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## Original Research

# COVID or not COVID: attributing and reporting cause of death in a community cohort



B.M.J. Lampl<sup>a, b, \*</sup>, M. Lang<sup>a</sup>, C. Jochem<sup>b</sup>, M.F. Leitzmann<sup>b</sup>, B. Salzberger<sup>c</sup>

<sup>a</sup> Regensburg Department of Public Health, Altmühlstr. 3, 93059, Regensburg, Germany

<sup>b</sup> Department of Epidemiology and Preventive Medicine, Faculty of Medicine, University of Regensburg, University Hospital Regensburg, Franz-Josef-Strauß-Allee 11, 93053, Regensburg, Germany

<sup>c</sup> Department of Infection Control and Infectious Disease, University of Regensburg, University Hospital Regensburg, Franz-Josef-Strauß-Allee 11, 93053, Regensburg, Germany

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## ABSTRACT

**Objectives:** In Germany, deaths of SARS-CoV-2–positive persons are reported as ‘death related to SARS-CoV-2/COVID-19’ to the Robert Koch Institute, Germany’s main infectious disease institution. In 177 COVID-19–associated deaths reported in Regensburg, Germany, from October 2020 to January 2021, we investigated how deaths following SARS-CoV-2 infection were reported and whether cases with a death attributed to SARS-CoV-2 (COVID-19 death [CD]) differed from cases with a reported death from other causes (non–COVID-19 death [NCD]).

**Study design:** This was an observational retrospective cohort study.

**Methods:** We analysed descriptive data on the numbers of cases, deaths, age, sex, symptoms and hospitalizations. We calculated odds ratios (ORs) with 95% confidence intervals (95% CIs) and performed Chi-squared/Fisher’s exact test for categorical variables and the Wilcoxon rank-sum test for comparison of medians.

**Results:** Deaths attributed to COVID-19 occurred primarily in elderly patients. The mortality rate and the case fatality ratio (CFR) increased with age. The median age and the prevalence of risk factors were similar between CD and NCD. Respiratory symptoms and pneumonia at the time of diagnosis were associated with death reported as CD. The odds of CD attribution in cases hospitalized because of COVID-19 were 6-fold higher than the odds of NCD (OR: 6.00; 95% CI: 1.32 to 27.22).

**Conclusions:** Respiratory symptoms/pneumonia at the time of diagnosis and hospitalization due to COVID-19 were associated with attributing a death to COVID-19. Numbers of COVID deaths need to be interpreted with caution. Criteria that facilitate attributing the cause of death among SARS-CoV-2 cases more uniformly could make these figures more comparable.

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## Introduction

The SARS-CoV-2 pandemic has a severe impact on health systems and economies.<sup>1</sup> While the total burden of disease due to COVID-19 is difficult to quantify, the number of deaths attributed to COVID-19 is often used as a surrogate parameter and is regarded as crucial in assessing the severity of the pandemic. Far-reaching consequences for societies worldwide are derived from these

figures. Numbers of deaths are often related to the total number of cases (case fatality ratio [CFR]) or to the total number of infections (infection fatality ratio [IFR]), of which the latter is challenging to assess.

In individual cases, it is difficult to determine whether SARS-CoV-2 infection was the direct cause of death, significantly contributed to death or merely coincided with death.<sup>2</sup> Autopsy studies typically comprise small sample sizes of mainly hospitalized patients.<sup>3,4</sup> In a recent study on deaths during the first COVID-19 wave in 2020 in Munich, Germany, autopsies were performed in only 11% of verified fatal COVID-19 cases.<sup>5</sup> To date, there are no uniform criteria to differentiate deaths likely caused by COVID-19 (‘due to’) from deaths coinciding with COVID-19 (‘together with’)

\* Corresponding author. Regensburg Department of Public Health Division of Infection Control and Prevention, Altmühlstr. 3, 93059, Regensburg, Germany. Tel.: +49 941 4009 523; Fax: +49 941 4009 764.

E-mail address: [benedikt.lampl@landratsamt-regensburg.de](mailto:benedikt.lampl@landratsamt-regensburg.de) (B.M.J. Lampl).

in SARS-CoV-2–infected persons. Thus, deaths of SARS-CoV-2–positive persons are reported to the Robert Koch Institute (RKI) as ‘death related to SARS-CoV-2/COVID-19’ (according to § 6 of the German Act on Protection Against Infectious Diseases [Infektionsschutzgesetz, IfSG]). Comparisons of international and even national figures need to be handled with caution as determining the cause of death might vary between countries, across time and between individual practitioners and local institutions.<sup>6–8</sup>

In the present study, we focused on deaths in SARS-CoV-2–positive cases in Regensburg, Germany, that occurred during the second COVID-19 wave. Specifically, we aimed to investigate how cases of death following SARS-CoV-2 infection were reported to the public health authorities and whether cases with a death attributed to SARS-CoV-2 (‘due to SARS-CoV-2/COVID-19’) differed from cases with a death reportedly not caused by SARS-CoV-2 (‘together with SARS-CoV-2/COVID-19’).

## Methods

We collected epidemiologic data on COVID-19 cases in Regensburg residents during the second COVID-19 wave (October 12th, 2020, to January 24th, 2021) and retrospectively analysed cases and deaths. We report absolute numbers of cases and deaths, attack rate, CFR and COVID-19–specific mortality according to age group and sex. Within the study period, cases were included by the date of reporting and deaths were included by the reported date of death.

### Case definitions, symptoms/clinical conditions and risk factors at the time of diagnosis

We applied the case definition of COVID-19/SARS-CoV-2 according to criteria specified by the RKI.<sup>9</sup> The following symptoms/clinical conditions and risk factors (RFs) were recorded at the time of case investigation (using the RKI/Äsculab21 reporting software) and analysed retrospectively: sore throat, cough, pneumonia, rhinitis, acute respiratory distress syndrome (ARDS), respiratory disorder requiring ventilation, dyspnoea, fever, general feeling of illness, diarrhoea, smell disorder, taste disorder, tachycardia and tachypnoea; cardiovascular disease, diabetes mellitus, liver disease, neurological/neuromuscular disease, immunodeficiency/HIV, kidney disease, chronic lung disease and cancer. Furthermore, data on status and cause of hospitalization were assessed.

### Attribution of the cause of death

Reported deaths in SARS-CoV-2–positive cases were classified as deaths caused by COVID-19 (COVID-19 death [CD]) or deaths from a different cause (non-COVID-19 death [NCD]) primarily based on notifications by the reporting physician. If the cause of death was not clearly stated by the reporting physician, cases were classified using clinical information from discharge letters and death certificates. Clinical criteria for CD were COVID-19 as a diagnosis in a discharge letter from hospital, a diagnosis of pneumonia, ARDS, morphological findings in computed tomography, multiorgan failure or thromboembolic events stated in medical records or the death certificates associated with a positive polymerase chain reaction (PCR) result for SARS-CoV-2. CD or NCD was categorized by one author (M.L.).

In 28 deaths primarily not reported as having been due to COVID-19, SARS-CoV-2 or COVID-19 was stated as part of the order of events in the death certificate or medical reports. These deaths were reclassified resulting in 137 CDs and 32 NCDs. For 8 deaths, no death certificates were available and those cases were excluded

from further analysis (Fig. 1). The retrospective analysis was done by B.L. in a blinded manner.

## Statistics

We analysed descriptive data on the numbers of cases, deaths, age, sex, symptoms and hospitalizations. To assess associations, we calculated odds ratios (ORs) with 95% confidence intervals (95% CIs). A Chi-squared/Fisher's exact test was used for categorical variables, and the Wilcoxon rank-sum test was performed for comparison of medians (level of significance for both tests  $P < 0.05$ ). All analyses were done using Microsoft Excel 2016 and SPSS, version 26.0.

## Results

A total of 6649 cases were reported to the Regensburg Public Health Department during the study period. Overall, 177 deaths occurred in this period in patients with a SARS-CoV-2 infection. Initially, 109 deaths (61.2%) were reported as having been caused by COVID-19, whereas 68 deaths (38.4%) were reported as NCD. No deaths occurred in individuals younger than 56 years. Therefore, we limited our analysis to cases older than 50 years (2569 cases). The overall CFR based on all COVID-associated deaths was 2.7% (2.1% based on attributed CD), and the CFR among persons aged  $\geq 50$  years was 6.9%. Basic descriptive data, symptoms at diagnosis and RFs for all cases  $\geq 50$  years and CD and NCD cases separately are shown in Table 1.

### Age and sex distribution, CFR and COVID-19–related mortality

We analysed the age and sex distribution of cases and CFR and COVID-19–related mortality according to age group. Most cases were reported among individuals aged 50–59 years ( $n = 1003$ , 39% of cases  $\geq 50$ , Fig. 2 a). Most deaths occurred among individuals aged 80–89 years ( $n = 86$ , 48.6%). Women showed a slightly greater number of deaths than men ( $n = 95$  [53.7%] vs.  $n = 82$  [46.3%]). Figures per 100,000 individuals per age group (Fig. 2 b) showed that the highest incidence of cases and deaths occurred among persons older than 90 years, with deaths increasing with age. At the same time, the CFR increased in an almost linear fashion (Fig. 2 c). The attack rate was lowest in the group aged 70–79 years, and it peaked among those aged  $>90$  years (7.2%). The age-specific COVID-19–attributed mortality was highest in the age group  $>90$  years, amounting to 1.7% of all COVID-associated deaths and 1.3% of CD. In summary, the attack rate, mortality and CFR increased with age.

### Case characteristics of cases $\geq 50$ years of age, CD and NCD cases

There was no significant difference in age between CD and NCD cases (median age = 86 vs. 83 years, interquartile range [IQR]: 80 to 90 vs. 79.3–89 years;  $P = 0.32$ ). Most deaths occurred in the group aged 80–90 years in CD and NCD, with a comparable sex distribution (Fig. 3). The median time from the date of report (as a proxy for the date of diagnosis) to death did not differ significantly between CD and NCD (9.0 vs. 8.5 days; IQR: 5.0–15.5 vs. 3.0–14.75 days;  $P = 0.18$ ).

A total of 286 of 2569 cases (11.1%) were hospitalized, 133 cases (5.2%) because of COVID-19 and 105 cases (4.1%) due to a different cause; in 48 cases (1.9%), the cause was not reported. Of 137 CDs, 65 cases (47.4%) were hospitalized: 42 cases (30.7%) due to COVID-19 and 14 cases (10.2%) due to a different cause (cause not reported in 9 cases [6.5%]). In NCDs, 12 of 32 cases (37.5%) were hospitalized: 3 cases (9.4%) due to COVID-19, and 6 cases (18.8%) due to a different cause (cause not reported for 3 cases [9.4%]).

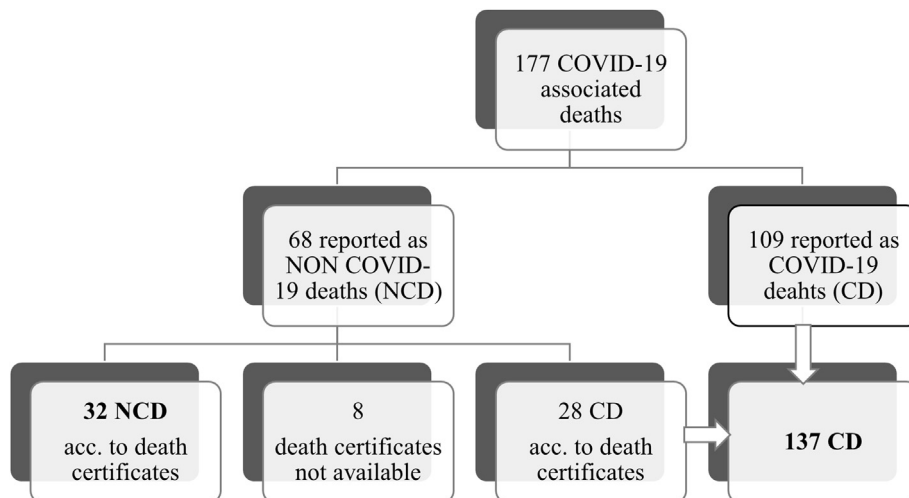


Fig. 1. Assignment of deaths to COVID death (CD) and non–COVID-19 death (NCD) group.

**Table 1**  
Case characteristics of all reported cases ≥50 years of age, COVID-19 deaths and non–COVID-19 deaths<sup>a</sup>.

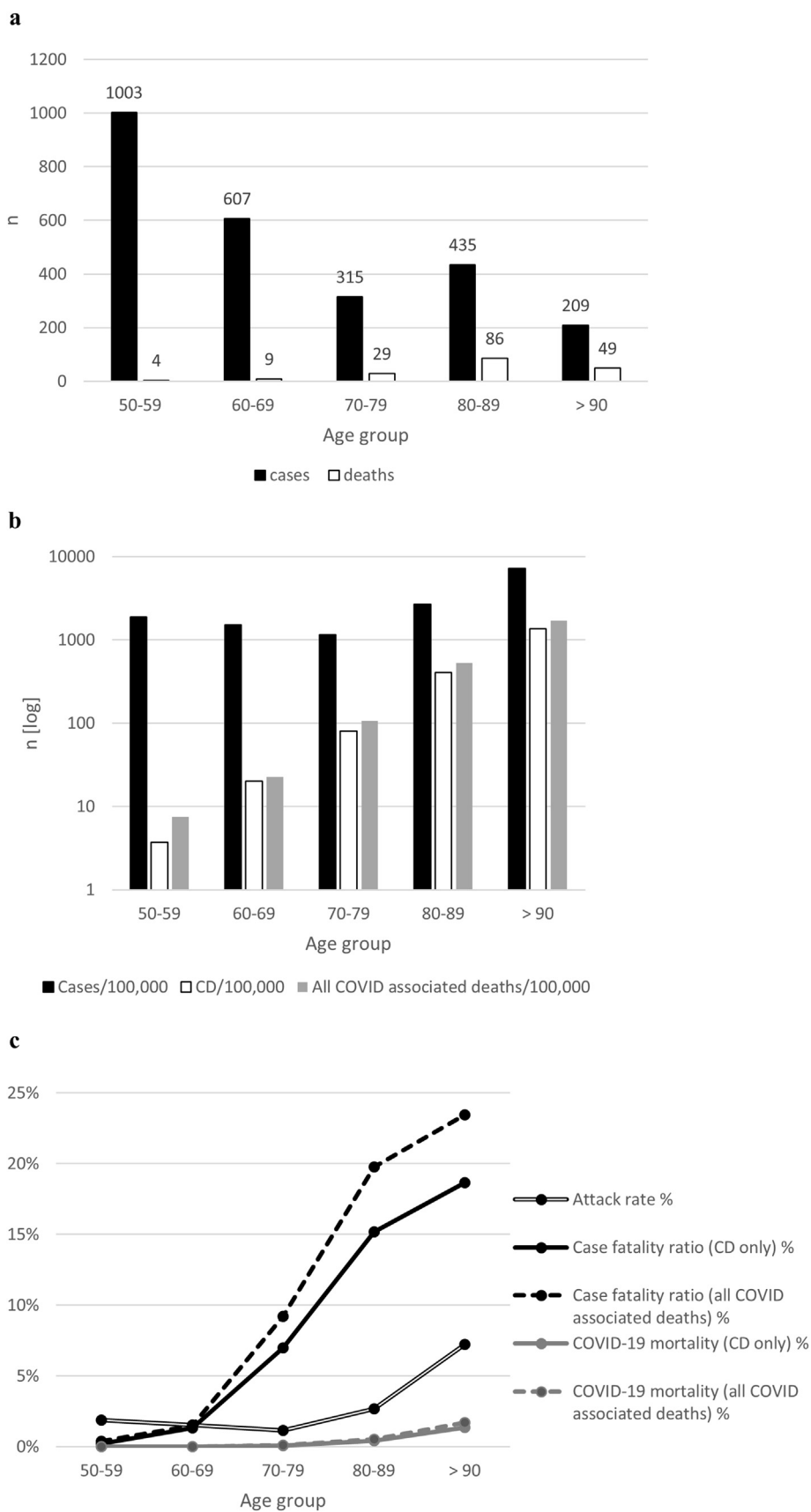
Study period	October 12, 2020, to January 24, 2021			
	All reported cases ≥ 50 years of age	CD	NCD	
Number [n] (%)	2569 (100)	137 (100)	32 (100)	
Male [n] (%)	1137 (44.3)	63 (46)	16 (50)	
Female [n] (%)	1432 (55.7)	74 (54)	16 (50)	
Mean age [y] (median; IQR)	67.3 (63; 56–80)	84.4 (86; 80–90)	82.8 (83; 79.3–89)	
Mean time from date of report to death [days] (median; IQR)	–	11.6 (9; 5–15.5)	8.9 (8.5; 3–14.75)	
Hospitalized [n] (%)	286 (11.1)	65 (47.4)	12 (37.5)	
■ due to COVID-19	133 (5.2)	42 (30.7)	3 (9.4)	
■ due to a different cause	105 (4.1)	14 (10.2)	6 (18.8)	
<b>Symptoms at diagnosis [n] (% of all cases/deaths)</b>				
Cough	662 (25.8)	21 (15.3)	0 (0)	
General feeling ill	587 (22.8)	22 (16.1)	7 (21.9)	
Fever	521 (20.3)	27 (19.7)	4 (12.5)	
Rhinitis	356 (13.9)	3 (2.2)	0 (0)	
Sore throat	312 (12.1)	4 (2.9)	0 (0)	
Taste disorder	189 (7.4)	5 (3.6)	0 (0)	
Odour disorder	143 (5.6)	0 (0)	0 (0)	
Dyspnoea	60 (2.3)	22 (16.1)	1 (3.1)	
Diarrhoea	60 (2.3)	3 (2.2)	0 (0)	
Pneumonia	43 (1.7)	30 (21.9)	1 (3.1)	
ARDS	9 (0.4)	4 (2.9)	1 (3.1)	
Respiratory disorder requiring ventilation	4 (0.2)	2 (1.5)	0 (0)	
Tachypnoea	4 (0.2)	2 (1.5)	0 (0)	
Tachycardia	3 (0.1)	2 (1.5)	0 (0)	
<b>Risk factors [n] (% of determinable /investigated RF)</b>				
Cardiovascular disease	1108 (77.9)	93 (85.3)	16 (72.7)	
Neurological/neuromuscular disease	379 (27.4)	52 (48.6)	13 (56.5)	
Diabetes mellitus	350 (25.3)	29 (27.1)	6 (28.6)	
Chronic lung disease (COPD)	210 (15.3)	25 (23.6)	4 (20)	
Kidney disease	176 (12.8)	30 (28.8)	7 (35)	
Cancer	155 (11.3)	18 (17)	5 (25)	
Liver disease	77 (5.6)	9 (8.7)	2 (10)	
Immunodeficiency, incl. HIV	74 (5.4)	5 (4.8)	0 (0)	

IQR = interquartile range; COPD = chronic obstructive pulmonary disorder; ARDS = acute respiratory distress syndrome.

<sup>a</sup> CD = COVID-19 deaths; NCD = non–COVID-19 deaths.

Cough (25.8%), general feeling of illness (22.8%) and fever (20.3%) were the most common symptoms reported among all cases (Table 1). Cough was not reported as a symptom at the time of reporting in NCD and was less frequent in CD (15.3%) than in all cases ≥50 years (25.8%). Fever was less common in NCD as an initial symptom (12.5% vs 19.7% in CD and 20.3% in all cases). Pneumonia

and dyspnoea were more frequent as an initial symptom in CD (21.9% and 16.1%, respectively) than in NCD (3.1% and 3.1%, respectively) and among all cases (1.7% and 2.3%, respectively). ARDS was equal for CD and NCD (2.9% and 3.1%). RFs were not determinable or not investigated in a large proportion of cases (mean 47.6% for all RF in cases older than 50 years, 22.7% in CD, and



**Fig. 2.** Distribution of COVID-19 cases  $\geq 50$  years of age and deaths. (a) numbers of cases and deaths by age group. (b) Numbers of cases and deaths per 100,000 per age group (logarithmic scale) (c) Attack rate, case fatality ratio (CFR) and COVID-19 associated mortality per age group.

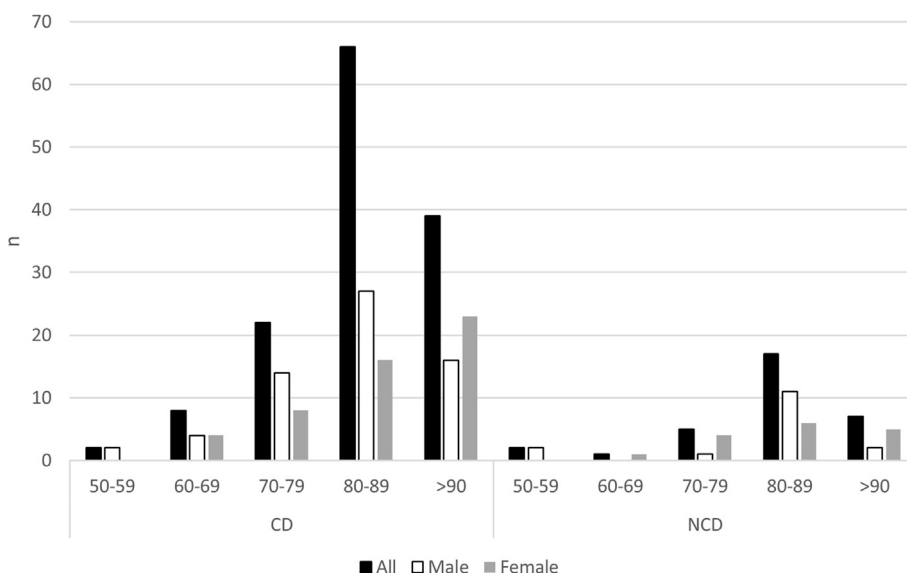


Fig. 3. Sex distribution of deaths per age group in COVID death (CD) and non-COVID-19 death (NCD).

35.2% in NCD). The leading RF in all cases with determinable RF was cardiovascular disease (77.9%), being more frequent in CD (85.3%) than in NCD (72.7) and among all cases aged ≥50 years (77.9%). Apart from immunodeficiency/HIV, all RFs were more frequent in CD than in all cases aged ≥50 years.

Association of symptoms/clinical conditions, RF and hospitalization with CD and NCD

For further analysis, CD and NCD were compared with respect to symptoms at diagnosis, RFs and hospitalization (Table 2). An association with CD was observed for pneumonia (OR: 8.69; 95% CI: 1.14 to 66.32; P = 0.01) and cough (P = 0.02). Dyspnoea was more

frequent in CD (22/115 vs 1/31; OR: 5.93; 95% CI: 0.77 to 45.74; P = 0.08). Cardiovascular disease as an RF was not significantly associated with CD (OR: 2.18; 95% CI: 0.74 to 6.41; P = 0.21). Hospitalization due to COVID-19 was associated with CD compared to hospitalization due to a different cause (OR: 6.00; 95% CI: 1.32 to 27.22; P = 0.01), but not hospitalization itself (OR: 1.33; 95% CI: 0.58 to 3.07; P = 0.50).

Discussion

The present study represents a retrospective analysis of a cohort from Regensburg, Germany. We focused on deaths in patients with SARS-CoV-2 during the second COVID-19 wave (October 2020 to

Table 2

Association of different symptoms, risk factors (RFs) and hospitalization at the time of reporting with CD and NCD<sup>a</sup>.

		Odds (yes/no) of CD vs NCD	OR (95% CI)	P value (Chi <sup>2</sup> /Fisher's exact test)
<b>Symptoms</b>	Pneumonia	30/107 vs 1/31	8.69 (CI: 1.14 to 66.32)	0.01
	Fever	27/110 vs 4/28	1.72 (CI: 0.56 to 5.31)	0.34
	Dyspnoea	22/115 vs 1/31	5.93 (CI: 0.77 to 45.74)	0.08 (Fisher's)
	Cough	21/116 vs 0/32	–	0.02 (Fisher's)
	General feeling ill	22/115 vs 7/25	0.68 (CI: 0.26 to 1.77)	0.432
	Taste disorder	5/132 vs 0/32	–	0.59 (Fisher's)
	Sore throat	4/133 vs 0/32	–	1.00 (Fisher's)
	ARDS	4/133 vs 1/31	0.93 (0.10–8.64)	1.00 (Fisher's)
	Diarrhoea	3/134 vs 0/32	–	1.00 (Fisher's)
	Respiratory disorder requiring ventilation	2/135 vs 0/32	–	1.00 (Fisher's)
	Rhinitis	3/134 vs 0/32	–	1.00 (Fisher's)
	Tachycardia	2/135 vs 0/32	–	1.00 (Fisher's)
	Tachypnoea	2/135 vs 0/32	–	1.00 (Fisher's)
	Odour disorder	0/137 vs 0/32	–	–
	<b>Risk factors (calculated for determinable/investigated RF)</b>	Cardiovascular disease	93/16 vs 16/6	2.18 (0.74–6.41)
Neurological/neuromuscular disease		52/55 vs 13/10	0.73 (0.29–1.80)	0.49
Diabetes mellitus		29/78 vs 6/15	0.93 (0.33–2.63)	0.89
Chronic lung disease		25/81 vs 4/16	1.24 (0.38–4.03)	1.00 (Fisher's)
Kidney disease		30/74 vs 7/13	0.75 (0.27–2.07)	0.58
Cancer		18/88 vs 5/15	0.61 (0.20–1.90)	1.00 (Fisher's)
Liver disease		9/95 vs 2/18	0.85 (0.17–4.28)	1.00 (Fisher's)
Immunodeficiency/HIV		5/99 vs 0/20	–	1.00 (Fisher's)
<b>Hospitalization</b>	due to COVID-19	65/61 vs 12/15	1.33 (0.58–3.07)	0.50
	due to other cause	42/14 vs 3/6	6.00 (1.32–27.22)	0.01

RF = risk factor; 95% CI = 95% confidence interval; ARDS = acute respiratory distress syndrome; OR = odds ratio.

If expected frequency in 2x2 table was <5, P value is stated according to Fisher's exact test.

<sup>a</sup> CD = COVID-19 death; NCD = non-COVID-19 death.



January 2021). Overall, mainly elderly and old patients died from COVID-19 or died in association with COVID-19. The attack rate and mortality increased with age, and the CFR culminated in a maximum of 23.4% calculated for all COVID-associated deaths aged  $\geq 90$  years. Pneumonia and cough at the time of diagnosis were significantly associated with death reported as CD. The odds for CD in cases hospitalized because of COVID-19 increased 6-fold compared to NCD. Time from diagnosis/date of report to death did not differ between the two groups. Thus, respiratory symptoms/pneumonia at the time of diagnosis and hospitalization due to COVID-19 seem to be associated with attributing deaths to COVID-19.

Taking only deaths with CD into account, the overall CFR of 2.1% in Regensburg was rather low compared to the literature.<sup>10,11</sup> If the CFR was based on all COVID-19-related deaths, it was 2.7%, which is slightly higher than in the first COVID-19 wave in spring 2020, which showed a CFR of 2.1%.<sup>12</sup> The observed increase in CFR, attack rate and mortality with age is well documented for COVID-19 in Europe and the US.<sup>13,14</sup>

In our cohort, we found that a number of deaths were initially not reported as CD to the public health authorities despite conflicting information in medical records or death certificates. Taking into account the information provided by death certificates, we reclassified nearly 16% of deaths in our cohort as CD. Divergent information between death reports and death certificates or discharge letters may reflect uncertainty in attributing the cause of death, particularly in older patients with comorbidities.

Studies on COVID-19-related deaths have mainly focused on hospitalized patients.<sup>3,4,15</sup> Studies attempting to identify associations of epidemiologic or clinical features with attribution of cause of death in general have been scarce.<sup>16</sup> Several RFs for death in COVID-19 cases have been identified thus far.<sup>17,18</sup> However, the presence of one or more RFs does not allow us to differentiate between CD and NCD as most of them are frequently present in elderly patients. Accordingly, we could not find significant differences in RFs between CD and NCD. Dyspnoea is described in the literature as a predictor of disease severity and death in COVID-19 patients.<sup>17,19</sup> We found significant associations with CD attribution only for pneumonia and cough.

Our study has several limitations. First, this is a retrospective study with a relatively small sample size. RFs and symptoms were collected as part of infection control investigations at one time point only and were provided by the individual case. The data on risk factors are incomplete due to the lack of verification and missing data. Associations of symptoms and cause of death attribution showed wide CIs. We did not adjust for potential confounding factors. To our knowledge, the autopsy rate in our cohort was 0, and no standard characteristics have been defined to decide, how deaths may be attributed to COVID-19 in different populations (e.g., outpatients) and timeframes after infection. Information from death certificates varied qualitatively and did not support a firm attribution of the cause of death in every case. Hence, our study cannot make solid statements about causes of death but only about the attribution of COVID-19 and its association with symptoms/clinical conditions and RF reported at the time of the first notification of the case. Generally, there is no unambiguous data source for the attribution of a death to SARS-CoV-2 infection as clinical assessments in discharge letters or death certificates (and even autopsies) must be regarded as arbitrary to some extent. So the number of deaths caused by COVID-19 has to be interpreted with caution.

To conclude, we have in a (cautious) exclusion process identified a number of deaths which were not attributed to COVID-19 in the judgement of the treating physician. There are some clinical characteristics present in this group which support our findings that not

every death in a patient with a positive SARS-CoV-2 PCR is caused strictly by SARS-CoV-2. On the other hand, asymptomatic (undiagnosed) fatalities may be missed and misclassification of deaths has to be assumed. Defined criteria might at least facilitate attributing the cause of death more uniformly and comparing death counts in different regions and countries. Efforts have to be made to improve the quality of the data on the suspected cause of death in the absence of widely used autopsies. Clinicians should be encouraged to deliver complete reports of clinical conditions in deceased patients and a complete and logical chain of causation in filling in death certificates. Awareness of the described problem and further research on the topic are necessary.

## Author statements

### Ethical approval

Not applicable.

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### Competing interests

None declared.

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