# COVID-19: A scoping review

**Brhane Berhe**
Adigrat University College of Health Sciences
**Haftom Legese**
Adigrat University College of Health Sciences
**Hagos Degefa**
Adigrat University College of Health Sciences
**Gebre Adhanom**
Adigrat University College of Health Sciences
**Aderajew Gebrewahd**
Adigrat University College of Health Sciences
**Fitsum Mardu**
Adigrat University College of Health Sciences
**Kebede Tesfay**
Adigrat University College of Health Sciences
**Getachew Kahsu**
Adigrat University College of Health Sciences
**Miglas Welay**
Adigrat University College of Health Sciences
**Hadush Negash** ( hadunegash@gmail.com )
Adigrat University College of Health Sciences https://orcid.org/0000-0001-8581-1766

**Research**

**Keywords:** Burden, Challenges, COVD-19, Epidemiology, impact, pathogenesis, prevention, scoping review

**Posted Date:** June 2nd, 2020

**DOI:** https://doi.org/10.21203/rs.3.rs-26166/v2

# Abstract

Background: Globally, the novel coronavirus is a pandemic disease with public health concern causing human infections. The severe acute respiratory syndrome 2 is causing severe infection and life-threatening complications. Now, it becomes a pandemic with a growing number of cases and deaths.

Methods: A scoping review was conducted following the methodological framework. In this scoping review, 70 records as of May 21, 2020 were included and discussed to better understand the current updates of the virus. PubMed, BioRxiv, MedRxiv, Global Health and google scholars were searched comprehensively for articles, preprints, grey literatures, reports, conference proceedings and expert information. Studies conducted in human and published in the English language were included in the review. All the findings and statements of the review regarding the outbreak are based on published data.

Results: We identified 408 records, of which 70 studies met the inclusion criteria. We synthesized the data from the included records and dug out the deep insights of them and pooled into this review. The burden of the outbreak is worsening due to overcrowding, presence of asymptomatic carriers, scarcity of test kits, the immune escaping ability of the virus and lack of community awareness.

Conclusions and recommendations: Due to the fast-spreading nature of severe acute respiratory syndrome 2 the prevention and control strategies become challenging. It is imposing social, psychological, and socio-economic impacts. We recommended strict adherence to physical distancing, quarantining suspects, using personal protective equipment, health education and introducing appropriate handwashing practices, avoiding contact with animals, improved controlling, and prevention strategies.


# Introduction

Globally, the novel coronavirus (COVID-19), is a pandemic disease-causing respiratory syndrome that needs urgent attention [1]. It was not reported to cause serious and life-threatening respiratory complications in humans until the outbreak of severe acute respiratory syndrome (SARS-CoV) that occurred early in 2003 that infected 8000 people, with a death rate of 9.5% [2]. This was followed by middle east respiratory syndrome (MERS-CoV) occurrence during 2012-2015 that infected 2500 people with a case fatality rate of 35% [2,3]. COVID-19 is a new disease  caused by the strain severe acute respiratory syndrome 2 (SARS-CoV-2) that has been identified to cause serious infection among humans [4] and has now become a pandemic with a rapidly growing number of cases and deaths up to 4,789,205 confirmed cases and 318,789 deaths as of 20 May 2020 [5].

SARS-CoV-2 is a viral agent in the family of coronaviridae which are a positive sense, enveloped, non-segmented RNA viruses. SARS-CoV-2 is classified under the genus of beta coronavirus that have a zoonotic origin whereby first isolated from humans in 1960s [1]. The origin of the virus is supported by a speculation during natural selection in an animal and human host before zoonotic transfer [6]. The novel coronavirus, previously designated 2019-nCoV, causes a cluster of pneumonia-like infections in China

during the late 2019. On 31 December 2019, four cases of an acute respiratory syndrome with unknown etiology were reported in China among people linked to a local seafood market [1, 3]. From 31 December 2019 to 3 January 2020, a total of 44 pneumonia cases with unknown etiology were reported to world health organization (WHO) from China. Within one month of the outbreak a total of 11, 791 confirmed cases and 213 deaths were reported from 19 countries [4, 5].

WHO declared SARS-CoV-2 as a global public health emergency [7] after about 118 598 confirmed cases reported from more than 100 countries [7, 8]. As of 21 May 2020, SARS-CoV-2 affected **213 countries and 2 territories** [9]. As per the report from a previous study the median age of the confirmed cases was 59 years (15 to 89 years) with the majority being males [8]. The incubation period of SARS-CoV-2 is from 2 to 14 days (sometimes ranging up to 27 days) [10, 11]. The outbreak has distributed throughout the globe. WHO and national guidelines have endorsed preventive strategies for the current outbreak. However, the current prevention and control strategy of SARS-CoV-2 is facing challenges.  Hence, we conducted this scoping review to assess the current SRARS-CoV-2 pandemic.

# Methods

## Methodological framework

We used the following methodological framework to conduct this scoping review. (1) Identification of review question (2), Developing review objectives, (3) Developing search strategy and identification of search sources, (4) Screening records and data extraction and (5) Setting eligibility criteria.

## Search strategy and searching sources

A search strategy was developed using specific key concepts in our research question: “COVID-19 AND epidemiology”, “COVID-19 AND burden”, “COVID-19 AND pathogenesis”, “COVID-19 AND immune system”, “COVID-19 AND diagnosis”, “COVID-19 AND immune-invading”, “COVID-19 AND preventions” and “COVID-19 AND challenges OR innovations”. We comprehensively searched PubMed, Cochrane, Global Health and google scholars. To avoid missing relevant studies we included preprints and grey literatures using BioRxiv, MedRxiv, World Health Organization and Centers for Disease Control and Prevention reports, conference proceedings and expert information.

## Study selection and data extraction

After the literature search, all the references were imported to Zotero. Four researchers (BB, HD, HL and HN) independently screened studies for eligibility and relevance. A fifth researcher (GA) was consulted for discrepancies. We resolved differences in opinion through discussion.

## Eligibility criteria

Articles, reports, preprints, expert opinions, articles conducted among human participants records published in the English language and records that briefly explained either the epidemiology,

pathogenesis, diagnosis, intervention and current innovations, prevention or future recommendations regarding SARS-CoV-were included.

# Results And Discussion

### Characteristics of the included studies and reports

Most of the records were retrieved from WHO, CDC reports and Global health. Out of the 70 included articles (**Figure 1**) more than half were reports and expert opinions.

### Three months Global burden of SARS-CoV-2 in terms of total confirmed cases and deaths

The confirmed cases of SARS-CoV-2 are increasing. In the first two months, the numbers of cases were higher among countries in the west pacific Asian region than other regions with the lowest cases were reported in Africa. As of 21 May 2020, the number of cases were exponentially increased among countries in the European, American, and Eastern Mediterranean regions (**Figure 2**). Furthermore, the number of deaths were higher in the western pacific Asian region in January and February 2020. However, the reported deaths outnumbered among countries in the European region by since March 2020 up to date (**Figure 3**).

### Virology, pathogenesis, and clinical syndrome of SARS-CoV-2

SRARS-CoV-2 is an RNA virus, with a typical crown-like appearance under an electron microscope due to the presence of glycoprotein spikes on its envelope that is caused by SARS-CoV-2 [12]. Even though its origin remains vague, it was isolated in environmental samples of the Huanan seafood market by China center for disease control and prevention, implying the origin of the outbreak [13]. SARS-CoV-2 was first isolated in the Broncho alveolar lavage fluid of three suspects in Wuhan Jinyintan Hospital during the late 2019 and later considered as a member of β-CoVs [14, 15].

Genome phylogenetic analysis indicates that SARS-CoV-2 shares 79.5% and 50% sequence similarity to SARS-CoV and MERS-CoV, respectively [6, 14, 15]. Possesses a nucleocapsid composed of genomic RNA and phosphorylated nucleocapsid protein. The nucleocapsid is buried inside phospholipid bilayers and covered by spike proteins. The membrane and envelope proteins are located among the S proteins in the viral envelope [16].

Individuals infected with COVID-19 presented with early symptoms of high fever ($39^0$c), headache and abnormal respiratory findings such as cough, and difficult breathing. The virus is theorized to pass through the mucous membranes, especially nasal and larynx mucosa entering the lungs through the respiratory tract [17]. After the virus reaches in the lung it spreads to peripheral blood, causing viremia. Then the virus would adhere and express to the angiotensin-converting enzyme 2 (ACE2), of the organs like lungs, heart, renal, gastrointestinal tract. Patients infected with the virus have a higher number of leukocytes, and increased plasma pro-inflammatory cytokines [14, 18, 19-]. The main pathogenesis of

COVID-19 infection as a respiratory system targeting virus was severe pneumonia, viremia, combined with the incidence of acute cardiac injury [13].

## Host immune response to SARS-CoV-2

The immune system is responsible for controlling, resolution and immunopathogenesis of Coronavirus (CoV) infections. The immune system recognizes the viral agent through pathogen-associated molecular patterns and the pattern recognition receptors. Usually, Toll-like receptor (TLR) 3, TLR7, TLR8, and TLR9 sense viral RNA and DNA in the endosome [21, 24]. The most important recognition mechanisms of RNA viruses are viral RNA receptor (retinoic-acid inducible gene I), cytosolic receptor (melanoma differentiation-associated gene 5) and nucleotide transferase cyclic GMP-AMP synthase [23, 24]. This complex signaling recruits adaptors, including TLR domain-containing adaptor protein, mitochondrial antiviral-signaling protein [25] and stimulator of interferon genes protein [26] to trigger downstream cascade molecules. This will also be involved in adaptor molecule MyD88 and lead to the activation of the transcription factor nuclear factor-κB, interferon regulatory factor 3, the production of type I Interferons and a series of pro-inflammatory cytokines [27,28].

## Innate immunity

To mount an antiviral response, innate immune cells need to recognize the invasion of the SARS-CoV-2. The recognition is through PAMPs and PRRs. In the innate immunity there is activation and regulation of the immune system to eliminate the virus, otherwise results in immunopathology. A few plasma cytokines and chemokines like IL-1, IL-2, IL- 4, IL-7, IL-10, IL-12, IL-13, IL-17, GCSF, macrophage colony-stimulating factor, IP-10, MCP-1, MIP-1α, hepatocyte growth factor, IFN-γ and TNF-α were abnormally high among SARS-CoV-2 infected individuals [13-29]. SARS-CoV-2 causes lung injury due to an inflammatory response in the lower respiratory tract that induces cytokine storm. This is associated with the critical and life-threatening conditions among cases [30].

Like SARS-CoV and MERS-CoV, early high rise in the serum levels of pro-inflammatory cytokines occurred among SARS-CoV-2 infected individuals [31], suggesting a cytokine storm-mediated disease severity [32, 33]. The effective innate immune response against SARS-CoV-2 involves the action of interferon responses and its downstream cascade that controls viral replication and induction of effective adaptive immune response [15]. The recognition site is present in a subset of lung cells called type 2 alveolar cells [14].

## Adaptive immune response

Unlike the other coronaviruses, limited serology details of SARS-CoV-2 were reported. In a previous study, peak IgM antibodies were observed after day 9 of disease onset. Additionally, sera from 5 patients of confirmed cases showed some cross-reactivity with SARS-CoV. Furthermore, SARS-CoV-2 is suggested to be neutralized by the antibodies produced against SARS-CoV in an in vitro plaque assay, suggesting a possible successful mounting of the humeral responses [14]. Although the antibody response against

SARS-CoV-2 is currently under investigation, the previous study revealed that humoral immunity triggers S and N-specific IgM response. This humoral response reached peak and isotype switching to IgG 3 weeks of post symptoms onsets. After 3 weeks IgM decreases and IgG increases [34]. Another study reported that CD8+ T cell responses were more frequently observed than CD4+ T cells. Generally, the virus-specific T cells were the central memory phenotypes with a significantly higher frequency of polyfunctional CD4+ T cells (IFNγ, TNFα, and IL-2) and CD8+ T cells (IFNγ and TNFα). Previously published report revealed that a strong T cell response was correlated significantly with higher neutralizing antibodies [35].

### Immune Evasion Mechanisms

Current observations indicate that coronaviruses are particularly adapted to evade immune detection and dampen human immune responses. This partly explains why they tend to have a longer incubation period, 2-14 days [36]. Hence the viral antigen can escape host immune detection at the early stage. The immune evasion mechanism is potentially like SARS-CoV and MERS-CoV. The other immune escaping mechanism is inhibition of innate immune responses, inhibition of interferon recognition and signaling, immune modulation including membrane or nonstructural proteins (NS4a, NS4b, NS15), viral mutations and immune exhaustion [37-9]. Furthermore, in the adaptive immune response, the evasion mechanism is due to downregulation of antigen presentation via MHC class I and MHC class II [40].

### Suggested strategies to trigger immune system

In the presence of controversial ideas between the immune system and SARS-CoV-2, some scientist and reports suggested that taking items listed below are some supplements to trigger the immune system.

- **Reducing stress**: Stress has negative impact on the production of lymphocytes. As stress increases the risk of viral disease increases [41, 42].
- **Exercise**: Regular exercise promotes cardiovascular health, lowers blood pressure, helps control body weight, and offers protection against diseases. Exercise also improves blood circulation, allowing immune system cells to move through the body more freely and do their job more effectively. Exercise also helps to improve cholesterol and lowers blood pressure and the risk for heart disease [41-43]
- **Eat a balanced diet with fruits, vitamins, and vegetables:** Previous evidence suggested that a lack of these nutrients can alter the immune response [42, 44].
- **Get enough sleep:** Studies showed that people who get an optimal sleep (sleeping 7-8 hours for adults and up to 10 hours for children and teenagers) are less likely to be at risk of viral infections [42, 44].
- **Nutritional supplements:** Such as Vitamin A, B, C and D, Zinc Selenium and iron can boost the immune system against SARS-CoV-2 [45, 46].

### Transmission, laboratory diagnosis and current treatment

**Transmission:** the virus has two main transmissions**,** zoonotic transmission like the outbreak of SARS-CoV in 2003 and MERS-CoV in 2012/2015 [47] and anthroponotic, via direct contact or through droplets spread while coughing or sneezing. Moreover, there is no evidence of congenital transmission for SARS-CoV-2 [16].

### Laboratory diagnosis

The following laboratory diagnostic techniques are used to detect SARS-CoV-2.

1. **Viral nucleic acid test:** Is the routine confirmation test for COVID-19 based on detecting a unique sequence that shows the presence or absence of the virus. The sensitivity and specificity of real-time RT-PCR is greater than 90%. Some factors like contamination, mutations in the primer and probe-target regions of SARS-CoV-2 indicated to have false results [48, 49]. Another study revealed that RT-PCR is a gold standard with 100% sensitivity and specificity [50].
2. **Serology test:** Used for outbreak investigation. These serological tests play a role in research and surveillance which includes antigen and antibody testing. Serum antibody can be detected using ELISA coating a Specific antibody of SARS-CoV-2. Diagnosing SARS-CoV-2 with serology lies with 65-80% sensitivity and 93-100% specificity [51].
3. **Viral sequencing:** After the virus is detected by nucleic acid test viral sequencing is important for monitoring genome mutation [52, 53].
4. **Viral culture:** It is not a routine test but used for further investigation [52, 53].
5. **Haematological test:** Is a supportive test to the routine tests for screening the distribution of complete blood cells [52, 53].
6. **Chest CT Scan:** It aids as a supportive diagnostic method to show pneumonia. This test should be considered to confirm COVID-19 when we are under investigating of this virus [52, 53]. It has higher sensitivity (86-98%) and low specificity (25%) because the imaging features overlap with other viral pneumonia [54, 55].
7. **Blood oxygen saturation test:** This test also uncommon and not routinely applied as a confirmatory test rather used as further investigation of the virus [52].
8. **Detecting Indicators of the inflammatory response:** It is recommended to conduct tests of C-reactive protein, procalcitonin, ferritin, D-dimer, total and subpopulations of lymphocytes, IL-4, IL-6, IL-10, TNF-α, INF-γ and other indicators of inflammation and immune status, which can help evaluate clinical progress, alert severe and critical tendencies, and provide a basis for the formulation of treatment strategies [56].

### Current treatment

Neither an effective vaccine nor anti-viral therapeutic agent is approved to treat SARS-CoV-2. Hence, we mostly focus on supportive care. Rapid public health interventions with antibodies, anti-viral or novel vaccine strategies are highly essential. As per previous reports, passive antibody therapy limits SARS-

CoV-2 pandemic which can recognize epitope regions in the foreign virus particle and reduce the virus replication [57, 58]. Although there is no specific treatment, some reports recommended that using some anti-bacterial or antimalarial and antiviral drugs are important as pre or shortly after the onset of the virus as prophylaxis to reduce infectiousness to others by reducing viral shedding in the respiratory secretions [57]. Some of the prophylactic drugs are listed below.

**Azithromycin:** This antibacterial drug acts by down regulating inflammatory responses and reduces the excessive cytokine production associated with respiratory viral infections [58].

**Chloroquine:** This anti-malarial drug with anti-inflammatory and immunomodulatory activities, has gained significant interest as a potential therapeutic option for the management of COVID-19 which acts by inhibiting the viral enzymes or processes such as viral DNA and RNA polymerase, viral protein glycosylation, virus assembly, new virus particle transport, and virus release. It also involves angiotensin-converting enzyme 2 (ACE2) cellular receptor inhibition, acidification at the surface of the cell membrane inhibiting fusion of the virus, and immunomodulation of cytokine release [58].

**Lopinavir and Ritonavir:** These ant viral drugs act by binding to Mpro, a key enzyme for coronavirus replication [59].

**Alpha interferon:** It is used during immunomodulation as an adjuvant treatment [60].

**Acetaminophen**: It is a temperature controller [61].

**Serum therapy**: It is the use of monoclonal antibodies with serum therapy and intravenous immunoglobulins preparations as passive immunization [59, 62]. This can be achieved by using peptide fusion inhibitors, anti-SARS-CoV-2 neutralizing antibodies, anti- -ACE-2 and protease inhibitors. The spike protein present on the viral membrane plays a vital role in virus entry and is the principal antigenic component responsible for inducing immune response [60-63].

### Antithrombotic treatment

SARS-CoV-2 has been associated with inflammation and a prothrombotic state, with increases in fibrin and fibrin degradation products which are currently added to the treatment guidelines. This treatment is recommended for careful monitoring, evaluating, and treating hospitalized patients with COVID-19 [64].

### Drugs under investigations

**Remdesivir:** This is not approved therapy by the Food and Drug Administration. However, it available through an FDA emergency use authorization for the treatment of hospitalized clients with COVID-19. It is suggested to be highly selective for viral polymerases, low toxicity and have a high genetic barrier to resistance with a long half-life that allows for once-daily dosing [64, 65, 66]

**Hydroxychloroquine**: Have better tolerability than chloroquine but the FDA precautioned that should not be used outside the hospital [67].

**Immune globulin administration**: Administration of convalescent plasma is recommended therapy which is currently under trial for COVID-19 treatment options [55, 64].

**Interleukin inhibitors**: To limit the cytokine storm following the immune response against SARS-CoV-2 interleukin inhibitors are undergoing phase trial for treatment option [55, 64].

### Economical and psychological impact of SARS-CoV-2

Following the index case of SARS-CoV-2 infected individual in China by December 2019 it started to spread to the rest of the world. It is then declared as a pandemic outbreak by WHO. Since the declaration of the outbreak, it leads to several economical and psychological problems. Some of the impacts include disruption of the global chain supply due to the closing their border, a slowdown of the investment, loss of revenue due to debt, increment in health spending cost, shortage of food and drugs, decrement of business travel and tightening domestic financial markets [68, 69]. Besides this, the outbreak leads to psychological trauma like fears, sadness, anxiety, and depression of the people [70].

**Risk groups:** Individuals with obesity, cardiovascular disease, respiratory diseases like chronic obstructive pulmonary disease, asthma, bronchitis, sinusitis, seasonal allergies/toxic mold exposure, dysbiosis, auto-immune diseases, fibromyalgia, neuro-degenerative disease, cancer, fatty liver, biotoxin illness and diabetes are highly susceptible to SARS-CoV-2 due to the depletion of immunological barrier mechanisms and cellular dysfunction [60].

To minimize the risk of vulnerable individuals, preventative strategies like cleaning and disinfecting in home and areas that people touch the most should be used. Adhering the same preventive measures as people went out and contacting healthcare providers are very crucial to minimize the risk of getting infected. Furthermore, individuals must limit shared spaces when having guests and keeping recommended physical distancing [71].

### Challenges and future prevention of SARS-CoV-2

**Challenges:** The challenges for the effective controlling of SARS-CoV-2include absence validated vaccine and treatment [60, 72], ability of the viral antigen to stay hours and even longer in the air, socio-cultural behaviour of people, lack of awareness, viral capacity to stay in inanimate objects for weeks [73], overcrowding environment, presence of asymptomatic carriers [74], presence of wide host range [61], lack of adherence to the recommended physical distancing protocols, variation of interpreting physical distancing,  unclear infective dose of the viral agent, unclear duration of infectiousness prior the onset of clinical manifestation and after recovery [65, 67].

### Future preventions and recommendations

**At government level:** International, National, regional governments should participate by allocating budget for training, isolation of suspects, testing and supportive cares and awareness creation.

**At health institutions:** Health institutions should also screen and early detection, giving supportive care and treatment, distributing medical protective equipment, give health education and introducing handwashing practices to customers and preparing isolation rooms [75].

At **the** community level: Creating community awareness on the transmission and early prevention, active case detection, distribution and preparing handwashing jars, utilization of hand sanitizers and respirators [75, 76], avoiding over-crowding [75], avoiding intimate contact with animals [76] and applying hand glove to protect touching different contaminates [75] should be practiced.

**At churches and University levels:** Minimizing conferences and Sunday schools, avoiding movement along with different places, avoid lecturing in classes and replace with alternative lecture methods, creating awareness using posters, preparing and distributing handwashing jars for the university community at the entry and exit and empowering the community on the usefulness of social distancing and handwashing practices.

**For upcoming researchers**: Researchers should develop validated vaccine and treatment.

# Conclusion

Due to the rapid spreading nature of SARS-CoV-2 the prevention and control strategies become challenging. Generally, the SARS-CoV-2 pandemic is imposing social, psychological, and socio-economic impacts. Curative treatments and vaccines are trying to be administered to humans and some are on clinical trials. Moreover, the most important preventing strategies for the pandemic up to date are physical distancing, isolation, and quarantine of suspects, using personal protective equipment, health education and improving handwashing practices, avoiding contact with animals. Hence, individuals have to strictly follow these prevention methods. There are limitations in implementing the prevention strategies.

# Abbreviations

ACE =Angiotensin converting enzyme, CD= Cluster of differentiation, CDC= Center of Disease Control, COPD = Chronic obstructive pulmonary disease, COVID-19= Novel corona virus-19, MERS-CoV=Middle East respiratory syndrome, PRISMA= Preferred Reporting Items for Systematic Reviews and Meta-analyses Protocol, RNA= Ribonucleic acid, SARS-CoV= Severe acute respiratory syndrome, WHO= World health organization, TH= T helper cells TLR=Toll-like receptor

# Declarations

### Competing interests

The authors declare that they have no competing interests.

### Declarations

### Ethics approval and consent to participate

Not applicable

### Consent for publication

Not applicable

### Availability of data and material

All data are incorporated into the manuscript.

### Funding

Not applicable

### Authors' contributions

All authors contributed equally to conduct this review, read, and approved the final manuscript.

### Acknowledgements

Not applicable

## References

1. Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z *et al*. Epidemiology and Transmission of COVID-19 in Shenzhen China: Analysis of 391 cases and 1,286 of their close contacts, 2020 (Unpublished).
2. Guarner J. Three Emerging Coronaviruses in Two Decades. *Am J Clin Pathol* doi: 10.1093/ajcp/aqaa029.
3. Su S, Wong G and Shi W. Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses. *Trends Microbiol* 2016; 24:490-502.
4. Adhikari SP, Meng S, Ju Wu Y, Ping Mao Y, Xue Ye R, Zhi Wang Q *et al*. Epidemiology, causes, clinical manifestation and diagnosis, prevention, and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infectious Diseases of Poverty, 2020 [cited 2020 Mar 27]. Available from: https://idpjournal.biomedcentral.com/articles/10.1186/s40249-020-00646-x
5. World Health Organization. Coronavirus disease 2019 (COVID-19) situation report-121.
6. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, *et al*. Genomic characterization, and epidemiology of novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020; **395**:565-574.
7. World Health Organization. Coronavirus disease 2019 (COVID-19) situation report-51. Geneva, Switzerland: World Health Organization; 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200311-sitrep-51-covid-19.pdf?sfvrsn=1ba62e57_10

8. European Centre for Disease Prevention and Control. Novel coronavirus disease 2019 (COVID-19) pandemic: increased transmission in the EU/EEA and the UK-sixth update-12 European Centre for Disease Prevention and Control. Novel coronavirus disease, Stockholm. Novel coronavirus disease 2019 (COVID-19) pandemic: increased transmission in the EU/EEA and the UK-sixth update. 2020;28
9. Coronavirus disease 2019 (COVID-19) situation report-103, 02 May 2020.
10. World Health Organization (WHO). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19) 2020 [cited 2020 1 March]. Available from: https://www.who.int/docs/default-source/coronaviruse/who-china-jointmission-on-covid-19-final-report.pdf.
11. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y *et al*. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med*. 2020. https://doi.org/10.1056/NEJMoa2001316.
12. Perlman S, and Net land J. Coronaviruses post-SARS: Update on replication and pathogenesis. *Rev. Microbiol.* 2009; **7**:439-450.
13. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y *et al*. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet (Lond. Engl).* 2020; **395**:497-506.
14. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J *et al*. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *Engl. J. Med*. 2020.
15. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W *et al.* A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.* 2020, 1-4.
16. Wu F, Zhao S, Yu B, Chen YM, Wang W, HuY *et al*. Complete genome characterization of a novel coronavirus associated with severe human respiratory disease in Wuhan, China. BioRxiv 2020.
17. Guan W J, Ni Z Y, and Hu Y. Clinical characteristics of 2019 novel coronavirus infection in China. *N Engl J Med*. 2020; undefined: undefined. doi: 10.1056/NEJMoa2002032.
18. Lei J, Li J, Li X and Qi X. CT imaging of the 2019 novel coronavirus (2019-nCoV) pneumonia, Radiology (2020); 200236, https://doi.org/10.1148/radiol. 2020200236.
19. Munster VJ, Koopmans M, van Doremalen N, van Riel D and de Wit E. A Novel Coronavirus Emerging in China - Key Questions for Impact Assessment. *N Engl J Med* 2020 Jan 24. doi: 10.1056/NEJMp2000929. [Epub ahead of print]
20. Alexopoulou L, Holt AC, Medzhitov R and Flavell RA. Recognition of double stranded RNA and activation of NF-kappaB by toll-like receptor. *Nature*. 2001; **413**(6857):732-8.
21. Wu J and Chen ZJ. Innate immune sensing and signaling of cytosolic nucleic acids. *Annu Rev Immunol*. 2014; **32**:461-88.
22. Yoo JS, Kato H and Fujita T. Sensing viral invasion by RIG-I like receptors. *Curr Opin Microbiol*. 2014; **20**:131-8.
23. Wu J, Sun L, Chen X, Du F, Shi H, Chen C *et al*. Cyclic GMP-AMP is an endogenous second messenger in innate immune signaling by cytosolic DNA. Science. 2013; **339**(6121):826-30.

24. Seth RB, Sun L, Ea CK and Chen ZJ. Identification and characterization of MAVS, a mitochondrial antiviral signaling protein that activates NF-kappa B and IRF3. Cell. 2005; **122**(5):669-82.
25. Ishikawa H and Barber GN. STING is an endoplasmic reticulum adaptor that facilitates innate immune signaling. 2008; **455**(7213):674-8.
26. Kawai T and Akira S. The role of pattern-recognition receptors in innate immunity: update on toll-like receptors. *Nat Immunol*. 2010; **11**(5):373-84.
27. Takeuchi O and Akira S. Innate immunity to virus infection. *Immunol Rev*. 2009; **227**(1):75-86.
28. Chen C, Zhang XR, Ju ZY and He WF. Advances in the research of cytokine storm mechanism induced by Corona Virus Disease 2019 and the corresponding immunotherapies. Zhonghua Shaoshang Zazhi. 2020; **36**(0): E005.
29. Liu Y, Zhang C, Huang F, Yang Y, Wang F, Yuan J *et al*. 2019-novel coronavirus (2019-nCoV) infections trigger an exaggerated cytokine response aggravating lung injury. 2020. http://www.chinaxiv.org/abs/202002.00018. Accessed 18 Feb 2020.
30. Liu Q, Wang R, Qu G, Wang Y, Liu P, Zhu Y *et al*. General anatomy report of novel coronavirus pneumonia death corpse. *J Forensic Med*. 2020; **36**(1):19-21.
31. Wu F, Zhao S, Yu B, Chen YM, Wang W and Song ZG *et al*. A new coronavirus associated with human respiratory disease in China. Nature [Preprint]. 2020 [cited 2020 Feb 16]: [19 p.]. Available from: https://doi.org/10.1038/s41586-020-2008-3.
32. Mahallawi WH, Khabour OF, Zhang Q, Makhdoum HM and Suliman BA. MERS-CoV infection in humans is associated with a pro-inflammatory Th1 and Th17 cytokine profile. Cytokine. 2018; **104**:8-13.
33. Wong CK, Lam CW, Wu AK, Ip WK, Lee NL, Chan IH *et al*. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. *Clin Exp Immunol*. 2004; **136**(1):95-103.
34. Xiao DAT, Gao DC, and Zhang DS. Profile of specific antibody to SARS-CoV-2: The first report. J Infect. 2020. DOI: http://10.1016/j.jinf.2020.03.012
35. Li CK, Wu H, Yan H, Ma S, Wang L, Zhang M *et al.* T cell responses to whole SARS coronavirus in humans. *J Immunol*. 2008; **181**(8):5490-500.
36. Lessler J, Reich NG, Brookmeyer R, Perl TM, Nelson KE and Cummings DA. Incubation periods of acute respiratory viral infections: a systematic review. *Lancet Infect Dis*. 2009; **9**(5):291-300.
37. Faure E, Poissy J, Goffard A, Fournier C, Kipnis E, Titecat M *et al*. Distinct immune response in two MERS-CoV-infected patients: can we go from bench to bedside? *PLoS One*. 2014; **9**(2):e88716.
38. Yi Y, Lagniton PNP, Ye S, Li E and Xu R-H. COVID-19: what has been learned and to be learned about the novel coronavirus disease. *Int J Biol Sci* 2020; **16**:1753-66. https://doi.org/10.7150/ijbs.45134.
39. Prompetchara E, Ketloy C and Palaga T. Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic. *Asian Pac J Allergy Immunol* https://doi.org/10.12932/AP-200220-0772.

40. Shokri S, Mahmoudvand S, Taherkhani R and Farshadpour F. Modulation of the immune response by Middle East respiratory syndrome coronavirus. *J Cell Physiol*. 2019; **234**(3):2143-51.
41. Center for disease control and prevention. People who are at high risk for severe illness. 2020. https://www.cdc.gov/coronavirus/2019-ncov/specific-groups/people-at-higher-risk.html
42. Centers for Disease Control and Prevention. Interim guidance for persons who may have 2019 Novel Coronavirus (2019-nCoV) to prevent spread in homes and residential communities. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-prevent-spread.html?Val=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019 ncov%2Fguidance-prevent-spread.html. [Accessed on 18 May2020].
43. National Center for Complementary and Integrative Health. Yoga: what you need to know. Available at: https://nccih.nih.gov/health/yoga/intro duction.htm. [Accessed on May 18 2020].
44. Peijie Chen, Lijuan Mao, George P. Nassis, Peter Harmer d, Barbara E. Ainsworth, Fuzhong Li. Coronavirus disease (COVID-19): The need to maintain regular physical activity while taking precautions. *J Sport Health Sci*. 2020; **9**:1034. (http://creativecommons.org/licenses/by-nc-nd/4.0/).
45. Kahled MB and Benejiba N. The role of nutrition in strengthening the immune system against newly emerging viral diseases: A case of SARS-CoV-2. *The northern African journal of food and nutrition research*. 2020; **04**(07): 240-244.
46. Derbyshire E and Delange J. COVID-19: Is there a role for immune-nutrition, particularly in the over 65s. *BMJ nutrition, prevention, and health*. 2020; **0**:1-6. Doi: http://10.1136/bmjnph-2020-000071.
47. Pan African Health Organization (PAHO). Laboratory Guidelines for Detection and Diagnosis of the Novel Coronavirus (2019-nCoV) Infection February 01, 2020.
48. Tahamtan A and Ardebili A. Real-time RT-PCR in COVID-19 detection: issues affecting the results EXPERT REVIEW OF MOLECULAR DIAGNOSTICS,2020https://doi.org/10.1080/14737159.2020.1757437
49. Yan C, Cui J, Huang L, Du B, Chen L, Xue G *et al*. Rapid and visual detection of 2019 novel coronavirus (SARS-CoV-2) by a reverse transcription loop mediated isothermal amplification assay, Clinical Microbiology and Infection, https://doi.org/10.1016/j.cmi.2020.04.001
50. Derrick Crook. Evaluation of antibody testing for SARS-CoV-2 using ELISA and lateral flow immunoassays. United Kingdom, 2020. (unpublished)
51. Rothan HA and Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *Journal of Autoimmunity* 2020:102433. https://doi.org/10.1016/j.jaut.2020.102433.
52. China CDC Weekly. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) -China, 2020 n.d.
53. Laboratory testing for coronavirus disease 2019 (COVID-19) in suspected human cases. Interim guidance 2 March 2020.
54. Udugama B, Kadhiresan P, Kozlowski HN, Malekjahani A, Osborne M, Li VYC *et al*. Diagnosing COVID-19: The Disease and Tools for Detection. *ACS Nano*, 2020.

55. Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W *et al*. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology* 2020, 2020, 200642.
56. Handbook of COVID-19 Prevention and Treatment. The First Affiliated Hospital, Zhejiang University School of Medicine Compiled According to Clinical Experience. Accessed date may 18, 2020.
57. FDA: https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/coronavirus-disease-2019-covid-19.
58. Smith T, Bushek J, and Prosser T. COVID-19 Drug Therapy-Potential Options. *Clinical Drug Information / Clinical Solutions* March 26, 2020.
59. Liu X and Wang XJ. Potential inhibitors for 2019-nCoV coronavirus M protease from clinically proven medicines. J Genet Genomics 2020 Feb 13. [Epub ahead of print] PMID: 32173287
60. Jin Y, Cai L and Cheng Z. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Military Med Res* 2020; **7**:4.
61. FDA: https://www.fda.gov/drugs/drug-safety-and-availability/fda-advises-patients-use-non-steroidal-anti-inflammatory-drugs-nsaids-covid-19.
62. Mitja O, and Clotet B. Use of antiviral drugs to reduce COVID-19 transmission. *Lancet Glob Health* 2020 https://doi.org/10.1016/ S2214-109X (20)30114-5.
63. Wan Y, Shang J, Graham R, Baric RS and Li F. Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS. *J Virol* [Preprint]. 2020. Available: https://jvi.asm.org/content/jvi/early/2020/01/23/JVI.00127-20.full.pdf
64. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://covid19treatmentguidelines.nih.gov/. Accessed date (18 may, 2020).
65. United Nations economic commissions for Africa. Economic Impact of the COVID-19 on Africa. Addis Ababa, Ethiopia March 13, 2020.
66. Mental health and psychosocial considerations during the COVID-19 outbreak, 18 March 2020.
67. Guidelines for elderly and high-risk groups to safeguard from COVID-19 Outbreak,1753503/2020/O/O IDSP-NCDC.
68. What you need to know about coronavirus disease 2019 (COVID-19) n.d.
69. Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P *et al*. Coronavirus infections and immune responses. *Journal of Medical Virology* 2020; 92:424-32. https://doi.org/10.1002/jmv.25685.
70. Cassella C. New Study Indicates How Long Coronaviruses Can Survive on a Surface. ScienceAlert n.d. https://www.sciencealert.com/study-shows-just-how-long-coronaviruses-can-stick-around-on-a-surface (accessed March 24, 2020).
71. Rapid risk assessment of European center for disease prevention and control (ECDC) coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK-eighth update, 8 April 2020.

72. Coronavirus Disease 2019 (COVID-19)-Prevention & Treatment. Centers for Disease Control and Prevention 2020. https://www.cdc.gov/coronavirus/2019-ncov/prepare/prevention.html (accessed March 23, 2020).
73. International Labour Organization (ILO) Note. COVID-19 and the world of work: Impact and policy responses 18 March 2020.
74. United Nations economic commissions for Africa. Economic Impact of the COVID-19 on Africa. Addis Ababa, Ethiopia March 13, 2020.
75. Coronavirus Disease 2019 (COVID-19) - Preventing COVID-19 Spread in Co. Centers for Disease Control and Prevention 2020. https://www.cdc.gov/coronavirus/2019-ncov/community/index.html (accessed March 23, 2020).
76. McIntosh K. COVID-19: epidemiology, virology, and clinical features - GOV.UK n.d. https://www.gov.uk/government/publications/wuhan-novel-coronavirus-background-information/wuhan-novel-coronavirus-epidemiology-virology-and-clinical-features (accessed March 23, 2020).

# Figures

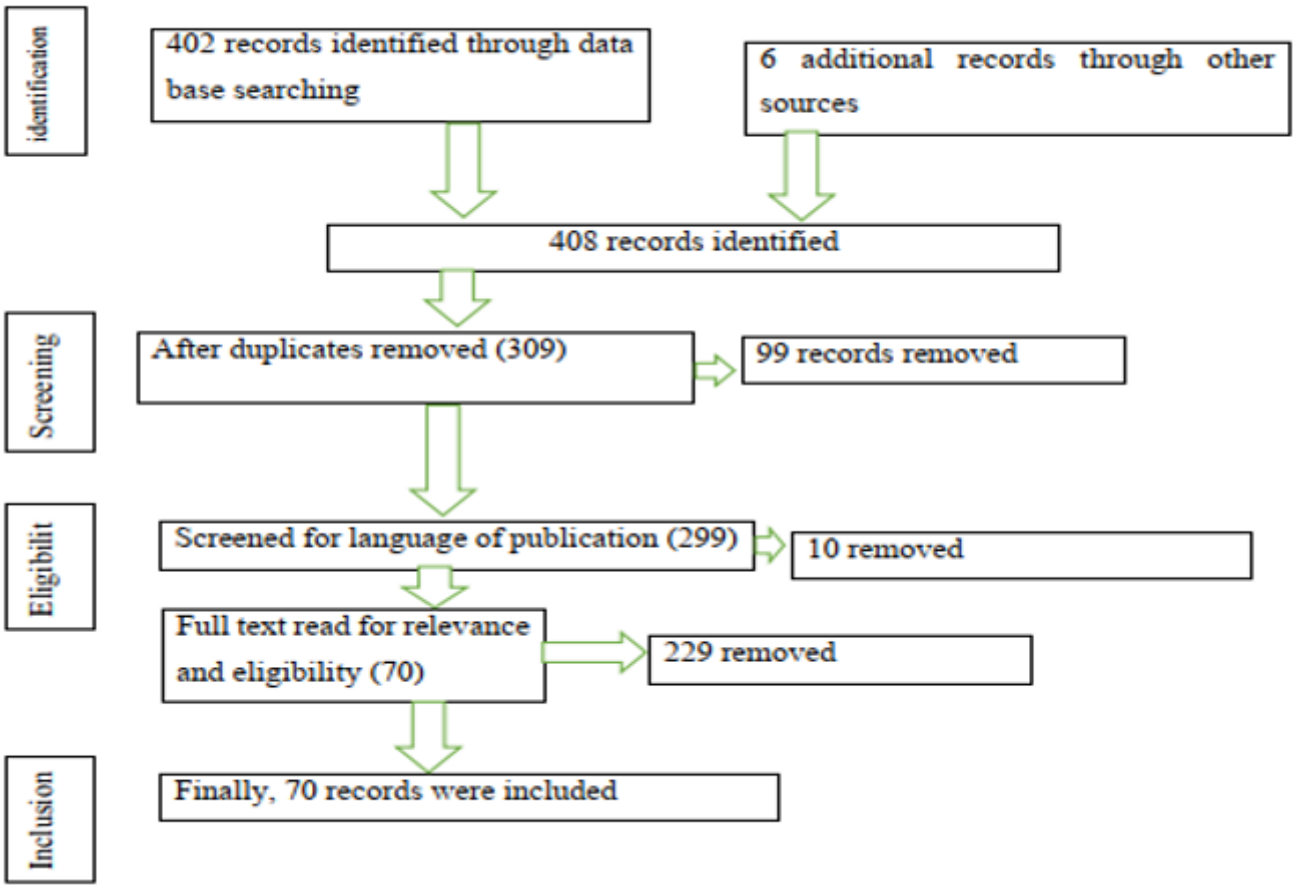


**Figure 1**

PRISMA diagram of included records

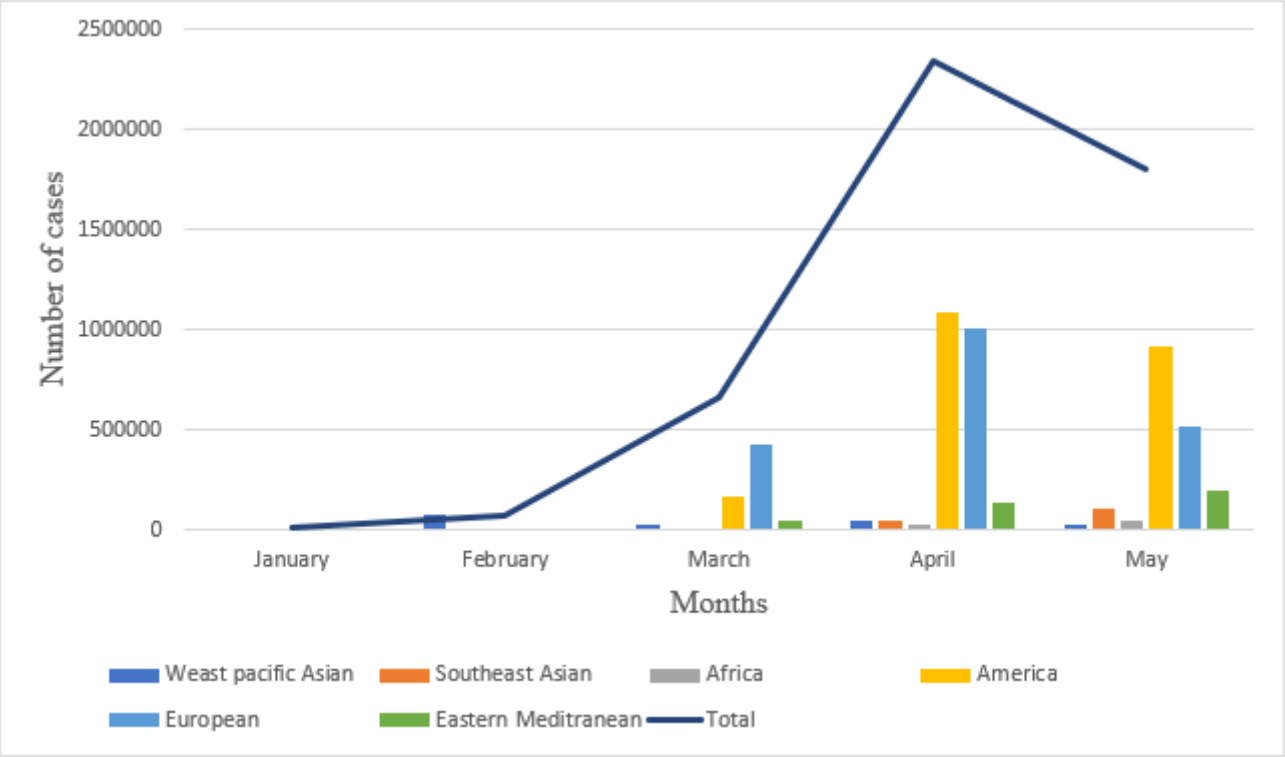


**Figure 2**

Distribution of confirmed SARS-CoV-2 cases in the recent five months in all WHO regions

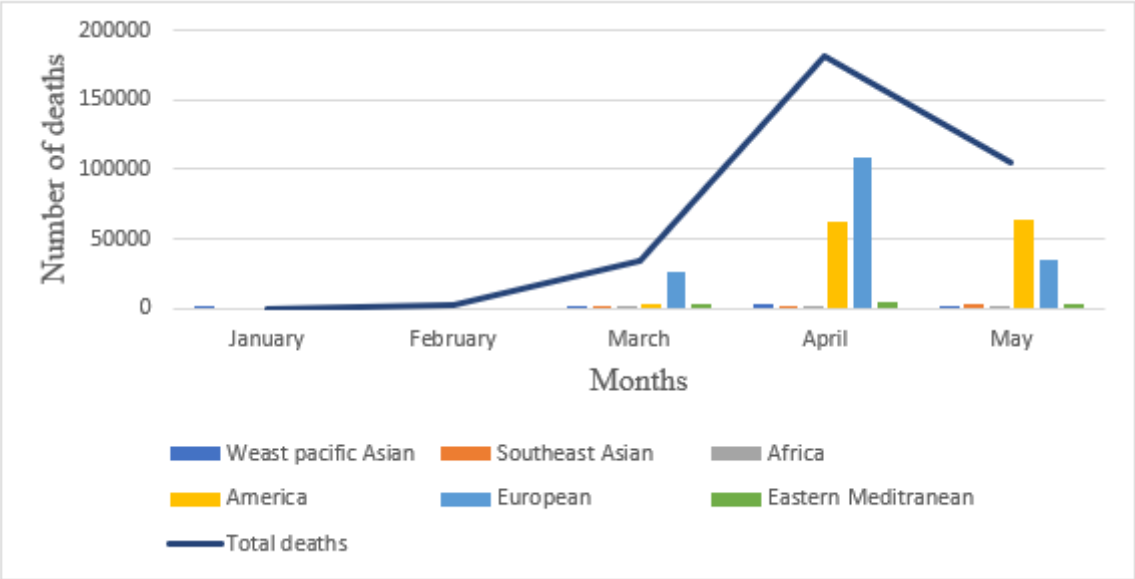


**Figure 3**

Total distribution of SARS-CoV-2 deaths in the recent five months with the WHO regions