Best-bet: The mortality rate of COVID-19

Title	What is the mortality rate in confirmed COVID-19 patients?
Report by	Tom Germeys * en Marie Groffi *
Search checked by	Dr. Nicolas Delvaux **
Clinical scenario	An ongoing outbreak of SARS-CoV-2 (COVID-19) started in December 2019, what is the mortality rate of this novel virus?
Answerable question	In the [general population], what is the [mortality rate] after confirmed [COVID-19 infection]?
Search terms	Pubmed: ((corona[All Fields] AND ("viruses"[MeSH Terms] OR "viruses"[All Fields] OR "virus"[All Fields])) OR ("COVID-19"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019-nCoV"[All Fields] OR "SARS-CoV-2"[All Fields] OR "2019nCoV"[All Fields] OR "sars cov 2"[All Fields]) OR "sars cov 2"[All Fields])) AND (("mortality"[Subheading] OR "mortality"[All Fields] OR "mortality"[MeSH Terms]) OR ("death"[MeSH Terms] OR "death"[All Fields])) Embase: ('covid 19' OR '2019 novel coronavirus' OR '2019-ncov' OR 2019ncov OR 'sars cov 2' OR 'severe acute respiratory syndrome coronavirus 2') AND (mortality OR death) Cochrane: (SARS coronavirus 19):ti,ab,kw OR (SARS covid 19):ti,ab,kw OR (COVID-19):ti,ab,kw OR (SARS CoV-2):ti,ab,kw
Search date	18/03/2020
Search outcome (number of hits)	182 (Pubmed 117, Embase 63, Cochrane 2)
Relevant papers (number of final inclusions)	10

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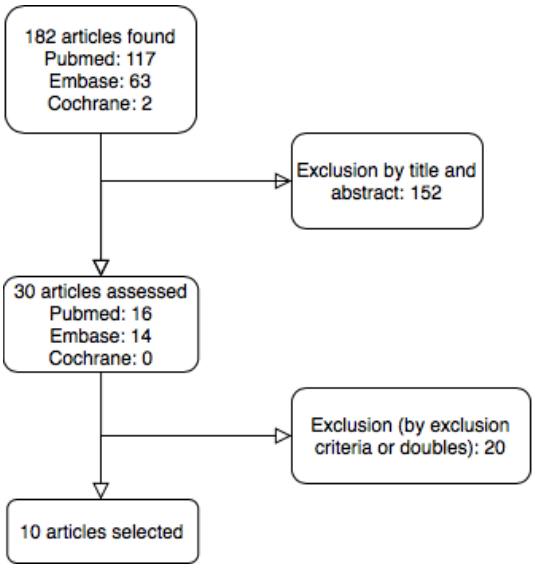
Flow chart	
Inclusion and exclusion criteria	• **Based on title and abstract** 1) Inclusion: (n=30) - Patient: general population or subpopulation - Intervention: confirmed COVID-19 infection/ SARS-CoV-2/ SARS nCoV - Outcome: mortality 2) Exclusion: (n=152) - Intervention: Infection with coronavirus other than COVID-19 - Outcome: no mortality outcome - Study type: opinions, editorials, case report - Language: publication in language other than English - Published before December 1, 2020 • **Based on full text** 1) Inclusion: (n=10) - Population: general population or meaningful subpopulation (epicenter or severely affected area) - Outcome: mortality rate and used calculation method. 2) Exclusion: (n=20) - No full text available - No calculation method mortality - Article included in review - Review included in meta-analysis

Evidence Table

Author, date and country	Study type (level of evidence)	Patient characteristics	Intervention	Comparison	Outcome	Key Results	Main risk of bias
Sun P et al.; China, 26/2/2020 (1)	Meta-analysis (2a)	50466 patients with SARS-CoV-2 infection from 10 retrospective studies	COVID-19 positive	Controls (no COVID-19)	Clinical characteristics of COVID-19 positive patients; The case fatality rate (CFR).	CFR: 4,3%	- Based on retrospective studies, not on systematic reviews - Mainly Chinese subjects, difficult to extrapolate - Lack of study details (method of mortality calculation) - Publication bias
Sohrabi C et al.; London, 24/2/2020 (2)	Narrative Review (2a)	**World population**	COVID-19 positive	Controls (no COVID-19)	Confirmed COVID-19 cases and mortality up to March 3, 2020, Time from onset of symptoms to death.	90870 cases (COVID-19 positive), 3112 death, Mortality: 3,4%; Median time from onset to death: 14 days; Median time >70 years: 11,5 days	- No clear criteria for inclusion - No information about search strategy - No check for validity - Lack of details of included studies
Wang Y et al.; China, 05/03/2020 (3)	Narrative Review (2a)	82623 reported cases and 2858 deaths **globally** (up to 27/02). 58,3% of cases in Wuhan city. Rest of China (excluding Hubei province) 13045 cases with 109 deaths. Outside of China (46 countries) with 3664 cases and 67 deaths.	COVID-19 positive	Controls (no COVID-19)	Case fatality rate	Global case mortality of 3.46%. Wuhan city 4,42%, rest of China except Hubei province 0,84%. Outside China 1.83% case mortality rate. Among 138 hospitalized patients, mortality rate was 4.3%. Case fatality rate among critical patients (4,7% of all cases) was 49%. Case fatality rate was higher for patients with comorbidities (CV disease 10,5%, diabetes 7,3%, chronic respiratory disease 6,5%, hypertension 6%, cancer 5,6%) compared to patients with no comorbidities (0,9%).	- No clear criteria for inclusion - No information about search strategy - No check for validity - Lack of details of included studies

Evidence Table

Baud D et al.; Switzerland 12/3/2020 (4)	Observational, retrospective Study (2b)	**World population**	COVID-19 positive	Controls (no COVID-19)	COVID-19 Mortality rate, time delay based (14 days) - up to March 1, 2020	China: 79 968 cases (2873 death), outside China: 7169 cases (104 death); Mortality rate China: 5,6%; Mortality rate outside China: 15,2%, Global mortality rate: 5,7%	- Selection bias - Detection bias
She J et al.; China, 20/2/2020 (5)	Narrative Review (2a)	**Chinese population**	COVID-19 positive	Controls (no COVID-19)	Mortality of COVID-19 in China up to February 10, 2020	Mortality in China: 2,3% (SARS was 9,6%, MERS 34,4%)	- Lack of search strategy - No inclusion/exclusion criteria - Lack of details of the used studies - No validity check of studies - Not representative for world population
Mizumoto K et al., China, 13/3/2020 (6)	Observational, retrospective Study (2b)	Residents in **China**, devided into China (excluding Hubei), Wuhan and Hubei Province (excluding Wuhan)	COVID-19 positive	Controls (no COVID-19)	**time-delay adjusted case-fatality rate** (d-CFR) and observed **crude CFR** (o-CFR), up to Februari 11, 2020	China total: 44795 cases (1117 death), Wuhan: 19559 cases (820 death), Hubei (excluding Wuhan): 13894 (248 death); Wuhan: d-CFR 12,2%, o-CFR 4,2% ; Hubei excluding Wuhan: d-CFR 4,2%, o-CFR 1,8%; China, excluding Hubei: d-CFR 0,9%, o-CFR 0,43%	- Ascertainment bias - Heterogeneity in calculation method for mortality, difficult to compare to other studies - Detection bias - Not representative for world population
Yang S et al.; China, 12/2/2020 (7)	Observational, retrospective Study (2b)	**Chinese population**, devided into China (excluding Hubei), Wuhan and Hubei Province (excluding Wuhan)	COVID-19 positive	Controls (no COVID-19)	estimated case fatality rate (**simple linear regression model**) between January 10, 2020 and February 3, 2020	CFR Wuhan: 5,25%; CFR Hubei (without Wuhan): 1,41%; CFR China (without Hubei): 0,15%; CFR China (total): 2,10%	- Selection bias - Detection bias - Heterogeneity in mortality calculation method, difficult to compare to other studies - Not representative for world population

Evidence Table

Jung S et al.; Japan, 14/02/2020 (8)	Observational, retrospective study (2b)	Data from 20 exported cases and estimated cumulative incidence in **China** up to 24/01 (6924 or 19,289 cases according to two calculated scenarios)	COVID-19 positive	Controls (no COVID-19)	c-CFR **(time-adjusted case fatality rate** of confirmed cases)	The estimated cCFR value was 5.3% or 8.4% in two different calculated scenarios.	- no clear criteria/definition of inclusions - No controls - Possible confounder - Selection bias - Detection bias
Wang W et al.; China, 29/01/2020 (9)	Narrative Review (2a)	In **Wuhan, China**: 1975 reported cased, 56 deaths (up to 25/01). 17 first deaths were 14 male and 3 female. Median age of death was 75 (range 48-89)	COVID-19 positive	Controls (no COVID-19)	Mortality, time from onset of illness to death	Mortality (up to 25/01) was 2,84%. Median number of days of first symptom to death was 14, shorter in >70 (11.5) than <70 (20) (p=0,033). 11 were complicated with other diseases before admission, and 5 had past surgery history	- No clear criteria for inclusion - No check for validity
Nishiura H et al.; Japan, 4/2/2020 (10)	Observational, prospective Study (2b)	565 **Japanese citizens evacuated from Wuhan** between 29 and 31 January 2020	COVID-19 positive	Controls (no COVID-19)	Ascertainment rate of infection; Infection Fatality Risk (IFR)	Ascertainment rate of infection (= risk of death among all infected individuals): 9,2%; Infection fatality risk (IFR): 0,3%-0,6%	- Selection bias - Detection bias - No controls - Possible confounders

Comments

The mortality rate of COVID-19 is difficult to determine as the global pandemic is still happening at this moment. Since the first reported cases in the epicenter of Wuhan city, the mortality has changed depending on time and space of the calculation.

Most studies defined the mortality rate at 2,2% - 4,8% in China. Wuhan has a higher estimated mortality rate than other places in China. In fact, the further away from Wuhan, the lower the mortality. This is the only place where such a distribution is seen. The mortality rate outside of China used to be very low (<1%), but in the last two weeks a shift has been seen as the infection becomes widespread across Europe. In the latest WHO situation report from 19/03/2020, Europe has an estimated mortality rate of 4,7%, while the global mortality rate is 4,2%. Especially Italy has become a new epicenter and has the highest mortality rate at the moment which was estimated at 7,2% on 15/03/2020 (11,12).
The latest numbers according to John Hopkins Coronavirus Resource Center, show that of all cases with an outcome (death or recovery) 10,7% of patients died (13).

Besides the varying rates depending on time and space, these calculated mortality rates can both be over- or underestimated. Overestimation of the fatal cases can be seen because not every person is tested for this disease, as many patients are asymptomatic or experience very mild symptoms without hospitalization (observer bias). Guidelines for testing for COVID-19 vary not only in place but are also continuously adapted.
Also, underestimation is a possible factor: at the moment of calculation, there will be a group of patients who is infected but not yet deceased (right censoring). Some studies have tried to cope with this last problem by calculating the mortality risk using a delay of approximately 14 days (mean time between onset of the symptoms and death). This generates a more reality-based mortality rate (14).

Some studies determined hospital mortality rates, which were higher with even rates up to >60% of ICU admission cases.

Mortality rates are also higher when clinical information is taken into account. Mostly male patients, old age and comorbidities are important factors in mortality (15). Comorbidities with higher risk are cardiovascular disease, diabetes, chronic respiratory disease, hypertension and cancer (mortality rates between 5-10%).

Clinical bottom line

The mortality rate in confirmed COVID-19 patients varies between 0,15% and 12,2% (in the epicenter, Wuhan). The mortality rate is very dynamic, because the rate depends on the used calculation method, the availability of medical care and the guidelines for testing for COVID-19. These guidelines vary between countries, even between cities and change in time.

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