Exhibit A

Centers for Disease Control and Prevention

Coronavirus Disease 2019 (COVID-19)

Are You at Higher Risk for Severe Illness?

Groups at higher risk

Older adults and people of any age who have serious underlying medical conditions may be at higher risk for more serious complications from COVID-19. These people who may be at higher risk of getting very sick from this illness, includes:

- **Older adults**
- **People who have serious underlying medical conditions** like:
  - Heart disease
  - Diabetes
  - Lung disease

People at higher risk for severe illness

Older Adults

People with HIV

People with Asthma

Steps to Prevent Getting Sick

Pregnant Women

More information

How to prepare

Symptoms & testing

If you are sick

Page last reviewed: March 20, 2020

Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19)

16-24 February 2020

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(a) **Transmission in health care settings and among health care workers (HCW)** – The Joint Mission discussed nosocomial infection in all locations visited during the Mission. As of 20 February 2020, there were 2,055 COVID-19 laboratory-confirmed cases reported among HCW from 476 hospitals across China. The majority of HCW cases (88%) were reported from Hubei.

Remarkably, more than 40,000 HCW have been deployed from other areas of China to support the response in Wuhan. Notwithstanding discrete and limited instances of nosocomial outbreaks (e.g. a nosocomial outbreak involving 15 HCW in Wuhan), transmission within health care settings and amongst health care workers does not appear to be a major transmission feature of COVID-19 in China. The Joint Mission learned that, among the HCW infections, most were identified early in the outbreak in Wuhan when supplies and experience with the new disease was lower. Additionally, investigations among HCW suggest that many may have been infected within the household rather than in a health care setting. Outside of Hubei, health care worker infections have been less frequent (i.e. 246 of the total 2055 HCW cases). When exposure was investigated in these limited cases, the exposure for most was reported to have been traced back to a confirmed case in a household.

The Joint Team noted that attention to the prevention of infection in health care workers is of paramount importance in China. Surveillance among health care workers identified factors early in the outbreak that placed HCW at higher risk of infection, and this information has been used to modify policies to improve protection of HCW.

(b) **Transmission in closed settings** – There have been reports of COVID-19 transmission in prisons (Hubei, Shandong, and Zhejiang, China), hospitals (as above) and in a long-term living facility. The close proximity and contact among people in these settings and the potential for environmental contamination are important factors, which could amplify transmission. Transmission in these settings warrants further study.

Children

Data on individuals aged 18 years old and under suggest that there is a relatively low attack rate in this age group (2.4% of all reported cases). Within Wuhan, among testing of ILI samples, no children were positive in November and December of 2019 and in the first two weeks of January 2020. From available data, and in the absence of results from serologic studies, it is not possible to determine the extent of infection among children, what role children play in transmission, whether children are less susceptible or if they present differently clinically (i.e. generally milder presentations). The Joint Mission learned that infected children have largely been identified through contact tracing in households of adults. Of note, people interviewed by the Joint Mission Team could not recall episodes in which transmission occurred from a child to an adult.

The signs, symptoms, disease progression and severity

Symptoms of COVID-19 are non-specific and the disease presentation can range from no symptoms (asymptomatic) to severe pneumonia and death. As of 20 February 2020 and

based on 55924 laboratory confirmed cases, typical **signs and symptoms** include: fever (87.9%), dry cough (67.7%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), and hemoptysis (0.9%), and conjunctival congestion (0.8%).

People with COVID-19 generally develop signs and symptoms, including mild respiratory symptoms and fever, on an average of 5-6 days after infection (mean incubation period 5-6 days, range 1-14 days).

Most people infected with COVID-19 virus have mild disease and recover. Approximately 80% of laboratory confirmed patients have had **mild to moderate disease**, which includes non-pneumonia and pneumonia cases, 13.8% have **severe disease** (dyspnea, respiratory frequency ≥30/minute, blood oxygen saturation ≤93%, PaO2/FiO2 ratio <300, and/or lung infiltrates >50% of the lung field within 24-48 hours) and 6.1% are **critical** (respiratory failure, septic shock, and/or multiple organ dysfunction/failure). **Asymptomatic infection** has been reported, but the majority of the relatively rare cases who are asymptomatic on the date of identification/report went on to develop disease. The proportion of truly asymptomatic infections is unclear but appears to be relatively rare and does not appear to be a major driver of transmission.

Individuals at **highest risk** for severe disease and death include people aged over 60 years and those with underlying conditions such as hypertension, diabetes, cardiovascular disease, chronic respiratory disease and cancer. Disease in **children** appears to be relatively rare and mild with approximately 2.4% of the total reported cases reported amongst individuals aged under 19 years. A very small proportion of those aged under 19 years have developed severe (2.5%) or critical disease (0.2%).

As of 20 February, 2114 of the 55,924 laboratory confirmed cases have died (**crude fatality ratio** [CFR[2]] 3.8%) (note: at least some of whom were identified using a case definition that included pulmonary disease). The overall CFR varies by location and intensity of transmission (i.e. 5.8% in Wuhan vs. 0.7% in other areas in China). In China, the overall CFR was higher in the early stages of the outbreak (17.3% for cases with symptom onset from 1-10 January) and has reduced over time to 0.7% for patients with symptom onset after 1 February (Figure 4). The Joint Mission noted that the standard of care has evolved over the course of the outbreak.

Mortality increases with age, with the highest mortality among people over 80 years of age (CFR 21.9%). The CFR is higher among males compared to females (4.7% vs. 2.8%). By occupation, patients who reported being retirees had the highest CFR at 8.9%. While patients who reported no comorbid conditions had a CFR of 1.4%, patients with comorbid conditions had much higher rates: 13.2% for those with cardiovascular disease, 9.2% for diabetes, 8.4% for hypertension, 8.0% for chronic respiratory disease, and 7.6% for cancer.

[2] The Joint Mission acknowledges the known challenges and biases of reporting crude CFR early in an epidemic.

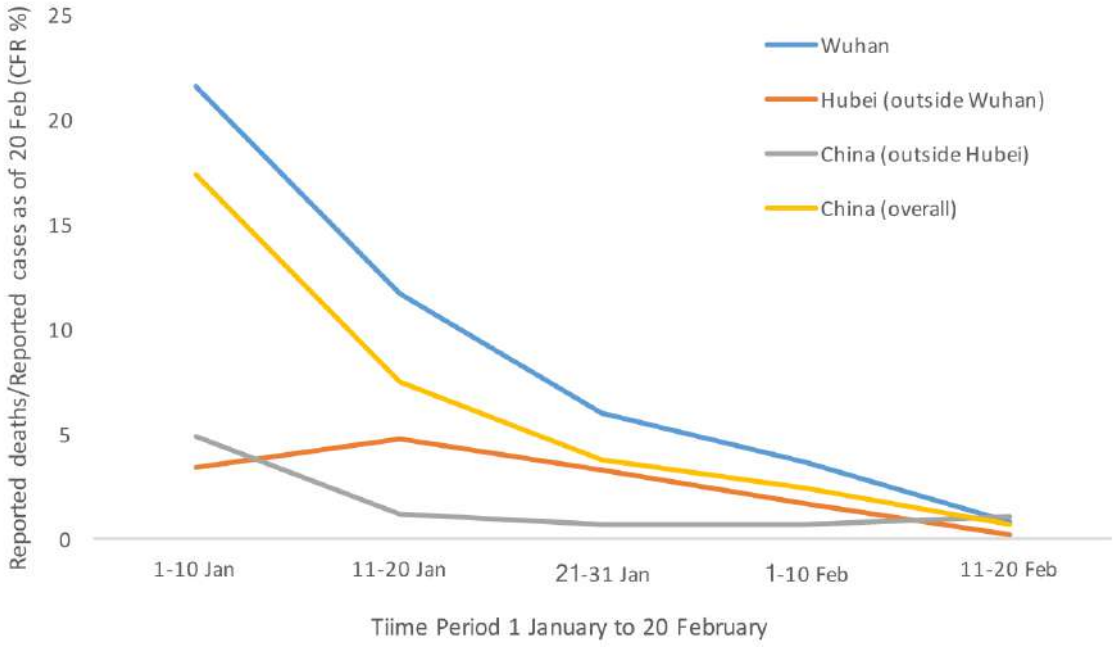

Figure 4 Case fatality ratio (reported deaths among total cases) for COVID-19 in China over time and by location, as of 20 February 2020

Data on the **progression of disease** is available from a limited number of reported hospitalized cases (Figure 5). Based on available information, the median time from symptom onset to laboratory confirmation nationally decreased from 12 days (range 8-18 days) in early January to 3 days (1-7) by early February 2020, and in Wuhan from 15 days (10-21) to 5 days (3-9), respectively. This has allowed for earlier case and contact identification, isolation and treatment.

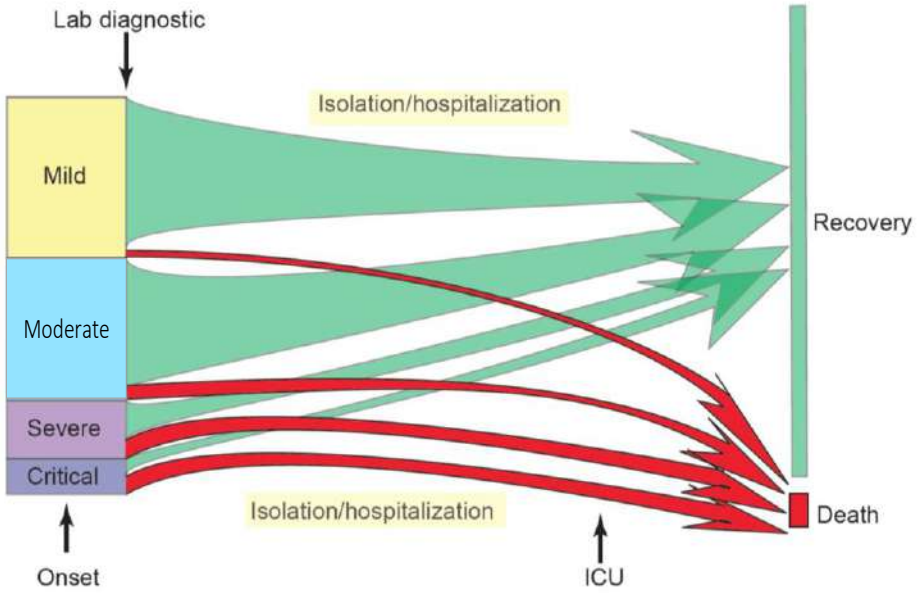

Figure 5. Pattern of disease progression for COVID-19 in China

Note: the relative size of the boxes for disease severity and outcome reflect the proportion of cases reported as of 20 February 2020. The size of the arrows indicates the proportion of cases who recovered or died. Disease definitions are described above. Moderate cases have a mild form of pneumonia.

Using available preliminary data, the median time from onset to clinical recovery for mild cases is approximately 2 weeks and is 3-6 weeks for patients with severe or critical disease. Preliminary data suggests that the time period from onset to the development of severe disease, including hypoxia, is 1 week. Among patients who have died, the time from symptom onset to outcome ranges from 2-8 weeks.

An increasing number of patients have **recovered**; as of 20 February, 18264 (24%) reported cases have recovered. Encouragingly, a report on 20 February from the Guangdong CDC suggests that of 125 severe cases identified in Guangdong, 33 (26.4%) have recovered and been released from hospital, and 58 (46.4%) had improved and were reclassified as having mild/moderate disease (i.e. + milder pneumonia). Among severe cases reported to date, 13.4% have died. Early identification of cases and contacts allows for earlier treatment.

The China response

Upon the detection of a cluster of pneumonia cases of unknown etiology in Wuhan, the CPC Central Committee and the State Council launched the national emergency response. A **Central Leadership Group for Epidemic Response** and the **Joint Prevention and Control Mechanism** of the State Council were established. General Secretary Xi Jinping personally directed and deployed the prevention and control work and requested that the prevention and control of the COVID-19 outbreak be the top priority of government at all levels. Prime Minister Li Keqiang headed the Central Leading Group for Epidemic Response and went to Wuhan to inspect and coordinate the prevention and control work of relevant departments and provinces (autonomous regions and municipalities) across the country. Vice Premier Sun Chunlan, who has been working on the frontlines in Wuhan, has led and coordinated the frontline prevention and control of the outbreak.

The prevention and control measures have been implemented rapidly, from the early stages in Wuhan and other key areas of Hubei, to the current overall national epidemic. It has been undertaken in **three main phases**, with two important events defining those phases. First, COVID-19 was included in the statutory report of Class B infectious diseases and border health quarantine infectious diseases on 20 January 2020, which marked the transition from the initial partial control approach to the comprehensive adoption of various control measures in accordance with the law. The second event was the State Council's issuing, on 8 February 2020, of The Notice on Orderly Resuming Production and Resuming Production in Enterprises, which indicated that China's national epidemic control work had entered a stage of overall epidemic prevention and control together with the restoration of normal social and economic operations.

The first stage

During the early stage of the outbreak, the main strategy focused on preventing the exportation of cases from Wuhan and other priority areas of Hubei Province, and preventing the importation of cases by other provinces; the overall aim was to control the source of infection, block transmission and prevent further spread. The response mechanism was initiated with multi-sectoral involvement in joint prevention and control measures. Wet markets were closed, and efforts were made to identify the zoonotic source. Information on the epidemic was notified to WHO on 3 January, and whole genome sequences of the COVID-19 virus were shared with WHO on 10 January. Protocols for COVID-19 diagnosis and

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Pathogenicity and transmissibility of 2019-nCoV—A quick overview and comparison with other emerging viruses

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ABSTRACT

A zoonotic coronavirus, tentatively labeled as 2019-nCoV by the World Health Organization (WHO), has been identified as the causative agent of the viral pneumonia outbreak in Wuhan, China, at the end of 2019. Although 2019-nCoV can cause a severe respiratory illness like SARS and MERS, evidence from clinics suggested that 2019-nCoV is generally less pathogenic than SARS-CoV, and much less than MERS-CoV. The transmissibility of 2019-nCoV is still debated and needs to be further assessed. To avoid the 2019-nCoV outbreak turning into an epidemic or even a pandemic and to minimize the mortality rate, China activated emergency response procedures, but much remains to be learned about the features of the virus to refine the risk assessment and response. Here, the current knowledge in 2019-nCoV pathogenicity and transmissibility is summarized in comparison with several commonly known emerging viruses, and information urgently needed for a better control of the disease is highlighted.

2019-nCoV is the third coronavirus to cross species to infect human populations (probably transmitted from bats or another host) in the past two decades [1–3]. The previous two are the severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012 [4,5]. Since 2019-nCoV can cause a severe respiratory illness like SARS and MERS and was found to be adept at human-to-human transmission, China launched an emergency response at an early stage of the outbreak. The World Health Organization (WHO) has not yet, but may soon declare the outbreak a global health emergency (PHEIC). Successful isolation of the 2019-nCoV [4,5] has promoted the understanding of viral origin and the feature of its infectivity, however, at this stage much remains unclear and to be investigated.

1. Pathogenicity of 2019-nCoV

Of the first 41 cases of laboratory confirmed infections with 2019-nCoV, all had viral pneumonia and almost a third of the patients developed acute respiratory distress syndrome (ARDS) requiring intensive care and 6 patients (14.6%) died [6]. Since the fatality rate of the early reported case is often high due to bias towards more severe cases, the true mortality risk might be much lower. As of Jan 27, 2020, about 3000 cases have been confirmed in China, and cases were also reported in Japan, South Korea, Thailand, Singapore, the United States, and Australia, all of which were exported from China. The total number of deaths from the pneumonia-related disease accounts for less than 3%. In addition, most of those who have died had underlying health conditions such as hypertension, diabetes or cardiovascular disease that compromised their immune systems. Although the fatality rate will continue to change until all infected people recover, it appears that 2019-nCoV is less pathogenic than SARS-CoV (~10%), and much less than MERS-CoV (~40%).

Coronaviruses are a group of viruses that cause a significant percentage of all common colds in human adults and children. Four human coronavirus including 229E, OC43, NL63, and HKU1 are prevalent and typically cause common cold symptoms in immunocompetent individuals. SARS-CoV which causes SARS, has a unique pathogenesis because it causes both upper and lower respiratory tract infections. 2019-nCoV is classified as a novel betacoronavirus belonging to the sarbecovirus subgenus of Coronaviridae family. The genome sequence of 2019-nCoV is about 89% identical to bat SARS-like-CoVZXC21 and 82% identical to human SARS-CoV [7]. It has been reported that 2019-nCoV uses the same cell entry receptor, ACE2, to infect humans, as SARS-CoV [8], so clinical similarity between the two viruses could be expected,

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particularly in severe cases. Notably, there are signs, from what is still very limited data, that the clinical features of 2019-nCoV seem to be more variable.

2. Transmissibility of 2019-nCoV

The 2019-nCoV outbreak was started from a local seafood market in winter, similar environment as SARS. Two-thirds of the first 41 confirmed cases were found to have a link with the Huanan Seafood Wholesale Market (also sold live animals). Initial reports indicated that human-to-human transmission of the virus was nonexistent or limited, however, it is now quite clear that efficient human-to-human transmission exists and is a requirement for the large-scale spread of 2019-nCoV [9]. Like SARS-CoV, 2019-nCoV can be passed directly from person to person by respiratory droplets, and emerging evidence suggested that it may also be transmitted through contact and fomites. Further investigations are required to explore the origin of 2019-nCoV and to reveal how easily the virus can pass between humans. In addition, the asymptomatic incubation period for individuals infected with 2019-nCov was estimated to range from 1 to 14 days (most likely 3–10 days), longer than that of SARS-CoV. Although it remains unclear whether those without symptoms have high enough viral titers for spreading the virus, great attention should be paid to minimize related risks.

A very important threshold quantity associated with the viral transmissibility is the basic reproduction number, which is usually denoted by R_0 (pronounced "R naught"). The epidemiological definition of R_0 is the average number of people who will catch a disease from one contagious person. It specifically applies to a population of people who were previously free of infection and not vaccinated. Three possibilities exist for the potential spread or decline of a disease, depending on its R_0 value: 1. If R_0 is less than 1, each existing infection causes less than 1 new infection. In this case, the disease will decline and eventually disappear. 2. If R_0 equals 1, the disease will stay alive, but there won't be an epidemic. 3. If R_0 is greater than 1, cases could grow exponentially and cause an epidemic or even a pandemic. From what we currently know, the calculated R_0 value for 2019-nCoV is significantly greater than 1. A preliminary R_0 estimate of 1.4–2.5 was presented in WHO's statement regarding the outbreak of 2019-nCoV, 23 Jan 2020 [1]. S. Zhao et al. estimated the mean R_0 for 2019-nCoV in the early phase of the outbreak ranging from 3.3 to 5.5 (likely to be below 5 but above 3 with rising report rate) [10], which appeared slightly higher than those of SARS-CoV (R_0: 2–5). In contrast, previous studies have suggested that the R_0 for MERS-CoV is less than 1, meaning that it is unlikely to cause a pandemic [11]. Super-spreading events have been implicated in 2019-nCoV transmission, as that in SARS-CoV and MERS-CoV, but their relative importance is still unclear and the super-spreaders are difficult to track. J Read. et al. estimated the R_0 for 2019-nCoV to be 3.6–4.0, indicating that 72–75% of transmissions must be prevented in order to stop the increasing trend [12], however, the authors assumed that there is little heterogeneity in reproductive numbers, so the true R_0 value could be smaller. Nevertheless, in view of avoiding the 2019-nCoV outbreak turning into an epidemic or even a pandemic, it is better to overestimate rather than underestimate the transmissibility of 2019-nCoV.

It should be noted that estimation of R_0 during the pre-epidemic stage can be plagued by data uncertainty and variability [13]. For example, the estimated R_0 was 0.80 (95% CI 0.54–1.13) for pre-epidemic SARS-CoV in southeast Asia (2002–2003). Additionally, R_0 might change seasonally according to climate or yearly gatherings such as the Chinese Spring Festival that put individuals in closer proximity to one another. Because of these, China is now under enormous pressure to make difficult decisions with an incomplete and rapidly changing understanding of the viral transmissibility. Considering the complexity of R_0, continuing research is required, including updated R_0 estimates and methodological refinements. Fortunately, a main trend is that the estimated R_0 value for 2019-nCoV is getting reduced as case information accumulates. And with the control measures implemented, the effective reproduction number (R_e) has been shown to drop to 2.08 (1.99–2.18) as of 22 Jan 2020 [14].

3. Relationship between viral pathogenicity and transmissibility

The severity of disease is most often an important indirect factor in a virus's ability to spread. Because coronaviruses have error-prone RNA-dependent RNA polymerases (RdRP), mutations and recombination events frequently occur [4], resulting in quasispecies diversity that is closely associated with adaptive evolution and the capacity to cause disease. Previous studies have shown that SARS-CoV mutated over the 2002–2004 epidemic to better bind to its cellular receptor and replication in human cells, enhancing virulence. It is thus important to examine whether 2019-nCoV behaves like SARS-CoV to adapt to the human host and whether this would increase the R_0 value and change its virulence. By contrast, MERS-CoV has not mutated substantially since it was discovered, which may be due to that the functional cellular receptor (CD26) used by MERS-CoV is quite unique so the virus has a very limited potential to mutate without losing fitness. Notably, ACE2, the receptor protein of both SARS-CoV and 2019-nCoV, is abundantly present in humans in the epithelia of the lung and small intestine [15], and coronaviruses can infect the upper respiratory and gastrointestinal tract of mammals. In this regard, identifying the possible route of infection will also have implications for the pathogenesis and treatment of disease caused by 2019-nCoV.

Table 1 gives estimates of case fatality rate as well as R_0 value of several commonly known emerging virus infections based on data collected from literatures [16,17], WHO and CDC. It is clear that airborne viruses tend to have a higher R_0 value than those spread through contact. Besides, from the table, we can find a trend that higher pathogenicity is often associated with lower transmissibility, which may also apply to a certain virus of different subtypes and strains. A good example is the influenza virus. Whereas the pandemic H1N1 virus binding to receptors in the upper respiratory tract caused relatively mild disease and became endemic in the population, the H7N9 virus binding to receptors in the lower respiratory tract has a fatality rate of approximately 40% and has so far resulted in only a few small clusters of human-to-human transmission. Another example is that Measles virus and

Table 1
Case fatality rate and R_0 value of commonly known emerging virus infections.

Virus	Case Fatality Rate (%)	R_0
2019-nCoV	3	1.4–5.5[a]
SARS-CoV	10	2–5
MERS-CoV	40	<1
Avian H7N9 (2013)	40	<1
H1N1 (2009)	0.03	1.2–1.6
H1N1 (1918)	3	1.4–3.8
Measles Virus	0.3	12–18
Rhinovirus	<0.01	6
Ebola Virus	70	1.5–2.5
HIV	80[b]	2–4
Small Pox Virus	17	5–7

[a] WHO: 1.4–2.5; S. Zhao et al.: 3.3–5.5; J. Read et al.: 3.6–4.0; M. Shen et al.: 4.5–4.9.
[b] Without therapy.

Rhinovirus have strong transmissibility but low mortality rate. But this is not a given: CoV-NL63 uses the same receptor (ACE2) as 2019-nCoV, whereas it causes disease of very different severity. In the case of 2019-nCoV, there have been some clues suggested that, sometimes, an individual with highly severe 2019-nCoV disease will only cause a few infections, conversely, individuals with a moderate disease or latent infection can occasionally cause many infections, though the molecular mechanism is not yet understood. A possible consequence of this is that viral mutations that pose a low health threat on the individual level may pose a high risk on the population level. Further studies are thus required to fill the knowledge gap in viral mutations and pathogenicity and transmissibility. Related information can help to reveal how the virus is evolving and adapting to new conditions and whether the outbreak has the potential to persist.

Based on above discussions, the current 2019-nCoV seems to have relatively low pathogenicity and moderate transmissibility. However, more information on the biological and epidemiological features of the virus are urgently needed to further refine the risk assessment and response, which will ultimately benefit the 2019-nCoV control and prevention. Besides, because that anti-coronaviral drugs and vaccines are still under development [18,19], fear plays a role in the economic and social consequences, which was also a feature of SARS-CoV outbreak. Educating the communities and strengthening public confidence will thus be important. As long as the transmission of the virus from one person to another could be substantially and consistently interrupted ($R < 1$), it is entirely possible that the outbreak could be controlled and even eradicated, and this requires the joint efforts of the whole society.

Declaration of Competing Interest

The author declared no competing interests.

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Anxiety and Related Disorders and Physical Illness

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Abstract

Anxiety and related disorders are the most prevalent mental disorders in the general population. There is a strong bidirectional association between anxiety and related disorders and co-occurring general medical conditions. The co-occurrence of anxiety and related disorders and general medical conditions is associated with significant impairment, morbidity and economic costs. At the same time, recognition of anxiety and related disorders in people with medical illness may be challenging when comorbid with physical illness due in part to overlap in symptomatology. Furthermore, there is a relatively limited evidence base of randomized controlled trials in this population. Additional work is needed to improve screening for anxiety and related disorders in medical illness, to enhance diagnosis and assessment, and to optimize treatment.

Anxiety disorders, obsessive-compulsive and related disorders, and trauma- and stressor-related disorders are the most prevalent psychiatric disorders in the general population [1, 2], with generalized anxiety disorder the most common anxiety disorder in primary care populations [3]. Indeed, these anxiety and related disorders occur frequently with a range of general medical disorders [4, 5], including gastrointestinal disease [6], pulmonary disease [7, 8], cardiovascular disease [9], endocrine disorders [10], dermatological disorders [11] and cancer [12], as well as neuropsychiatric disorders such as chronic pain [13, 14], migraines [15], dementia [16] and Parkinson's disease [17]. In this chapter we review the epidemiology of comorbid anxiety and related disorders and physical illness, the growing evidence of a bidirectional relationship between these sets of conditions [18] and relevant randomized controlled trials in this area.

Epidemiology

Anxiety and related disorders are the most common psychiatric disorders worldwide, with a 12-month prevalence worldwide of between 4 and 20% [2]. The onset of anxiety and related disorders usually happens in childhood or adolescence, with many individuals first presenting with physical symptoms in primary care settings

Table 1. Common medical conditions associated with anxiety

Endocrine disorders	diabetes mellitus [32], thyroid disease [10], catecholamine-secreting pheochromocytoma
Gastrointestinal disorders	peptic ulcers [27], celiac disease [33], irritable bowel syndrome [26]
Musculoskeletal disorders	fibromyalgia/chronic fatigue syndrome [34], arthritis [35]
Neurological disorders	migraines [15], epilepsy, neurodegenerative illness [17]
Cardiorespiratory disease	asthma [30], angina [25], chronic obstructive pulmonary disease [7], mitral valve prolapse [36], cystic fibrosis [8], obesity [24, 37, 38]
Chronic pain	burns [14], cancer [12]
Infectious disease	HIV [39], tuberculosis [39]

[4]. Anxiety and related disorders are prevalent throughout life [19–22]. Furthermore, while the prevalence of comorbid anxiety and related disorders in those with chronic medical illness is not as well studied as depression in medical conditions, studies which have been done indicate it is as common [22–25]. A large cross-sectional study demonstrated that generalized anxiety disorder was the most prevalent anxiety disorder in primary care settings [3].

Systematic reviews have established that anxiety disorders are particularly prevalent in gastrointestinal disorders, pulmonary disease, cardiovascular disease, endocrine disease and cancer, as well as neuropsychiatric disorders such as chronic pain and migraines. In irritable bowel syndrome, up to 95% of patients have generalized anxiety disorder or panic disorder [26]. Similarly, panic disorder and generalized anxiety disorder were more prevalent in those with peptic ulcer disease [27]. In asthma, anxiety disorders occur in at least 25% of patients [28, 29]. In multiple studies of adolescents and adults with asthma, the prevalence of panic disorder and agoraphobia is almost three times that of the general population [30, 31]. Another anxiety disorder that co-occurs with respiratory illness is generalized anxiety disorder [31]. Table 1 outlines medical conditions associated with anxiety symptoms and disorders.

The co-occurrence of anxiety and general medical conditions is associated with significant impairment, morbidity and economic costs [36, 40–42]. For example, in a study of almost 500 medically ill persons diagnosed with anxiety disorders, those with posttraumatic stress disorder, panic disorder and social anxiety disorder were found more likely to be frequent consumers of healthcare, and to remain unable to maintain their roles and responsibilities, including work [43]. Medical comorbidities with anxiety disorders have also been shown to elevate suicide risk [44]. Adequate management of anxiety symptoms can improve outcomes of physical ill-health, and reduce the use of healthcare resources [4, 45]. In addition, some work suggests that quality of life and functional ability may be improved with optimal treatment of comorbid general medical and anxiety disorders [46–48].

Etiology

There is a growing body of evidence for a strong bidirectional association between anxiety and related disorders and co-occurring general medical

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conditions [14, 29, 49]. On the one hand, medical disorders may lead to fears about diagnosis, hospitalization, painful procedures and a foreshortened lifespan, while certain medical disorders may be linked physiologically to the development of anxiety and related disorders [50]. On the other hand, anxiety and related disorders may lead to vulnerability for various medical conditions. There may also be underlying factors that contribute to susceptibility for both anxiety disorders and physical conditions [51].

There is ongoing work to determine the precise nature of the relationships between anxiety disorders and physical illness in a number of areas. Thus, in irritable bowel syndrome, it has been suggested that infection or inflammation of the gastrointestinal tract lead to anxiety [29], while in asthma it has been postulated that increased partial pressure of carbon dioxide is responsible for panic attacks [52]. On the other hand, neurotransmitter disturbances and hypothalamic-pituitary-adrenal axis dysfunction have been postulated to play a key role in explaining how anxiety symptoms and disorders lead to medical illnesses [53].

The common underlying factors that may contribute to both anxiety disorders and comorbid physical illness have also received ongoing study. Genetic factors may, for example, predispose to both general medical conditions and anxiety disorders [54, 55]. In the World Mental Health Surveys, there were strong relationships between early adversity and subsequent onset of both anxiety disorders and various physical disorders, including chronic spinal pain, chronic headache, heart disease, asthma, diabetes and hypertension [56, 57].

Clinical Features

Recognition of anxiety disorders in people with medical illness can be challenging for several reasons. Firstly, anxiety symptoms are an understandable response to the diagnosis of medical conditions. A medical condition can be sufficient enough to be a stressor for an individual to develop an adjustment disorder, and in some cases even posttraumatic stress disorder. Secondly, anxiety symptoms may overlap with symptoms of an underlying medical disorder; thus, since patients with cancer may have insomnia and fatigue, conditions such as generalized anxiety disorder are overlooked. Similarly, medications used in the treatment of physical disorders may lead to anxiety symptoms [20, 49, 58].

In a patient with anxiety symptoms, a range of different diagnoses can be considered. Table 2 tabulates the main features of key anxiety and related disorders. Posttraumatic stress disorder is the anxiety and related disorder that is most commonly associated with gastrointestinal, cardiac, endocrine, chronic pain, migraines and Parkinson's disease [14, 22]. Symptoms of generalized anxiety disorder arguably most closely resemble those of many general medical conditions, particularly in the older population [20]. Panic disorder may, however, mimic a number of physical illnesses. Indeed, a broad range of different anxiety and related disorders have been associated with various physical illnesses.

Management

Early identification of anxiety symptoms and disorders in individuals with chronic illness is important in determining better outcomes for individuals with both sets of disorders [60–62]. The therapeutic alliance and collaboration between medical professionals may contribute to successful management of symptoms [50]. There is, however, a paucity of robust evidence in the treatment of chronically ill patients with comorbid anxiety and related disorders [51].

Cognitive behavioral therapy has been undertaken in a number of studies of individuals with medical illness and anxiety and related disorders. A systematic review of 32 psychotherapy

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Table 2. Anxiety and related disorders commonly seen in medically ill adult patients [14, 59]

Generalized anxiety disorder	characterized by a pervasive and excessive worry about everyday life events; this worry is difficult to control and is accompanied by somatic symptoms which impair the individual's functioning
Specific phobia	characterized by excessive, irrational and persistent fear of specific objects, situations or activities such as heights, flying and spiders
Social anxiety disorder	characterized by an intense and excessive fear of scrutiny and humiliation in social situations which then leads to avoidance of these situations, or development of panic attacks when the situations are endured
Panic disorder	characterized by recurrent unexpected panic attacks described as discrete events in which the individual experiences symptoms that peak within a few minutes and resolve spontaneously, coupled with anticipatory anxiety about future panic attacks
Posttraumatic disorder	a disorder in which the individual experiences a traumatic event; the disorder is then characterized by recurrent distressing re-experiencing phenomena, increased arousal, persistent avoidance of reminders and stimuli associated with the event, and negative cognitions and mood
Hypochondriasis	characterized by preoccupation with having a severe disease; the individual cannot be reassured despite medical investigations
Obsessive-compulsive disorder	characterized by recurrent intrusive distressing thoughts or images (obsessions) which are neutralized by some other thought or repetitive mental act/behavior (compulsions)
Substance/medication-induced anxiety disorder	characterized by anxiety symptoms which are directly related to the physiological effects of a substance or medication
Adjustment disorder with anxiety	characterized by a time-limited, maladaptive anxiety response to an identifiable stressor
Separation anxiety disorder	characterized by excessive, developmentally inappropriate anxiety upon separation of the child from the home or from significant attachment figures
Anxiety disorder not otherwise specified	diagnosed when the individual's symptoms are severe and distressing but do not meet diagnostic criteria for any other anxiety disorder

trials in patients with irritable bowel syndrome and anxiety disorders indicates the efficacy of cognitive behavioral therapy in reducing somatic distress [63–65]. A systematic review of 20 studies of cognitive-behavioral interventions in nearly 3,000 participants found that they may be effective in the management of HIV-/AIDS-associated anxiety [66]. Cognitive behavioral therapy has also been shown to reduce anxiety symptoms and distress in patients with cardiac disease and anxiety in one randomized controlled trial [67].

Behavioral strategies in anxiety disorders and comorbid medical illnesses include biofeedback, relaxation training and meditation [68, 69]. Two randomized controlled trials examining the effects of biofeedback in the management of asthma [69], and another two randomized controlled trials looking at relaxation therapy showed a reduction in the use of bronchodilator agents and improved quality of life [70].

Hypnotherapy and interpersonal therapy are other treatment modalities showing promise in the management of pain related to procedures for

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cancer therapies [71, 72], but rigorous studies are lacking in this area [14, 64].

In patients with physical illness and anxiety and related disorders, there are relatively few randomized controlled trials to guide treatment choices. Thus, medications should be selected based on studies of efficacy in anxiety disorders, and on minimizing adverse events and drug-drug interactions. The selective serotonin reuptake inhibitors sertraline, citalopram and escitalopram have relatively few adverse events and are safe in interaction with other agents [73]. The serotonin-noradrenaline reuptake inhibitors venlafaxine and duloxetine have the potential advantage of being beneficial for pain symptoms, but venlafaxine has the disadvantage of requiring blood pressure monitoring [74]. Drugs such as mirtazapine and the tricyclic antidepressants may be efficacious in the treatment of some anxiety disorders, but carry a significant side-effect profile and may have worrisome drug-drug interactions [74]. Benzodiazepines and sedative-hypnotic agents may be helpful for anxiety symptoms, but should be used cautiously due to concerns of dependence [6]. The second-generation antipsychotic quetiapine is anxiolytic at low doses, and is efficacious in the treatment of some anxiety and related disorders [50], but its metabolic, cardiac and autonomic side-effect burden should be taken into consideration.

Conclusion

Anxiety and related disorders are frequently comorbid with chronic medical conditions. There is growing understanding of the bidirectional relationships between these sets of disorders. Recognition can be delayed due to the similarity of primary anxiety symptoms and anxiety secondary to general medical conditions. Pharmacotherapy management can be effective, but clinicians need to be aware of the side-effect burden of psychotropics in medical conditions as well as potential drug-drug interactions. There is a growing database of studies of cognitive-behavioral therapy showing efficacy in individuals with anxiety disorders and comorbid medical illness. Further work is needed to improve screening for anxiety and related disorders in medical illness, to enhance diagnosis and assessment, and to optimize treatment.

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Management of physical health conditions in adults with severe mental disorders

WHO GUIDELINES

World Health Organization

Guidelines for the management of physical health conditions in adults with severe mental disorders

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Executive summary

INTRODUCTION

The global burden of disease due to mental disorders continues to rise, especially in low- and middle-income countries (LMIC). In addition to causing a large proportion of morbidity, mental disorders – especially severe mental disorders (SMD) – are linked with poorer health outcomes and increased mortality. SMD are defined as a group of conditions that include moderate to severe depression, bipolar disorder, and schizophrenia and other psychotic disorders. People with SMD have a two to three times higher average mortality compared to the general population, which translates to a 10-20 year reduction in life expectancy. While people with SMD do have higher rates of death due to unnatural causes (accidents, homicide, or suicide) than the general population, the majority of deaths amongst people with SMD are attributable to physical health conditions, both non-communicable and communicable. Furthermore, people with SMD are more likely to engage in lifestyle behaviours that constitute risk factors for non-communicable diseases (NCDs) such as tobacco consumption, physical inactivity and consuming unhealthy diets.

Most studies reporting the excess mortality in people with SMD are from high income countries. The situation may be much worse in LMIC where the resources are inadequate, the institutions are not well managed and access to quality mental health care and physical care is limited.

Equitable access to comprehensive health services remains out of reach for the majority of people with SMD. Unfortunately, people with SMD often lack access to health services or receive poor quality care, including promotion and prevention, screening, and treatment. It is crucial to address the disparities in health care access and provision for people with SMD. Following the principle of non-discrimination and universal health coverage as elaborated in target 3.4 of the United Nations Sustainable Development Goals ("By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote of mental health and well-being"), people with SMD should be offered at least the same level of treatment for physical health conditions and their risk factors as the general population.

The WHO *Comprehensive Mental Health Action Plan (2013-2020)* outlines a vision where people living with mental disorders are able to exercise the full range of human rights and to access high quality, culturally-appropriate health and social care in a timely way to promote recovery. In service of this vision and as part of WHO's Mental Health Gap Action Programme (mhGAP), these *Guidelines on the management of physical health conditions in adults with severe mental disorders* will provide up-to-date, evidence-based recommendations to support the scale-up of care for physical health conditions and their risk factors affecting people living with SMD globally.

Accordingly, the objective of these guidelines is:

To improve the management of physical health conditions in adults with SMD and support the reduction of individual health behaviours constituting risk factors for these illnesses, with the aim of decreasing morbidity and premature mortality amongst people with SMD.

Existing WHO guidelines for the general population are relevant to the physical health conditions that increase the morbidity and mortality for people with SMD. For example, the *Package of Essential Noncommunicable (PEN) Disease Interventions for Primary Health Care in Low-Resource*

Settings Geneva, WHO, 2010 provides guidelines and recommendations for tobacco cessation, weight management, cardiovascular disease prevention including diabetes management and prevention of complications, treatment and prevention of chronic respiratory diseases in the general population. Other WHO guidelines for infectious disease are also relevant such as the *Consolidated guidelines on HIV prevention, diagnosis, treatment, and care for key populations. WHO, 2016 update* and *Guidelines for treatment of drug-susceptible tuberculosis and patient care, 2017 update. WHO, 2017.*

GUIDELINE DEVELOPMENT METHODS

The process of development of these guidelines followed the *WHO handbook for guideline development* and involved: (1) recruitment of the Guideline Development Group (GDG); (2) declaration of interest by GDG members and peer reviewers; (3) scoping review to formulate questions and select outcomes (4) identification, appraisal and synthesis of available evidence; (5) formulation of recommendations with inputs from a wide range of stakeholders; and (6) preparation of documents and plans for dissemination.

The GDG, an international group of experts, provided input into the scope of the guideline and assisted the steering group in developing the key questions. A total of one background question and seven PICO (Population, Intervention, Comparison, and Outcome) questions were developed.

To address the PICO questions, a series of searches for systematic reviews was conducted and GRADE evidence profiles prepared. During a meeting at WHO headquarters in Geneva, 9 – 10 May 2018, the GDG discussed the evidence, sought clarifications, and interpreted the findings in order to develop recommendations. The GDG considered the relevance of the recommendations for people with SMD including the balance of benefit and harm of each intervention; values and preferences of people with SMD; costs and resource use; and other relevant practical issues for providers in LMIC.

When making a strong recommendation, the GDG was confident that the desirable effects of the intervention outweigh any undesirable effects. When the GDG was uncertain about the balance between the desirable and undesirable effects, the GDG issued a conditional recommendation. Strong recommendations imply that most individuals would want the intervention and should receive it while conditional recommendations imply that different choices may be appropriate for individual people and they may require assistance at arriving at management decisions. The GDG members reached an unanimous agreement on all the recommendations and ratings.

3.7
OTHER INFECTIOUS DISEASES (TUBERCULOSIS, HEPATITIS B/C)

For people with SMD and infectious diseases (Tuberculosis, Hepatitis B/C), what pharmacological and nonpharmacological (social, psychological) interventions are effective for treatment of infectious diseases (i.e. tuberculosis, hepatitis B, hepatitis C)?

Population:
People with SMD and infectious diseases (Tuberculosis, Hepatitis B/C)

Intervention:
- Pharmacological interventions for infectious diseases
- Nonpharmacological (social, psychological) interventions for infectious diseases

Comparison:
One treatment versus another or care as usual

Outcomes:
- Critical
  – Infectious disease-related outcomes
- Important
  – Frequency of adverse events/side-effects

BACKGROUND

People with SMD are at greater risk than the general population for exposure to infectious diseases, including tuberculosis (TB) and chronic hepatitis(Rosenberg *et al.*, 2010). Infectious diseases appear to contribute to an increased risk of death in persons with SMD, with a 4- to 8-fold risk of death due to infection compared to the general population.

Tuberculosis and SMD share common risk factors including homelessness, HIV positive serology, alcohol/substance abuse and migrant status leading to frequent co-morbidity. There are widespread discriminatory attitudes and behaviours towards patients with TB and SMD in the community which affects health-related quality of life. In people with SMD and TB, there may be a negative impact on health behaviours such as medication adherence leading to greater morbidity, mortality, amplification of drug-resistance, transmission and all the associated social costs of these outcomes (Alene *et al.*, 2018).

The WHO End TB strategy calls to provide TB care through an integrated approach in collaboration with other public health programmes including mental health services such as tailoring TB care delivery models to the specific needs of populations with mental health problems.

There is also a high prevalence of hepatitis B and C in people with SMD. There is evidence that hepatitis C infection itself may be directly associated with psychiatric symptoms, independent of pre-existing psychiatric disorders. Stigmatization and the fact that people have to cope with a chronic infectious disorder increase the risk of depression. As is seen with TB, mental health problems during antiviral treatment have a strong impact on quality of life, may reduce treatment compliance and are risk factors for treatment failure.

For people with SMD and TB or hepatitis B/C, pharmacological and non-pharmacological interventions need to be considered as in the general population.

RECOMMENDATIONS AND CONSIDERATIONS

RECOMMENDATION 1:

For people with severe mental disorders and TB, pharmacological management should be considered in accordance with the *WHO guidelines for the treatment of drug-susceptible tuberculosis and patient care*, and the *WHO treatment guidelines for drug-resistant tuberculosis*.

(Strength of the recommendation: strong; Quality of the evidence: Low).

WHO guidelines for the treatment of drug-susceptible tuberculosis and patient care

(http://apps.who.int/iris/bitstream/handle/10665/255052/9789241550000-eng.pdf?sequence=1)

In patients with drug-susceptible pulmonary TB, the 6-month rifampicin-based regimen 2HRZE/4HR and daily dosing is the recommended regimen and dosing frequency.

WHO treatment guidelines for drug-resistant tuberculosis

(http://apps.who.int/iris/bitstream/handle/10665/250125/9789241549639-eng.pdf?sequence=1).

Note: The guidelines are currently being updated and the recommendations will be replaced with the revised ones as soon as they are available.

1) Shorter MDR-TB regimen

In patients with RR-TB or MDR-TB who were not previously treated with second-line drugs and in whom resistance to fluoroquinolones and second-line injectable agents was excluded or is considered highly unlikely, a shorter MDR-TB regimen of 9–12 months may be used instead of the longer regimens (conditional recommendation, very low certainty in the evidence).

2) Longer MDR-TB regimens

2a) In patients with RR-TB or MDR-TB, a regimen with at least five effective TB medicines during the intensive phase is recommended, including pyrazinamide and four core second-line TB medicines – one chosen from Group A, one from Group B, and at least two from Group C2 (conditional recommendation, very low certainty in the evidence). If the minimum number of effective TB medicines cannot be composed as given above, an agent from Group D2 and other agents from Group D3 may be added to bring the total to five.

2b) In patients with RR-TB or MDR-TB, it is recommended that the regimen be further strengthened with high-dose isoniazid and/or ethambutol (conditional recommendation, very low certainty in the evidence).

(Group A=levofloxacin, moxifloxacin, gatifloxacin; Group B=amikacin, capreomycin, kanamycin, (streptomycin); Group C= ethionamide (or prothionamide), cycloserine (or terizidone), linezolid, clofazimine).(Group D2=bedaquiline, delamanid; Group D3=p-aminosalicylic acid, imipenem–cilastatin, meropenem, amoxicillin clavulanate, (thioacetazone)).

RECOMMENDATION 2:

For people with severe mental disorders and TB, non-pharmacological (social, psychological) management should be considered in accordance with the WHO guidelines for the treatment of drug-susceptible tuberculosis and patient care, and the WHO treatment guidelines for drug-resistant tuberculosis.

(Strength of the recommendation: strong; Quality of the evidence: Low).

Cross-cutting interventions for drug-susceptible TB and drug-resistant TB: effectiveness of patient care and support interventions

(http://apps.who.int/iris/bitstream/handle/10665/255052/9789241550000-eng.pdf?sequence=1)

RECOMMENDATIONS:

Health education and counselling on the disease and treatment adherence should be provided to patients on TB treatment. (Strong recommendation, moderate certainty in the evidence)

A package of treatment adherence interventions may be offered to patients on TB treatment in conjunction with the selection of a suitable treatment administration option. (Conditional recommendation, low certainty in the evidence)

One or more of the following treatment adherence interventions (complementary and not mutually exclusive) may be offered to patients on TB treatment or to health-care providers: a) tracers and/or digital medication monitor (Conditional recommendation, very low certainty in the evidence) b) material support to patient (Conditional recommendation, moderate certainty in the evidence) c) psychological support to patient (Conditional recommendation, low certainty in the evidence) d) staff education (Conditional recommendation, low certainty in the evidence).

[The GDG suggests that psychological support* should be provided to patients with TB (conditional recommendation, low certainty of evidence). *Psychological support includes counselling sessions and peer-group support.]

Psychological support was varied and could include self-help groups, alcohol cessation counselling and TB clubs. Patients who had access to psychological support had higher rates of treatment completion and cure, as well as lower rates of treatment failure and loss to follow-up. When considering this data, it should also be noted that psychological support types are very broad and may not be adequately represented in this review. To maximize health equity, psychological support should be targeted at the most marginalized populations.

RECOMMENDATION 3:

For people with severe mental disorders and hepatitis B, treatment should be considered in accordance with the WHO guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection.

(Strength of the recommendation: strong; Quality of the evidence: Low)

Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. March 2015

http://apps.who.int/iris/bitstream/handle/10665/154590/9789241549059_eng.pdf?sequence=1

In all adults, adolescents and children aged 12 years or older in whom antiviral therapy is indicated, the nucleos(t)ide analogues (NAs) which have a high barrier to drug resistance (tenofovir or entecavir) are recommended. Entecavir is recommended in children aged 2–11 years. *(Strong recommendation, moderate quality of evidence)*

RECOMMENDATION 4:

For people with severe mental disorders and hepatitis C, treatment should be considered in accordance with the WHO guidelines for the screening care and treatment of persons with chronic hepatitis C infection.

(Strength of the recommendation: strong; Quality of the evidence: Low)

Guidelines for the screening care and treatment of persons with chronic hepatitis C infection. Updated version, April 2016

http://www.who.int/hepatitis/publications/hepatitis-c-guidelines-2016/en/

Treatment with direct-acting antiviral agents: it is recommended that direct-acting antivirals (DAA) regimens be used for the treatment of persons with hepatitis C infection rather than regimens with pegylated interferon and ribavirin. *(Strong recommendation, moderate quality of evidence)*

BEST PRACTICE STATEMENT:

For people with severe mental disorders and TB, Hepatitis B/C prescribers should take into account the potential for drug-drug interactions between TB medicines, medicines for hepatitis B and C with psychotropic medicines.

Additional considerations

People with SMD may be at an increased risk of Hepatitis B and C for example due to injection drug use. The CDC in the USA has reported outbreaks of Hepatitis A in people who inject drugs, which may also be through the sharing of contaminated instruments and needles or through faeco-oral transmission. Therefore members of the GDG recommended that in people with SMD who also inject drugs, Hepatitis A and Hepatitis B vaccination, and Hepatitis B and Hepatitis C testing should be undertaken. This has also been recommended by the CDC, USA (https://www.cdc.gov/hepatitis/populations/idu.htm).

SUPPORTING EVIDENCE AND RATIONALE

No reviews were identified for interventions in people with SMD and comorbid TB, Hepatitis B/C. A recent systematic review reported that programmes that included educational, psychological, and/or material support were associated with better TB outcomes, and can now be considered best practice(Alipanah *et al*., 2018). Some trial evidence shows effectiveness of treatment of pulmonary TB in people with SMD (Mishin *et al* 2008) and of a brief intervention to deliver best practice services for infectious diseases to people with mental disorders in increasing participation and acceptance of core services, including testing for hepatitis B/C; immunization for hepatitis A and B; increased hepatitis knowledge reduction of substance use (Rosenberg *et al*., 2010).

The drug-drug interaction review showed that major interactions exist between medicines used for TB, hepatitis B/C and psychotropic medicines (Annex 6). These require close clinical monitoring and dose adjustments and in some cases use of alternate psychotropic medicines with less potential for interaction.

These recommendations are based on indirect evidence of TB/Hepatitis treatment in the general population that are provided in existing WHO guidelines as the GDG concluded that the same pathophysiological mechanisms for these conditions would apply to people with SMD. The GDG provided strong recommendations as they agreed that the benefits of the interventions outweighed the harms while noting the need to consider drug interactions. The GDG also agreed that there was no important uncertainty about or variability in how much people value the main outcomes and that the interventions would increase health equity. The GDG agreed that people with SMD would need additional support for adherence to TB treatments and provided a strong recommendation for this intervention drawing from existing general population guidelines.

Exhibit B

CORONAVIRUS

Coronavirus could 'wreak havoc' on U.S. jails, experts warn

"People are freaking out about it, and we don't have the resources," said an official of the union that represents federal prison workers.

JosefHanus / Getty Images/iStockphoto

March 12, 2020, 1:04 PM EDT

By Rich Schapiro

Several jail staffers took notice when an inmate arrived at a federal detention center in Miami last week wearing a mask.

Word spread rapidly inside the FDC Miami that the man had flu-like symptoms, two workers said, triggering fears that the inmate was infected with the coronavirus.

"A lot of staffers are in an uproar because they don't know if they're going to get exposed," an employee told NBC News at the time.

It turned out that the inmate had a bacterial infection, a Bureau of Prisons official said, not coronavirus. But concern about the potential spread of COVID-19 inside a detention facility has only grown since then as the number of confirmed cases has exploded across the country.

An outbreak of the deadly virus inside the walls of a U.S. prison or jail is now a question of when, not if, accor health experts. And interviews with several jail staffers, prisoner advocates and former correctional medical

personnel revealed deep concerns over the potential for the illness to wreak havoc behind bars.

Full coverage of the coronavirus outbreak

"We're in a very perilous stage right now," said Dr. Homer Venters, the former chief medical officer of the New York City jail system. "It's just a matter of time before we see cases inside jails and prisons."

Coronavirus declared a pandemic by World Health Organization

MARCH 11, 202002:31

Venters regularly visits jails and prisons across the country as an expert consultant on health services in correctional settings. He said it's common to see facilities lacking the kind of basic germ-fighting tools necessary to help prevent the spread of an illness like the coronavirus.

"Let's say there are three sinks for 40 people," said Venters, who is the president of Community Oriented Correctional Health Systems, a nonprofit that works to improve health care behind bars.

"Rarely do I ever see most of them working, plus soap and paper towels. Some of the most basic elements of infection control that we take for granted, like your ability to wash your hands and dry them, remain out of reach for many people in detention."

The U.S. has roughly 5,000 adult detention facilities – a mix of jails, which house inmates awaiting trial or serving short sentences, and prisons, where people convicted of serious crimes go to serve time. No cases have yet been reported in any of the facilities.

But the environments, with inmates packed together in often grimy spaces with limited ventilation, provide a prime breeding ground for the spread of infectious diseases, experts say.

Jails are seen as being especially vulnerable, given the constant flow of prisoners in and out. Several jail systems have announced coronavirus countermeasures, such as stepped-up cleaning and ramped-up medical screening of new arrivals.

But more dramatic measures, such as restricting inmate visitation, had yet to be put in place on a grand scale until late Thursday, when several states announced that they were suspending visitation until further notice.

Prisoner advocates worry that the virus has already made its way inside the walls of the nation's detention facilities.

"My fear is it will be similar to the assisted living facility in Washington state, where no one's going to know until it becomes a very serious matter somewhere," said Maria Morris, a senior staff attorney with the American Civil Liberties Union's National Prison Project.

Morris said the combination of staffers moving in and out of prisons and the already unsanitary conditions inside many of them increase the likelihood of serious coronavirus outbreaks.

Download the NBC News app for full coverage of the coronavirus outbreak

"Once it gets in, if there's not a well-thought-out plan to address it, it seems very likely that it'll wreak havoc on facilities quite quickly," she said.

Countries hard hit by the coronavirus have already experienced major problems inside their prisons. Deadly riots broke out in facilities across Italy amid efforts to contain the virus. In China, where it originated, at least 500 prisoners have been infected. And Iran took the extraordinary step of temporarily releasing more than 50,000 prisoners in hope of slowing the spread of the virus.

Joe Rojas, the Southeast regional vice president for the Council of Prison Locals, the union that represents federal prison workers, said he fears the potential for riots to erupt.

"When there's fear among inmates without a plan for containment, you can have a riot," Rojas said.

He said that many federal prisons are also dealing with staffing shortages in their medical departments and that a lack of guidance from the Bureau of Prisons has fueled workers' fears.

"People are freaking out about it, and we don't have the resources," Rojas said.

A spokeswoman for the Bureau of Prisons said: "Out of an abundance of caution, the BOP provided guidance to health-care professionals throughout the system and has a screening tool in place for use in the event an inma staff member is exposed or symptomatic. The BOP has an internal web-based system for reporting infectious and outbreaks, allowing access to health care and correctional professionals system-wide."

Federal prisons are not stocking COVID-19 test kits, the spokeswoman said, but medical personnel working with local health authorities can facilitate inmate testing.

"Every BOP facility has contingency plans in place to address a large range of concerns, to include infectious diseases, and is fully equipped to implement these plans as necessary," the spokeswoman added.

Unlike prisons, the majority of local and county jails lack in-house medical staffs, experts say, making it far more difficult to combat a fast-spreading illness like the coronavirus.

"There are jails where the sheriff's deputies are handing out medications and making medical decisions for the individuals," said Sheriff Dave Mahoney, who operates a 1,000-bed facility in Dane County, Wisconsin.

Mahoney, who is the incoming president of the National Sheriffs' Association, said he and his counterparts around the country are having ongoing discussions about a range of potential countermeasures – from instituting video-only visitation to increasing alternatives to incarceration for lesser crimes.

"With the flu, we could at least warn people to get the flu shot at the beginning of the year and reduce the volume of the virus, and even if they got the flu, they could mitigate the effects by getting a Tamiflu shot," Mahoney said. "Well, those things don't exist for the coronavirus."

In January, the Henderson County Detention Center in central Kentucky had a trial run of sorts for dealing with a coronavirus outbreak when more than 200 inmates came down with a mysterious stomach bug.

The jail moved quickly to contain the spread of the illness, moving the sick inmates to a special wing where the recirculated air goes nowhere else and ramping up cleaning the old-fashioned way.

"Bleach and water," said head jailer Amy Brady, who runs the facility. "We had inmates running in shifts."

The symptoms disappeared after 12 hours. The same month, an area doctor who treats inmates at the detention center offered sage advice: stock up on specialized masks amid reports of a worsening virus in China.

The masks, known as N95 respirators, are now in short supply across the country.

"We have 250 of them," Brady said. "I feel pretty good. But like anything else with the jails, there's always the likelihood that it's going to spread."

Rich Schapiro

Rich Schapiro is a reporter for the NBC News Investigative Unit.

Coronavirus COVID-19 and the Correctional Facility

For the Correctional Healthcare Worker

Anne C. Spaulding MD MPH
March 9, 2020
Emory Center for the
Health of Incarcerated Persons
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EMORY | ROLLINS SCHOOL OF PUBLIC HEALTH

Outline

- COVID-19 Overview for a Congregate Environment
  - Spread
  - Prevention
  - Symptoms & Diagnosis
  - Treatment
  - Adverse Outcomes
- Implications for Correctional Healthcare
  - Overview
  - Correctional Facility Case Examples
    - Coordination
    - A Cautionary Tale

COVID-19 Overview: Spread

- COVID-19 is a viral disease
  - *The virus' official name is "SARS-CoV-2"; COVID-19 is the name of the disease*
- Transmission
  - The virus is thought to spread mainly from person-to-person.
  - Between people who are in close contact with one another (within about 6 feet)
  - Via respiratory droplets produced when an infected person coughs or sneezes.
  - Droplets can land in mouths or noses of people nearby or possibly be inhaled into lungs.

- May spread from inanimate objects that have virus on them,
  but this is not the main way it spreads.
- People are thought to be most contagious when they are the sickest.
- Some spread might be possible before people show symptoms,
  but this is not the main way it spreads.

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COVID-19 Overview: Spread

- The first cases were in the Hubei province of China.
- It has now spread to many countries.
- As of March 2020, some areas of the US have local transmission.
- Keep up with your state and local health department to learn what's happening where your correctional facility is located.

Persons entering correctional facilities can have infections either

- ➢Because of travel from, or through, a highly prevalent region, OR
- ➢From acquisition of the infection close to home…

If it's spreading in your community, it's likely to show up in your local jail or prison.

COVID-19 Overview: Prevention

- Avoid close contact with people who are sick.
- Avoid touching your eyes, nose, and mouth.
- Cover your cough or sneeze with a tissue, then throw the tissue in the trash.
- Wash your hands with soap and water frequently.
  - Wash for 20 seconds—as long as it takes to sing the Happy Birthday song.

- Clean and disinfect frequently touched objects and surfaces using a hospital-grade disinfectant.

- Follow CDC's recommendations for using a facemask, and isolation of infected persons.
- Correctional staff should stay off from work if they feel sick.

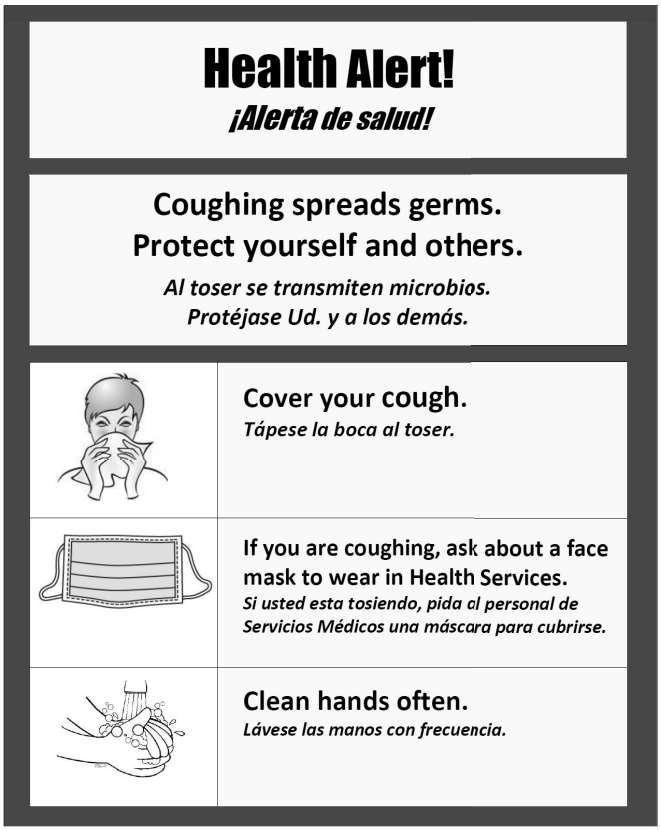
Have a cough, fever and/or shortness of breath? Stay home.
If illness becomes worse, seek medical care; call ahead before you go!

This slide can be printed out and used as a hand out for staff

Health Alert Signage for the Health Services Unit—same as used for flu.

Feel free to copy in color or black and white.

Adapted from: https://www.bop.gov/resources/pdfs/seasonal_influenza_guidance.pdf

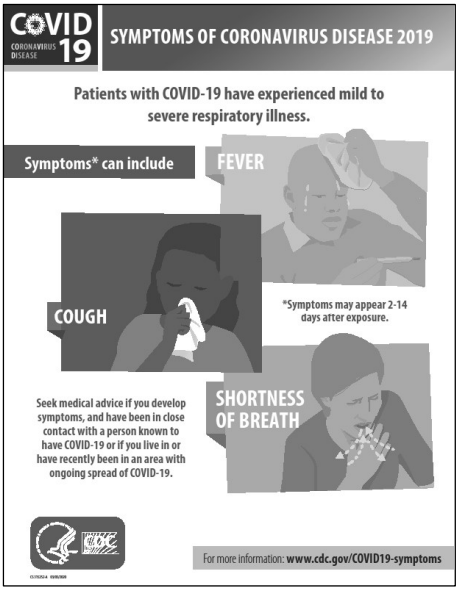


Overview: Symptoms & Diagnosis

- Many people are asymptomatic or only have mild symptoms.
- Can appear soon (~ 2 days) or long (~2 weeks) after exposure.
  - Or sometime between "soon" and "long after"!
- Some common symptoms: fever, cough, shortness of breath.

Which sounds an awful lot like the flu…

Tip: To prevent influenza, and possible unnecessary evaluation for COVID-19: use your flu vaccine stock now!



Overview: Symptoms & Diagnosis

To review, the common symptoms are : 1) fever, 2) cough, and 3) shortness of breath.

Diagnostic guidelines, best tests are evolving, so check your local and state health department for latest updates. Also: go to CDC.gov

1. CHECK where patient has been within 14 days of the onset of symptoms—
   -- Any place on current list of areas where there is local transmission??
2. ASK about contact with an infected person.
3. ASSESS Symptoms—especially worrisome if 2 or more of the above symptoms.

IF APPROPRIATE EXPOSURE HISTORY & SYMPTOMS:

Put a simple surgical face mask on patient.

Place them in a separate, closed room and shut the door.

- Ideally, use an airborne infection isolation room (AIIR) with neg. pressure.

Healthcare and custody staff : wear personal protective equipment in room

- N-95masks/gowns/gloves, etc.

Assess stability of patient—in respiratory distress needing hospital transfer?

Or do you want to test them on site? Call your local health department for help.

COVID-19, the new type of coronavirus

For those not needing hospital transfer:

- Treatment
  - Rest
  - Drink fluids to prevent dehydration
  - Take medicine to reduce fever (for example, acetaminophen)
  - Research is ongoing on the use of already-developed medications
  - Health care staff should be notified if patient worse symptoms develop, such as difficulty breathing.
- Vaccination
  - There is no vaccine for COVID-19 as of early March 2020,

  but scientists around the world are actively working on a vaccine.

This slide can be printed out and used as a hand out for patients.

COVID-19 Complications Overview

- Anyone can have a coronavirus infection that can become serious or be fatal.
- Serious disease and death are most common in older persons and/or those with underlying medical conditions
- Think of your patients in chronic care clinics, your pregnant patients and how you will keep them safe from disease.

(See CDC website for guidance for particular groups, such as pregnant women.)

Implications for <u>Correctional Health Staff</u>

<u>Are correctional facility populations at risk? Yes.</u>

1. Healthcare staff should be aware of ongoing updates to clinical guidelines.

2. Share with your local health department the role of your facility in prevention, identification, and management of infectious disease. Remind them that you are in their territory.

- Just because you have a healthcare staff…
  (which may be hired via a private vendor)

…doesn't mean that the health department should not consider how the presence of a jail and prison, and movement of citizens in and out of the facility, impacts the health of the public.

3. Work with your facility on planning now: where to cohort persons (placing persons diagnosed with coronavirus together, but at a distance from folks who are well) if many people are getting sick at the same time.

Health Services: Check with your local health department and https://www.cdc.gov/coronavirus/ website as needed for latest guidelines on:

1. How to isolate persons—when is negative pressure room indicated?
2. How long to quarantine those who are exposed, those who are infected?
3. What personal protective equipment is needed, and for whom: N95 or surgical mask, eye shield, gloves, gowns?
4. How to handle those exposed to a case of COVID-19, especially after first test is negative: when to repeat before infection can be ruled out?
5. When can isolation be lifted?

Implications for Correctional Custody Staff

Are people who live and work in correctional facilities at risk? Yes.

- Jurisdictions need to understand that incarceration of persons defying quarantine orders could lead to exponential increases in jail cases and cases in the community.
  - Measures other than detention should be considered, such as at-home electronic monitoring.
  - Custody should plan on future absenteeism of ill correctional officers.
  - Supply chains (medicines, food, etc.) may become disrupted.
  - Consider alternatives to incarceration, in order to keep stock population down (diversionary courts, community corrections) .
  - If COVID-19 is in your jurisdiction, consider restriction of movement in and out (visitors, non-essential vendors, tours).

Implications for Correctional Healthcare: A Florida Jail Case Example with Zika:

PLAN now, before the epidemic reaches your jurisdiction

1. A protocol for the jail was developed with the help of local health department.
2. When a symptomatic entrant to the jail was confirmed with Zika infection, the Florida jail maintained close relationship with the local health department.

Call your local health department <u>now</u>, even if the epidemic has not yet hit your town, to make sure that correctional health services are being considered in regional planning…

Make sure they have your contact info

Other Issues for Correctional Healthcare

- Think of your supply chain for medications and medical supplies: realize that a continued epidemic may disrupt distribution of goods. Consider making sure your stocks are full, but don't hoard.
- Make sure persons confined in your facility have access to soap for hand washing; tissue for nasal discharge, etc.
- Consider what will happen if health care workers are themselves sick and need to stay home, or if they are at home caring for others.
- Prepare for absenteeism, and discourage "presentism": when sick staff members insist on coming to work, and possibly infecting your patients.

Implications for Correctional Healthcare: Two Cautionary Tales

- Prisons and jails are enclosed environments, where individuals dwell in close proximity. Incarcerated persons sleep in close quarters, eat together, recreate in small spaces. Staff are close by. Both those incarcerated and those who watch over them are at risk for airborne infections.
- A prison and jail is a self-contained environment.

Implications for Correctional Healthcare: Two Cautionary Tales

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- A prison and jail is a self-contained environment.

- Some make an analogy with a cruise ship.

Photo: Fox News

- Cautionary tale #1: think of the spread of COVID-19 on the Diamond Princess Cruise Ship, January 2020.
- Cautionary tale #2: Hundreds of cases diagnosed in Chinese prisons.

Photo: S. China Post, from Weibo

Resources:

- https://www.cdc.gov/coronavirus/2019-ncov/index.html

Many correctional systems have developed pandemic flu plans. These plans can be readily adapted to COVID-19 and readapted as we learn more about this new pathogen, e.g., incubation period, transmission, and morbidity factors. The BOP plan is available online:

- https://www.bop.gov/resources/pdfs/seasonal_influenza_guidance.pdf

- Questions? Aspauld@emory.edu
- Emory Center for the Health of Incarcerated Persons, Atlanta GA

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3/9/2020

CORONAVIRUS

When Purell is Contraband, How Do You Contain Coronavirus?

Handwashing and sanitizers may make people on the outside safer. But in prison it can be impossible to follow public health advice.

By **KERI BLAKINGER** and **BETH SCHWARTZAPFEL**

Reporting on the COVID-19 pandemic, criminal justice and immigration.

When Lauren Johnson reached for a squirt of hand sanitizer on her way out of the doctor's office, she regretted it immediately.

In the Central Texas prison where she was housed, alcohol-based hand sanitizer was against the rules—and the on-duty officer was quick to let her know it.

"He screamed at me," she said.

Then, she said, he wrote her up and she lost her recreation and phone privileges for 10 days.

The incident was a minor blip in Johnson's last prison stay a decade ago, but the rules hold true today and underscore a potential problem for combating coronavirus: Behind bars, some of the most basic disease prevention measures are against the rules or simply impossible.

“Jails and prisons are often dirty and have really very little in the way of infection control,” said Homer Venters, former chief medical officer at New York City’s notorious Rikers Island jail complex. “There are lots of people using a small number of bathrooms. Many of the sinks are broken or not in use. You may have access to water, but nothing to wipe your hands off with, or no access to soap.”

So far, the respiratory virus has sickened more than 97,000 people worldwide and at least 200 in the U.S. More than 3,300 people have died. As of late Thursday there were no reported cases in American prisons, though experts say it’s just a matter of time.

To minimize further spread, the Centers for Disease Control and Prevention suggests things like avoiding close contact with people who are sick, covering your mouth with a tissue when you cough or sneeze, disinfecting frequently-used surfaces and washing your hands or using alcohol-based hand sanitizer.

But these recommendations run up against the reality of life in jails and prisons. Behind bars, access to toilet paper or tissues is often limited and covering your mouth can be impossible if you’re handcuffed, either because of security status or during transport to another facility.

Typically, facilities provide some access to cleaning products for common areas and individual cells, but sometimes those products aren’t effective, and Johnson recalled women stealing bleach and supplies so they could clean adequately.

Hand sanitizer is often contraband because of the high alcohol content and the possibility for abuse (the alcohol can be separated out from the gel). A spokesman clarified Thursday that the Texas prison system now sells sanitizer on commissary, though it is a non-alcohol-based alternative, which is not what the CDC recommends.

Even something as basic as hand-washing can be difficult in facilities with spotty water access or ongoing concerns about contamination, such as in the recent Legionnaires’ outbreak at one federal prison complex in Florida. (Legionnaires is caused by contaminated water, though the source of that water is not clear in Florida).

Aside from all that, prisons and jails are large communities where a sicker-than-average population is crammed into close quarters where healthcare is often shoddy, and medical providers are often understaffed. In an infectious disease outbreak, health experts recommend separating sick people from well people to prevent the disease from spreading, but in prison that can be nearly impossible, since prisoners are already grouped according to security and other logistical considerations.

Given all that, correctional facilities often respond to outbreaks with the same set of tools: lockdowns, solitary confinement and visitation restrictions. That’s what some prisons and jails did

during the 2009 swine flu pandemic, and it's what happened more recently in the Florida federal prison complex struck by Legionnaires'. In Texas and other states, prison officials regularly shut down visitation or institute partial lockdowns during mumps and flu outbreaks.

This time, though, some public health officials—including former Rikers health official Venters—are proposing a different solution: large-scale releases, like those already underway in Iran. There, officials approved the temporary release of more than 54,000 prisoners in an effort to combat the spread of the new virus.

"That's a gauntlet for the U.S.," said Jody Rich, a professor of Medicine and Epidemiology at Brown University. " Really? Iran's going to do it better than we are?"

Advocates in Indiana on Thursday called on the governor to consider releasing large numbers of elderly and sick prisoners, who are at highest risk of complications from coronavirus. People with chronic illnesses are vastly overrepresented in U.S. prisons and jails, and elderly inmates are the fastest-growing share of prisoners.

Some in law enforcement immediately criticized the proposal.

"I don't think a viable solution for the safety of our community is to have mass releases from jails," said Joe Gamaldi, president of the Houston police union. "As much as we have to balance the dangers that coronavirus poses to the community, we also have to balance that against the danger of letting violent criminals back out on the streets."

It's not yet clear whether any prisons or jails are seriously considering widespread releases. A spokeswoman for the federal prison system did not respond to questions about the idea, instead saying that the isolating nature of prisons could be an asset in handling any potential outbreak.

"The controlled environment of a prison allows the Bureau of Prisons to isolate, contain and address any potential medical concern quickly and appropriately," said Nancy Ayers, the spokeswoman. "Every facility has contingency plans in place to address a large range of concerns."

Open Letter to ICE From Medical Professionals Regarding COVID-19

Acting Director Matthew T. Albence
U.S. Immigration and Customs Enforcement
500 12th St. SW
Washington, D.C. 20536

Dear Acting Director Albence,

As concerned clinicians, we are writing this letter to urge U.S. Immigration and Customs Enforcement (ICE) officials to release individuals and families from immigration detention while their legal cases are being processed to prevent the spread of COVID-19 and mitigate the harm of an outbreak.

In light of the rapid global outbreak of the coronavirus disease 2019 (COVID-19), we want to bring attention to the serious harms facing individuals in immigration detention facilities under the custody of ICE. Health and Human Services Secretary Azar declared a public health emergency on January 31, 2020. As of March 13, 2020, there have been over 132,000 confirmed cases worldwide with nearly 5,000 deaths.

Conditions of Detention Facilities

Detention facilities, like the jails and prisons in which they are housed, are designed to maximize control of the incarcerated population, not to minimize disease transmission or to efficiently deliver health care. This fact is compounded by often crowded and unsanitary conditions, poor ventilation, lack of adequate access to hygienic materials such as soap and water or hand sanitizers, poor nutrition, and failure to adhere to recognized standards for prevention, screening, and containment. The frequent transfer of individuals from one detention facility to another, and intake of newly detained individuals from the community further complicates the prevention and detection of infectious disease outbreaks. A timely response to reported and observed symptoms is needed to interrupt viral transmission yet delays in testing, diagnosis and access to care are systemic in ICE custody. Further, given the patchwork regulatory system, it is unclear whether ICE or the county and state health departments are responsible for ensuring public health oversight of facilities.

For these reasons, transmission of infectious diseases in jails and prisons is incredibly common, especially those transmitted by respiratory droplets. It is estimated that up to a quarter of the US prison population has been infected with tuberculosis[1], with a rate of active TB infection that is 6-10 times higher than the general population.[2] Flu outbreaks are regular occurrences in jails and prisons across the United States.[3],[4] Recent outbreaks of vaccine-preventable illnesses including mumps, influenza, and varicella have similarly spread throughout immigration detention facilities. From September of 2018 to August 2019, 5 cases of mumps ballooned to nearly 900 cases among staff and individuals detained in 57 facilities across 19 states, a number that represents about one third of the total cases in the entire US in that time frame.[5] With a mortality rate 10 times greater than the seasonal flu and a higher R0 (the average number of individuals who can contract the disease from a single infected person)[6] than Ebola, an outbreak of COVID-19 in immigration detention facilities would be devastating.

Risks of a COVID-19 Outbreak in Detention

Emerging evidence about COVID-19 indicates that spread is mostly via respiratory droplets among close contacts[7] and through contact with contaminated surfaces or objects. Reports that the virus may be viable for hours in the air are particularly concerning.[8] Though people are most contagious when they are symptomatic, transmission has been documented in absence of symptoms. We have reached the point where community spread is occurring in the United States. The number of cases is growing exponentially, and health systems are already starting to be strained. Social distancing measures recommended by the Centers for Disease Control (CDC)[9] are nearly impossible in immigration detention and testing remains largely unavailable. In facilities that are already at maximum capacity large-scale quarantines may not be feasible. Isolation may be misused and place individuals at higher risk of neglect and death. COVID-19 threatens the well-being of detained individuals, as well as the corrections staff who shuttle between the community and detention facilities.

Given these facts, it is only a matter of time before we become aware of COVID-19 cases in an immigration detention system in which detainees live in close quarters, with subpar infection control measures in place, and whose population represents some of the most vulnerable. In this setting, we can expect spread of COVID-19 in a manner similar to that at the Life Care Center of Kirkland, Washington, at which over 50% of residents have tested positive for the virus and over 20% have died in the past month. Such an outbreak would further strain the community's health care system. Considering the extreme risk presented by these conditions in light of the global COVID-19 epidemic, it is impossible to ensure that detainees will be in a "safe, secure and humane environment," as ICE's own National Detention Standards state.

In about 16% of cases of COVID-19 illness is severe including pneumonia with respiratory failure, septic shock, multi organ failure, and even death. Some people are at higher risk of getting severely sick from this illness. This includes **older adults over 60** and people who have **serious chronic medical conditions like heart disease, liver disease, diabetes, lung disease, and who are immunocompromised**. There are currently no antiviral drugs licensed by the U.S. Food and Drug Administration (FDA) to treat COVID-19, or post-exposure prophylaxis to prevent infection once exposed.

As such, we strongly recommend that ICE implement community-based alternatives to detention to alleviate the mass overcrowding in detention facilities. Individuals and families, particularly the most vulnerable—the elderly, pregnant women, people with serious mental illness, and those at higher risk of complications— should be released while their legal cases are being processed to avoid preventable deaths and mitigate the harm from a COVID-19 outbreak.

*This letter was written by physician members of the New York Lawyers for the Public Interest Medical Providers Network and Doctors for Camp Closure.

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[1] Hammett TM, Harmon MP, Rhodes W. The burden of infectious disease among inmates of and releases from US correctional facilities, 1997, *Am J Public Health*, 2002, vol. 92 (pg. 1789-94)

[2] Centers for Disease Control Prevention (CDC). Prevention and control of tuberculosis in correctional and detention facilities: recommendations from CDC, *MMWR Morb Mortal Wkly Rep*, 2006, vol. 55 (pg. 1-48)

[3] Dober, G. Influenza Season Hits Nation's Prisons and Jails. *Prison Legal News,* June, 2018 (pg. 36) https://www.prisonlegalnews.org/news/2018/jun/5/influenza-season-hits-nations-prisons-and-jails/

[4] Pandemic influenza and jail facilities and populations, Laura Maruschak, et. al., American Journal of Public Health, September 2009

[5] Leung J, Elson D, Sanders K, et al. *Notes from the Field:* Mumps in Detention Facilities that House Detained Migrants — United States, September 2018–August 2019. MMWR Morb Mortal Wkly Rep 2019;68:749–750. https://www.cdc.gov/mmwr/volumes/68/wr/mm6834a4.htm?s_cid=mm6834a4_x

[6] The R0 is the reproduction number, defined as the expected number of cases directly generated by one case in a population where all individuals are susceptible to infection.

[7] Close contact is defined as—

a) being within approximately 6 feet (2 meters) of a COVID-19 case for a prolonged period of time; close contact can occur while caring for, living with, visiting, or sharing a health care waiting area or room with a COVID-19 case

b) having direct contact with infectious secretions of a COVID-19 case (e.g., being coughed on)

[8] https://www.medrxiv.org/content/10.1101/2020.03.09.20033217v1.full.pdf

[9] https://www.cdc.gov/coronavirus/2019-ncov/community/homeless-shelters/plan-prepare-respond.html

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