Scoping Search Results

Research question or topic:

"What workforce do we need to effectively treat and support people with, and after, COVID-19?"

This question was split into two searches (this document answers part b)

a) Literature discussing the workforce implications
b) Incidence and prevalence of key symptoms (physical, cognitive and psychological) – clinical presentation and health outcomes of COVID-19 to help determine the likely skill mix, training and education needed"

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Search comments

There is an abundance of literature being published about COVID-19. To answer your question I split the search into two parts - part a includes literature that discusses what the workforce implications of the virus might be, or anything that examines a post-COVID environment. Part b covers the clinical presentation/ symptoms of COVID-19 and potential health outcomes which could be used to think through the kinds of skills that might be required – the results of this part are detailed below. Lots of literature was available so what is included was intended as a "scoping exercise" to give you an idea of the kinds of topics being discussed, not a definitive list of everything published under each sub-theme. If you require a more in-depth search of any of the themes or topics included, I would be happy to conduct these for you.

A full list of results is available below and they have been grouped under "clinical presentation and symptoms" and "health outcomes" and organised further by theme (see contents list).

The WHO and PHE have both issued lists of symptoms, and identified some as more common than others, though as you will see from the literature there are ongoing discussions about the commonality of different symptoms, and the evidence base continues to emerge. On the 18th May 2020 it was reported that loss of smell and taste had been added to the symptoms list in the UK.

Please note that some of papers included may be preprints. Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behaviour and should not be reported in news media as established information.

Search results

Clinical presentation and symptoms

Range of symptoms

Coronavirus Symptoms World Health Organisation

COVID-19 affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization.

Most common symptoms:

- fever.
- · dry cough.
- tiredness.

Less common symptoms:

- aches and pains.
- sore throat.
- diarrhoea.
- · conjunctivitis.
- headache.
- loss of taste or smell.
- a rash on skin, or discolouration of fingers or toes.

Check if you have coronavirus symptoms NHS

Use the 111 online coronavirus service if you have either:

- a high temperature this means you feel hot to touch on your chest or back (you do not need to measure your temperature)
- a new, continuous cough this means coughing a lot for more than an hour, or 3 or more coughing episodes in 24 hours (if you usually have a cough, it may be worse than usual)
- loss or change to your sense of smell or taste this means you've noticed you
 cannot smell or taste anything, or things smell or taste different to normal

These are the main symptoms of coronavirus.

On the 18th May 2020 it was announced that loss of smell and taste had been added to the UK symptoms list.

Video: Spotlight on COVID: Tracking the symptoms 5th May 2020, King's College London

Professor Richard Trembath, Executive Dean, Faculty of Life Sciences & Medicine, interviews Tim Spector, Professor of Genetic Epidemiology and Head of the Department of Twin Research

& Genetic Epidemiology in the School of Life Course Sciences, to discuss the COVID Symptom Tracker app.

<u>COVID symptoms partly influenced by genetics according to app data</u> 27th April 2020, King's College

Data from the COVID Symptom Tracker app suggests some symptoms, including fever, fatigue and anosmia, have genetic influences.

<u>Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized</u> With COVID-19 in the New York City Area 22nd April 2020, JAMA Network

Question What are the characteristics, clinical presentation, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19) in the US? Findings In this case series that included 5700 patients hospitalized with COVID-19 in the New York City area, the most common comorbidities were hypertension, obesity, and diabetes. Among patients who were discharged or died (n = 2634), 14.2% were treated in the intensive care unit, 12.2% received invasive mechanical ventilation, 3.2% were treated with kidney replacement therapy, and 21% died. Meaning This study provides characteristics and early outcomes of patients hospitalized with COVID-19 in the New York City area.

<u>Clinical Presentation of COVID-19: A Systematic Review Focusing on Upper Airway Symptoms</u>
April 2020, Ear, nose and throat journal

AIMPharyngodynia, nasal congestion, rhinorrhea, smell, and taste dysfunctions could be the presenting symptoms of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2. The aim was to perform a systematic review of current evidences on clinical presentation of COVID-19, focusing on upper airway symptoms in order to help otolaryngologists identifying suspected cases.METHODSWe searched PubMed and Web of Science electronic databases.RESULTSWe included 5 retrospective clinical studies for a total of 1556 hospitalized patients with COVID-19, 57.5% were male and mean age was 49.1 years. Pooled data revealed that pharyngodynia was present in 12.4% of patients, nasal congestion in 3.7%, and rhinorrhea was rare. No reports on COVID-19 and olfactory/gustative disorders matched inclusion criteria but preliminary evidences suggested they could be present. Common symptoms were fever (85.6%), cough (68.7%), and fatigue (39.4%). Frequent comorbidities were hypertension (17.4%), diabetes (3.8%), and coronary heart disease (3.8%); 83% of patients had alterations on chest computed tomography that were bilateral in 89.5% of cases. Ground-glass opacity was the most common finding (50%). Lymphopenia (77.2%) and leucopenia (30.1%) were common. Critical cases with complications were 9%, intensive care unit admission was required in 7.3%, invasive ventilation in 3.4%, and mortality was 2.4%.CONCLUSIONOtolaryngologists should know that pharyngodynia, nasal congestion, olfactory, and gustative disorders could be the presenting symptoms of COVID-19. Clinical presentation together with radiological and laboratory findings could help to identify suspected cases.

<u>Clinical Course and Outcomes of Patients with Severe Acute Respiratory Syndrome</u>
<u>Coronavirus 2 Infection: a Preliminary Report of the First 28 Patients from the Korean Cohort Study on COVID-19 April 2020, Journal of Korean Medical Science</u>

BACKGROUNDSevere acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected pneumonia emerged in Wuhan, China in December 2019. In this retrospective multicenter study, we investigated the clinical course and outcomes of novel coronavirus disease 2019 (COVID-19) from early cases in Republic of Korea.METHODSAll of the cases confirmed by real time polymerase chain reaction were enrolled from the 1st to the 28th patient nationwide. Clinical data were collected and analyzed for changes in clinical severity including laboratory, radiological, and virologic dynamics during the progression of illness.RESULTSThe median age was 40 years (range, 20-73 years) and 15 (53.6%) patients were male. The most common symptoms were cough (28.6%) and sore throat (28.6%), followed by fever (25.0%). Diarrhea was not common (10.7%). Two patients had no symptoms. Initial chest X-ray (CXR) showed infiltration in 46.4% of the patients, but computed tomography scan confirmed pneumonia in 88.9% (16/18) of the patients. Six patients (21.4%) required supplemental oxygen therapy, but no one needed mechanical ventilation. Lymphopenia was more common in severe cases. Higher level of C-reactive protein and worsening of chest radiographic score was observed during the 5-7 day period after symptom onset. Viral shedding was high from day 1 of illness. especially from the upper respiratory tract (URT). CONCLUSIONThe prodromal symptoms of COVID-19 were mild and most patients did not have limitations of daily activity. Viral shedding from URT was high from the prodromal phase. Radiological pneumonia was common from the early days of illness, but it was frequently not evident in simple CXR. These findings could be plausible explanations for the easy and rapid spread of SARS-CoV-2 in the community.

Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis March 2020, Travel medicine and infectious diseases

INTRODUCTIONAn epidemic of Coronavirus Disease 2019 (COVID-19) began in December 2019 in China leading to a Public Health Emergency of International Concern (PHEIC). Clinical. laboratory, and imaging features have been partially characterized in some observational studies. No systematic reviews on COVID-19 have been published to date.METHODSWe performed a systematic literature review with meta-analysis, using three databases to assess clinical, laboratory, imaging features, and outcomes of COVID-19 confirmed cases. Observational studies and also case reports, were included, and analyzed separately. We performed a random-effects model meta-analysis to calculate pooled prevalences and 95% confidence intervals (95%CI).RESULTS660 articles were retrieved for the time frame (1/1/2020-2/23/2020). After screening, 27 articles were selected for full-text assessment, 19 being finally included for qualitative and quantitative analyses. Additionally, 39 case report articles were included and analyzed separately. For 656 patients, fever (88.7%, 95%CI 84.5-92.9%), cough (57.6%, 95%CI 40.8-74.4%) and dyspnea (45.6%, 95%CI 10.9-80.4%) were the most prevalent manifestations. Among the patients, 20.3% (95%CI 10.0-30.6%) required intensive care unit (ICU), 32.8% presented with acute respiratory distress syndrome (ARDS) (95%CI 13.7-51.8), 6.2% (95%Cl 3.1-9.3) with shock. Some 13.9% (95%Cl 6.2-21.5%) of hospitalized patients had fatal outcomes (case fatality rate, CFR). CONCLUSION COVID-19 brings a huge burden to healthcare facilities, especially in patients with comorbidities. ICU was required for approximately 20% of polymorbid, COVID-19 infected patients and hospitalization was associated with a CFR of >13%. As this virus spreads globally, countries need to urgently prepare human resources, infrastructure and facilities to treat severe COVID-19.

<u>Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei</u> (<u>epicenter</u>) and outside Hubei (<u>non-epicenter</u>): A Nationwide Analysis of China April 2020, The European Respiratory Journal

BACKGROUNDDuring the outbreak of coronavirus disease 2019 (COVID-19), consistent and considerable differences in disease severity and mortality rate of patients treated in Hubei province compared to those in other parts of China has been observed. We sought to compare the clinical characteristics and outcomes of patients being treated inside and outside Hubei province, and explore the factors underlying these differences.METHODSCollaborating with the National Health Commission, we established a retrospective cohort to study hospitalised COVID-19 cases in China. Clinical characteristics, the rate of severe events and deaths, and the time to critical illness (invasive ventilation or intensive care unit admission or death) were compared between patients in and outside of Hubei. The impact of Wuhan-related exposure (a presumed key factor that drove the severe situation in Hubei, as Wuhan is the epicenter as well the administrative center of Hubei province) and the duration between symptom onset and admission on prognosis were also determined. RESULTSUpon data cut-off (Jan 31st, 2020). 1590 cases from 575 hospitals in 31 provincial administrative regions were collected (core cohort). The overall rate of severe cases and mortality was 16.0% and 3.2%, respectively. Patients in Hubei (predominantly with Wuhan-related exposure, 597/647, 92.3%) were older (mean: 49.7 versus 44.9 years), had more cases with comorbidity (32.9% versus 19.7%), higher symptomatic burden, abnormal radiologic manifestations, and, especially, a longer waiting time between symptom onset and admission (5.7 versus 4.5 days) compared with patients outside Hubei. Patients in Hubei [severe event rate 23.0% versus 11.1%, death rate 7.3% versus 0.3%, hazards ratio (HR) for critical illness 1.59, 95%CI 1.05-2.41] have a poorer prognosis compared with patients outside of Hubei after adjusting for age and comorbidity. However, among patients outside of Hubei, the duration from symptom onset to hospitalisation (mean: 4.4 versus 4.7 days) and prognosis (HR 0.84, 95%CI 0.40-1.80) were similar between patients with or without Wuhan-related exposure. In the overall population, the waiting time, but neither treated in Hubei nor Wuhan-related exposure, remained an independent prognostic factor (HR 1.05, 1.01-1.08).CONCLUSIONThere were more severe cases and poorer outcomes for COVID-19 patients treated in Hubei, which might be attributed to the prolonged duration of symptom onset to hospitalisation in the epicenter. Future studies to determine the reason for delaying hospitalisation are warranted.

Clinical and Epidemiological Characteristics of 1,420 European Patients with mild-to-moderate Coronavirus Disease 2019 April 2020, Journal of Internal Medicine

BACKGROUNDThe clinical presentation of European patients with mild-to-moderate Covid-19 infection is still unknown.OBJECTIVETo study the clinical presentation of Covid-19 in Europe.METHODSPatients with positive diagnosis of Covid-19 were recruited from 18 European hospitals. Epidemiological and clinical data were obtained through a standardized questionnaire. Bayesian analysis was used for analyzing the relationship between outcomes.RESULTS1,420 patients completed the study (962 females, 30.7% of health care

workers). The mean age of patients was 39.17±12.09 years. The most common symptoms were headache (70.3%), loss of smell (70.2%), nasal obstruction (67.8%), cough (63.2%), asthenia (63.3%), myalgia (62.5%), rhinorrhea (60.1%), gustatory dysfunction (54.2%) and sore throat (52.9%). Fever was reported by on 45.4%. The mean duration of Covid-19 symptoms of mild-to-moderate cured patients was 11.5±5.7 days. The prevalence of symptoms significantly varied according to age and sex. Young patients more frequently had ear, nose, and throat complaints, whereas elderly individuals often presented fever, fatigue and loss of appetite. Loss of smell, headache, nasal obstruction and fatigue were more prevalent in female patients. The loss of smell was a key symptom of mild-to-moderate Covid19 patients and was not associated with nasal obstruction and rhinorrhea. Loss of smell persisted at least 7 days after the disease in 37.5% of cured patients.CONCLUSIONThe clinical presentation of mild-to-moderate Covid-19 substantially varies according to the age and the sex characteristics of patients. Olfactory dysfunction seems to be an important underestimated symptom of mild-to-moderate Covid-19 that needs to be recognized as such by the WHO.

A Comprehensive Literature Review on the Clinical Presentation, and Management of the Pandemic Coronavirus Disease 2019 (COVID-19) April 2020, Cureus

Coronavirus disease 2019 (COVID-19) is a declared global pandemic. There are multiple parameters of the clinical course and management of the COVID-19 that need optimization. A hindrance to this development is the vast amount of misinformation present due to scarcely sourced manuscript preprints and social media. This literature review aims to presents accredited and the most current studies pertaining to the basic sciences of SARS-CoV-2, clinical presentation and disease course of COVID-19, public health interventions, and current epidemiological developments. The review on basic sciences aims to clarify the jargon in virology, describe the virion structure of SARS-CoV-2 and present pertinent details relevant to clinical practice. Another component discussed is the brief history on the series of experiments used to explore the origins and evolution of the phylogeny of the viral genome of SARS-CoV-2. Additionally, the clinical and epidemiological differences between COVID-19 and other infections causing outbreaks (SARS, MERS, H1N1) are elucidated. Emphasis is placed on evidence-based medicine to evaluate the frequency of presentation of various symptoms to create a stratification system of the most important epidemiological risk factors for COVID-19. These can be used to triage and expedite risk assessment. Furthermore, the limitations and statistical strength of the diagnostic tools currently in clinical practice are evaluated. Criteria on rapid screening, discharge from hospital and discontinuation of self-quarantine are clarified. Epidemiological factors influencing the rapid rate of spread of the SARS-CoV-2 virus are described. Accurate information pertinent to improving prevention strategies is also discussed. The penultimate portion of the review aims to explain the involvement of micronutrients such as vitamin C and vitamin D in COVID19 treatment and prophylaxis. Furthermore, the biochemistry of the major candidates for novel therapies is briefly reviewed and a summary of their current status in the clinical trials is presented. Lastly, the current scientific data and status of governing bodies such as the Center of Disease Control (CDC) and the WHO on the usage of controversial therapies such as angiotensin-converting enzyme (ACE) inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs) (Ibuprofen), and corticosteroids usage in COVID-19 are discussed. The composite collection of accredited studies on each of these subtopics of COVID-19 within this review will enable clarification and focus on the current status and direction in the planning of the management of this global pandemic.

<u>COVID-19 diagnosis and management: a comprehensive review</u> April 2020, Journal of Internal Medicine

Severe acute respiratory syndrome coronavirus (SARS-CoV)-2, a novel coronavirus from the same family as SARS-CoV and Middle East respiratory syndrome coronavirus, has spread worldwide leading the World Health Organization to declare a pandemic. The disease caused by SARS-CoV-2, coronavirus disease 2019 (COVID-19), presents flu-like symptoms which can become serious in high-risk individuals. Here, we provide an overview of the known clinical features and treatment options for COVID-19. We carried out a systematic literature search using the main online databases (PubMed, Google Scholar, MEDLINE, UpToDate, Embase and Web of Science) with the following keywords: 'COVID-19', '2019-nCoV', 'coronavirus' and 'SARS-CoV-2'. We included publications from 1 January 2019 to 3 April 2020 which focused on clinical features and treatments. We found that infection is transmitted from human to human and through contact with contaminated environmental surfaces. Hand hygiene is fundamental to prevent contamination. Wearing personal protective equipment is recommended in specific environments. The main symptoms of COVID-19 are fever, cough, fatigue, slight dyspnoea, sore throat, headache, conjunctivitis and gastrointestinal issues. Real-time PCR is used as a diagnostic tool using nasal swab, tracheal aspirate or bronchoalveolar lavage samples. Computed tomography findings are important for both diagnosis and follow-up. To date, there is no evidence of any effective treatment for COVID-19. The main therapies being used to treat the disease are antiviral drugs, chloroquine/hydroxychloroquine and respiratory therapy. In conclusion, although many therapies have been proposed, guarantine is the only intervention that appears to be effective in decreasing the contagion rate. Specifically designed randomized clinical trials are needed to determine the most appropriate evidence-based treatment modality.

<u>Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19</u> April 2020, Clinical Microbiology and infection

OBJECTIVESDetailed knowledge on the prevalence of asymptomatic cases of COVID-19 and the clinical characteristics of mild COVID-19 is essential for effective control of the COVID-19 pandemic. We determined the prevalence of asymptomatic cases of COVID-19 and characterized the symptoms of patients with mild COVID-19.METHODSWe recruited the study participants from a community facility designated for isolation of patients without moderate-tosevere symptoms of COVID-19 in South Korea. The prevalence of asymptomatic patients at admission and the detailed symptoms of mild COVID-19 were evaluated through a questionnaire-based survey. Diagnosis of COVID-19 was confirmed by real-time RT-PCR.RESULTSOf the 213 patients with COVID-19, 41 (19.2%) were asymptomatic until admission. Among the remaining patients with mild COVID-19, the most common symptom was cough (40.1% [69/172]), followed by hyposmia (39.5% [68/172]) and sputum (39.5%, [68/172]). Of the 68 patients with hyposmia, 61 (90%) patients had accompanying symptoms such as hypogeusia, nasal congestion, or rhinorrhea. Fever (>37.5 °C) was only observed in 20 (11.6%). CONCLUSIONSAs much as one-fifth of patients with COVID-19 had remained asymptomatic from exposure to admission. Hyposmia was quite frequent among patients with mild COVID-19, whereas fever was not. Social distancing should be strongly implemented to prevent disease transmission from asymptomatic patients or those with mild and inconspicuous symptoms.

<u>Clinical characteristics of Coronavirus Disease 2019 and development of a prediction model for prolonged hospital length of stay April 2020, Annals of translation medicine</u>

BackgroundThe epidemic of Coronavirus Disease 2019 (COVID-19) has become a global health emergency, but the clinical characteristics of COVID-19 are not fully described. We aimed to describe the clinical characteristics of COVID-19 outside of Wuhan city; and to develop a multivariate model to predict the risk of prolonged length of stay in hospital (ProLOS). Methods The study was conducted in a tertiary care hospital in Zhejiang province from January to February 20, 2020. Medical records of all confirmed cases of COVID-19 were retrospectively reviewed. Patients were categorized into the ProLOS and non-ProLOS groups by hospital length of stay greater and less than 14 days, respectively. Conventional descriptive statistics were applied. Multivariate regression model was built to predict the risk of ProLOS, with variables selected using stepwise approach. Results A total of 75 patients with confirmed COVID-19 were included for quantitative analysis, including 25 (33%) patients in the ProLOS group. ProLOS patients were more likely to have history of traveling to Wuhan (68% vs. 28%; P=0.002). Patients in the ProLOS group showed lower neutrophil counts [median (IQR): 2.50 (1.77-3.23) ×109/L vs. 2.90 (2.21-4.19) ×109/L; P=0.048], higher partial thrombin time (PT) (13.42±0.63 vs. 13.10±0.48 s; P=0.029), lower D-Dimer [0.26 (0.22-0.46) vs. 0.44 (0.32-0.84) mg/L; P=0.012]. There was no patient died and no severe case in our cohort. The overall LOS was 11 days (IQR, 5-15 days). The median cost for a hospital stay was 7,388.19 RMB (IQR, 5,085.39-11,145.44). The prediction model included five variables of procalcitonin, heart rate. epidemiological history, lymphocyte count and cough. The discrimination of the model was 84.8% (95% CI: 75.3% to 94.4%). Conclusions Our study described clinical characteristics of COVID-19 outside of Wuhan city and found that the illness was less severe than that in the core epidemic region. A multivariate model was developed to predict ProLOS, which showed good discrimination.

<u>Clinical characteristics of 3,062 COVID-19 patients: a meta-analysis</u> April 2020, Journal of Medical Virology

OBJECTIVEWe aim to systematically review the clinical characteristics of Coronavirus disease 2019 (COVID-19).METHODSSeven datebases were searched to collect studies about the clinical characteristics of COVID-19 from 1 January 2020 to 28 February 2020. Then, metaanalysis was performed by using Stata12.0 software.RESULTSA total of 38 studies involving 3 062 COVID-19 patients were included. Meta-analysis showed that a higher proportion of infected patients were male (56.9%). The incidence rate of respiratory failure or ARDS was 19.5% and the fatality rate was 5.5%. Fever (80.4%), fatigue (46%), cough (63.1%) and expectoration (41.8%) were the most common clinical manifestations. Other common symptoms included muscle soreness (33%), anorexia (38.8%), chest tightness (35.7%), shortness of breath (35%), dyspnea (33.9%). Minor symptoms included nausea and vomiting (10.2%), diarrhea (12.9%), headache (15.4%), pharyngalgia(13.1%), shivering (10.9%) and abdominal pain (4.4%). Patients with asymptomatic was 11.9%. Normal leukocytes counts (69.7%), lymphopenia (56.5%), elevated C-reactive protein levels (73.6%), elevated ESR (65.6%) and oxygenation index decreased (63.6%) were observed in most patients. About 37.2% of patients with elevated D-dimer, 25.9% of patients with leukopenia, along with abnormal levels of liver function (29%) and renal function (25.5%). Other findings included leukocytosis (12.6%) and elevated procalcitonin (17.5%). Only 25.8% of patients had lesions involving single lung and 75.7% of patients had lesions involving bilateral lungs. CONCLUSIONSThe most commonly

experienced symptoms of COVID-19 patients were fever, fatigue, cough and expectoration. A relatively small percentage of patients were asymptomatic. Most patients showed normal leucocytes counts, lymphopenia, elevated levels of C-reactive protein and ESR. Bilateral lungs involvement was common.

Review of the Clinical Characteristics of Coronavirus Disease 2019 (COVID-19) May 2020, Journal of General Internal Medicine

In late December 2019, a cluster of cases with 2019 Novel Coronavirus pneumonia (SARS-CoV-2) in Wuhan, China, aroused worldwide concern. Previous studies have reported epidemiological and clinical characteristics of coronavirus disease 2019 (COVID-19). The purpose of this brief review is to summarize those published studies as of late February 2020 on the clinical features, symptoms, complications, and treatments of COVID-19 and help provide guidance for frontline medical staff in the clinical management of this outbreak.

COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis March 2020, Journal of Medical Virology

The aim of this study was to analyze the clinical data, discharge rate, and fatality rate of COVID-19 patients for clinical help. The clinical data of COVID-19 patients from December 2019 to February 2020 were retrieved from four databases. We statistically analyzed the clinical symptoms and laboratory results of COVID-19 patients and explained the discharge rate and fatality rate with a single-arm meta-analysis. The available data of 1994 patients in 10 literatures were included in our study. The main clinical symptoms of COVID-19 patients were fever (88.5%), cough (68.6%), myalgia or fatigue (35.8%), expectoration (28.2%), and dyspnea (21.9%). Minor symptoms include headache or dizziness (12.1%), diarrhea (4.8%), nausea and vomiting (3.9%). The results of the laboratory showed that the lymphocytopenia (64.5%), increase of C-reactive protein (44.3%), increase of lactic dehydrogenase (28.3%), and leukocytopenia (29.4%) were more common. The results of single-arm meta-analysis showed that the male took a larger percentage in the gender distribution of COVID-19 patients 60% (95% CI [0.54, 0.65]), the discharge rate of COVID-19 patients was 52% (95% CI [0.34,0.70]), and the fatality rate was 5% (95% CI [0.01,0.11]).

Clinical characteristics of coronavirus disease 2019 (COVID-19) in China: A systematic review and meta-analysis April 2020, The Journal of infection

OBJECTIVETo better inform efforts to treat and control the current outbreak with a comprehensive characterization of COVID-19.METHODSWe searched PubMed, EMBASE, Web of Science, and CNKI (Chinese Database) for studies published as of March 2, 2020, and we searched references of identified articles. Studies were reviewed for methodological quality. A random-effects model was used to pool results. Heterogeneity was assessed using I2. Publication bias was assessed using Egger's test.RESULTS43 studies involving 3600 patients

were included. Among COVID-19 patients, fever (83.3% [95% CI 78.4-87.7]), cough (60.3% [54.2-66.3]), and fatigue (38.0% [29.8-46.5]) were the most common clinical symptoms. The most common laboratory abnormalities were elevated C-reactive protein (68.6% [58.2-78.2]), decreased lymphocyte count (57.4% [44.8-69.5]) and increased lactate dehydrogenase (51.6% [31.4-71.6]). Ground-glass opacities (80.0% [67.3-90.4]) and bilateral pneumonia (73.2% [63.4-82.1]) were the most frequently reported findings on computed tomography. The overall estimated proportion of severe cases and case-fatality rate (CFR) was 25.6% (17.4-34.9) and 3.6% (1.1-7.2), respectively. CFR and laboratory abnormalities were higher in severe cases, patients from Wuhan, and older patients, but CFR did not differ by gender.CONCLUSIONSThe majority of COVID-19 cases are symptomatic with a moderate CFR. Patients living in Wuhan, older patients, and those with medical comorbidities tend to have more severe clinical symptoms and higher CFR.

<u>Epidemiological and clinical features of asymptomatic patients with SARS-CoV-2 infection</u> April 2020, Journal of Medical Virology

Few studies reported the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected patients with completely asymptomatic throughout the disease course. We investigated the epidemiological and clinical features of patients infected by SARS-CoV-2 without any symptoms. Patients with confirmed SARS-CoV-2 infection were retrospectively recruited. The demographic characteristics, clinical data, treatment, and outcomes of SARS-CoV-2 infected patients without any symptoms were analyzed. Fifteen (4.4%) of 342 SARS-CoV-2 infected patients did not develop any symptom during the course of the disease. The median time from exposure to diagnosis was 7.0 days (interquartile range [IQR]: 1.0-15.0 days). Of the 15 patients, 14 patients were diagnosed by tested positive for SARS-CoV-2 in throat swabs, while one patient was only tested positive for SARS-CoV-2 in anal swabs. During hospitalization, only 1 (6.7%) patient developed lymphopenia. Abnormalities of chest computed tomography examinations were detected in 8 (53.4%) patients on admission. As of 8 March 2020, all patients have been discharged. The median time of SARS-CoV-2 tested negative from admission was 7.0 days (IQR: 4.0-9.0 days). Patients without any symptoms but with SARS-CoV-2 exposure should be closely monitored and tested for SARS-CoV-2 both in anal and throat swabs to excluded the infection. Asymptomatic patients infected by SARS-CoV-2 have favorable outcomes.

Real-time tracking of self-reported symptoms to predict potential COVID-19 May 2020, Nature Medicine

A total of 2,618,862 participants reported their potential symptoms of COVID-19 on a smartphone-based app. Among the 18,401 who had undergone a SARS-CoV-2 test, the proportion of participants who reported loss of smell and taste was higher in those with a positive test result (4,668 of 7,178 individuals; 65.03%) than in those with a negative test result (2,436 of 11,223 participants; 21.71%) (odds ratio = 6.74; 95% confidence interval = 6.31-7.21). A model combining symptoms to predict probable infection was applied to the data from all app users who reported symptoms (805,753) and predicted that 140,312 (17.42%) participants are likely to have COVID-19.

<u>Coronavirus Disease (COVID-19): A primer for emergency physicians</u> March 2020, The American Journal of Emergency Medicine

INTRODUCTIONRapid worldwide spread of Coronavirus Disease 2019 (COVID-19) has resulted in a global pandemic.OBJECTIVEThis review article provides emergency physicians with an overview of the most current understanding of COVID-19 and recommendations on the evaluation and management of patients with suspected COVID-19.DISCUSSIONSevere Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for causing COVID-19, is primarily transmitted from person-to-person through close contact (approximately 6 ft) by respiratory droplets. Symptoms of COVID-19 are similar to other viral upper respiratory illnesses. Three major trajectories include mild disease with upper respiratory symptoms, nonsevere pneumonia, and severe pneumonia complicated by acute respiratory distress syndrome (ARDS). Emergency physicians should focus on identifying patients at risk, isolating suspected patients, and informing hospital infection prevention and public health authorities. Patients with suspected COVID-19 should be asked to wear a facemask. Respiratory etiquette, hand washing, and personal protective equipment are recommended for all healthcare personnel caring for suspected cases. Disposition depends on patient symptoms, hemodynamic status, and patient ability to self-quarantine. CONCLUSIONThis narrative review provides clinicians with an updated approach to the evaluation and management of patients presenting to the emergency department with suspected COVID-19.

<u>Clinical Characteristics of Coronavirus Disease 2019 in China</u> April 2020, The New England Journal of Medicine

BACKGROUNDSince December 2019, when coronavirus disease 2019 (Covid-19) emerged in Wuhan city and rapidly spread throughout China, data have been needed on the clinical characteristics of the affected patients.METHODSWe extracted data regarding 1099 patients with laboratory-confirmed Covid-19 from 552 hospitals in 30 provinces, autonomous regions, and municipalities in mainland China through January 29, 2020. The primary composite end point was admission to an intensive care unit (ICU), the use of mechanical ventilation, or death.RESULTSThe median age of the patients was 47 years; 41.9% of the patients were female. The primary composite end point occurred in 67 patients (6.1%), including 5.0% who were admitted to the ICU, 2.3% who underwent invasive mechanical ventilation, and 1.4% who died. Only 1.9% of the patients had a history of direct contact with wildlife. Among nonresidents of Wuhan, 72.3% had contact with residents of Wuhan, including 31.3% who had visited the city. The most common symptoms were fever (43.8% on admission and 88.7% during hospitalization) and cough (67.8%). Diarrhea was uncommon (3.8%). The median incubation period was 4 days (interquartile range, 2 to 7). On admission, ground-glass opacity was the most common radiologic finding on chest computed tomography (CT) (56.4%). No radiographic or CT abnormality was found in 157 of 877 patients (17.9%) with nonsevere disease and in 5 of 173 patients (2.9%) with severe disease. Lymphocytopenia was present in 83.2% of the patients on admission.CONCLUSIONSDuring the first 2 months of the current outbreak, Covid-19 spread rapidly throughout China and caused varying degrees of illness. Patients often presented without fever, and many did not have abnormal radiologic findings.

<u>Symptom Criteria for COVID-19 Testing of Heath Care Workers</u> May 2020, Academic Emergency Medicine

BACKGROUNDLimitations on testing availability has been a challenge during the COVID-19 pandemic. An evidence based symptom criteria for identifying heath care workers (HCW) for testing, based on the probability of positive COVID-19 test results, would allow for a more appropriate use of testing resources.METHODSThis was an observational study of outpatient COVID-19 testing of HCW. Prior to testing, HCW were asked about the presence of 10 symptoms. Their responses were then compared to their subsequent pharyngeal swab COVID-19 Polymerase Chain Reaction test results. These data were used to derive and evaluate a symptom based testing criteria.RESULTS961 HCW were included in the analysis, of which 225 (23%) had positive test results. Loss of taste or smell was the symptom with the largest positive likelihood ratio (3.33). Dry cough, regardless of the presence or absence of other symptoms, was the most sensitive (74%) and the least specific (32%) symptom. The existing testing criteria consisting of any combination of one or more of three symptoms (fever, shortness of breath, dry cough) was 93% sensitive and 9% specific (AUC = 0.63, 95% CI: 0.59 - 0.67). The derived testing criteria consisting of any combination of one or more of two symptoms (fever, loss of taste or smell) was 89% sensitive and 48% specific (AUC = 0.75, 95% CI: 0.71 - 0.78). The hybrid testing criteria consisting of any combination of one or more of four symptoms (fever, shortness of breath, dry cough, loss of taste or smell) was 98% sensitive and 8% specific (AUC = 0.77, 95% CI: 0.73 - 0.80). CONCLUSIONAn evidence based approach to COVID-19 testing which at least includes fever and loss of taste or smell should be utilized when determining which HCW should be tested.

Clinical and imaging features of COVID-19 2020, Radiology of Infectious Diseases

Since December 2019, multiple cases of 2019 coronavirus disease (COVID-19) have been reported in Wuhan in China's Hubei Province, a disease which has subsequently spread rapidly across the entire country. Highly infectious, COVID-19 has numerous transmission channels and humans are highly susceptible to infection. The main clinical symptoms of COVID-19 are fever, fatigue, and a dry cough. Laboratory examination in the early stage of the disease shows a normal or decreased white blood cell count, and a decreased lymphocyte count. While CT examination serves as the screening and diagnostic basis for COVID-19, its accuracy is limited. The nucleic acid testing is the gold standard for the diagnosis of COVID-19, but has a low sensitivity is low. There is clearly a divide between the two means of examination. This paper reviews the published literature, guidelines and consensus, and summarizes the clinical and imaging characteristics of COVID-19, in order to provide a reliable basis for early diagnosis and treatment.

A comparative-descriptive analysis of clinical characteristics in 2019-coronavirus-infected children and adults 2020, Journal of Medical Virology

Acute respiratory disease caused by 2019 novel coronavirus (2019-nCoV) has rapidly spread throughout China. Children and adults show a different clinical course. The purpose of the

current study is to comparatively analyze the clinical characteristics of 2019-nCoV infection in children and adults and to explore the possible causes for the discrepancies present. The medical records of 25 adults and 7 children confirmed cases of 2019-2019-nCoV acute respiratory diseases were reviewed retrospectively. All children were family clusters. The total adult patients were differentiated into the local residents of Wuhan, a history of travel to Wuhan and direct contact with people from Wuhan. The numbers were 14 (56%), 10 (40%), and 1 (4%), respectively. The median incubation period of children and adults was 5 days (ranged, 3-12 days) and 4 days (ranged, 2-12 days), respectively. Diarrhoea and/or vomiting (57.1%) were demic by World Health Organiza more common in children, whereas for adults it was myalgia or fatigue (52%). On admission, the percentage of children having pneumonia (5%, 71.4%) was roughly the same as adults (20%, 80%). A total of 20% of adults had leucopoenia, but leukocytosis was more frequently in children (28.6%, P=.014). A higher number of children had elevated creatine kinase isoenzyme (57.1% vs 4%, P=.004). Antiviral therapy was given to all adult patients but to none of the children. In summary, knowledge of these differences between children and adults will not only be helpful for the clinical diagnosis of 2019-nCoV disease, but also for a future discussion on age-specific coronavirus infection

<u>Upper airway symptoms in coronavirus disease 2019 (COVID-19)</u> 2020, American Journal of Otolaryngology

Dear Editor.

A novel member of human RNA coronavirus was newly identified in Wuhan, China. International Committee on Taxonomy of Viruses (ICTV) officially named it as Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) [1]. World Health Organization (WHO) recently named the disease caused by SARS-CoV-2, as Coronavirus Disease 2019 (COVID-19). Clinical evidence has demonstrated that this virus was transmissible from person to person [2]. SARS-CoV-2 cases increased rapidly in Wuhan and Hubei Province and extended with transmission chains throughout China. Outside China, imported cases and secondary cases have been reported in many countries and territories, and WHO declared COVID-19 outbreak a pandemic on March 11th, 2020 [3]. In Italy, we are experiencing a constant increase of infected patients and there is now concern regarding the Italian national health system's capacity to effectively respond to the needs of patients who are infected and require intensive care for SARS-CoV-2 pneumonia [4]. On March 27th, 2020 in Italy, 66,414 patients tested positive to the virus, 36,653 (55.2%) were isolated at home, 26,029 (39.2%) were hospitalized and 3732 (5.6%) were admitted to intensive care unit [5].

Clinical Characteristics of Covid-19 in China May 2020, New England Journal of Medicine

According to the World Health Organization (WHO), the case definition for surveillance of returning travelers requires that they need to present with fever and at least one respiratory symptom to be considered as having suspected cases of coronavirus disease 2019 (Covid-19).¹ In their article regarding 1099 patients with laboratory-confirmed Covid-19 at hospitals across China during the first 2 months of the pandemic, Guan et al. (Feb. 28 online publication, available at NEJM.org)² present compelling data supporting the need for a reassessment of these criteria. The authors found that only 43.8% of the patients presented with fever on admission, although fever developed in 88.7% during hospitalization. That means that if those travelers were returning from affected areas, more than half would not be suspected of having

Covid-19, which would result in undetected patients who can spread the virus. This issue may be particularly relevant in low-income countries with less structured health care systems, which could not provide adequate follow-up of these travelers.

ARDS (Acute Respiratory Distress syndrome)

Comparison of Hospitalized Patients With ARDS Caused by COVID-19 and H1N1 March 2020, Chest

BACKGROUNDSince the outbreak of coronavirus disease 2019 (COVID-19) in China in December 2019, considerable attention has been focused on its elucidation. However, it is also important for clinicians and epidemiologists to differentiate COVID-19 from other respiratory infectious diseases such as influenza viruses.RESEARCH QUESTIONThe aim of this study was to explore the different clinical presentations between COVID-19 and influenza A (H1N1) pneumonia in patients with ARDS.STUDY DESIGN AND METHODSThis analysis was a retrospective case-control study. Two independent cohorts of patients with ARDS infected with either COVID-19 (n = 73) or H1N1 (n = 75) were compared. Their clinical manifestations, imaging characteristics, treatments, and prognosis were analyzed and compared.RESULTSThe median age of patients with COVID-19 was higher than that of patients with H1N1, and there was a higher proportion of male subjects among the COVID-19 cohort (P < .05). Patients with COVID-19 exhibited higher proportions of nonproductive coughs, fatigue, and GI symptoms than those of patients with H1N1 (P < .05). Patients with H1N1 had higher Sequential Organ Failure Assessment (SOFA) scores than patients with COVID-19 (P < .05). The Pao2/Fio2 of 198.2 mm Hg in the COVID-19 cohort was significantly higher than the Pao2/Fio2 of 107.0 mm Hg in the H1N1 cohort (P < .001). Ground-glass opacities was more common in patients with COVID-19 than in patients with H1N1 (P < .001). There was a greater variety of antiviral therapies administered to COVID-19 patients than to H1N1 patients. The in-hospital mortality of patients with COVID-19 was 28.8%, whereas that of patients with H1N1 was 34.7% (P = .483). SOFA score-adjusted mortality of H1N1 patients was significantly higher than that of COVID-19 patients, with a rate ratio of 2.009 (95% CI, 1.563-2.583; P < .001).INTERPRETATIONThere were many differences in clinical presentations between patients with ARDS infected with either COVID-19 or H1N1. Compared with H1N1 patients, patients with COVID-19-induced ARDS had lower severity of illness scores at presentation and lower SOFA score-adjusted mortality.

Acute respiratory failure in COVID-19: is it "typical" ARDS? May 2020, Critical Care

In December 2019, an outbreak of coronavirus disease 2019 (COVID-19) was identified in Wuhan, China. The World Health Organization (WHO) declared this outbreak a significant threat to international health. COVID-19 is highly infectious and can lead to fatal comorbidities especially acute respiratory distress syndrome (ARDS). Thus, fully understanding the characteristics of COVID-19-related ARDS is conducive to early identification and precise treatment. We aimed to describe the characteristics of COVID-19-related ARDS and to elucidate the differences from ARDS caused by other factors. COVID-19 mainly affected the respiratory system with minor damage to other organs. Injury to the alveolar epithelial cells was the main cause of COVID-19-related ARDS, and endothelial cells were less damaged with

therefore less exudation. The clinical manifestations were relatively mild in some COVID-19 patients, which was inconsistent with the severity of laboratory and imaging findings. The onset time of COVID-19-related ARDS was 8-12 days, which was inconsistent with ARDS Berlin criteria, which defined a 1-week onset limit. Some of these patients might have a relatively normal lung compliance. The severity was redefined into three stages according to its specificity: mild, mild-moderate, and moderate-severe. HFNO can be safe in COVID-19-related ARDS patients, even in some moderate-severe patients. The more likely cause of death is severe respiratory failure. Thus, the timing of invasive mechanical ventilation is very important. The effects of corticosteroids in COVID-19-related ARDS patients were uncertain. We hope to help improve the prognosis of severe cases and reduce the mortality.

Respiratory conditions in coronavirus disease 2019 (COVID-19): Important considerations regarding novel treatment strategies to reduce mortality April 2020, Medical Hypotheses

A novel virus named 2019 novel coronavirus (2019-nCoV/SARS-CoV-2) causes symptoms that are classified as coronavirus disease (COVID-19). Respiratory conditions are extensively described among more serious cases of COVID-19, and the onset of acute respiratory distress syndrome (ARDS) is one of the hallmark features of critical COVID-19 cases. ARDS can be directly life-threatening because it is associated with low blood oxygenation levels and can result in organ failure. There are no generally recognized effective treatments for COVID-19, but treatments are urgently needed. Anti-viral medications and vaccines are in the early developmental stages and may take many months or even years to fully develop. At present, management of COVID-19 with respiratory and ventilator support are standard therapeutic treatments, but unfortunately such treatments are associated with high mortality rates. Therefore, it is imperative to consider novel new therapeutic interventions to treat/ameliorate respiratory conditions associated with COVID-19. Alternate treatment strategies utilizing clinically available treatments such as hyperbaric oxygen therapy (HBOT), packed red blood cell (pRBC) transfusions, or erthropoiesis-stimulating agent (ESA) therapy were hypothesized to increase oxygenation of tissues by alternative means than standard respiratory and ventilator treatments. It was also revealed that alternative treatments currently being considered for COVID-19 such as chloroquine and hydroxychloroquine by increasing hemoglobin production and increasing hemoglobin availability for oxygen binding and acetazolamine (for the treatment of altitude sickness) by causing hyperventilation with associated increasing levels of oxygen and decreasing levels of carbon dioxide in the blood may significantly ameliorate COVID-19 respiratory symptoms. In conclusion, is recommend, given HBOT, pRBC, and ESA therapies are currently available and routinely utilized in the treatment of other conditions, that such therapies be tried among COVID-19 patients with serious respiratory conditions and that future controlled-clinical trials explore the potential usefulness of such treatments among COVID-19 patients with respiratory conditions.

<u>COVID-19 Pandemic ARDS Survivors: Pain after the Storm?</u> April 2020, Anesthesia and analgesia

Key points

• Setting up a multidisciplinary commission of experts to issue recommendations in order to

identify risks for chronic pain and other physical and psychological sequelae during the emergency phase of the COVID-19 pandemic and to recommend adequate therapeutic strategies. (See link for full list of points)

<u>Treatment for severe acute respiratory distress syndrome from COVID-</u>19 May 2020, The Lancet Respiratory Medicine

In The Lancet Respiratory Medicine, Kollengode Ramanathan and colleagues1provide excellent recommendations for the use of extracorporeal membrane oxygenation (ECMO) for patients with respiratory failure from acute respiratory distress syndrome (ARDS) secondary to coronavirus disease 2019 (COVID-19). The authors describe pragmatic approaches to the challenges of delivering ECMO to patients with COVID-19, including training health-care personnel, resolving equipment and facilities issues, implementing systems for infection control and personal protection, providing overall support for health-care staff, and mitigating ethical issues. They also address some of the anticipated challenges with local and regional surges in COVID-19 ARDS cases; although there has been an increase in hospitals with the capacity to provide ECMO, the potential demand might exceed the available resources. Furthermore, some health-care systems offer advanced therapies such as ECMO but lack a coordinated local, regional, or national referral protocol.

COVID-19 pneumonia: ARDS or not? April 2020, Critical Care

Even though it can meet the ARDS Berlin definition [1,2], the COVID-19 pneumonia is a specific disease with peculiar phenotypes. Its main characteristic is the dis-sociation between the severity of the hypoxemia and the maintenance of relatively good respiratory mechanics. Indeed, the median respiratory system compliance is usually around 50 ml/cmH2O. Of note, the patients with respiratory compliance lower or higher than the median value experience hypoxemia of similar severity. We propose the presence of two types of patients ("non-ARDS,"type 1, and ARDS, type 2) with different patho-physiology. When presenting at the hospital, type 1 and type 2 patients are clearly distinguishable by CT scan(Fig.1). If the CT scan is not available, the respiratory system compliance and possibly the response to PEEP are the only imperfect surrogates we may suggest

<u>Simultaneous ventilation of two simulated ARDS patients in COVID-19 pandemic</u> May 2020, Critical Care

TheCOVID-19pandemiccreatedashortageofventilatorsin many parts of the world. Models predict that the number of patients that will require a ventilator ranges between 1.4and 31 patients per available ventilator [1]. Given this potential, numerous groups have proposed modification of ventilator circuit to enable using a single ventilator to support multiple patients. Previous works demonstrated the feasibility of this method in models of healthy lungs, animals ,and healthy volunteers [2–4]. In the current study, we used lung models with varying compliances, to investigate whether such simultaneous ventilation is feasible.

<u>Differentiating COVID-19 Pneumonia from Acute Respiratory Distress Syndrome (ARDS) and</u> High Altitude Pulmonary Edema (HAPE): Therapeutic Implications May 2020, Circulation

COVID-19 is an acute respiratory illness caused by a droplet-borne coronavirus, SARS-CoV-2. By May1st 2020 the pandemic had resulted in ~3.3 million infections, over 235,000 deaths and global disruption of trade. While 80% of people with COVID-19 suffer a minor, acute respiratory infection, the mortality ranges from 2-7%. Patients with COVID-19 pneumonia maydecompensate due to hypoxemic respiratory failure. Autopsy data show inflammation, diffusealveolar damage (DAD), alveolar fluid accumulation, and occasional hyaline membranes, consistent with acute respiratory distress syndrome (ARDS). Understanding the causes of hypoxemia in COVID-19 is complicated by a paucity of hemodynamic and autopsy data; however the presentation of COVID-19 patients is atypical of ARDS in that the hypoxemia is often profound without appropriate dyspnea, occurs despite relatively preserved lung compliance and is associated with a large intrapulmonary shunt. These traits suggest a failure of the body's homeostatic O₂-sensing system (HOSS), which includes the pulmonary circulation, carotid body, adrenomedullary cells, and neuroepithelial bodies. The HOSS optimizes oxygen uptake and systemic oxygen delivery. Hypoxic pulmonary vasoconstriction (HPV) is the pulmonary circulation's homeostatic response to airway hypoxia in lung diseases, such as pneumonia. HPV constricts pulmonary arteries (PA) serving hypoxic lung segments, diverting blood to better-ventilated alveoli, optimizing ventilation/perfusion (V/Q) matching. The carotid body senses hypoxemia, increasing respiratory drive. COVID-19 hypoxemia is variably attributed to ARDS, impaired HPV and a high altitude pulmonary edema (HAPE)-physiology (Figure 1). We propose that the best explanation is profound impairment of HPV and carotid body function, sometimes combined with virally-induced, ARDS.

Smell and taste disorders (anosmia and ageusia)

New AI diagnostic can predict COVID-19 without testing, loss of taste and smell strong predictor of infection 14th May 2020, Kings College London

A joint effort between researchers at Massachusetts General Hospital, health science company ZOE, King's School of Biomedical Engineering & Imaging Sciences, Department of Twin Research & Genetic Epidemiology, and London Medical Imaging and AI Centre for Value Based Healthcare has seen the development of an artificial intelligence diagnostic that can predict whether someone is likely to have COVID-19 based on their symptoms.

Their findings were published this week in <u>Nature Medicine</u>. Researchers from the London AI Centre helped develop the AI model which uses data from the COVID Symptom Study app to predict COVID-19 infection by comparing people's symptoms and the results of traditional COVID tests.

Real-time tracing to self-reported symptoms to predict potential COVID-19 11th May 2020, NatureMedicine

A total of 2,618,862 participants reported their potential symptoms of COVID-19 on a smartphone-based app. Among the 18,401 who had undergone a SARS-CoV-2 test, the

proportion of participants who reported loss of smell and taste was higher in those with a positive test result (4,668 of 7,178 individuals; 65.03%) than in those with a negative test result (2,436 of 11,223 participants; 21.71%) (odds ratio = 6.74; 95% confidence interval = 6.31–7.21). A model combining symptoms to predict probable infection was applied to the data from all app users who reported symptoms (805,753) and predicted that 140,312 (17.42%) participants are likely to have COVID-19.

<u>Literature search on "loss of sense of smell" as a symptom conducted on 22nd April 2020 by Salisbury NHS FT Library Service</u>

Acute-onset smell and taste disorders in the context of COVID-19: a pilot multicenter PCR-based case-control study 22nd April 2020, European Journal of Neurology

Background: Specific respiratory tract infections, including Covid-19, may cause smell and/or taste disorders (STD) with increased frequency. We aim to determine whether new-onset STD are more frequent among Covid-19 patients than influenza patients. Methods: Case-control study including hospitalized patients of two tertiary care centers. Consecutive patients positive for Covid-19 PCR (cases) and patients positive for influenza PCR (historical control sample) were assessed during specific periods, employing a self-reported STD questionnaire. Results: Seventy-nine cases and 40 controls were included. No significant differences were found in basal features between both groups. New-onset STD were significantly more frequent among cases (31, 39.2%) than in the control group (5, 12.5 %), adjusted OR 21.4 (2.77-165.4, p=0.003). Covid-19 patients with new-onset STD were significantly younger than Covid-19 patients without STD (52.6 \pm 17.2 vs. 67.4 \pm 15.1, p<0,001). Among Covid-19 patients who presented STD, 22 (70.9%) recalled an acute onset and was an initial manifestation in 11 (35.5%). Twenty-five (80.6%) presented smell disorders (mostly anosmia, 14, 45.2%), and 28 (90.3%) taste disorders (mostly ageusia, 14, 45.2%). Only four (12.9 %) reported concomitant nasal obstruction. Mean duration of STD was 7.5 ± 3.2 days and 12 patients (40%) manifested complete recovery after 7.4 ± 2.3 days of onset. Conclusion: New-onset STD were significantly more frequent among Covid-19 patients than influenza patients, they usually had an acute onset and were commonly an initial manifestation. We suggest the use of STD assessment in anamnesis as a hint for Covid-19 and to support individuals' self-isolation in the current epidemic context.

Anosmia and ageusia are emerging as symptoms in patients with COVID-19: What does the current evidence say? 2020, Ecancermedicalscience

There have been several reports noting anosmia and ageusia as possible symptoms of COVID-19. This is of particular interest in oncology since patients receiving some cancer treatments such as chemotherapy or immune therapy often experience similar symptoms as side-effects. The purpose of this report was to summarise the evidence on the existence of anosmia and ageusia an emerging COVID-19 symptoms in order to better inform both oncology patients and

clinicians. Currently, there is no published evidence or case reports noting anosmia or ageusia as symptoms of COVID-19. Nevertheless, experts in rhinology have suggested that the onset of such symptoms could either act as a trigger for testing for the disease where possible, or could be a new criterion to self-isolate. Whilst more data is currently needed to strengthen our knowledge of the symptoms of COVID-19, oncology patients who are concerned about anosmia or ageusia in the context of their systemic anti-cancer therapy should contact their acute oncology support line for advice.

<u>Loss of smell or taste as the only symptom of COVID-19</u> May 2020, Tidsskrift for den Norske laegeforening: tidsskrift for praktisk medicin, ny raekke

BACKGROUNDOlfactory and taste disorders (OTDs) have recently been reported among patients with COVID-19, and it has been hypothesised that oral and nasal tissues may contain host cells of SARS-CoV-2. We report on two cases (spouses) with SARS-CoV-2 infection with self-reported OTDs, but otherwise no typical respiratory symptoms of COVID-19.CASE PRESENTATIONA man in his nineties (index patient) had respiratory symptoms and dysgeusia, and was diagnosed with COVID-19. His daughter-in-law and son had no respiratory COVID-19 symptoms. However, they experienced complete loss of smell and taste, respectively, 7 and 10 days after their first close contact with the index patient. Both tested positive for SARS-CoV-2 RNA.INTERPRETATIONOur case histories support recent reports hypothesising that anosmia and ageusia may be the only symptoms of SARS-CoV-2 infection, and that SARS-CoV-2 may infect oral and nasal tissues. Together, these findings may inform future research, diagnosis, prevention and treatment of COVID-19.

Anosmia as a prominent symptom of COVID-19 infection April 2020, Rhinology *Abstract only** (ePub ahead of print)

According to WHO recommendations, everyone must protect themselves against Coronavirus disease 2019 (COVID-19), which will also protect others. Due to the lack of current effective treatment and vaccine for COVID-19, screening, rapid diagnosis and isolation of the patients are essential (1, 2). Therefore, identifying the early symptoms of COVID-19 is of particular importance and is a health system priority. Early studies from COVID-19 outbreak in China have illustrated several non-specific signs and symptoms in infected patients, including fever, dry cough, dyspnea, myalgia, fatigue, lymphopenia, and radiographic evidence of pneumonia (3, 4). Recently, a probability of association between COVID-19 and altered olfactory function has been reported in South Korea, Iran, Italy, France, UK and the United States (5-8). However, to our knowledge, the definite association between COVID-19 and anosmia has not been published.

<u>The Prevalence of Olfactory and Gustatory Dysfunction in COVID-19 Patients: A Systematic Review and Meta-analysis</u> May 2020, Otolaryngology – head and neck surgery

OBJECTIVETo determine the pooled global prevalence of olfactory and gustatory dysfunction in patients with the 2019 novel coronavirus (COVID-19). DATA SOURCESLiterature searches of PubMed, Embase, and Scopus were conducted on April 19, 2020, to include articles written in English that reported the prevalence of olfactory or gustatory dysfunction in COVID-19 patients.REVIEW METHODSSearch strategies developed for each database contained keywords such as anosmia, dysgeusia, and COVID-19. Resulting articles were imported into a systematic review software and underwent screening. Data from articles that met inclusion criteria were extracted and analyzed. Meta-analysis using pooled prevalence estimates in a random-effects model were calculated.RESULTSTen studies were analyzed for olfactory dysfunction (n = 1627), demonstrating 52.73% (95% CI, 29.64%-75.23%) prevalence among patients with COVID-19. Nine studies were analyzed for gustatory dysfunction (n = 1390), demonstrating 43.93% (95% CI, 20.46%-68.95%) prevalence. Subgroup analyses were conducted for studies evaluating olfactory dysfunction using nonvalidated and validated instruments and demonstrated 36.64% (95% CI, 18.31%-57.24%) and 86.60% (95% CI, 72.95%-95.95%) prevalence, respectively.CONCLUSIONSOlfactory and gustatory dysfunction are common symptoms in patients with COVID-19 and may represent early symptoms in the clinical course of infection. Increased awareness of this fact may encourage earlier diagnosis and treatment, as well as heighten vigilance for viral transmission. To our knowledge, this is the first meta-analysis to report on the prevalence of these symptoms in COVID-19 patients.

<u>High prevalence of olfactory and taste disorder during SARS-CoV-2 infection in outpatients</u> May 2020, Journal of Medical Virology

Prevalent symptoms of SARS-CoV-2 in reports and metaanalyses refer to cough, fatigue, myalgia and respiratory distress. These represent clinically acknowledged relevant findings of valuable importance, particularly with the requirement for ventilation and hospital bed occupancy in ICUs. There is however a wide discordance with the actual picture of clinical presentation and symptoms in Italy. Here we comment on Sun and coll Metaanlysis with particular nuance to olfactory and taste disorders that very often herald SARS-CoV-2 in our country, particularly in outpatients, and are not reported so far in the medical literature from China. This article is protected by copyright. All rights reserved.

Gastrointestinal symptoms

Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection June 2020, Gut

OBJECTIVETo study the GI symptoms in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infected patients. DESIGNWe analysed epidemiological, demographic, clinical and laboratory data of 95 cases with SARS-CoV-2 caused coronavirus disease 2019. Real-time reverse transcriptase PCR was used to detect the presence of SARS-CoV-2 in faeces and GI tissues. RESULTSAmong the 95 patients, 58 cases exhibited GI symptoms of which 11 (11.6%) occurred on admission and 47 (49.5%) developed during hospitalisation. Diarrhoea (24.2%), anorexia (17.9%) and nausea (17.9%) were the main symptoms with five (5.3%), five (5.3%) and three (3.2%) cases occurred on the illness onset, respectively. A substantial proportion of

patients developed diarrhoea during hospitalisation, potentially aggravated by various drugs including antibiotics. Faecal samples of 65 hospitalised patients were tested for the presence of SARS-CoV-2, including 42 with and 23 without GI symptoms, of which 22 (52.4%) and 9 (39.1%) were positive, respectively. Six patients with GI symptoms were subjected to endoscopy, revealing oesophageal bleeding with erosions and ulcers in one severe patient. SARS-CoV-2 RNA was detected in oesophagus, stomach, duodenum and rectum specimens for both two severe patients. In contrast, only duodenum was positive in one of the four non-severe patients.CONCLUSIONSGI tract may be a potential transmission route and target organ of SARS-CoV-2.

Conjunctivitis

Conjunctivitis can be the only presenting sign and symptom of COVID-19 2020, IDcasess

Five cases of non-remitting conjunctivitis turned out to be the sole presenting sign and symptom of COVID-19. These patients tested positive on RT-PCR of naso-pharyngeal swabs and developed no fever, malaise, or respiratory symptoms throughout the course of their illness. They all fully recovered. In the current efforts to fight the spread of this virus, authors want to emphasize that atypical clinical presentations of COVID-19 can occur and a high level of suspicion should be maintained. Ocular involvement and transmission of SARS-CoV-2 should never be overlooked. In fact, conjunctival mucosae are susceptible to respiratory viruses and remain an important point of entry. For this reason, eye protection in the form of goggles or a face shield should be considered essential for all healthcare providers, even when taking care of patients who are not showing typical symptoms of COVID-19.Copyright

Diarrhoea

<u>Diarrhea: An underestimated symptom in Coronavirus disease 2019</u> 2020, Clinics and Research in Hepatology and Gastroenterology

In a retrospective study in the Nord Franche-Comte hospital conducted between March 1st and March 17th 2020, and compared to the review of Li et al., diarrhea was a main symptom in patients with COVID-19. Out of the 114 patients, 55 (48%) had diarrhea; it was the fifth most common symptom. In the group of patients with diarrhea, the median age was 56 years (+/- 18) and 32 (58%) were female. Only 2 patients (3.6%) had a past history of inflammatory bowel disease. Fifty-six percent of patients (n = 30/54) were hospitalised. Diarrhea appeared 4.5 days (+/- 1.8) after the onset of the first other symptoms in COVID-19. Of the 55 patients with diarrhea, 29 (52.7%) had at least one simultaneous gastrointestinal (GI) symptom other than diarrhea. Twenty-five patients (45.5%) had nausea, 19 patients (34.5%) had abdominal pain and 9 (16.3%) had vomiting. Myalgia, sore throat, sneezing and the other GI symptoms were statistically more frequent in the group with diarrhea than in the group without diarrhea (P < 0.05).

Patients with diabetes

<u>Clinical characteristics and outcomes of patients with severe covid-19 with diabetes</u> April 2020, BMJ Open Diabetes

OBJECTIVEThis study explores the clinical characteristics of patients with diabetes with severe covid-19, and the association of diabetes with survival duration in patients with severe covid-19.RESEARCH DESIGN AND METHODSIn this single-center, retrospective, observational study, the clinical and laboratory characteristics of 193 patients with severe covid-19 were collected. 48 patients with severe covid-19 had diabetes, and 145 patients (ie, the controls) did not have diabetes. A severe case was defined as including at least one of the following criteria: (1) Respiratory rate >30/min. (2) Oxygen saturation ≤93%. (3) PaO2/FiO2≤300 mm Hg. (4) Patients, either with shock or respiratory failure, requiring mechanical ventilation, or combined with other organ failure, requiring admission to intensive care unit (ICU).RESULTSOf 193 patients with severe covid-19, 48 (24.9%) had diabetes. Compared with patients with severe covid-19 without diabetes, patients with diabetes were older, susceptible to receiving mechanical ventilation and admission to ICU, and had higher mortality. In addition, patients with severe covid-19 with diabetes had higher levels of leukocyte count, neutrophil count, highsensitivity C reaction protein, procalcitonin, ferritin, interleukin (IL) 2 receptor, IL-6, IL-8, tumor necrosis factor α, D-dimer, fibrinogen, lactic dehydrogenase and N-terminal pro-brain natriuretic peptide. Among patients with severe covid-19 with diabetes, more non-survivors were men (30 (76.9%) vs 9 (23.1%)). Non-survivors had severe inflammatory response, and cardiac, hepatic. renal and coagulation impairment. Finally, the Kaplan-Meier survival curve showed a trend towards poorer survival in patients with severe covid-19 with diabetes than patients without diabetes. The HR was 1.53 (95% CI 1.02 to 2.30; p=0.041) after adjustment for age, sex, hypertension, cardiovascular disease and cerebrovascular disease by Cox regression. The median survival durations from hospital admission in patients with severe covid-19 with and without diabetes were 10 days and 18 days, respectively. CONCLUSIONThe mortality rate in patients with severe covid-19 with diabetes is considerable. Diabetes may lead to an increase in the risk of death.

Cancer patients

<u>Clinical characteristics and outcomes of cancer patients with COVID-19</u> May 2020, Journal of Medical Virology Abstract only*

OBJECTIVEThis retrospective study aimed to analysis clinical characteristics and outcomes of cancer patients with novel coronavirus disease-19 (COVID-19).METHODMedical records, laboratory results and radiologic findings of 52 cancer patients with COVID-19 were collected, clinical characteristics and outcomes were summarized.RESULTSA total of 52 cancer patients with COVID-19 were included. Median age of 52 cancer patients with COVID-19 was 63 years (34-98). 33(63.5%) patients were mild and 19(36.5%) were severe/critical. Lung cancer was the most frequent cancer type (10, 19.2%). The common symptoms were as follows: fever (25%), dry cough (17.3%), chest distress (11.5%) and fatigue (9.6%).There were 33(63.5%) patients had comorbidities, the most common symptom was hypertension (17, 51.5%). 26(78.8%) patients developed pneumonia on admission. Lymphocytes (0.6×109 /L) decreased in both mild and severe/critical patients. Median levels of D-dimer, C-reactive protein(CRP), procalcitonin (PCT) and lactate dehydrogenase(LDH) were 2.8 mg/L, 70.5 mg/L, 0.3 ng/mL, and 318 U/L respectively, which increased significantly in severe/critical patients compared to the mild

patients. Interleukin 6(IL-6) (12.6 pg/ml) increased in both mild and severe/critical patients, there was a significant difference between them. Complications were observed in 29(55.8%) patients, such as liver injury (19, 36.5%), acute respiratory distress syndrome (ARDS) (9, 17.3%), sepsis (8, 15.4%), myocardial injury (8, 15.4%), renal insufficiency (4, 7.7%), and multiple organ dysfunction syndrome (MODS) (3, 5.8%).11(21.2%) cancer patients died.CONCLUSIONThe infection rate of severe acute respiratory syndrome coronavirus 2(SARS-COV-2) in cancer patients was higher than the general population, cancer patients with COVID-19 showed deteriorating conditions and poor outcomes.

Appendicular syndrome

SARS-CoV-2 infection may result in appendicular syndrome: Chest CT scan before appendectomy April 2020, Journal of Visceral Surgery

The initial clinical presentation of coronavirus disease 2019 may be appendicular syndrome. An abdominal CT scan ruled out a diagnosis of appendicitis and a chest CT scan yielded a diagnosis of SARS-CoV-2 infection. CT scan is required before considering emergency surgery for acute appendicitis.

Skin symptoms

<u>Vascular skin symptoms in COVID-19: a french observational study April</u> 2020, Journal of the European Academy of Dermatology and Venerology

Coronavirus 19 (COVID-19) was declared as a pandemic viral infection by the World Health organization on March 11th 2020. Usual clinical manifestations of COVID-19 infection include fever, fatigue, myalgia, headache, diarrhea, dry cough, dyspnea that may lead to acute respiratory distress syndrome and death (1). Skin symptoms of COVID-19 have been poorly described but may include erythematous rash, urticaria and chicken pox like lesions (2-7). Angiotensin-converting enzyme 2 (ACE2) is a cellular receptor for COVID-19.

Health outcomes

Rehabilitation

Rehabilitation in the wake of Covid-19: a phoenix rising from the ashes British Society of Rehabilitation Medicine, 11th May 2020

Rehabilitation forms a critical component of the acute care pathway, helping to relieve pressure on the acute and frontline services. It is shown to be both effective and cost-effective, whether through improving independence and societal reintegration; or managing the impacts of long-term disability including neuro-palliative care. The Covid-19 pandemic has already led to a marked increase in the burden of disease and disability and will continue to do so. It has produced many new challenges:

- •A diminished workforce due to sickness, shielding and redeployment to frontline services.
- The many impacts of social distancing including
- osocio-economic and psychosocial effects
- oisolation of patients from their families
- orestrictions on interventions that involve hands-on treatment, group interventions or aerosol generating procedures.
- •An as yet unquantifiable additional case-load of patients with post-Covid disability presenting with a wide range of problems due to cardio-pulmonary, musculoskeletal, neurological and psychological/psychiatric complications of the disease, compounded in many cases by deconditioning from prolonged stays in ICU.As NHS services re-boot in the wake of the pandemic, there is an important opportunity to work collaboratively to rebuild services on a better, more cooperative model —a phoenix from the ashes. This document sets out the BSRM's recommendations for rehabilitation services for adults aged 16 years and over in the wake of the Covid-19 pandemic -in particular, the role of specialist rehabilitation to support patients with more complex rehabilitation needs. The guidance is not just for patients who have had Covid-19, but for all patients leaving intensive and acute care after severe illness

Rehabilitation of adults who are hospitalised due to COVID-19: physiotherapy service delivery 14th May 2020, Chartered Society of Physiotherapy

These standards are underpinned by national guidance and standards, in particular by National Institute for Health and Care Excellence (NICE), government and profession-specific guidance on Covid-19. Targeted, expert peer review has been used to ask reviewers specific questions about the draft standards and complete a pragmatic accuracy check. We will review and update the standards as the knowledge base and expert experience develop.

<u>Evidence search: [PH Bulletin] COVID post-discharge support</u>. Lisa Burscheidt. (15th April, 2020). ILFORD, UK: Aubrey Keep Library and Knowledge Service.

<u>Evidence search: Rehabilitation of recovering Covid 19/coronavirus patients</u> [literature as at 20 April 2020]. Paul Lee. (20th April, 2020). LONDON, UK: Reay House Library and Knowledge Service.

<u>Evidence search: COVID-19 and dysphagia the role of speech and language therapists</u>. Rhys Whelan. (20th April, 2020). ABERTAWE/SWANSEA, UK: Bwrdd Iechyd Prifysgol Bae Abertawe Library Services.

Literature Search - Prehabilitation and Covid 19 (Royal United Hospitals Bath)

<u>Evidence search: Post COVID-19 psychological rehabilitation.</u> Karen Skinner. (27th April, 2020). REDHILL, UK: Surrey and Sussex Library and Knowledge Services.

Systematic rapid "living" review on rehabilitation needs due to covid-19: update to March 31st 2020 April 2020, European Journal of Physical and Rehabilitation Medicine

BACKGROUNDThe outbreak of Covid-19 epidemics has challenged the provision of health care worldwide, highlighting the main flaws of some national health systems with respect to their capacity to cope with the needs of frail subjects. People experiencing disability due to Covid-19 express specific rehabilitation needs that deserve a systematic evidence-based approach.OBJECTIVESTo provide the rehabilitation community with updates on the latest scientific literature on rehabilitation needs due to Covid-19. The first rapid "living" review will present the results of a systematic search performed up to March 31st, 2020.METHODSA systematic search on PubMed, Pedro and Google Scholar was performed using the search terms: "Covid-19", "Coronavirus", "severe acute respiratory syndrome coronavirus 2", "rehabilitation", "physical therapy modalities", "exercise", "occupational therapy", and "late complications". Papers published up to March 31st, 2020, in English, were included.RESULTSOut of the 2758 articles retrieved, 9 were included in the present review. Four of them are "calls for action", 3 provide recommendations about rehabilitation interventions in the acute phase, 2 address the needs of people quarantined at home or with restricted mobility due to the lockdown, and 1 provides a Core Outcome Set to be used in clinical trials to test the efficacy of health strategies in managing Covid-19 patients.CONCLUSIONSAII selected papers were based on previous literature and not on the current Covid-19 pandemic. Main messages included: 1) early rehabilitation should be granted to inpatients with Covid-19; 2) people with restricted mobility due to quarantine or lockdown should receive exercise programs to reduce the risk of frailty, sarcopenia, cognitive decline and depression; 3) telerehabilitation may represent the first option for people at home. Further updates are warranted in order to characterize the emerging disability in Covid-19 survivors and the adverse effects on the health of chronically disabled people.

Recommendations for respiratory rehabilitation in adults with COVID-19 April 2020, Chinese Medical Journal

Coronavirus disease-2019 (COVID-19) is a highly infectious respiratory disease that leads to respiratory, physical, and psychological dysfunction in patients. Respiratory rehabilitation is an important intervention as well as cure for clinical patients. With increased understanding of COVID-19 and the accumulation of clinical experience, we proposed recommendations for respiratory rehabilitation in adults with COVID-19 based on the opinions of frontline clinical experts involved in the management of this epidemic and a review of the relevant literature and

evidence. Our recommendations are as follows: 1. for inpatients with COVID-19, respiratory rehabilitation would relieve the symptoms of dyspnea, anxiety, and depression and eventually improve physical functions and the quality of life; 2. for severe/critical inpatients, early respiratory rehabilitation is not suggested; 3. for patients in isolation, respiratory rehabilitation guidance should be conducted through educational videos, instruction manuals, or remote consultation; 4. assessment and monitoring should be performed throughout the respiratory rehabilitation process; 5. proper grade protection should be used following the present guidelines. These recommendations can guide clinical practice and form the basis for respiratory rehabilitation in COVID-19 patients.

Recovery

<u>Follow-up studies in COVID-19 recovered patients - is it mandatory?</u> April 2020, The science of the total environment

The novel Coronavirus disease 2019 (COVID-19) is an illness caused due to Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The World Health Organization (WHO) has declared this outbreak a global health emergency and as on April 24, 2020, it has spread to 213 countries, with 25,91,015 confirmed cases and 742,855 cases have been recovered from COVID-19. In this dreadful situation our team has already published an article in the Science of the Total Environment, which elaborates the various aspects of the SARS-CoV-2 infection. In this situation, it is imperative to understand the possible outcome of COVID-19 recovered patients and determine if they have any other detrimental illnesses by longitudinal analysis to safeguard their life in future. It is necessary to follow-up these recovered patients and performs comprehensive assessments for detection and appropriate management towards their psychological, physical, and social realm. This urges us to suggest that it is highly important to provide counselling, moral support as well as a few recommended guidelines to the recovered patients and society to restore to normalcy. Epidemiological, clinical and immunological studies from COVID-19 recovered patients are particularly important to understand the disease and to prepare better for potential outbreaks in the future. Longitudinal studies on a larger cohort would help us to understand the in-depth prognosis as well as the pathogenesis of COVID-19. Also, follow-up studies will help us provide more information for the development of vaccines and drugs for these kinds of pandemics in the future. Hence, we recommend more studies are required to unravel the possible mechanism of COVID-19 infection and the after-effects of it to understand the characteristics of the virus and to develop the necessary precautionary measures to prevent it.

<u>Urgent need of a management plan for survivors of COVID-19</u> April 2020, The European Respiratory Journal

The current pandemia of COVID-19 affects primarily adults and particularly those affected by one or more chronic diseases[11].Because most of the severe COVID-19 are due to pneumonia associated with respiratory failure[11, 12], it is likely that similarly to patients with exacerbations of COPD and/or community acquired pneumonia, the survivors of COVID will be at high risk of

cardiovascular events and mortality following the acute phase of the disease. We would like to call attention to this vulnerable period, and recommend that patients be closely followed with a management plan that pays special attention to the prompt recognition of cardiovascular complications, especially in the 30 days following the resolution of the acute phase of the event. It would be a pity that those survivors of COVID-19 pneumonia, would then succumb from a relatively preventable consequence.

Post viral fatigue syndrome

Concern coronavirus may trigger post-viral fatigue syndromes April 2020, New Scientist

COULD the coronavirus sweeping around the world have a second illness following in its wake? We may expect to see an outbreak of post-viral fatigue syndromes in some people who have had covid-19, according to some researchers. Viral infections have previously been linked to problems with long-term fatigue symptoms. For example, chronic fatigue syndrome (CFS), which is also called myalgic encephalomyelitis (ME), sometimes occurs after viral infections. People who have CFS experience extreme fatigue and a range of other symptoms, such as pain and sensitivity to light, but the condition is poorly understood.

Post Intensive Care Syndrome

Post Intensive Care Syndrome: a call for action April 2020, Journal of Rehabilitation Medicine

Although we are currently overwhelmed by the astonishing speed of infection of the Covid-19 pandemic, and the daily onslaught of new, and ever-worsening predictions, it is vital that we begin to prepare for the aftershocks of the pandemic. Prominent among this will be the cohort of post-intensive case survivors who have been mechanically ventilated and will like experience short- and medium-term consequences. The notion that patients surviving intensive care and mechanical ventilation for several weeks can be discharged home without further medical attention is a dangerous illusion. Post Intensive Care Syndrome and other severe conditions will require not only adequate screening but early rehabilitation and other interventions. Action must be taken now to prepare for this inevitable aftershock to the healthcare system.

Mental Health

The Effect of COVID-19 on Youth Mental Health April 2020, The Psychiatric Quarterly

The purposes of this study was to assess the youth mental health after the coronavirus disease 19 (COVID-19) occurred in China two weeks later, and to investigate factors of mental health among youth groups. A cross-sectional study was conducted two weeks after the occurrence of COVID-19 in China. A total of 584 youth enrolled in this study and completed the question about cognitive status of COVID-19, the General Health Questionnaire(GHQ-12), the PTSD Checklist-Civilian Version (PCL-C) and the Negative coping styles scale. Univariate analysis and univariate logistic regression were used to evaluate the effect of COVID-19 on youth mental health. The results of this cross-sectional study suggest that nearly 40.4% the sampled youth were found to be prone to psychological problems and 14.4% the sampled youth with Post-

traumatic stress disorder (PTSD) symptoms. Univariate logistic regression revealed that youth mental health was significantly related to being less educated (OR = 8.71, 95%CI:1.97-38.43), being the enterprise employee (OR = 2.36, 95%CI:1.09-5.09), suffering from the PTSD symptom (OR = 1.05, 95%CI:1.03-1.07) and using negative coping styles (OR = 1.03, 95%CI:1.00-1.07). Results of this study suggest that nearly 40.4% of the youth group had a tendency to have psychological problems. Thus, this was a remarkable evidence that infectious diseases, such as COVID-19, may have an immense influence on youth mental health. Therefor, local governments should develop effective psychological interventions for youth groups, moreover, it is important to consider the educational level and occupation of the youth during the interventions.

<u>Progression of Mental Health Services during the COVID-19 Outbreak in China</u> 2020, International Journal of Biological Sciences

The novel coronavirus disease (COVID-19) has been rapidly transmitted in China, Macau, Hong Kong, and other Asian and European counterparts. This COVID-19 epidemic has aroused increasing attention nationwide. Patients, health professionals, and the general public are under insurmountable psychological pressure which may lead to various psychological problems, such as anxiety, fear, depression, and insomnia. Psychological crisis intervention plays a pivotal role in the overall deployment of the disease control. The National Health Commission of China has summoned a call for emergency psychological crisis intervention and thus, various mental health associations and organizations have established expert teams to compile guidelines and public health educational articles/videos for mental health professionals and the general public alongside with online mental health services. In addition, mental health professionals and expert groups are stationed in designated isolation hospitals to provide on-site services. Experts have reached a consensus on the admission of patients with severe mental illness during the COVID-19 outbreak in mental health institutions. Nevertheless, the rapid transmission of the COVID-19 has emerged to mount a serious challenge to the mental health service in China.

<u>People with Suspected COVID-19 Symptoms Were More Likely Depressed and Had Lower Health-Related Quality of Life: The Potential Benefit of Health Literacy</u> March 2020, Journal of Clinical Medicine

The coronavirus disease 2019 (COVID-19) epidemic affects people's health and health-related quality of life (HRQoL), especially in those who have suspected COVID-19 symptoms (S-COVID-19-S). We examined the effect of modifications of health literacy (HL) on depression and HRQoL. A cross-sectional study was conducted from 14 February to 2 March 2020. 3947 participants were recruited from outpatient departments of nine hospitals and health centers across Vietnam. The interviews were conducted using printed questionnaires including participants' characteristics, clinical parameters, health behaviors, HL, depression, and HRQoL. People with S-COVID-19-S had a higher depression likelihood (OR, 2.88; p < 0.001), lower HRQoL-score (B, -7.92; p < 0.001). In comparison to people without S-COVID-19-S and low HL, those with S-COVID-19-S and low HL had 9.70 times higher depression likelihood (p < 0.001), 20.62 lower HRQoL-score (p < 0.001), for the people without S-COVID-19-S, 1 score increment of HL resulted in 5% lower depression likelihood (p < 0.001) and 0.45 higher HRQoL-score (p <

0.001), while for those people with S-COVID-19-S, 1 score increment of HL resulted in a 4% lower depression likelihood (p = 0.004) and 0.43 higher HRQoL-score (p < 0.001). People with S-COVID-19-S had a higher depression likelihood and lower HRQoL than those without. HL shows a protective effect on depression and HRQoL during the epidemic.

COVID-19, anxiety, sleep disturbances and suicide June 2020, Sleep Medicine

Suicide is an important public health problem. During the epidemic of a highly contagious coronavirus 2019 disease (COVID-19) that was identified in China at the end of 2019, the risk of suicide may be exacerbated. COVID-19 has spread to other Asian countries, Europe, Australia, North and South America, and Africa. The COVID-19 epidemic is associated with anxiety, depression, distress, sleep disturbances, and suicidality [1], [2], [3], [4], [5], [6], [7]].

Researchers in China examined psychological responses during the initial stage of the COVID-19 epidemic in the general population [3]. They found that 53.8% of respondents rated the psychological impact of the outbreak as moderate or severe, 16.5% reported moderate to severe depressive symptoms, and 28.8% reported moderate to severe anxiety symptoms. Another nationwide survey of more than 50,000 people in China during the COVID-19 epidemic showed that about 35% of the respondents experienced psychological distress [4]. Another research group in China sampled and analyzed the online posts from about 18,000 Chinese social media users before and after the declaration of COVID-19 in China on January 20, 2020 [5]. Researchers found that negative emotions such as anxiety, depression, and anger increased, while positive emotions and life satisfaction decreased.

COVID-19 and Depression 2020, Clinical Therapeutics

The COVID-19 pandemic embodies overwhelming stresses-unemployment, death, and isolation, among others. When called upon, clinicians must try to sort out demoralization from depression. This commentary discerns the characteristics of demoralization versus depression, and suggests solutions for both, together with a cautionary word on the use chloroquine and hydroxychloroquine in patients with COVID-19

<u>Coronavirus Anxiety Scale: A brief mental health screener for COVID-19 related anxiety</u> August 2020, Death Studies

Mental health concerns of people impacted by the coronavirus pandemic have not been adequately addressed. The objective of this study was to develop and evaluate the properties of the Coronavirus Anxiety Scale (CAS), which is a brief mental health screener to identify probable cases of dysfunctional anxiety associated with the COVID-19 crisis. This 5-item scale, which was based on 775 adults with anxiety over the coronavirus, demonstrated solid reliability and validity. Elevated CAS scores were found to be associated with coronavirus diagnosis, impairment, alcohol/drug coping, negative religious coping, extreme hopelessness, suicidal ideation, as well as attitudes toward President Trump and Chinese products. The CAS discriminates well between persons with and without dysfunctional anxiety using an optimized

cut score of ≥ 9 (90% sensitivity and 85% specificity). These results support the CAS as an efficient and valid tool for clinical research and practice.

Ptsd as the second tsunami of the sars-cov-2 pandemic April 2020, Psychological Medicine

Since the first cases, the coronavirus disease (COVID-19) rapidly spread around the world, with hundred-thousand cases and thousands of deaths. Post-traumatic stress disorder (PTSD) is a common consequence of major disasters. Exceptional epidemic situations also promoted PTSD in the past. Considering that humanity is undergoing the most severe pandemic since Spanish Influenza, the actual pandemic of COVID-19 is very likely to promote PTSD. Moreover, COVID-19 was renamed severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2). With a poor understanding of viruses and spreading mechanisms, the evocation of SARS is generating a great anxiety contributing to promote PTSD. Quarantine of infected patients evolved to quarantine of 'infected' towns or popular districts, and then of entire countries. In the families of cases, the brutal death of family members involved a spread of fear and a loss of certainty, promoting PTSD. In the context of disaster medicine with a lack of human and technical resources, healthcare workers could also develop acute stress disorders, potentially degenerating into chronic PTSD. Globally, WHO estimates 30-50% of the population affected by a disaster suffered from diverse psychological distress. PTSD individuals are more at-risk of suicidal ideation, suicide attempt, and deaths by suicide – considering that healthcare workers are already at-risk occupations. We draw attention towards PTSD as a secondary effect of the SARS-Cov-2 pandemic, both for general population, patients, and healthcare workers. Healthcare policies need to take into account preventive strategy of PTSD, and the related risk of suicide, in forthcoming months

Occurrence, prevention and management of the psychological effects of emerging virus outbreaks on healthcare workers: rapid review and meta-anlayis 23rd April 2020, BMJ

OBJECTIVETo examine the psychological effects on clinicians of working to manage novel viral outbreaks, and successful measures to manage stress and psychological distress.DESIGNRapid review and meta-analysis.DATA SOURCESCochrane Central Register of Controlled Trials, PubMed/Medline, PsycInfo, Scopus, Web of Science, Embase, and Google Scholar, searched up to late March 2020. ELIGIBILITY CRITERIA FOR STUDY SELECTIONAny study that described the psychological reactions of healthcare staff working with patients in an outbreak of any emerging virus in any clinical setting, irrespective of any comparison with other clinicians or the general population.RESULTS59 papers met the inclusion criteria: 37 were of severe acute respiratory syndrome (SARS), eight of coronavirus disease 2019 (covid-19), seven of Middle East respiratory syndrome (MERS), three each of Ebola virus disease and influenza A virus subtype H1N1, and one of influenza A virus subtype H7N9. Of the 38 studies that compared psychological outcomes of healthcare workers in direct contact with affected patients, 25 contained data that could be combined in a pairwise metaanalysis comparing healthcare workers at high and low risk of exposure. Compared with lower risk controls, staff in contact with affected patients had greater levels of both acute or posttraumatic stress (odds ratio 1.71, 95% confidence interval 1.28 to 2.29) and psychological distress (1.74, 1.50 to 2.03), with similar results for continuous outcomes. These findings were the same as in the other studies not included in the meta-analysis. Risk factors for psychological distress included being younger, being more junior, being the parents of

dependent children, or having an infected family member. Longer quarantine, lack of practical support, and stigma also contributed. Clear communication, access to adequate personal protection, adequate rest, and both practical and psychological support were associated with reduced morbidity. CONCLUSIONS Effective interventions are available to help mitigate the psychological distress experienced by staff caring for patients in an emerging disease outbreak. These interventions were similar despite the wide range of settings and types of outbreaks covered in this review, and thus could be applicable to the current covid-19 outbreak.

Neurological

<u>Neurological complications of coronavirus and COVID-19</u> May 2020, Revista de neurologia *Abstract only in English*

INTRODUCTIONClinical and experimental studies have shown that the coronavirus family has a certain tropism for the central nervous system. Seven types of coronavirus can infect humans.DEVELOPMENTCoronaviruses are not always confined to the respiratory tract, and under certain conditions they can invade the central nervous system and cause neurological pathologies. The potential for neuroinvasion is well documented in most human coronaviruses (OC-43, 229E, MERS and SARS) and in some animal coronaviruses (porcine haemagglutinating encephalomyelitis coronavirus). Neurological symptoms have been reported in patients affected by COVID-19, such as headache, dizziness, myalgia and anosmia, as well as cases of encephalopathy, encephalitis, necrotising haemorrhagic encephalopathy, stroke, epileptic seizures, rhabdomyolysis and Guillain-Barre syndrome, associated with SARS-CoV-2 infection.CONCLUSIONSFuture epidemiological studies and case records should elucidate the real incidence of these neurological complications, their pathogenic mechanisms and their therapeutic options.

Alcohol use disorder

COVID-19 Hangover: A Rising Tide of Alcohol Use Disorder and Alcohol-Associated Liver Disease May 2020, Hepatology *Abstract only**

The coronavirus disease 2019 (COVID-19) pandemic has had a tremendous global impact since it began in November of 2019. However, there are concerns that the COVID-19 pandemic will not affect all equally and some populations will be particularly vulnerable. Relevant to liver disease, patients with alcohol use disorder (AUD) and alcohol-associated liver disease (ALD) may be amongst the populations that are the most severely impacted. The reasons for this include being at a higher risk of severe COVID-19 infection due to a depressed immune system and high-risk underlying comorbidities, the injurious effect of COVID-19 on the liver, the inability to attend regular visits with providers, diversion of hospital resources, and social isolation leading to psychological decompensation and increased drinking or relapse. As a result, we fear that there will be a dramatic rising tide of alcohol relapse, admissions for decompensated ALD, and an increase in newly diagnosed patients with AUD/ALD post-COVID-19 pandemic. Providers and their institutions should implement pre-emptive strategies such as telehealth and aggressive patient outreach programs now to curb this anticipated problem. Liver transplantation (LT) centers should adapt to the pandemic by considering leniency to some LT candidates with ALD who cannot access appropriate alcohol treatment due to the current

situation. In conclusion, the COVID-19 pandemic will likely be especially detrimental to patients with AUD/ALD and actions need to be taken now to limit the scope of this anticipated problem.

Disabilities

<u>Up to 2.2 million people experiencing disability suffer collateral damage each day of Covid-19</u> lockdown in Europe May 2020, European Journal of Physical Rehabilitation and Medicine

BACKGROUNDThe Covid-19 pandemic is having a great impact on health services. Patients not receiving care due to closure of outpatient services suffer a collateral damage. Our aim was to provide first data on impact of Covid-19 on people experiencing disability in Europe.METHODSWe developed an estimation from a survey and publicly available data. Thirty-eight countries have been inquired through the European Bodies of Physical and Rehabilitation Medicine - the rehabilitation medical specialty. The 9-questions focused on March 31st, 2020. We used the following indicators: for inpatients, acute and rehabilitative hospital beds; for outpatients, missing uniform European data, we used information from Italy, Belgium and UK, and estimated for Europe basing on population, number of rehabilitation physicians, physiotherapists, and people with self-reported limitations. FINDINGSThirty-five countries (92%) including 99% of the population (809.9 million) answered. Stop of admissions to rehabilitation, early discharge and reduction of activities involved 194,800 inpatients in 10 countries. Outpatient activities stopped for 87%, involving 318,000 patients per day in Italy, Belgium and UK, leading to an estimate range of 1,3-2,2 million in Europe. Seven countries reported experiences on rehabilitation for acute Covid-19 patients.INTERPRETATIONCovid-19 emergency is having a huge impact on rehabilitation of people experiencing disability. This may lead to future cumulative effects due to reduced functional outcome and consequent increased burden of care. When the emergency will fade, rehabilitation demand will probably grow due to an expected return wave of these not well treated patients, but probably also of post-Covid-19 patients' needs.

Cardiovascular disease

<u>Cardiovascular Disease in the Post-COVID-19 Era - the Impending Tsunami?</u> April 2020, Heart, lung and circulation

The dramatic impacts on health care provisions, social behaviours as well as economic strategies from governments throughout the world have resulted in a significant shift in public behaviours in an effort to reduce the spread of the virus with the aim to "flatten the curve". One of the unintended consequences of the current pandemic has been a reduction in patients presenting for management of other chronic health conditions, in particular, cardiovascular health conditions. There is gathering data with respect to declining rates of patients presenting with ST elevation myocardial infarction (STEMI) throughout the world, with a reduction of 70% in the north of Italy, 40% in Spain [1], and up to 50% across the United States [2]. A number of theories have been suggested, including a tangible change in diet andlifestyle, whereby a reduction in aerobic exercise may reduce risk of acute plaque rupture [3], whilst less psychological stress by staying at home may also reduce risks of acute coronary syndromes [4]. Furthermore with fewer cars on the roads, there may be a reduction in particulate air pollution[5]. However, worryingly, initial data from Hong Kong has suggested that patients are presenting later to hospital with STEMI, presumably in an effort to minimise interaction with the

health care system, in an effort to avoid COVID-19infection [6]. Furthermore, emerging data from New York, at time of writing the epicentre for the pandemic suggests that rates of out of hospital cardiac arrests have increased by800% [7,8].

Appendix

Sources and Databases Searched

GOVuk, World Health Organisation (WHO) and the Cochrane Library were searched. Healthcare Databases Advanced Search (HDAS) was used to search the following databases: Medline; Embase; CINAHL; PsycINFO.

Search Strategy

Key words included: coronavirus infections; covid19; sars-cov-2; "clinical outcome*"; survival; recover*; PTSD; "post traumatic stress disorder"; anxiety; depression; "post viral fatigue; "health impact*"; "health outcome*"; ARDS; "acute respiratory distress syndrome"; "post intensive care syndrome"

This is not an exhaustive list of the terminology used. Please see the full search strategy embedded below.

HDAS



Searching the literature retrieved the information provided. We recommend checking the relevance and critically appraising the information contained within when applying to your own decisions, as we cannot accept responsibility for actions taken based on it. Every effort has been made to ensure that the information supplied is accurate, current and complete, however for various reasons it may not represent the entire body of information available.

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