelines during public health emergencies is needed to ensure rigorous methods and the inclusion of vulnerable populations. 2836 studies were identified; of which 2794 were excluded after screening. Forty-two guidelines were considered eligible for inclusion with 18 being specific to covid-19. Overall; the clinical guidelines lacked detail and covered a narrow range of topics. Recommendations varied in relation to for example; the use of antiviral drugs. The overall quality was poor particularly in the domains of stakeholder involvement applicability and editorial independence. Links between evidence and recommendations were limited. Minimal provision [317] was made for vulnerable groups such as pregnant women children and older people.

COVID-19 pandemic has posed dilemmas for the oncology community [318] across the globe. Guidelines based on limited evidence show discordance and need to be interpreted with caution. Crowd sourcing could help collate the data related to COVID-19 and generate high quality evidence-based guidelines. Majority guidelines for various types of cancers favoured a delay in treatment or a nonsurgical approach wherever feasible. These guidelines are based on a low level of [318] evidence and have significant discordance for the role and timing of surgery; especially in early tumours.

Telemedicine is a useful tool for managing patients of diabetes [319] during this lockdown period. However; there is limited data and further research is required. In view of restrictions on mobility of patients because of COVID-19 pandemic face-to-face consultations are difficult. We sought to study the feasibility of telemedicine in this scenario. PubMed and Google Scholar search engines were searched using the key terms telemedicine diabetes COVID-19 up to 31st March 2020. In addition; existing guidelines including those by Ministry of Health and Family Welfare (MOHFW) Government of India were accessed. We discuss evidence and general guidelines [319] regarding role of telemedicine in patients with diabetes along with its utility and limitations.

The severity of COVID-19 disease ranges from an asymptomatic infection [320] or mild illness to mild or severe pneumonia with respiratory failure and/or death. COVID-19 dramatically affects the pulmonary system. There is a lack of knowledge about the long-term outcomes of the

disease and the possible sequelae and rehabilitation. This clinical practice guideline includes pulmonary rehabilitation (PR) recommendations for adult COVID-19 patients and has been developed in the light of the guidelines on the diagnosis and treatment of COVID-19 provided by the World Health Organization and Republic of Turkey Ministry of Health recently published scientific literature; and PR recommendations for COVID-19 regarding basic principles of PR. In this guideline; the contagiousness of COVID-19 recommendations on limited contact of patient with healthcare providers and the evidence about [320] possible benefits of PR were taken into consideration [321] (Figure 76).

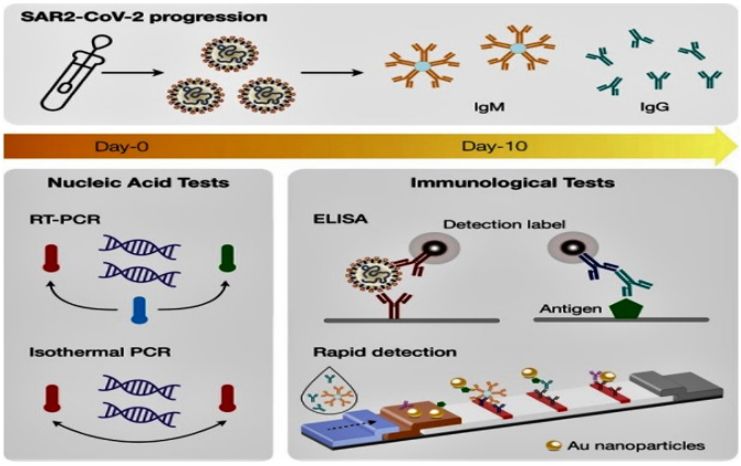


Figure 76: Tugba Kilic, et al. [321].

As the number of new COVID-19 cases and deaths [322] continue to rise steadily around the world the common goal of healthcare providers scientists and government officials worldwide has been to identify the best way to detect the novel coronavirus named SARS-CoV-2 and to treat the viral infection COVID-19. Accurate detection timely diagnosis effective treatment and future prevention are the vital keys to management of COVID-19 and can help curb the viral spread. Traditionally; biomarkers play a pivotal role in the early detection of disease aetiology diagnosis treatment and prognosis. To assist myriad ongoing investigations and innovations we developed this current article that overviews known and emerging biomarkers for SARS-CoV-2 detection COVID-19 diagnostics treatment and prognosis; and ongoing work to identify and develop more biomarkers for new drugs and vaccines. Moreover; biomarkers of socio-psychological stress the [322] high technology quest for new virtual drug screening and digital applications are described [323] (Figure 77).

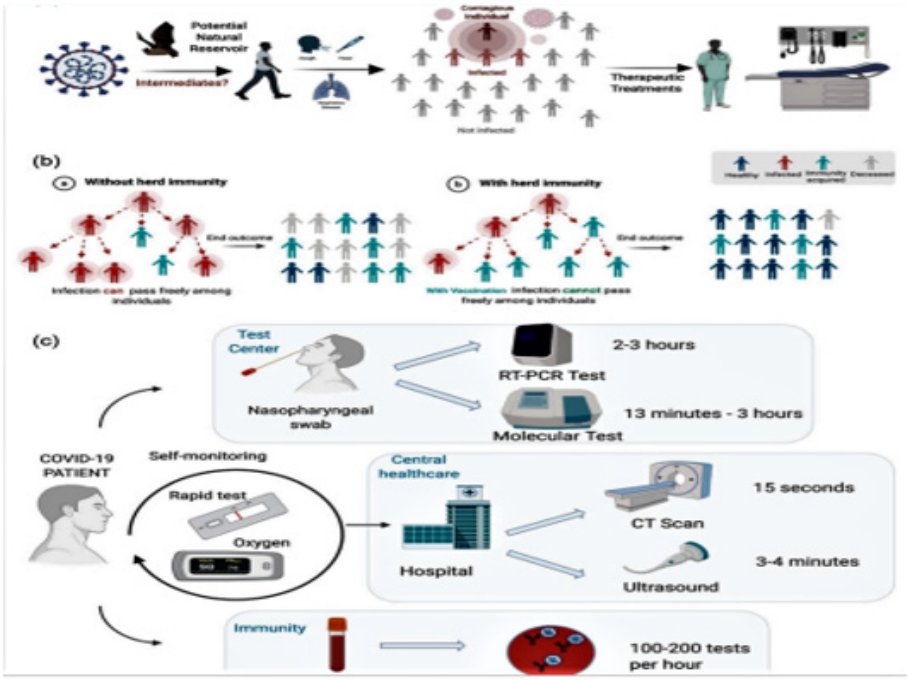


Figure 77: COVID-19 origins, transmission, immunity, and diagnostics Mayar Allam, et al. [323].

Many anaesthesia COVID-19 guidelines have emerged [324] whose underlying management principles include minimizing aerosol contamination and protecting healthcare workers. These guidelines originate from Australia and New Zealand; Canada; China; India; Italy; Korea; Singapore; the United States and the United Kingdom. These difficult airway guidelines require modifications in order to align with the principles of the anaesthetic COVID-19 guidelines. In turn most of the anaesthetic COVID-19 guidelines do not or only briefly discuss an airway strategy after failed tracheal intubation. We combine the principles from both sets of guidelines and explain the necessary modifications to the airway guidelines to form a failed tracheal intubation airway strategy in the COVID-19 patient. Valuing and a greater understanding of these [324] differences and modifications may lead to greater adherence to the new COVID-19 guidelines.

If RT-qPCR is not available the [325] combination of chest CT and IC assay may be useful for diagnosing COVID-19. We examined 139 serum specimens collected from 112 patients with COVID-19 and 48 serum specimens collected from 48 non-COVID-19 patients. The presence of IgM/IgG antibody for SARS-COV2 was determined using the One Step Novel Coronavirus (COVID-19) IgM/IgG Antibody Test. Chest CT was performed in COVID-19 patients on admission. Of the139 COVID-19 serum specimens IgM was detected in 27.8 % 48.0 %; and 95.8 % of the specimens collected within 1 week 1–2 weeks; and >2 weeks after symptom onset and IgG was detected in 3.3 %; 8.0 %; and 62.5 %; respectively. The diagnostic sensitivity of CT scan alone and in combination with the IC assay was 57.9 % (22/38) and 68.4 % (26/38) for the [325] asymptomatic patients and 74.3 % (55/74) and 82.4 % (61/74) for the symptomatic patients respectively.

COVID-19 Genome Sequence

It is well known that host cellular [326] miRNAs can directly target both viral 3 UTR and coding region of the viral genome to induce the antiviral effect. In this study we did in silico analysis of human miRNAs targeting SARS (4 isolates) and COVID-19 (29 recent isolates from different regions) genome and correlated our findings with aging and underlying conditions. We found 848 common miRNAs targeting the SARS genome and 873 common microRNAs targeting the COVID-19 genome. Out of a total of 848 miRNAs from SARS only 558 commonly present in all COVID-19 isolates. Interestingly 315 miRNAs are unique for COVID-19 isolates and 290 miRNAs unique to SARS. We also noted that out of 29 COVID-19 isolates 19 isolates have identical miRNA targets. The COVID-19 isolates Netherland (EPI_ISL_422601) Australia (EPI_ISL_413214) and [326] Wuhan (EPI_ISL_403931) showed six; four; and four unique miRNAs targets respectively.

SARS-CoV-2 transmits mainly through droplets and [327] close contact and the elder or people with chronic diseases are high-risk population. People affected by SARS-CoV-2 can be asymptomatic which brings about more difficulties to control the transmission. COVID-19 has become pandemic rapidly after onset and so far; the infected people have been above 2 000 000 and more than 130 000 died worldwide according to COVID-19 situation dashboard of World Health Organization (https://covid19.who.int). Here; we summarized the current known knowledge regarding epidemiological pathogenesis pathology clinical features comorbidities [327] and treatment of COVID-19/ SARS-CoV-2 as reference for the prevention and control COVID-19.

Significant to COVID-19 ACE2 is postulated to [328] serve as a major entry receptor for SARS-CoV-2 in human cells as it does for SARS-CoV. Many infected individuals develop COVID-19 with fever; cough; and shortness of breath that can progress to pneumonia. Disease progression promotes the activation of immune cells platelets and coagulation pathways that can lead to multiple organ failure and death. ACE2 is expressed by epithelial cells of the lungs at high level a major target of the disease as seen in post-mortem lung tissue of patients who died with COVID-19 which reveals diffuse alveolar damage with cellular fibro myxoid exudates bilaterally. Comparatively ACE2 is expressed at low level by vascular endothelial cells of the heart and kidney but may also be targeted by the virus in severe COVID-19 cases. Interestingly SARS-CoV-2 infection downregulates ACE2 [328] expression which may also play a critical pathogenic role in COVID-19.

As the time for finding a definitive and safe cure as a [329] vaccine for novel Corona Virus Disease 2019 (Covid-19) is still far there is need to study in depth about the other potential drugs which can save millions of lives due to Covid-19 pandemic. Right at the centre of the debate is the use of drug “Hydroxychloroquine” as a prophylaxis as well as a treatment strategy against Covid-19 in conjunction with azithromycin. Without a therapeutic vaccine or specific antiviral drugs and with a desperate attempt to find a cure against novel Corona Virus Disease 2019 (Covid-19). Initial studies of Covid-19 patients treated with hydroxychloroquine with or without azithromycin were shown to have mixed results with more [329] scrutiny being raised over the lack of proper design of these studies [330] (Figure 78).

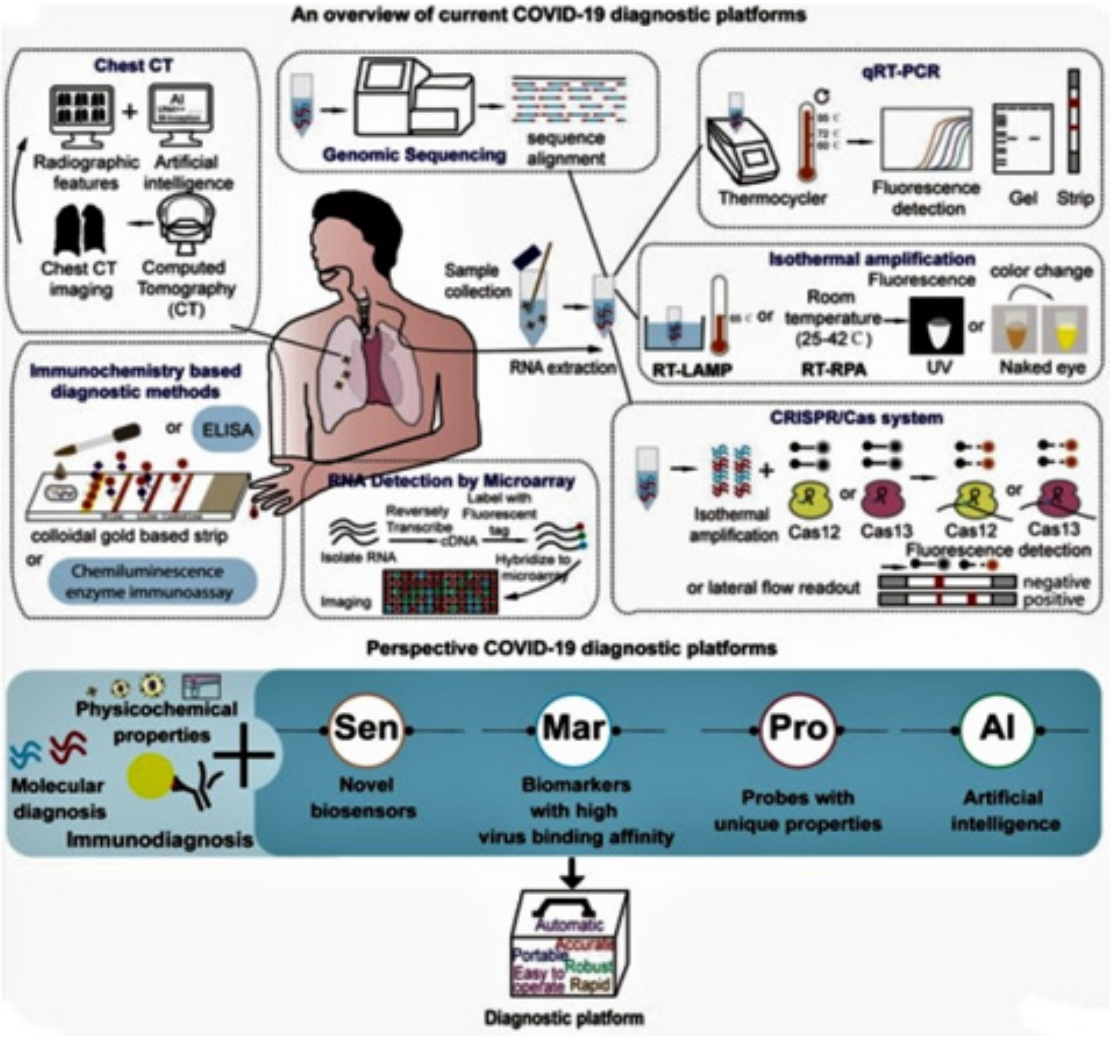


Figure 78: Xi Yuan, et al. [330].

Despite great efforts worldwide to [331] control SARS-CoV-2 the spread of the virus has reached a pandemic. Infection prevention and control of this virus is the primary concern of public health officials and professionals. Currently several therapeutic options for COVID-19 are proposed and vaccine development has been initiated for prevention purposes. In this review we will discuss treatment options including anti-inflammatory drugs angiotensin-converting enzyme inhibitors/angiotensin receptor blockers nucleoside analogues protease inhibitors monoclonal antibodies; and convalescent plasma therapy. Some other agents such as vitamin D and melatonin which were recommended as potential adjuvant treatments for COVID-19 infection are also presented. Moreover; the potential use of [331] convalescent plasma for treatment of COVID-19 infection was described.

The coronavirus disease-2019 (COVID-19) pandemic has [332] resulted in a proliferation of clinical trials designed to slow the spread of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2). Many therapeutic agents that are being used to treat patients with COVID-19 are repurposed treatments for influenza Ebola or for malaria that were developed decades ago and are unlikely to be familiar to the cardiovascular and cardio-oncology communities. Here we provide a foundation for cardiovascular and cardio-oncology physicians on the front-line providing care to patients with COVID-19 so that they may better understand the emerging cardiovascular epidemiology and the biological rationale for the clinical trials [332] that are ongoing for the treatment of patients with COVID-19.

The severe acute respiratory syndrome [333] coronavirus 2 (SARS-CoV-2) is a positive sense single stranded RNA virus that causes the potentially lethal Covid-19 respiratory tract infection. It does so by binding to host cell angiotensin converting enzyme 2 (ACE2) receptors leading to endocytosis with the receptor and subsequently using the host cell's machinery to replicate copies of itself and invade new cells. The extent of the spread of infection in the body is dependent on the pattern of ACE2 expression and overreaction of the immune system. Hundreds

of clinical trials on existing approved drugs from different classes acting on a multitude of targets in the virus life cycle are ongoing to examine potential effectiveness for the prevention and treatment of the infection. [333] The viral life cycle provides potential targets for drug therapy.

A recent study has shown that remdesivir and [334] chloroquine effectively inhibit the replication and infection of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2; 2019-nCov) in vitro. Here we systemically discuss the pharmacological therapeutics targeting RNA-dependent RNA polymerase (RdRp) proteinase and S protein for treatment of SARS-CoV-2 infection. We will discuss the viability and challenges in targeting RdRp and proteinase and application of natural product quinoline and its analog chloroquine for treatment of coronavirus infection. Finally determining the structural-functional relationships of the S protein of SARS-CoV-2 will provide new insights into inhibition of interactions between S protein and angiotensin-converting enzyme 2 (ACE2) and enable us to [334] develop novel therapeutic approaches for novel coronavirus SARS-CoV-2.

Many cancer patients frequently visit the hospital [335] for treatment and disease surveillance. They may be immunocompromised due to the underlying malignancy or anticancer therapy and are at higher risk of developing infections. Cancer patients appear to have an estimated twofold increased risk of contracting SARS-CoV-2 than the general population. The main management strategies for treating cancer patients during the COVID-19 epidemic include clear communication and education about hand hygiene infection control measures high-risk exposure and the signs and symptoms of COVID-19. Consideration of risk and benefit for active intervention in the cancer population must be individualized. Postponing elective surgery or adjuvant chemotherapy for cancer patients with low risk of [335] progression should be considered on a case-by-case basis.

COVID-19 Infection and Herd Immunity Either by Vaccination or Person Immunity After Previous Infection

In a sufficiently immune population herd immunity [336] provides indirect protection to susceptible individuals by minimizing the probability of an effective contact between a susceptible individual and an infected host. In its simplest form herd immunity will begin to take effect when a population reaches the herd immunity threshold namely when the proportion of individuals who are immune to the pathogen crosses 1 – 1/R0. There are two possible approaches to build widespread SARS-CoV-2 immunity

1. A mass vaccination campaign which requires the development of an effective and safe vaccine or

2. Natural immunization of global populations with the virus over time. However; the consequences of the latter are serious and far reaching a large fraction of the human population would need to become infected with the virus and millions would succumb to it. Thus; in the absence of a vaccination program [336] establishing herd immunity should not be the ultimate goal.

Outlining potential public health actions including [337] hygiene measures social distancing and face masks and realistic future advances this paper focuses on the consequences of taking no public health action. The role of natural changes such as weather the adverse public health consequences of lockdowns testing for surveillance and research purposes testing to identify cases and contacts. Including the role of antibody tests the public health value of treatments mobilising people who have recovered population (a synonym for herd) immunity through vaccination and through natural infection involving the entire population and the need for public debate. Until there is a vaccine population immunity is going to occur only from infection. Allowing infection in those at very low risk while making it safer for them and wider society needs consideration but is currently taboo. About 40–50% population immunity is sufficient to suppress an [337] infection with a reproduction number of about 1 or slightly more [338] (Figures 79 & 80).

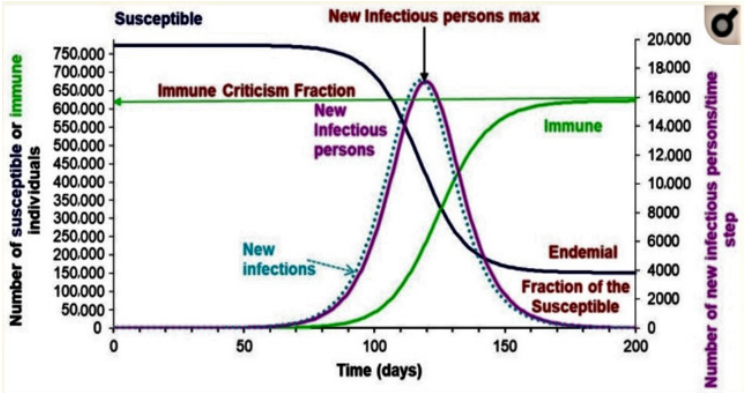


Figure 79: Susceptible, Exposed, Infected, nd Resistant (SEIR) model simulation of the coronavirus disease 2019 (COVID-19) propagation dynamics in a standard population with random circulation (Vicente Clemente-Suárez, Alberto Hopgood, Manuel Jiménez, Juan Benitez-A et al, 2020).

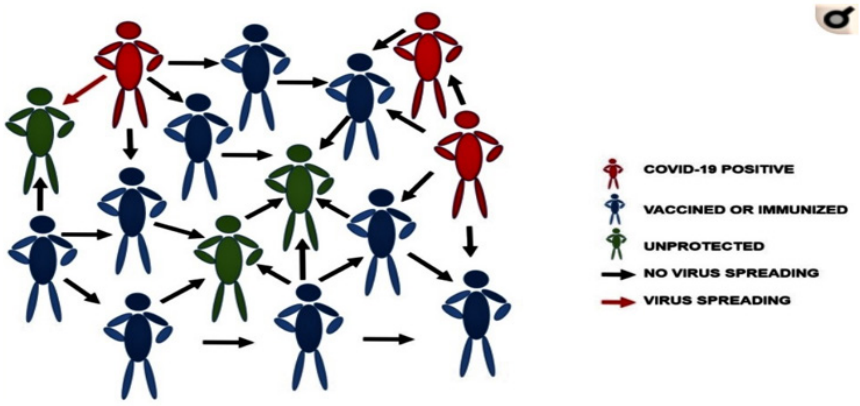


Figure 80: Herd immunity for the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). (Vicente Clemente-Suárez, Alberto Holgado, Manuel Jiménez, Juan Benitez-A et al, 2020).

Induction of herd immunity by mass vaccination [339] has been a very successful strategy for preventing the spread of many infectious diseases. Hence protecting the most vulnerable population groups unable to develop immunity for example individuals with immunodeficiencies or a weakened immune system due to underlying medical or debilitating conditions. Therefore; vaccination represents one of the most promising counter pandemic measures to COVID-19. However; to date no licensed vaccine exists neither for SARS-CoV-2 nor for the closely related SARS-CoV or Middle East respiratory syndrome-CoV. Although COVID-19 vaccine development is currently accelerated via so-called [339] fast-track programs vaccines may not be timely available to have an impact on the first wave of the ongoing COVID-19 pandemic.

Recent outbreaks such as SARS in [340] 2003 Ebola in 2014 MERS in 2015 and currently COVID-19 have forced citizens around the world to confront and reconsider the high social and economic costs of epidemic control. A vaccination game is defined in which costly commitments vaccination are required of a fraction of the population to reach the critical level needed for herd immunity without which defectors are punished by the natural contagion of epidemics. Our experimental implementation of a vaccination game in a controlled laboratory setting reveals that endogenous epidemic punishment is a credible threat resulting in voluntary vaccination to obtain herd immunity for [340] which the orthodox principle of positive externalities fails to account.

Despite various levels of preventive measures in 2020 [341] many countries have suffered severely from the coronavirus 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. We show that population heterogeneity can significantly impact disease-induced immunity as the proportion infected in groups with the highest contact rates is greater than in groups with low contact rates. We estimate that if R0 = 2.5 in an age-structured community with mixing rates fitted to social activity then the disease-induced herd immunity level can be around 43% which is substantially less than the classical herd immunity level of 60% obtained through homogeneous immunization of the population. Our estimates should be interpreted as an illustration of how population heterogeneity affects [341] herd immunity rather than an exact value or even a best estimate.

To quantify the economic value of the [342] costs and benefits of a policy of continued limited reopening with social distancing relative to alternative COVID-19 response strategies in the United States. We estimate the number and value of quality-adjusted life-years (QALY) gained from mortality averted with a value of $125;000 per QALY and compare these benefits to the associated costs in terms of plausible effects on US GDP under a policy of continued limited reopening with social distancing relative to a policy of full reopening toward herd immunity. QALY benefits from mortality averted by continued social distancing and limited reopening relative to a policy of [342] full reopening exceed projected GDP costs if an effective vaccine or therapeutic can be developed within 11.1 months from late May 2020.

Vaccination is an effective measure to control [343] the diffusion of infectious disease such as COVID-19. This paper analyses the basic reproduction number in South Korea which enables us to identify a necessary level of vaccine stockpile to achieve herd immunity. A susceptible-infected-susceptible model is adopted that allows a stochastic diffusion. The result shows that the basic reproduction number of South Korea is approximately 2 which is substantially lower than those of the other regions. The herd immunity calculated from economic epidemiological model suggests that at least 62% of the [343] susceptible population be vaccinated when COVID-19 vaccine becomes available.

The analyses presented in this study demonstrated [344] that India has less mortality rate of COVID-19 as its total infected population is concern. Particularly India is in the process of scaling up public health and social measures based on local epidemiology and on local risk

assessments such as continuously four full lockdown restricted local movement and educational institutes are implementing the distance learning and businesses to teleworking and regulated international and national travel measures. Finally; the death rate is likely to be connected with many cultures demonstrated [344] related behaviours and to the presumed diversity in health conditions of the people.

Leaders of Meritus Health a western Maryland [345] community hospital in an area of low-density population used a predictive modelling tool to anticipate the impact of the novel coronavirus pandemic on its 300-bed facility. In mid-March the projected surge showed a need for more than 200 beds for Covid-19 patients by early April. In response the team implemented aggressive testing and prevention efforts to flatten the curve while regularly monitoring a dashboard to spot any adverse developments. Aggressive testing yielded more than 18;000 results approximately 10% of the population and showed a low Covid-19 prevalence rate of 4.2%. The low positive rate demonstrates that herd immunity is far from reality and raises the [345] pressure on a vaccine as the ultimate answer to the pandemic.

Effective herd immunity against SARS-CoV-2 will be determined on [346] many factors the percentage of the immune population the length and effectiveness of the immune response and the stability of the viral epitopes. The required percentage of immune individuals has been estimated to be 50–66% of the population which given the current infection rates will take long to be achieved. Furthermore; data from SARS-CoV suggest that the duration of immunity may not be sufficiently significant while the immunity response against SARS-CoV-2 may not be efficiently effective in all patients as relapses have already been reported. In conclusion the development of an effective vaccine is an urgent necessity as long-term natural immunity to [346] SARS-CoV-2 may not be sufficient for the control of the current and future outbreaks.

Mucosal immunity including secretory IgA (sIgA) plays an [347] important role in early defences against respiratory pathogens. Salivary testing the most convenient way to measure sIgA has been used to characterize mucosal immune responses to many viral infections including SARS MERS influenza HIV; and RSV. However; its role has not yet been characterized in the COVID-19 pandemic. We successfully validated a qualitative salivary assay for SARS-CoV-2 IgA antibodies with positive and negative predictive values of 92% and 97% respectively and no observable cross-reactivity with any of seven potential confounders. Pre-COVID-19 saliva samples showed an 8-fold range of IgA concentrations suggesting a broad continuum of natural antibody resistance against the novel virus though at levels lower than [347] that observed in COVID-19 PCR-confirmed subjects.

COVID-19 Mode of Transmission and Mortality Rate

Until an effective treatment or a vaccine is developed the [348] current recommendations are to contain the disease and control its transmission. It is now clear that the primary mode of SARS-CoV-2 transmission is aerosol/droplet spread and by contacting virus contaminated surfaces acting as fomites (inanimate vectors). By virtue of the nature of the practice of dentistry where intrinsically a high volume of aerosols is produced as well as the close proximity of dentists and patients during treatment dentists and allied health staff are considered the highest risk health professional group for acquiring SARS-CoV-2 during patient management. Therefore; several organizations and specialty associations have proposed guidelines and [348] recommendations for limiting the transmission of SARS-COV-2 from carriers to dentists and vice versa.

The SARS-CoV-2 is mainly transmitted through [349] respiratory droplets and close contact. There is also evidence of transmission through aerosols and digestive tracts. Because orthodontic treatment involves a large population who need routine return visits it was significantly affected and suspended because of the COVID-19 pandemic and the shutdown of the dental clinics and hospitals. This is due to the fact that the asymptomatic carriers of SARS-CoV-2 or patients in the incubation period may cause the cross-infection between orthodontic practitioners and patients. The close proximity between the practitioners and the patients and the generation of [349] droplets and aerosols that contain saliva and blood during treatment further increase the risks of transmission [350] (Figure 81).

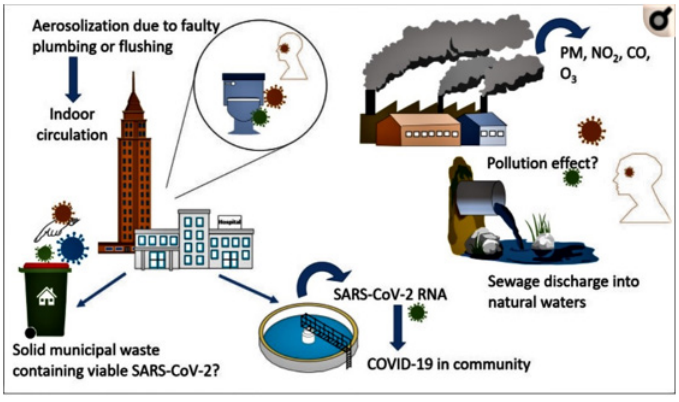


Figure 81: Khaled Huraimel, et al. [350].

SARS-CoV-2 is a novel and highly contagious [351] virus and there is no specific treatment for COVID-19 disease up to now. It must be taken into account that if no effective action is taken and if drugs vaccines and patient tracking measures are not widely implemented or effective intermittent social distancing is likely to continue until 2022. By that time COVID-19 might have affected 90% of the world population and kill over 40 million people. Therefore; it is wise to continue preventive methods and public health measures until an appropriate vaccine and effective drugs are discovered. Combinational therapies with some of the above-mentioned drugs or supplements plus an appropriate immunomodulatory diet [351] proper mental support and adherence to standards will eventually be effective against COVID-19.

There were no differences in the clinical characteristics of [352] pregnant women and non-pregnant COVID-19 patients. COVID-19 infection has caused higher incidence of fatal distress and premature labour in pregnant women. Although the possibility of vertical transmission in infected pregnant women is rare four neonates test results for COVID-19 infection were positive in this review. Overall; 21 articles were reviewed and clinical characteristics of 90 pregnant patients and 92 neonates born to mothers infected with COVID-19 were reviewed. The most common symptoms included fever cough and dyspnoea. The main laboratory findings included leucocytosis lymphopenia thrombocytopenia and elevated C-reactive protein. The most commonly reported complications were preterm labour and foetal distress. Three mothers were admitted to ICU and required mechanical ventilation among them one died and one was on extracorporeal membrane oxygenation. Overall; 86 neonates were tested for the possibility of vertical transmission and 82 cases [352] were negative in RT-PCR while 4 were positive. Out of 92 neonates one died and one was born dead [353] (Figure 82).

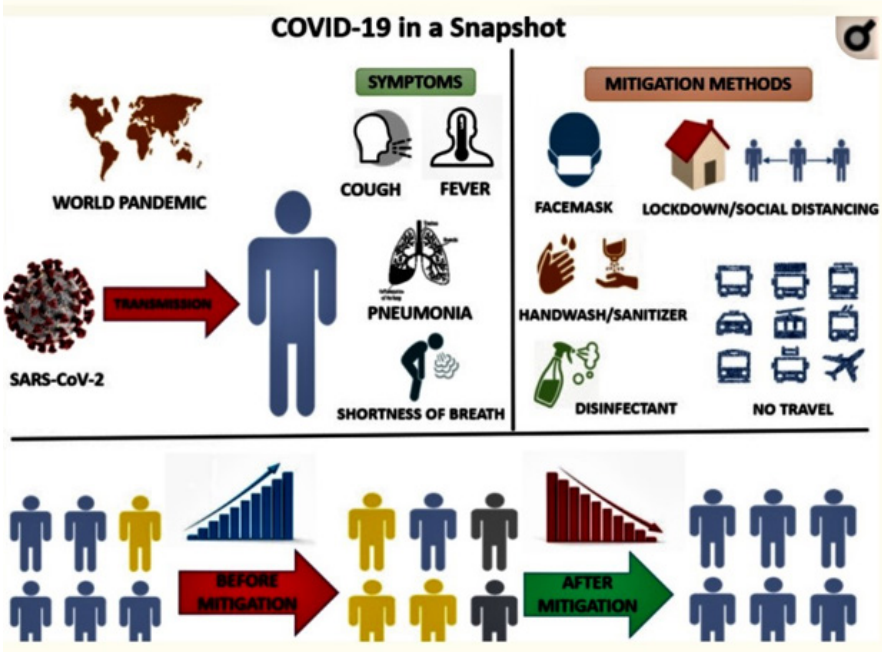


Figure 82: Transmission of COVID-19 symptom, mitigation measures adopted and effect on population. Satinder Kaur, et al. [353].

We obtained information on the scale of population migrated (Changqing Lin; Alexis Lau; Jimmy Fung; Cui G et al; 2020) from Wuhan the world epicentre of the COVID-19 outbreak into the study provinces/municipalities using mobile phone positioning system and big data techniques. The highest STRs were found in densely populated metropolitan areas and in cold provinces located in north eastern China. Population density had a non-linear relationship with disease spread (linearity index; 0.9). Among various meteorological factors only temperature was significantly associated with the STR after controlling for the effect of population density. The STR increased substantially as the temperature in north-eastern China decreased below 0 °C (the STR ranged from 3.5 to 12.3 when the temperature was between −9.41 °C and −13.87 °C); whilst the STR showed less temperature dependence in the study areas with (Changqing Lin; Alexis Lau; Jimmy Fung; Cui G et al; 2020) temperate weather conditions (the STR was 1.21 ± 0.57 when the temperature was above 0 °C).

The SARS-CoV-2 can be transmitted in various circumstances [354] and cluster infection plays important roles in the rapid evolution of COVID-19 transmission. Prevention and control measures such as social distance must be strictly implemented to contain the cluster infections. We searched all of the studies published between January 1 2020 and June 15; 2020 on the cluster infections of COVID-19 in the English electronic [354] databases including PubMed Embase Web of Knowledge and Scopus. As we could compare Previous century with current [355] modern era of Medical Sciences and latest inventions. Sick patients are getting more better medicines and latest treatment/

surgical procedures and they are living longer than ever before. The availability of health services and latest medicines has made our life easier and solving the small health problems easier than ever before. Getting free prescriptions from pharmacies in some [355] countries with easily buying medicines is making good effect in the community.

Public health resorted to non-pharmaceutical interventions [356] such as social distancing and lockdown to slow down the spread of the pandemic. We describe the motion of individual agents using a social force model. Each agent can be either susceptible infected quarantined immunized or deceased. The model considers both mechanisms of direct and indirect transmission. We parameterize the model to reproduce the early dynamics of disease spread in Italy. Next; we reveal that pre-symptomatic transmission accelerates the onset of the exponential growth of cases. After that we demonstrate that the persistence of SARS-CoV-2 on hard surfaces determines the number of cases reached during the peak of the epidemic. Then we show that the restricted movement of the individuals flattens the epidemic curve. Finally; model predictions [356] suggest that measures stricter than social distancing and lockdown were used to control the epidemic in Wuhan China.

Universal COVID-19 screening is generally the [357] preferred option. However; in locations with high COVID-19 prevalence or where the local societal cost of one HCW being unavailable is the highest such as in rural areas universal PPE may be cost-effective and preferred. This model may help to provide guidance regarding allocation of resources on L&D during these current and future pandemics. In the base case using a COVID-19 prevalence of 0.36% (the rate in the United States at the time) universal screening is the preferred strategy because while universal PPE is more effective at preventing COVID-19 transmission it is also more costly costing $4;175;229 and $3;413;251 to prevent one infection in the setting of spontaneous and induced labour respectively. For planned CD universal PPE is cost saving. At a higher cost-effectiveness [357] threshold the prevalence of COVID-19 can be lower for universal PPE to become cost-effective.

To support public health policymakers in Connecticut [358] as they begin phased lifting of social distancing restrictions; we developed a county-structured compartmental SEIR-type model of SARS-CoV-2 transmission and COVID-19 disease progression. We calibrated this model to the local dynamics of deaths and hospitalizations and the exact timing of state interventions including school closures and stay-at-home order. Our model results are consistent with high effectiveness of state lockdown measures but changes in human interaction patterns during the coming months are unknown. In addition; a lot of uncertainty remains with respect to several key epidemiological [358] parameters and the effectiveness of increased testing and contact tracing capacity.

This recent outbreak of novel coronavirus (CoV) was believed to [359] be originated from bats and causing respiratory infections such as common cold dry cough fever headache dyspnoea; pneumonia; and finally Severe Acute Respiratory Syndrome (SARS) in humans. For this widespread zoonotic virus human-to-human transmission has resulted in nearly 83 lakh cases in 213 countries and territories with 4;50;686 deaths as on 19 June 2020. This review presents a report on the origin transmission symptoms; diagnosis; possible vaccines; animal models; and immunotherapy for this novel virus and will provide ample references for the researchers toward the ongoing development of therapeutic agents [359] and vaccines and also preventing the spread of this disease.

COVID-19 Suspected Second Wave and When it is Happening?

The number of new Covid-19 cases reported in Italy has [360] risen sharply over the past two weeks. So how bad is the situation and what happens next? On Thursday Italy recorded 840 new cases of Covid-19 the highest number since lockdown eased. After 642 the previous day this continued the overall trend of rising case numbers over the last two weeks. Authorities began tightening restrictions on Sunday August 16th after cases rose from 200-300 a day to 600 within a week. Italy's strict lockdown one of the world's longest is credited with getting the initial major outbreak under control. The daily number of new Italian cases had hovered between 175-250 for much of July before starting to rise again. Italy is of course not alone in seeing this trend with many countries including France and Germany now recording new case numbers [360] equal to those last seen in April and May.

Natural Killer (NK) cells are innate immune responders [361] critical for viral clearance and immunomodulation. Despite their vital role in viral infection the contribution of NK cells in fighting SARS-CoV-2 has not yet been directly investigated. Insights into pathophysiology and therapeutic opportunities can therefore be inferred from studies assessing NK cell phenotype and function during SARS MERS and COVID-19. These studies suggest a reduction in circulating NK cell numbers and/or an exhausted phenotype following infection and hint toward the dampening of NK cell responses by coronaviruses. Reduced circulating NK cell levels and exhaustion may be directly responsible for the progression and severity of COVID-19. Conversely; in light of data linking inflammation with coronavirus disease severity it is necessary [361] to examine NK cell potential in mediating immunopathology.

The aim is to develop and psychometrically test [362] the COVID-19 prevention detection and home-management self-efficacy scale (COVID-19-SES). We conducted an observational cross-sectional study. Six-hundred and seventy-eight people participated in the study. Data

were collected between March and May 2020. The COVID-19-SES validity (content; criterion; and construct) reliability (internal consistency and test-retest reliability) and legibility were studied. The COVID-19-SES reliability was high (Cronbach's alpha = 0.906 intraclass correlation coefficient = 0.754). The COVID-19-SES showed good content validity (scale's content validity index = 0.92) and good criterion validity when the participants results on the COVID-19-SES were compared to their general self-efficacy ($r = 0.38$; $p < 0.001$). Legibility analysis [362] showed that the COVID-19-SES is easy to read and understand by laypeople.

We review the antibody response that is triggered by severe acute [363] respiratory syndrome coronavirus 2 (SARS-CoV-2) infection of humans and how it may inform vaccine research. The isolation and properties of neutralizing monoclonal antibodies from COVID-19 patients provide additional information on what vaccines should try to elicit. We summarize the immunogenicity of leading vaccine candidates tested to date in animals and humans and discuss the outcome and interpretation of virus challenge experiments in animals. By far the most immunogenic vaccine candidates for antibody responses are recombinant proteins which were not included in the initial wave of Warp Speed immunogens. A substantial concern for SARS-CoV-2 vaccines is adverse events which we review by considering what was seen in studies of SARS-CoV-1 [363] and Middle East respiratory syndrome coronavirus (MERS-CoV) vaccines.

Higher education both domestically and internationally [364] has been disrupted. Forecasts for the long shadow implications of COVID-19 range from a six-month to a five-year disruption. Forecasts predict anywhere from a 15 to 25% decline in enrolment depending on the part of the world. But the virus has also presented higher education with opportunities after the dangers of COVID-19 have passed or a vaccine is discovered that makes it safe to resume normal activities. How will colleges and universities worldwide respond to the residuals? The following five opportunities will exist for those who pursue them.

1. Create a vision statement for your school.
2. Create a yearlong academic program combining the best of in-person and online learning.
3. Create yearlong recruitment programs for both domestic and [364] international students.
4. Create new business models and financing options.
5. Replace competition with collaboration [365] (Figure 83).

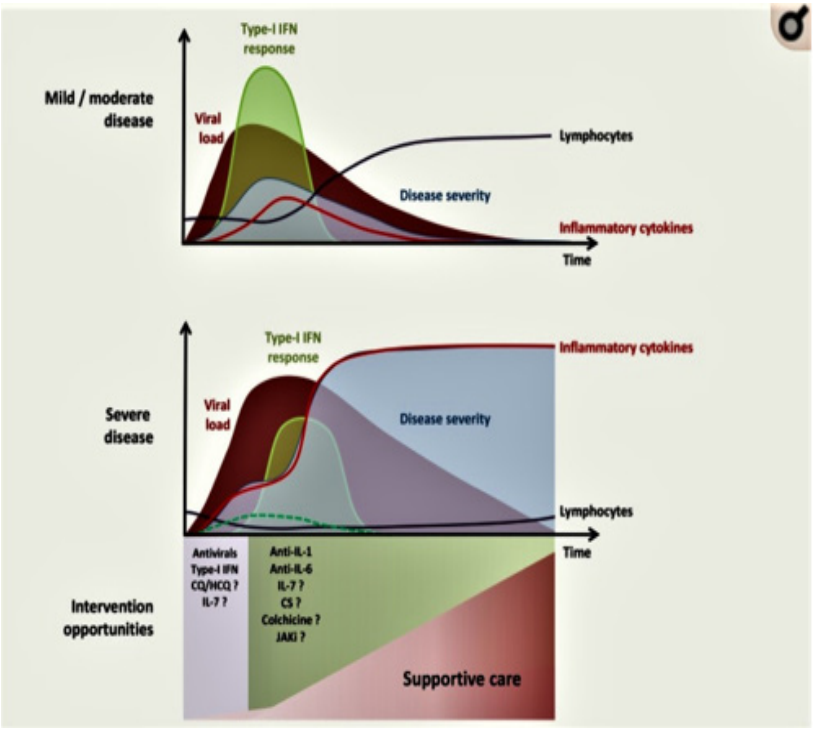


Figure 83: Kinetics and intensity of the antiviral response are decisive in COVID-19 outcome. In mild to moderate COVID-19 the early antiviral response mostly type-I interferon (IFN) allows the rapid reduction of viral load and prevents T-cell depletion and hyper cytokinemia. In severe COVID-19 delayed (solid green line) or low (dotted green line) antiviral response results in elevated lung cytokine/chemokine levels impaired virus-specific T-cell responses and acute clinical deterioration Yvan Jamilloux, et al. [365].

Until now Germany's coronavirus policymakers [366] have sworn by the country's federal system but with no real hot spot to speak of Germany's localized strategy could be about to take a U-turn. If compulsory masks in classrooms prevent school closures a similar rule could also be applied to schools across the board Kramp-Karrenbauer said. While masks have become standard practice on most school premises the western state of North-Rhine Westphalia (NRW) is so far the only state to require them during lessons for secondary school children. The biggest criticism regarding masks however remains how the rules are implemented. Penalties for mask shirkers vary enormously from state to state: in the German [366] capital fines can be up to €500 while the penalty in Rhineland-Palatinate in western Germany is just €10.

Although information about the mechanisms of immunity [367] are scant it appears that monocyte/macrophages and then CD8 T cells are important in eliminating the SARS-CoV-2 virus. This may be facilitated via anti-viral antibody responses that may prevent re-infection. However viral escape and infection of leucocytes to promote lymphopenia apparent CD8 T cell exhaustion coupled with a cytokine storm and vascular pathology appears to contribute to the damage in ARDS. In contrast to ablative haematopoietic stem cell therapy most multiple sclerosis related disease modifying therapies do not particularly target the innate immune system and few have any major long-term impact on CD8 T cells to limit protection against COVID-19. In addition; few block the formation of immature B cells within [367] lymphoid tissue that will provide antibody mediated protection from (re)infection.

Europe succeeded China as the epicentre of the virus [368] as it hit the continent hard from April to June in particular. A downturn in July allowed for a gradual reopening at varying rates with many countries desperate to reignite their battered economies. The evidence indicates that this period of suppression is over amid fears of a second wave. Germany this month had more than 1;000 cases in a day for the first time since May 7. Even more drastic spikes have been seen in France and Spain. Greece is also suffering after having handled the outbreak so effectively thus far. Still entry to Greece where the full details of all arrivals are logged is far more effectively martialled in terms of tracking than in France for example. From anecdotal experiences the cafes in Athens have hand sanitizer on every table whereas in French towns the sole bottle looks lonely and unused. Paris is on the verge of another lockdown with mandatory face mask rules in force in many [368] cities and towns across France.

Will There Be A Second Wave Of [369] COVID-19? In short? Yes; here most certainly will. Or looking at it from another perspective there might not be a second wave as the first one won't end. In any case which scenario is more probable depends on your country's leadership and decisions and whether people will be compliant enough to go along with the restrictions. Because how governments are preparing for it over the next few weeks will be crucial in the fight against the pandemic. The search is still on for a vaccine and it certainly won't be ready by the time experts say the second wave hits the stage. Technically to talk about a second wave the first wave needs to end. In some parts of the world we've seen that happening while we also see [369] record numbers in new infections elsewhere so the disease is on fire again.

Countries across Europe are seeing a resurgence in [370] COVID-19 cases after successfully controlling outbreaks early in the year. But how strong has the coronavirus comeback been and does it compare to the infection numbers seen in the spring? Countries in southern eastern Europe such as Albania Bulgaria Montenegro North Macedonia and Romania are seeing higher case numbers in August than they did earlier in the year. Serbia is one of the exceptions posting similar figures now to mid-April. Croatia Greece and Malta appear to be experiencing a surge in cases with even higher numbers this past week compared to the first wave. Belgium Italy and the UK among Europe's worst-hit countries are seeing a resurgence but so far at least nothing like March and April. France Poland the [370] Netherlands and Spain are likely dealing with the much-feared second wave and have started taking action to curb it.

Coronavirus is far from over. [371] Some countries are still dealing with large epidemics but even those currently controlling the virus fear the second wave. In the UK; health experts are warning ministers to prepare for one following the decision to further ease restrictions in England from early July. The second phase of Spanish flu a century ago was deadlier than the first. So; is a second wave inevitable? And how bad could it be? In order to say one wave has ended the virus would have been brought under control and cases fallen substantially. For a second wave to start you would need a sustained rise in infections. New Zealand which has its first cases after 24 days without coronavirus and Beijing which is facing an outbreak after 50 virus-free days are not in this position [371].

COVID-19 Incidence and Transmission and the Relationship of Zip Code in the USA?

Nearly 20% of U.S counties are disproportionately black [372] and they accounted for 52% of COVID-19 diagnoses and 58% of COVID-19 deaths nationally. County level comparisons can both inform COVID-19 responses and identify epidemic hot spots. Social conditions structural racism and other factors elevate risk for COVID-19 diagnoses and deaths in black communities. Counties with higher proportions of black people have higher prevalence of comorbidities and greater air pollution. Counties with higher proportions of black residents had more COVID-19 diagnoses (Rate Ratio (RR) 1.24; 95% confidence interval (1.17–1.33) and deaths (RR: 1.18; 95% confidence interval 1.00–1.40)

after adjusting for county-level characteristics such as age poverty comorbidities and epidemic duration. [372] COVID-19 deaths were higher in disproportionally black rural and small metro counties.

Newly released data from the Illinois Department of Public Health [373] shows the number of COVID-19 cases by zip code a new level of detail not previously available. The data shows most of the cases are in Cook County and Chicago with high concentrations of cases on the city's South and West sides. It also shows a growing number of cases in the suburbs particularly towns to the North and South of Chicago. Indiana officials haven't released similar numbers by zip code. But newly released data by Indiana county shows most of the cases there [373] concentrated in Marion County home to the state's capitol of Indianapolis.

ZIP codes with higher rates of [374] cases per 100;000 residents appear as a darker shade of blue than zip codes with lower rates of cases. These data do not necessarily mean that one zip code or neighbourhood is more or less safe than another. An increase in the number of tests completed in any one zip code can affect zip code case counts and rates. Zip codes with higher rates of cases per 100;000 residents appear as a darker shade of blue than zip codes with lower rates of cases. Some case counts and rates include cases associated with Long-Term Care Facilities (LTCFs) that are located within these zip codes. Some LTCFs have had clusters of reported COVID-19 cases which impacts the case rates for zip codes where LTCFs are located. Total cases reported for LTCFs include all [374] residents and staff associated cases regardless of zip code of residence.

Like a rubber ball bouncing down a hardwood [375] hallway COVID-19 continues to spread across the USA hitting some neighbourhoods hard while touching other parts of the same metro area only lightly according to a USA TODAY analysis of ZIP code-level data. The analysis shows that COVID-19 is more prevalent in poorer neighbourhoods. In ZIP codes where median household income is less than $35;000 the overall infection rate is more than twice as high as in neighbourhoods with household income of more than $75;000. In neighbourhoods with a majority of non-white residents the overall COVID-19 infection rate is nearly [375] five times higher than in areas where non-white population is less than 10%.

Using zip code level data for New York City [376] we analysed testing rates positivity rates and proportion positive. A spatial scan statistic identified clusters of high and low testing rates high positivity rates and high proportion positive. Boxplots and Pearson correlations determined associations between outcomes clusters and contextual factors. Clusters with less testing and low proportion positive tests had higher income education and white population whereas clusters with high testing rates and high proportion positive tests were disproportionately black and without health insurance. Correlations showed inverse associations of white race education and income with proportion [376] positive tests and positive associations with black race Hispanic ethnicity and poverty.

Colorado is also reporting like other states that [377] communities of colour and low-income persons are disproportionately affected by COVID-19. Overall; the greatest increase in COVID-19 incidence was in northern Colorado i.e. Weld County which reported the highest rates in the Urban Front Range. Social and health determinants associated with higher COVID-19-related deaths were population density and asthma indicative of urban areas and poverty and unemployment suggestive of rural areas. Furthermore; a spatial overlap of high rates of chronic diseases [377] with high rates of COVID-19 may suggest a broader health burden where comorbidities intersect with inequality of social determinants of health.

The number of dialysis stations [378] within a zip code correlates with the SARS-CoV-2 positivity rate per capita in Cook County IL and this correlation may be driven by population density and the demographics of the residents. These findings highlight the high risk of SARS-CoV-2 exposure for patients with end-stage kidney disease living in poor urban areas. Positive test results per capita also correlated significantly with number of households living in poverty ($r = 0.57$; 95% CI; 0.53-0.6; $P < 0.005$) and percentage of residents reporting Black race ($r = 0.28$; 95% CI; 0.23-0.33; $P < 0.005$) and Hispanic ethnicity ($r = 0.68$; 95% CI; 0.65-0.7; $P < 0.001$;). COVID-19 associated deaths per capita correlated significantly with the percentage of residents reporting Black race ($r = 0.24$; 95% CI; 0.19-0.29; $P < 0.005$) and [378] with percentage of households living in poverty ($r = 0.34$; 95% CI; 0.29-0.38; $P < 0.005$).

Over the past years it has become clear that early life adversity [379] plays a critical role biasing the immune system towards a pro-inflammatory and senescent phenotype many years later. Cytotoxic T lymphocytes (CTL) appear to be particularly sensitive to the early life social environment. As we understand more about the immune response to SARS-CoV-2 it appears that a functional CTL (CD8+) response is required to clear the infection and COVID-19 severity is increased as the CD8+ response becomes somehow diminished or exhausted. This raises the hypothesis that the ELA induced pro-inflammatory and senescent phenotype may play a role in determining the clinical course of COVID-19 and the convergence of ELA induced senescence and COVID-19 induced [379] exhaustion represents the worst-case scenario with the least effective T-cell response [380] (Figure 84).

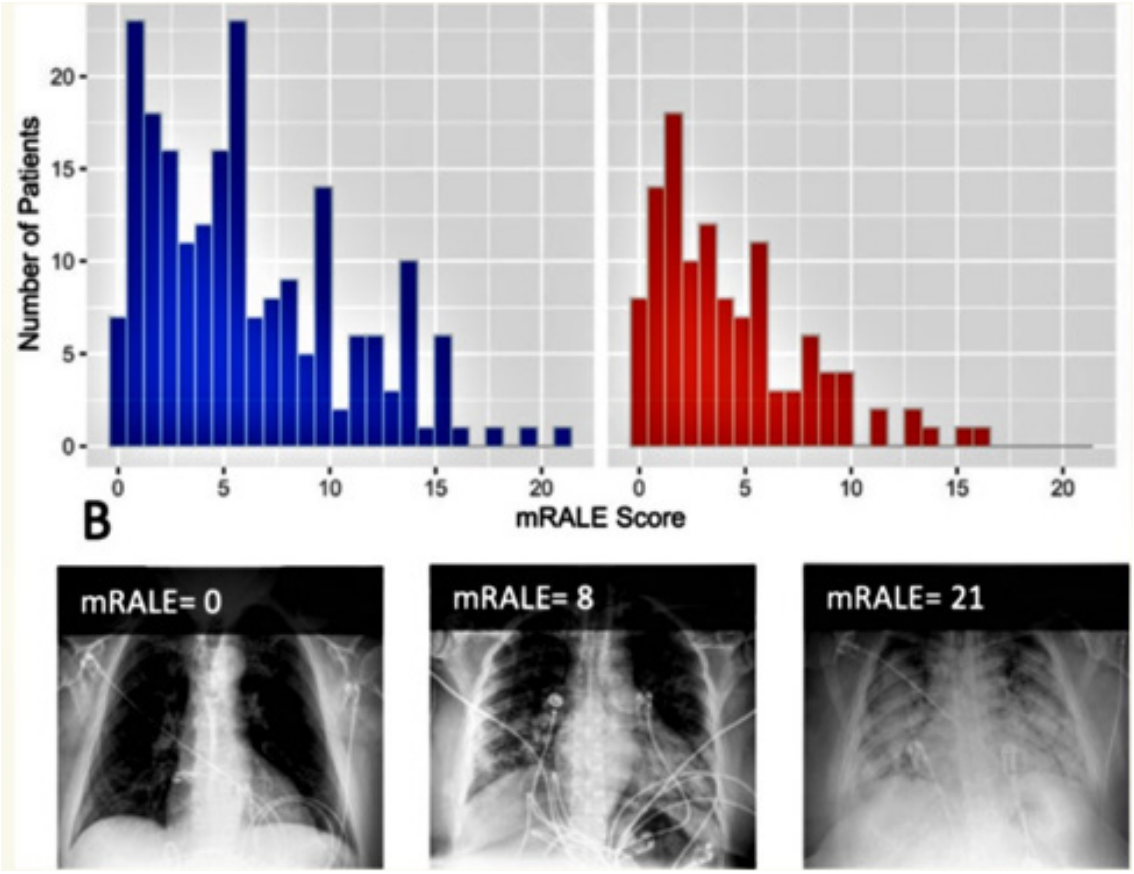


Figure 84: Histogram of mRALE Score Distribution Nicholos Joseph, et al. [380] by Race.

A) Distribution of mRALE categories on Admission Chest Radiograph by Race/Ethnicity. Non-White/Hispanic patients were more likely to have higher mRALE score categories compared with White/non-Hispanic patients (Coefficient 0.560, 95% CI 0.046 to 1.074 to, p = 0.033). On average, adjusted for potential confounders, Non-White patients presented with higher mRALE scores on admission CXR compared with White patients (average difference 1.60, 95%CI 0.50 to 2.71, p=0.005) in our multiple variable linear regression analyses.

B) Examples of modified Radiograph Assessment of Lung Edema (mRALE) annotations (Nicholos Joseph, Nicholas Reid, Avik Som, Matthew D L et al, 2020) for pulmonary disease severity in patients with COVID-19.

In New York City COVID-19 testing has not been [381] proportional to need existing socioeconomic and racial disparities in healthcare access have likely impacted public health response. There is urgent need for widespread testing and public health outreach for the most vulnerable communities in New York City. The number of total tests significantly increased with the increasing proportion of white residents (β=0.004; SE=0.001; p=0.0032) but not with increasing Hispanic composition or SES index score. The ratio of positive tests to total tests significantly decreased with the increasing proportion of white residents in the ZIP code Tabulation Area (β= −0.003; SE=0.000 6; p<0.001) and with [381] increasing SES index score (β= −0.001 6; SE=0.0007; p=0.0159).

Emerging evidence from a variety of countries [382] suggests that these inequalities are being mirrored today in the COVID-19 pandemic. COVID-19 has laid bare our longstanding social economic and political inequalities even before the COVID-19 pandemic life expectancy amongst the poorest groups was already declining in the UK and the USA and health inequalities in some European countries have been increasing over the last decade. It seems likely that there will be a post-COVID-19 global economic slump which could make the health equity situation even worse particularly if health-damaging policies of austerity are implemented again. It is vital that this time the right public policy responses are undertaken so that the COVID-19 pandemic does [382] not increase health inequalities for future generations. Public health must win the peace as well as the war.

The unfolding COVID-19 pandemic brings existing [383] health inequities to the forefront once again and highlights ways that behavioural science can provide important insights into managing the pandemic and urgent efforts on mitigating such inequities. While behavioural health

can contribute to the general understanding of health disparities among underserved communities e.g. applications for the implications of COVID-19 on minority health (e.g.; impacts of living in close quarters during quarantine limited access to telecommuting work-from-home options) are needed. To this end behavioural health should adopt multidisciplinary approaches (e.g.; applications from the economics literature) for understanding the realities [383] of social distancing measures among disadvantaged groups.

Substantial racial/ethnic disparities are observed in COVID-19 CF [384] and mortality with Blacks/AA disproportionately affected across the United States. The COVID-19 mortality CmI indicated Blacks/AA with 34% of the total mortality in the United States albeit their 13% population size. The COVID-19 CF was higher among Blacks/AA relative to Whites; Maryland; (2.7% vs. 2.5%); Wisconsin (7.4% vs. 4.8%); Illinois (4.8% vs. 4.2%); Chicago (5.9% vs. 3.2%); Detroit (Michigan); 7.2% and St. John the Baptist Parish (Louisiana); 7.9%. Blacks/AA compared to Whites in Michigan were 15% more likely to die; CmI risk ratio (CmIRR) = 1.15; 95% CI; 1.01-1.32. Blacks/AA relative to Whites in Illinois were 13% more likely to die; CmIRR = 1.13; 95% CI; 0.93-1.39; while Blacks/AA compared to Whites in Wisconsin were 51% more likely to die; CmIRR = 1.51; 95% CI; 1.10-2.10. In Chicago Blacks/AA [384] were more than twice as likely to die; CmIRR = 2.24; 95% CI; 1.36-3.88.

The role of Medical Sciences and Inventions to Save Human Lives by Diagnosing and Providing Latest Medical and Surgical Treatment

The author told the dangers and the [385] harmful effects done by the Avian flu and how this deadly disease spread in the communities silently and the health departments comes to know about this disease when it done its work; killing the innocent people; terrorize the whole community by its deadly results. This essay also points out the flaws in our health systems for example; are the health authorities is aware of the dangers of Avian flu are the health departments are serious about giving training to the members of health department to cope with this great threat of Avian flu; are they teaching local people how to cope [385] with this danger? No; I don't think that enough work is done to handle this great threat of Avian flu.

The purpose of this study was to evaluate [386] the neonatal outcomes in early and delayed cord clamping and to find their correlation in early and delayed cord clamping with different haematological parameters in neonates. The present study predicted that no correlation in either group existed between hemoglobin hematocrit and bilirubin with increasing cord clamping time. Furthermore; there was no association observed in neonates with anemia; low hematocrit; polycythemia [386] and high bilirubin with increasing cord clamping time.

The Article themed to provide idea [387] that people in Favor or against the use of Mobile Phones Internet and Gadgets to obtain Health services. Data Table and Data Analysis clearly provides that 75% out of 100% of the selected Articles Authors Opinion agreed in Favor of use of [387] Social media and Online accessing Health Information and taking Online Treatment.

The aim of the study was to evaluate association [388] of hematological parameters on gender basis in chronic myeloid leukemia patients admitted in medical oncology department. The present study predicted that considerable difference did not exist in various hematological parameters of male and female CML patients. However; there was significant difference [388] observed in myelocyte count of these patients on the basis of gender.

A total of 342 pregnant females in their third stage of labor were selected for this study. No correlation existed between hemoglobin and hematocrit with cord clamping time (p-value 0.661) and (p-value 0.439) respectively. Weak positive correlation (p=0.002; r = 0.169) existed between bilirubin levels with clamping time. No correlation was observed with cord clamping time and anemia; low hematocrit or polycythemia (p-value 0.422); (p-value 0.058) and (p-value 0.20) respectively while weak negative correlation (ρ = -0.221) existed between high bilirubin levels in neonates with increasing cord clamping time (p-value <0.001). According to our study no correlation exists between hemoglobin and hematocrit with cord clamping time but weak positive correlation was observed between bilirubin levels with clamping time in seconds.

Electrolyte derangement has been documented [389] during cancer chemotherapy leading to the electrolyte imbalance. So; we conducted this study to evaluate the type and frequency of affected electrolytes. Our study demonstrates that electrolyte imbalances are common during chemotherapy and monitoring should be done by medical [389] oncologist so to avoid future morbidity and mortality.

The mean age of Group 1 patients was 41.90±14.90 years [390] while that of group 2 was 42.35±13.17years. In our study; males had total leukocyte count 2076.30±1207.72 cells/cum; neutrophil count 29.91±20.68/mm3 and females had total leukocyte count 2862.36±1970.80 cells/ cum; neutrophil count 38.56±21.87/mm3 which is significantly different among two groups (p-value<0.05).Febrile neutropenia was found to be present in 96(57.1%) of males and 70(47.3%) of female patients in our study which was not statistically significant(p-value=0.080). Our study showed that among male and female cancer patients on chemotherapy more than half of [390] males were found to have febrile neutropenia; while fewer females had febrile neutropenia.

The aim of the study was to identify the correlation [391] of age with hematological parameters in patients admitted in medical oncology department. The present study predicted the median age of 40.29 years in patients suffering from chronic myeloid leukemia. Furthermore; no significant difference existed in hematological parameters and therefore no correlation observed [391] with age in various hematological parameters in these patients.

To compare the prevalence of clinical signs and symptoms of [392] hypertension among different gender and age-based groups of hypertensive patients. The prevalence of smoking; chest pain; vision problems; fatigue and confusion were found to be different between both genders. Furthermore; the prevalence of smoking; headache; vertigo; chest pain; vision problems; dyspnea; increased urinary frequency; nausea; sleep apnea; irregular heartbeat/palpitation [392] fatigue and confusion were found to be different between both age groups.

The cancer patients are most prone to developing electrolyte abnormalities. [393] This study aims to focus on changes in various electrolytes before and after chemotherapy in cancer patients and to establish a relationship between electrolytes with the duration of chemotherapy. This study predicted that there is difference in electrolyte levels before and after chemotherapy in cancer patients. Furthermore; no correlation was observed in various electrolytes with the duration of chemotherapy [393] although the difference in electrolyte levels is not clinically significant.

Our study showed that significant difference [394] exists in some of the hematological parameters including hemoglobin levels; platelet count; total leukocyte count; neutrophil count; monocyte count and absolute neutrophil count in patient treat with different chemotherapeutic drugs suffering from febrile neutropenia. can be managed promptly in less time. The mean age of Group 1 patients was 39.88 ± 15.2 years while that of group 2 was 44.84 ± 12.2 years. In our study significant difference exists in some of the hematological parameters. In our study; group 1 had total leukocyte count of 1411.0180 ± 641.48 cells/cmm; neutrophil count of 17.64 ± 14.01/mm3 and group 2 had total leukocyte count 3597.41 ± 1673.90 cells/cmm; neutrophil count 52.20±12.08/mm3 [394] which is significantly different among two groups (p-value < 0.05).

Vitamin A deficiency is a major [395] contributor to child mortality. There is increasing evidence that it also raises significantly risk of maternal death. Elimination of vitamin A deficiency as a public health problem should be considered as a principal element for child and women survival programs. This article discusses the problem of vitamin A deficiency diseases (VADD) in developing and under-developed countries as well as the magnitude of the VADD problem. In addition; this article also provides strategies for the prevention and elimination of the vitamin A deficiency. Recent years; Great progresses had taken place in many countries in combating vitamin A deficiency. However; urgent action was still needed to be taken to accelerate existing progress in order to rapidly [395] increase the number of countries where this potentially lethal disorder was under control.

One does not need to be too much of a cynic to argue [396] that the only reason affluent countries rediscovered their concern for this forgotten disease was self-interest [397;398]. TB showed that it could strike again [399]. Anywhere; at random and with devastating effect [399;400]. WHO's current slogan; there is no hiding place; is spot on [401]. After 1993; when TB was declared a global emergency by the WHO; Pakistan committed itself to a WHO guideline that of achieving 100 percent DOTS coverage by 2005 [402;403]. Realistically if we are looking at a significant reduction of TB prevalence in Pakistan [404]; we have to look at another 20 years; despite the target of reducing TB by at least 50 percent by the year 2010 [405]. TB is a deadly disease and is a big challenge for the public health departments and for WHO [406].


8
Chapter

Conclusion

The traces of COVID19 Pandemic starts from Wuhan province; China where it was initially reported to WHO in November 2019 and it was given the name COVID19 Novel corona virus. Current COVID19 pandemic has taught us a great lesson and it is similar to other SARS viruses but till date October 2020 there is no proven medical treatment or approved Vaccine to prevent against COVID19 Virus. Remdesivir; Lopinavir-Ritonavir; Ceftriaxone; Cephalexin; Azithromycin; Clarithromycin; Continuous Oxygen therapy; Dexamethasone; Plasma therapy has shown positive results in some of the patients and treated them well. Human trials for approved COVID19 Vaccination are conducted in Russia; USA; Europe and the UK; UAE; China and Pakistan; India and Saudi Arabia but still time is needed to be recommended by WHO; FDA USA; EU to use on mass scale to vaccinate local people. The author of this article has done systematic literature review of more than 450 articles and selected 60 articles for Critical literature review by Bray and Rees criteria of 12 Questionnaire to answer them and critically explain the articles and their written matter. The author has written and presented this book for the research on Epidemiology of COVID19 Virus; its Distribution; Incidence; Prevention and treatment; use of PPE to save the precious human lives. The aim is to provide the reliable research to find the treatment and approved vaccination for the COVID19 Novel corona virus.

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