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A Primer on SARS-CoV-2 and the Covid-19 Pandemic

Subramani Mani, MBBS, PhD[1]

Abstract

In this paper we first provide a primer on SARS-CoV-2 and Covid-19 delineating the etiopathogenesis, epidemiology, clinical features and the course of the disease. We then trace the evolution of the Covid-19 pandemic highlighting the characteristics of the epidemic in select countries of Europe and the US. We also project some possible trajectories for the mega cities of India based on the demographic characteristics of the cities in comparison to New York city.

Keywords

SARS-CoV-2; Covid-19; pandemic; primer; India; mortality rate; evolution

Introduction

Corona virus disease 2019 (Covid-19) caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) originated in the city of Wuhan, China in late 2019. After infecting tens of thousands of people in Wuhan and the province of Hubei where Wuhan is located the disease spread to various other cities of China and internationally. It is currently raging in many countries of Europe (Italy, Spain, France, Germany, United Kingdom), Asia (Iran, South Korea) and the United States. It has currently spread to more than 200 countries and is challenging the healthcare resources of both the developed and the developing world. With a global case count approaching 2.5 million with a mortality of more than 160,000 over a four-month period, the Covid-19 pandemic is threatening to become the most dangerous global infectious disease of the 21st century [2].

Humans are susceptible to a range of microbes which include parasites, bacteria and viruses. However, most of the newly identified emerging pathogens are viruses that are carried by vectors or cause primary disease in animals and then "jump" to humans (zoonotic). These are opportunistic viruses that mutate at high rates easily adapting to the new human host thereby enabling human-to-human transmission. The most prominent of these emerging pathogens are the Zika virus and the newer zoonotic respiratory coronaviruses [3, 4].

The first SARS-CoV outbreak occurred in late 2002 and soon became a pandemic in early 2003 resulting in the death of more than 700 people with a large cluster of fatalities reported from Hong Kong. This SARS-CoV virus is thought to have originated in a single or multiple species of bats [3]. A more recent coronavirus (CoV) pathogen is the Middle Eastern respiratory syndrome (MERS) CoV. It first emerged in 2012 in Saudi Arabia and spread to many countries in the region and by 2018 had infected more than two thousand people causing 803 deaths, the majority of them in Saudi Arabia. Camels and bats are considered to be reservoirs of this pathogen [5].

[1] Formerly associate professor of Medicine and Translational Informatics, University of New Mexico School of Medicine, Albuquerque, NM, USA. Email <subramani.tvm@gmail.com>

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Before the emergence of SARS, human coronaviruses typically caused only mild upper respiratory infections resulting in the common cold. All this changed with the emergence of SARS-CoV, MERS-CoV and the currently raging SARS-CoV-2 inspired Covid-19 pandemic.

Etiology

Covid-19 is caused by the recently identified respiratory tract virus SARS-CoV-2 which belongs to the viral family coronoviridae also referred to as the coronavirus family [6]. Other prominent members of the respiratory tract group are the rhinovirus, the respiratory syncytial virus (RSV) and the influenza and parainfluenza viruses. The coronaviruses are single-stranded RNA viruses containing an RNA inner core with an outer oily lipid envelope from which crownlike spikes of proteins project outwards. These characteristic crown-like projections on their surface give the virions the appearance of a solar corona in electron micrographs and hence the nomenclature "corona". See Figure 1. The corona viruses are heat sensitive and are susceptible to lipid solvents such as acetone, ether, and vinegar which contains acetic acid. The lipid envelope of the virus also breaks apart on contact with soap.

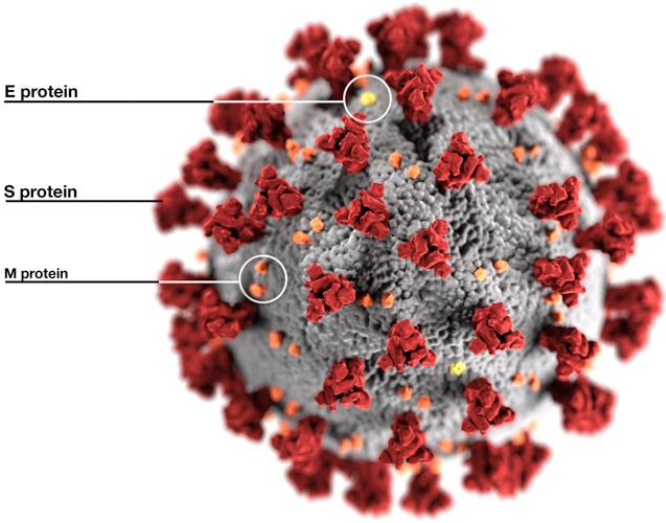

Figure 1: Eckert and Higgins illustration of SARS-CoV-2,

The viral sequence of SARS-CoV-2 identified by Zhu etal. contained 29,892 nucleotides [6] and the viral genome reported by Wu etal. contained 29903 nucleotides [7]. Phylogenetic analysis revealed the close relationship to SARS-like coronaviruses previously found in bats in China. The pangolin is also likely to be an intermediate host and a natural reservoir of SARS-CoV-2-like coronaviruses [8]. Recently a jump from human to a tiger in New York city has also been demonstrated when a Tiger in the Bronx zoo turned positive. See Figure 2.

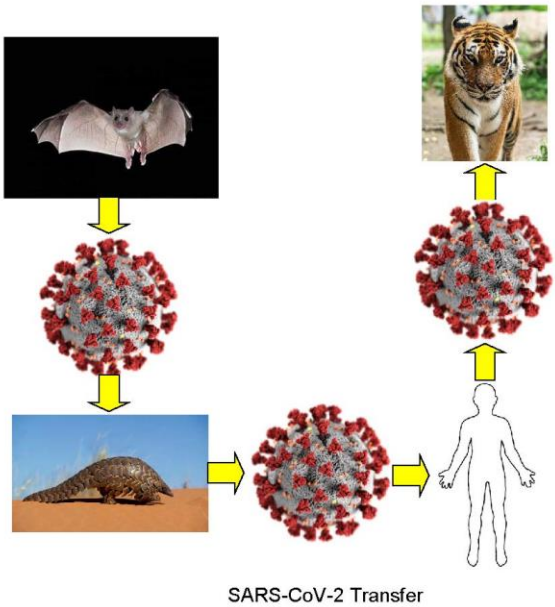

Figure 2: A transmission model from bat to man with pangolin as reservoir.

Laboratory diagnosis

The lab diagnosis of SARS-CoV-2 infection is performed by real-time reverse transcription polymerase chain reaction (RT-PCR) assay for a genetic sequence matching the genome of SARS-CoV-2. This is accomplished by SARS-CoV-2 specific primers and probes. SARS-CoV-2 is a respiratory virus which is shed in respiratory droplets. A swab taken from the deep nasopharynx is used to isolate the virus from an infected person.

Epidemiology

This description is based predominantly on five studies---the first 425 confirmed cases in Wuhan,

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China [9], the second reporting data on 1099 patients admitted to various hospitals in mainland China [10], the third on 138 hospitalized patients in Wuhan [11], the fourth a review article based on 19 studies (18 from China and 1 from Australia) which also included the three primary studies [12] and the fifth a retrospective cohort study of 191 hospitalized patients in Wuhan with follow-up [13].

Covid-19 is a highly contagious disease. The transmissibility or the basic reproductive number R_0 is defined as the number of new cases on average an existing case is likely to generate. The R_0 of Covid-19 is 2.2.

Incubation period

The incubation period is the duration from the time of exposure to the manifestation of symptoms of the disease. The mean incubation period is 5.5 days with a range of 2 days to 12 days. But there could be outliers and the following table adapted from [14] shows the number of positive cases which could be missed using a 14-day and 28-day protocol of isolation (see Table 1).

Table 1: Expected number of symptomatic SARS-CoV-2 infections missed during active monitoring using 14-day and 28-day protocols with varying risks for infection following exposure (modified from [14])

Isolation Period	**Missed Symptomatic Infections per 10,000 Monitored Persons**			
	Low Risk (1/10,000)	**Medium Risk (1/1000)**	**High Risk (1/100)**	**Infected Sample (1/1)**
14 days	0	0.1	1	101
28 days	0	0	0	1.4

The mode of transmission is by respiratory droplets but the virus has also been isolated from the stools of patients. Both symptomatic patients and asymptomatic persons infected with SARS-CoV-2 can transmit the virus [15]. The virus can remain suspended in aerosols for 3 hours and can remain viable for up to 72 hours on different surfaces as varied as plastic, steel, copper and cardboard [16].

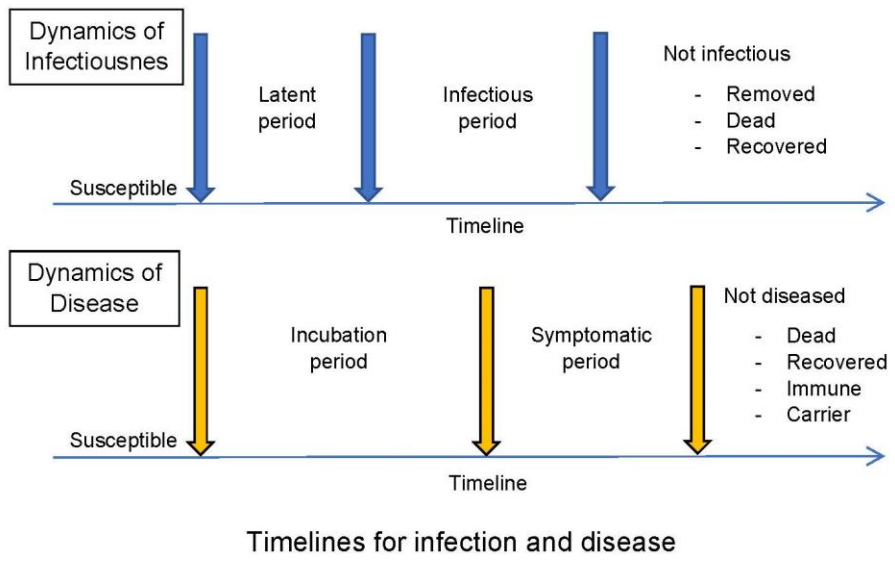

Figure 3: Dynamics of infection and disease (modified from [1])

Figure 3 provides the dynamics of infectiousness, susceptibility to infection and disease manifestation. The top panel shows how a person could get infected, remain asymptomatic and be contagious. The bottom panel shows how a person can be contagious during a part of the incubation period when the symptoms have not manifested.

Demographics

The median age of patients in different studies varied between 47 and 59 years. Males were disproportionately affected ranging from

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50-75 percent. Among the first 425 confirmed cases in Wuhan there were no children below 15 years of age. In the study of 1099 patients, the number of children below 15 years was 9. About 16% of the hospitalized patients were categorized as severe who were on average older by 7 years and were more likely have co-existing medical conditions compared to the less severe hospitalized group of patients.

Pathogenesis

The SARS-CoV2 virus enters the human body via droplets through the nose, mouth or eyes. The virus enters the cells in the airway by binding the viral surface spike protein to the human angiotensin converting enzyme 2 (ACE2) receptor. This follows activation of the spike protein by transmembrane protease serine 2 (TMPRSS2). ACE2 is expressed in the alveolar cells of the lung, heart, vascular endothelium and the kidneys but the main portal of viral entry seems to be the lung alveolar cells [17, 18].

Clinical characteristics

Fever was present in half the patients on admission and ninety percent of patients during the hospitalization period. Cough was the second most prevalent symptom and was reported by 70% of the patients. Half of the patients also reported feeling fatigued. Breathlessness was also observed in 40% of the patients. Nausea, vomiting, sore throat and headache were uncommon (less than 10%). A fourth of the patients had one or more co-exiting conditions such as high blood pressure, chronic obstructive pulmonary disease, diabetes or coronary artery disease and this was more pronounced among patients with severe disease.

Cardiovascular manifestations

There have been some reports of patients presenting with chest pain and showing ST-segment elevation in the EKG without any evidence of coronary artery disease. Echo revealed LV dysfunction with reduced ejection fraction and elevated cardiac biomarkers such as troponin. Patients with SARS-CoV-2 infection can also present with myocarditis, stress cardiomyopathy or cardiac failure or with palpitations and chest pain without fever and cough. The exact mechanism of cardiac pathogenesis is not clear [18].

Neurological manifestations

Patients have presented with altered sensorium and other clinical features suggestive of brain inflammation. A small subset of patients developed stroke and seizures. There are also reports of acute necrotizing encephalopathy in covid-19 patients. Some patients develop tingling and numbness in the upper and lower limbs referred to as acroparesthesia. In a study of Covid-19 patients in Wuhan based on a sample of 113 patients who died and 161 patients who recovered the researchers found that 20% of deceased patients developed hypoxic encephalopathy while among the recovered group of patients it was observed in only 1% [19].

Radiology and lab features

Eighty percent of the CT scans of patients with non-severe disease and 96% of the scans of patients in the severe disease category revealed abnormal findings. The typical patterns on chest CT were ground-glass opacity and bilateral patchy shadowing. These abnormal patterns were also visible in chest X-rays.

More than 80% of patients had a low lymphocyte count. About a third of patients had low white cell counts and another third had low platelet counts. Most patients also showed high levels of C-reactive protein and elevated ESR. The laboratory findings were more pronounced in patients with severe form of the disease.

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Treatment, clinical course and outcomes

No specific anti-viral treatment is currently available for Covid-19. A majority of the patients (60%) were given intravenous antibiotics and oxygen was administered to about 40% of the patients. Twenty percent of the patients typically needed admission to the intensive care unit out of whom half had to be put on ventilators. More than 90% had pneumonia, 10% of patients developed adult respiratory distress syndrome and five percent of patients went into shock. The median duration of hospitalization was 12-20 days in different studies. The mortality rate varied from 2 to 20 percent in various studies.

Drug pipeline

Two drugs that are undergoing studies for effectiveness in the treatment of Covid-19 are Remdesivir and Chloroquine. There is some preliminary evidence that these drugs have the potential to inhibit SARS-CoV-2 [20]. Remdesivir is an antiviral compound originally developed as a potential drug for Ebola and Chloroquine is a time-tested drug used in the treatment of malaria. Another drug Tocilizumab, an interlukin-6 receptor antagonist used in the treatment of rheumatoid arthritis is also being tested for the treatment of Covid-19 [18].

Vaccine trials

There are various candidate vaccines based on RNA and DNA as well as inactivated and live attenuated versions under pre-clinical evaluation. One candidate vaccine based on RNA being developed by Moderna in collaboration with the national institute of allergy and infectious diseases (NIAID) has moved on to phase I clinical trial [21].

Covid-19 pandemic story so far

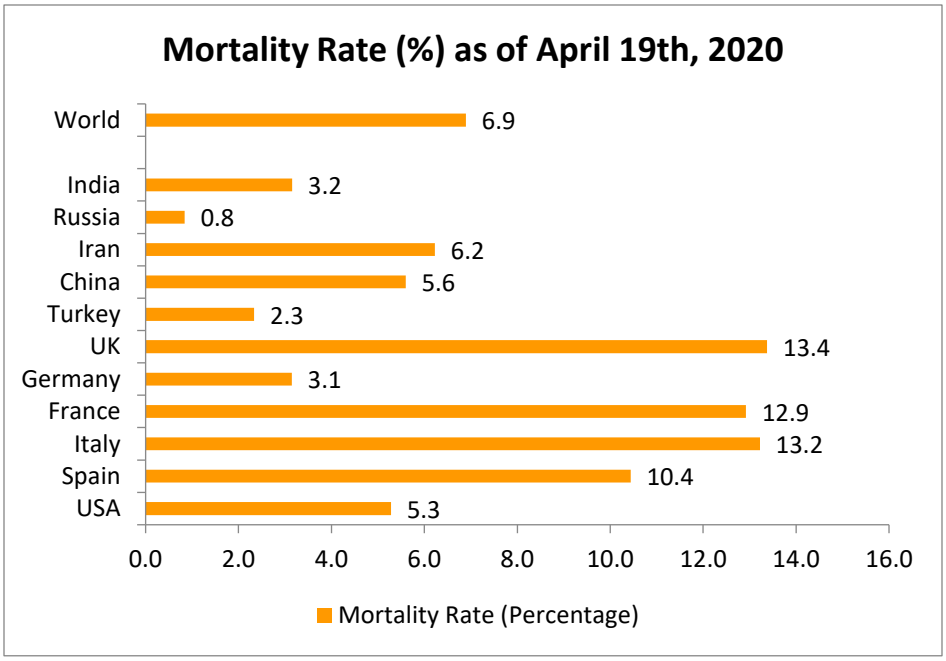

Figure 4: Covid-19 mortality rate

We present the story of the Covid-19 pandemic from an analytical perspective based on the numbers available from the *worldometer* website as of April 19, 2020 [2]. In this analysis we include numbers from the top ten countries based on the reported number of cases plus India and the global figures. A total of 2.5 million cases and more than 160,000 deaths have been reported worldwide. The United states tops the table with a reported total caseload totaling more than 0.75 million with more than 40,000 deaths. India has reported more than seventeen thousand cases and 560 deaths through April 19th. Spain,

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Italy, France and Germany have reported more than 150,000 cases each with a combined death toll exceeding 65,000. US also leads the countries in the total number of people tested with close to 4 million tests followed by Russia with 1.9 million people tested. But the testing rate (number of tests per million people) is highest in Italy with more than 22,000 people tested per million inhabitants.

Table 2: Fatality rate and reproductive rate (R_0) of common and emerging virus infections. Modified from [22]

Virus	**Fatality rate (%)**	**Transmissibility Factor (R_0)**	**Deaths**
SARS-CoV-2 (2019)	3	2.2	162,000+ (till April 19, 2020)
SARS-CoV (2002)	10	2-5	700
MERS-CoV (2012)	40	<1	800
H1N1 (2009)	0.03	1.2-1.6	18,600-300,000
H1N1 (1918)	3	1.4-3.8	17-50 million (1918-1920)
Measles virus	0.3	12-18	140,000 in 2018
Seasonal flu	<0.1	1.2-2.4	0.3-0.6 million per year currently
Ebola virus (2014-16)	40	1.5-2.5	11,300 (2014-2016)
HIV	80 (without drug therapy)	2-4	30 million total deaths so far
Small pox virus	17	5-7	300 million in 20th century

The number of new cases reported daily is an indicator of the evolution of the pandemic on a daily basis in each country. In this measure also US tops the list with close to thirty thousand new cases in one day. Figure 4 provides the mortality rate of Covid-19 for the various countries. The worldwide mortality rate is 6.9% with a range of 0.8% for Russia to 13.4% for UK. The mortality rate for India stands at 3.5% (see Figure 4). For an epidemiological comparison the fatality rates and reproductive rates of common and emerging virus infections are shown in Table 2.

Discussion

The pandemic continues to spread and evolve on a global scale. It has overwhelmed the healthcare capabilities and capacities of various cities and countries including Wuhan (China), Italy, Spain, France, UK and New York causing fatalities in the thousands and tens of thousands. As countries attempt to block the spread of Covid-19 by proclamations of stay-in-place and lockdown orders in cities, states and countries the economies of the various countries are taking a huge hit and sliding towards recession.

Recall that the transmissibility of a contagion is defined by the reproductive number R_0 in epidemiological terms. There are two basic strategies to tackle the spread of Covid-19 referred to as containment and mitigation. When the R_0 is two or greater there will be an exponential spread as each case will generate

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two or more new cases on average and the total number of cases in a community or a geographical region starts doubling every few days. A containment strategy is typically used at the beginning of an epidemic and involves testing persons exposed to the virus, isolating and quarantining them individually and tracing their contacts if they test positive or develop symptoms. In the containment approach the goal is to keep R_0 below one to break the community transmission. To tackle an exponential spread and when the number of cases overwhelm containment approaches a mitigation approach is taken using various types of non-pharmacological interventions (NPI) with the goal of lowering R_0 as much as feasible but not to reduce it to one or below one. The common NPIs involve the steps of extensive testing, isolation/quarantine and social distancing measures for certain population groups such as senior citizens and people with pre-existing medical conditions or the population as a whole with lockdowns and stay-in-place declarations. Mitigation steps also involve the closure of schools and colleges, shutting down places of entertainment such as performance venues, religious congregations and places of worship and sports events. Likewise, a drastic reduction in gatherings such as marriages and funerals are also enforced. Both these approaches may need to be applied in tandem in large parts of a country or geographical region facing the onslaught of Covid-19.

Covid-19 run in China, South Korea, Europe and US

China

The novel corona virus originated in December in the city of Wuhan in China and slowly made its spread in the province of Hubei which includes Wuhan. When cases started multiplying and authorities suspected human to human transmission of the new virus containment measures were instituted. By the end of December a viral sequence was completed and a week later the novel corona virus was officially announced as the causative pathogen of the outbreak by China CDC [9]. By 13th January a test kit became available for detecting SARS-CoV-2. Within a period of ten days hundreds of people had tested positive for the virus. Moreover, within that timespan more than two thousand people had started showing symptoms of the new disease and visiting hospitals in Wuhan. Even though the authorities hesitated initially the city of Wuhan was put under lockdown on January 23rd. By that time many other cities in China were also seeded with the virus as more than seven million residents of Wuhan left the city to celebrate the Chinese New Year. On January 24th fifteen other cities within Hubei province in which Wuhan is situated

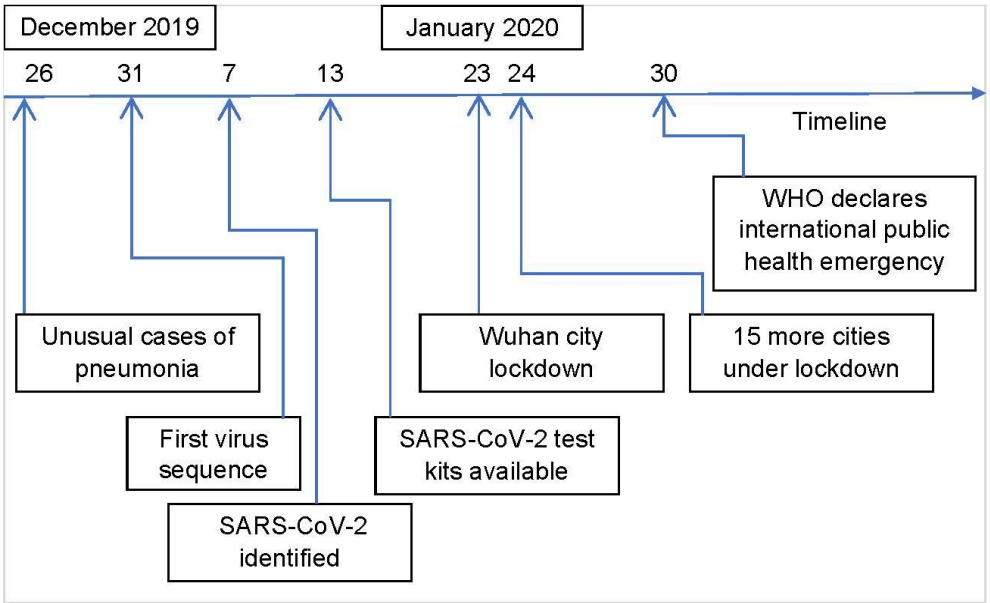

Figure 5: Wuhan Covid-19 outbreak timeline

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were also put under lockdown and on January 30th WHO declared an international public health emergency [23]. Figure 5 provides a timeline of the Wuhan outbreak.

China was able to control the smaller outbreaks that occurred outside Hubei province by initiating effective containment measures. However, in the city of Wuhan and broadly in the Hubei province the healthcare facilities were overwhelmed by the outbreak. The lockdown in the city of Wuhan was in place for 76 days and only recently restrictions on the movement of people put in place during the lockdown are being slowly relaxed. At the time of writing China has reported a total of 82000 cases and more than 4600 deaths mostly in Wuhan and the rest of Hubei province.

South Korea

The first case of Covid-19 was reported on January 20th and by February 21st the caseload increased to 346 with the outbreak concentrated in the city of Daegu in the southern part of the country [24]. South Korea cancelled mass gatherings in Daegu and instituted effecting containment measures incorporating mass testing, contact tracing, isolation of exposed individuals and quarantining those who tested positive. In late February and early March, the country reported more than 500 cases daily and by mid-March the outbreak was under control reporting less than 250 new cases. And by mid-April the number of daily new cases has come down to about 25. The total number of deaths through April 19th stands at 234 for a total positive case count of 10,600. South Korea did not institute a countrywide shutdown or social distancing measures applicable to the whole of the country.

Europe

The Covid-19 pandemic opened its account in Europe with the first reported case in France on January 21st and by April 19th the case count had gone up to more than 1.1 million. On April 19th, the total number of deaths has exceeded 100,000 in the whole of the European Union (EU) including UK [25]. We consider five countries—Italy, Spain, France, Germany and UK in additional detail here.

Italy

Covid-19 first emerged in Italy on January 31st when two tourists from China tested positive. Three weeks later a cluster of cases was reported from the Lombardy region of Italy which includes Milan and by early March positive cases were reported from many parts of the country [26]. By March 1st the daily case count had increased to more than 500. The epidemic raged in Italy throughout March and the first two weeks of April with the total case count reaching more than 178,000 with a death toll exceeding 23,600 by April 19th. And the peak appears to be flattening.

Spain

The country reported its first case on January 31st and by mid-March the disease had spread to all the 50 provinces [27]. By the 10th of March the daily new case count had increased to more than 500 and the country reached its peak during the last week of March and the plateau was sustained through the first week of April. As of April, 19th the total case count has reached close to 200,000 with a total death toll exceeding 20,000.

France

The epidemic raised its head first in France on January 24th and the first set of cases was in travelers returning from China. The annual assembly of the Christian Open Door Church attended by 2500 people was a significant watermark in the spread of the virus and almost half of the congregants contracted the virus [28]. By March 12th the number of daily reported new cases had gone up to more than 500 and the

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country reached its peak in the first week of April. By April 19th the total case count has exceeded 152,500 with a death toll nearing 20,000.

Germany

Covid-19 emerged in Germany in late January when the first case of confirmed near Munich on January, 27th. On March, 8th the government recommended cancellation of events with more than one thousand participants and in mid-March schools and nurseries were closed. Only the state of Bavaria declared a curfew on March 20th but after two days the federal government decided to forbid gatherings of more than two people and social distancing measures were introduced though no formal stay-in orders were issued [29]. At its peak in late March/early April the daily new case count exceeded 6,000 but by mid-April it has fallen to about 2,000. As of April, 19th the total case count exceeded 144,000 with a total fatality count more than 4,500.

United Kingdom

In UK also Covid-19 was detected first in late January and by the end of February community transmission within UK was also confirmed [30]. By March, 18th the number of daily reported new cases had exceeded 500 and it is not clear at the time of writing whether the country has reached the apex. As of April, 19th the total case count is more than 120,000 with a total death toll that is over 16,000.

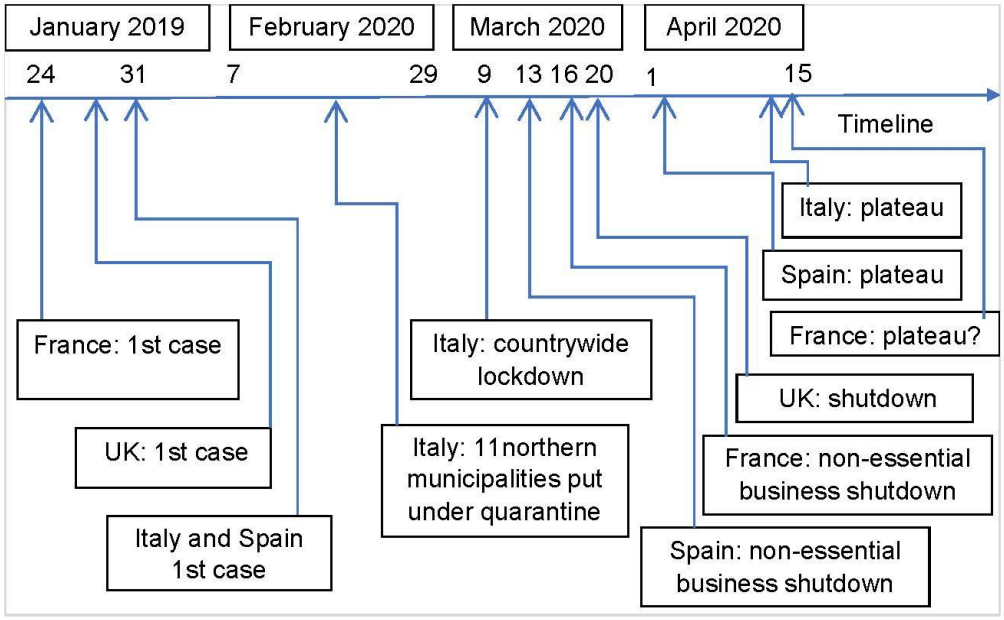

Figure 6: Italy Spain France and United Kingdom Covid-19 outbreak timeline

See Figure 6 for the evolution of the outbreak through mid-April and the interventions instituted by the respective authorities in Italy, Spain, France and the UK.

United States

The first Covid-19 case was reported in the US on January 20th when a person who had returned from Wuhan, China five days earlier tested positive for the virus. Community transmission was first confirmed in late February when a person without any history of recent international travel or exposure to a known infected individual tested positive [31]. The number of daily new cases exceeded 500 on March 13th. Though a travel restriction was instituted on passengers coming from China on January 31st, no significant intervention measures were instituted during the whole of February or the first two weeks of March. Containment measures such as extensive testing, isolation and quarantine measures lagged behind considerably. Starting mid-March when the total case count approached 4,000 various states started

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instituting mitigation strategies to enforce social distancing measures. Stay at home orders were issued in various states starting with California on March 19th and covering most states of US by April 7th.

New York has been the most affected state with a total case count nearing 250,000 with deaths exceeding 18,000 as of April, 19th. US also is the worst affected country with a total caseload exceeding 750,000 and fatalities exceeding 40,000 as of April, 19th.

India

Covid-19 raised its head in India in late January with a positive case reported on January, 30th in the state of Kerala [32]. By March, 24th the total case count had exceeded 500 and the same day the government declared a nationwide lockdown for three weeks which was further extended on April, 14th till May, 3rd with a phased relaxation of some restrictions expected to occur after April, 20th based on the success of containment of spread in various states. As of April, 19th the total case count exceeds 17,600 with a total death count of 559. For a country with a population of 1.37 billion the case count appears low but the country has tested only about 400,000 people with a testing rate of just 291 per one million people while the testing rate for Germany and Italy are seventy times more with a rate of 20,629 and 22,436 respectively per one million people.

There are some country-specific trends discernible in the evolution of the pandemic till now in terms of total number of deaths and the ability of the health systems in coping up with the increased demand on their resources. Let us consider the analogy of a primary and its concomitant secondary metastases to follow some of these trends. China had a clear source, it was unifocal and the outbreak started in Wuhan and more specifically at the Huanan seafood market there. Even though other regions of Hubei province and the rest of the country got multiple-seeded from this outbreak, containment measures were successful in controlling the epidemic outside Hubei province. In Wuhan and broadly in Hubei intervention measures began with containment but the hospitals were soon overwhelmed and they had to institute strong mitigation efforts in the city of Wuhan and the rest of Hubei province over a period of 75 days to suppress the community transmission. But the primary source was clear to them.

The South Korea outbreak was seeded by travelers from China but it became concentrated in the southern city of Daegu. The country quickly instituted containment measures with extensive testing of the population, contact tracing, isolation and quarantine. The hospitals were never overwhelmed with a total death toll under 300. Their testing rate stands at more than 10,000 per million population. The country could prevent a disastrous outbreak in a major population center such as Seoul.

Italy, Spain, France and the UK have some commonalities. They are all well connected globally with extensive travel among them and also with China. It is likely that they were all multiple-seeded and they were slow in scaling up containment measures starting with extensive testing and were also hesitant in the beginning to initiate strong mitigation efforts. Their health systems, in particular those of Italy, Spain and France were clearly overwhelmed with a combined death toll exceeding 65,000 by April, 19th. UK still hasn't peaked and its hospitals are under pressure.

Germany was much better prepared even though it is one of the most well-connected countries. The country quickly instituted strong containment measures with extensive testing in the early stages. Germany was also able to keep the mortality rate very low initially but it has since then crept up possibly because hospitalized people started dying after long stays. But the country's healthcare system was not overwhelmed.

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US is well connected to China, Europe and most other parts of the world. It is clear from the evolution of the Covid-19 pandemic that the public health infrastructure is lacking in the country. From the start the country ran into difficulties with its testing strategy. Though initially contact tracing of returning travelers who tested positive was instituted, the machinery for managing and organizing strong containment measures soon broke down and community transmission started occurring in many population centers in different parts of the country. The tri-state region of New York, New Jersey and Connecticut was severely affected with hot spots also popping up in Michigan, California and Louisiana. Some hot spots were brought under control by stay-at-home directives but New York city bore the brunt of the epidemic and many hospitals in the city were overwhelmed exacting a large death toll. Though the first wave of the outbreak is being brought under control it is not clear how the epidemic will evolve once social distancing measures are relaxed and the businesses open up.

Table 3: *Four mega cities of India compared with New York city*

City	Total Population in millions	Population Density/Sq. mile	Bed per 1000	Covid cases	Total deaths
NYC	8.7	28,000	3	131,000	11,000
Bombay	21	73,000	0.5	2187	126
Delhi	30	30000	0.5	1893	43
Calcutta	15	63000	0.5	11	
Chennai	11	69000	0.5	240	

India is a large populous country with many dense population centers. However, the health infrastructure lacks considerably when compared with the countries discussed earlier. For example, South Korea has 12 beds per thousand people while India has just 0.5. For Italy, China and US the number is close to 4. The first cluster of cases in India was from students traveling back from Wuhan to the state of Kerala in the southern part of India. Kerala instituted prompt containment measures with isolation of contacts and quarantining people testing positive. Soon other parts of the country also got seeded and dense population centers are now under serious threat. Testing lags considerably with a rate of 291 per million population. Though mitigation efforts in the form of a countrywide lockdown has been instituted relatively early when compared to many other countries, these cannot be sustained for months in the absence of resources to feed and sustain the population and the minimal healthcare facilities are likely to be overrun once the lockdown is relaxed. Based on the experience of New York city we provide an outbreak scenario for the four major population centers of India—Bombay, Delhi, Calcutta and Chennai. The projections are based on the total population, population density and the quality of healthcare infrastructure as reflected in the bed per one thousand population. See Table 3 for these parameters and see Figure 7 for the projected cases and fatalities. The lower projections are based on maintaining moderate social distancing measures in place and the higher range will be reached if mitigation efforts cannot be sustained and compliance is eroded. If mitigation efforts are totally withdrawn the counts could rise by an order of magnitude.

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The demographics of the state of Kerala provide a set of opportunities while posing some unique challenges. The state has a total population of 35 million with an average population density of 2,200 per sq. mile which is three times the national average. Again, the coastal regions are more than two times denser than the state average [33]. The coastal plains of Kerala running north south from Kasaragod to Trivandrum act as a metropolitan corridor well-connected by railways and long-distance buses. The region also has three major airports with frequent flights to the countries in the middle east and the rest of India.

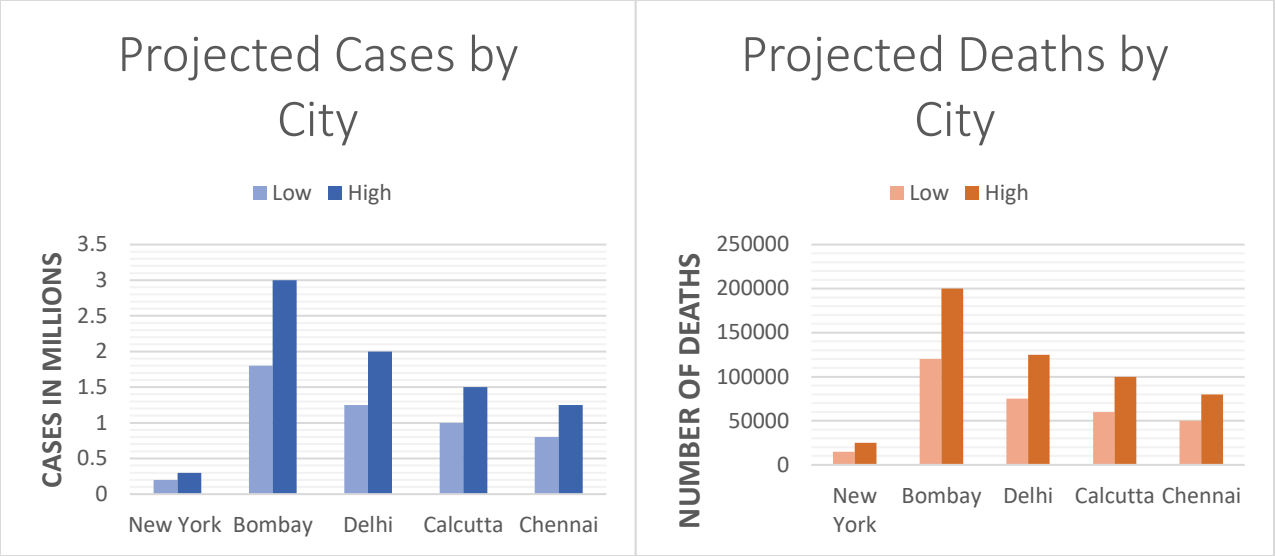

Figure 7: Projected cases and deaths for New York City, Bombay, Delhi, Calcutta and Chennai

Kerala also has a high human development index which informs favorably on the literacy, life expectancy and the public health infrastructure of the state in general. Kerala has managed to contain the spread of Covid-19 by testing travelers, isolating contacts and quarantining people testing positive. However, testing has lagged behind considerably in assessing penetration in the community to get a clear handle on the prevalence of Covid-19. There are four dense metro areas in the state with a population of 1-2 million—Kochi, Trivandrum, Calicut and Quilon and only by extensive testing hot spots can be quickly picked up and snuffed out in time preventing flare ups. Extensive testing is critical when social distancing measures are getting relaxed.

An outlook similar to India is likely in many of the densely populated countries of Asia (for example, Indonesia, Bangladesh, Pakistan, Japan) and most countries of Africa, South America and also Mexico. One worrying common denominator is the number of people tested per million which stands very much under 1,000 in all these regions.

There is also a line of thinking that opposes social distancing measures by means of shut downs and stay-in orders; they oppose closure of educational institutions, businesses and events. They want the younger working populace to acquire herd immunity and segregate the older people and others who are at risk of developing severe manifestations with poor outcomes. However, it is becoming clearer that many younger people are also getting hospitalized and losing their lives. Moreover, US alone lost more than 7,000 seniors to covid-19 in nursing homes where they are kept typically separate from the younger population. Moreover, in a country such as India with joint-family households where children, parents and grandparents live in the same household segregating seniors is not a viable proposition. Riding out

the pandemic without instituting containment and mitigation measures will overwhelm the healthcare system resulting in carnage in almost all population centers. For a contagious disease with a high mortality rate herd immunity has to be acquired with effective vaccines.

Summary and conclusion

Covid-19 originated in China ravaging it and quickly spread to many other countries in Asia, Europe and the Americas. It has also slowly found its way into many countries of Africa and has truly emerged as a global pandemic. But the magnitude and severity of the spread in different countries varies considerably. Currently Covid-19 is raging in many countries of Europe, Iran and the United States. The virus is like a slow-moving tsunami that has acquired the ability to launch outbreaks at the time and place of its choosing. There are some knowns but many unknowns surrounding the SARS-CoV-2 virus. An effective vaccine which can confer definitive protection against Covid-19 appears to be at least 18-24 months away though many scientists are on a race to develop such a vaccine and two candidate vaccines are currently in phase I trials. Likewise, there is no definitive drug treatment for the condition though a handful of drugs including the anti-viral drug Remdesivir and the anti-malarial drug Chloroquine are being evaluated in clinical studies for their efficacy. In the absence of vaccines and definitive drugs the only effective resistance against the contagion seems to be vigorous containment and mitigation efforts to alleviate the onslaught of Covid-19. The pandemic has reinforced the age-old but often sidelined aphorism that *prevention is better than cure*.

After providing a primer on Covid-19 we have charted the first phase of the pandemic which started in China and then moved quickly mainly to the countries of the western world picking through its health systems and decimating many senior living facilities. In phase two it is on the verge of spreading its tentacles to the developing countries of Asia, Africa and South America and it is likely to cycle back during fall into the countries ravaged earlier. Covid-19 might sustain itself and become endemic in many parts of the world till an effective vaccine emerges to stop the virus on its tracks.

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