

The foreshadow of a second wave: An analysis of current COVID-19 fatalities in Germany

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I. MAIN TEXT

A second wave of SARS-CoV-2 is unfolding in dozens of countries. However, this second wave manifests itself strongly in new reported cases, but less in death counts compared to the first wave. Over the past three months in Germany, the reported cases increased by a factor five or more, whereas the death counts hardly grew (Fig. 1, bottom). This discrepancy fueled speculations that the rise of reported cases would not reflect a second wave but only wider testing. We find that this apparent discrepancy can be explained to a large extent by the age structure of the infected, and predict a pronounced increase of death counts in the near future, as the spread once again expands into older age groups.

We investigated this apparent discrepancy using age-resolved case and death reports [1], and the age-dependent infection fatality rate (IFR). The IFR increases by an estimated factor of 10 for every 20 years of age, and is about 10% ($\pm 2.3\%$) at age 82 [2, 3]. With this age-resolved IFR, we predicted the COVID-19-associated deaths from the reported cases (see methods). The prediction (color) matches the actually observed deaths (black) well in each age group (Fig. 1, right). Even the absolute numbers match, suggesting a low rate of unobserved SARS-CoV-2 infection chains.

This age-resolved analysis explains the apparent discrepancy between the total reported infections and deaths: The rise in reported cases is mainly driven by younger generations (younger than 60), who contribute only little to the absolute death counts (Fig. 1, right). Only in early September, the reported cases in the older generations (≥ 60 years) started to increase, and did so very steeply. This indicates that the more vulnerable age groups are not protected well anymore. This failure of protecting the elderly is also reflected in an increased rate of positive tests by a factor four at almost constant test numbers [4].

Such a spill-over to the older generations is more likely

when new infection numbers are too high, so that test-trace-and-isolate (TTI) capacities are exceeded: Test results are obtained less quickly, and TTI misses more and more infection chains. Exceeding the TTI capacity presents a tipping point, beyond which increasingly more SARS-CoV-2 carriers remain unnoticed and thus transmit the virus inadvertently - also to people at risk [5–7].

The age groups 60+ apparently were protected fairly well during summer 2020: If the virus had been spreading independently of age, between 1.3 % and 2.0 % of the infected would have died. However, the case fatality rate (CFR) was as low as 0.39 % in August (see table II). Now, with the strongly increasing number of infections among the elderly (Fig. 1), the CFR will most likely increase soon. This indicates that protecting the people at risk might be possible whilst case numbers are low, but likely fails when incidence increases.

For the coming two weeks, the already reported cases clearly predict that the number of weekly deaths will almost double. Forecasts beyond two weeks are difficult, because the death counts depend on the not-yet-reported cases. To account for this uncertainty, we display three future scenarios, where reported cases are (A) derived from estimated spreading within and between the different age groups, or (B,C) extrapolated based on the past five weeks (see methods). The forecasts of these scenarios range between 150 and 300 weekly deaths in early November, but case numbers might even grow faster in case a second wave fully unfolds.

The second wave in Germany has not overwhelmed hospitals yet, however, it starts to surpass the TTI capacity. By losing this important means of control, the overall successful management of the pandemic in Germany is seriously put at risk. To re-establish control, and to avoid the tipping point when TTI capacity is exceeded, case numbers have to be lowered. Otherwise the control of the spread and the protection of vulnerable people will require more restrictive measures latest when the hospital

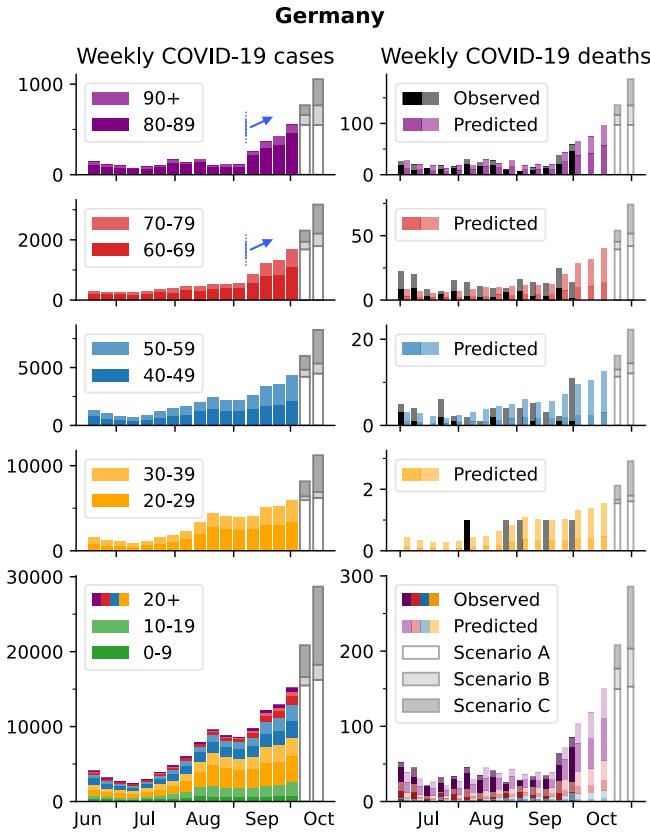


FIG. 1. The number of weekly COVID-19 case (left), and the number of predicted and actual COVID-19-associated deaths are displayed for each age group (right). Predicting the number of deaths from case numbers (color) matches the reported deaths (black) in each age group well. For this prediction, the age-dependent infection-fatality rate [2] was used. Despite a rise in total reported cases since mid July (bottom), cases in the older age groups only started to rise in September (blue arrows). As a consequence, a rise in deaths is expected to unfold soon (right). The forecast scenarios A,B,C (gray) predict a further increase in case numbers and deaths. The recent rise of infections in the older age groups together with the overall rise in cases clearly indicate a loss of control over the spreading, and the start of a second wave.

capacity is reached.

II. SUPPLEMENTARY METHODS SECTION

a. Data sources For Germany, the age-stratified data used in this document was retrieved from the national health agency, the Robert Koch Institute (RKI): both the number of reported SARS-CoV-2 cases and the number of deaths are available in age groups of ten years [1], and the reported cases are also available with 5-year resolution up to the age of 80 from [8]. It was verified that the number of cases in the two sources matches. The time points of the case and death numbers correspond to their *reporting* dates, and not necessarily to the actual testing or date of

death.

The population age distribution of Germany was retrieved from the United Nation's database [9].

b. IFR calculation The overall goal is to estimate death numbers from past reported cases per age group and compare them to the observed number of deaths. We used an age-dependent infection-fatality rate (IFR) equation, following recent meta-studies [2, 3]: Let a be the age of an infected person. Then the infection fatality rate for this age is estimated as

$$\text{IFR}(a) = 0.1 \cdot 10^{\frac{1}{20}(a-82)} \quad (1)$$

This equation formalizes that at 82 years, the IFR is 10% and decreases by a factor of 10 every 20 years. The age group 100+ is treated separately as 60%, in accordance with the supplementary calculations in [2]. In our analysis, we omit cases below the age of 20, as the weekly reported death numbers in that group are too low for any meaningful analysis. The equation (1) is very close to the published one [2], but has been rounded to integers for simplicity. For comparison see table I.

As reported cases are available with 5-year resolution, equation (1) was evaluated centered in the respective age group. For instance, the IFR of the age group 40-44 is approximated as:

$$\text{IFR}^{40-44} = \text{IFR}(42) = 0.1 \cdot 10^{\frac{1}{20}(42-82)} = 0.1\% \quad (2)$$

c. Estimating the number of deaths from the reported SARS-CoV-2 cases The number of deaths is estimated by multiplying the published weekly number of reported cases in 5-years-wide age groups by the associated IFR (equation (2)). To obtain the time point of the expected number of deaths, we delayed the number of reported cases by two weeks. This accounts for a one week delay between infection and case reporting, and a three weeks delay between infection and death. Thus, the total delay of two weeks between reported case and death amounts to the difference between the infection-case and infection-death delay. In addition, two weeks matches a median delay of 10 days, which can be derived from individual case information supplied by the RKI's publicly available database [10].

The observed number of deaths is only available in 10-years-wide age groups. Thus, to match the coarser stratification, we summed the corresponding two 5-years-wide age groups for all the plots.

d. Uncertainties of predictions Our estimations features a number of uncertainties: The IFR probably decreased over the course of the pandemic because of better treatments. This leads to some overestimation of the IFR as reported by Levin et al [2], which uses data from early in the pandemic. A fraction of cases remains unobserved, and people at risk may protect themselves better than earlier in the pandemic. Moreover, the assumed two-week delay between case detection and death is an approximation, the observed delay of individual cases

features a wider distribution. Overall however, the evidence indicates that in Germany half or more of all cases are currently detected [11]. In relative numbers across age-groups, uncertainties are smaller, because systematic errors in the IFR and the delay approximations are expected to effect all age groups similarly.

e. Accounting for non-matching age groups If reported cases are not available with a 5-year resolution, but only coarser, we distribute the reported cases of the coarser age groups in 5-years-wide age groups, proportional to the population-age distribution of the respective country [9]. This approach is necessary for ages above 80 years for Germany, where only 10-years-wide age groups are available: 80-89, 90-99 and 100+.

f. Prediction We consider three distinct scenarios for the future spread of the virus. *Scenario A* is based on a modified Susceptible-Exposed-Infectious-Recovered (SEIR) model with delay including inferred age-dependent transmission rates and interactions between age groups [12] fitted on reported cases. *Scenario B* is a linear extrapolation fitted to the reported cases in the respective age groups over the last 5 weeks, which we chose since linear growth can reflect the local and heterogeneous spreading of SARS-CoV-2. Furthermore, *Scenario C* is an exponential forecast using the latest reproduction rate $R_0 = 1.2$ given by the RKI [1] and reflects the worst of the three scenarios. For the forecast, the corresponding weekly increase of 37.5% is applied to the latest week of age-stratified case numbers.

g. Effective infection fatality rate The effective infection fatality rate IFR_{eff} is defined as the infection fatality rate given the age distribution of reported cases. It is calculated by weighting the IFR of the age groups (eq. (2)) by the number of current reported cases. This approach to calculate the effective IFR accounts for varying case distributions within the age groups, which therefore leads to a time-dependence of the effective IFR. Note that this IFR_{eff} is not a case-fatality rate, because only the age distribution of reported cases is used to weight the $\text{IFR}(a)$ in each age group appropriately; this is different from the case-fatality rate, which corresponds to the ratio of observed deaths to reported cases.

We calculated the evolution of the effective IFR in Germany for the period of June until September (table II). For comparison, $\text{IFR}_{\text{mix}}^{\text{DE}}$, the effective IFR for Germany assuming eq. (2) and a case distribution proportional to the population's age distribution is calculated: $\text{IFR}_{\text{mix}}^{\text{DE}} = 1.83$. Alternatively with values from [2] for the age-specific IFR (instead of eq. (2)), the corresponding effective IFR for Germany is $\text{IFR}_{\text{Levin}}^{\text{DE}} = 1.61[1.29; 2.02]$. Both IFR^{DE} represent an age-agnostic infection spread.

h. Case fatality rate In order to compare the theoretical effective infection fatality rate to the actual reported deaths, we calculated a case fatality rate. The approach was to divide the number reported deaths occurring two weeks later by the reported cases. This doesn't take into account the wide distribution of delays between infections and deaths. We mitigate the errors introduced by this

Age group	IFR (in percent)			[%] of pop.	cum. [%] of deaths pred. obs.
	Levin et al.	[]	Eq. (2)		
20-39	.007	.006	.009	.01	5.43
	.014	[.011	.017]	.0178	5.76
	.025	[.021	.03]	.0316	6.50
	.045	[.038	.053]	.0562	6.48
40-44	.081	[.07	.094]	.1	6.04
45-49	.148	[.129	.17]	.178	6.19
50-54	.269	[.234	.308]	.316	7.97
55-59	.488	[.425	.561]	.562	8.12
60-64	.887	[.764	.103]	1.	6.95
65-69	1.61	[1.37	1.9]	1.78	5.76
70-74	2.93	[2.44	3.52]	3.16	5.58
75-79	5.33	[4.34	6.53]	5.62	4.34
80-84	9.68	[7.71	12.2]	10.	3.89
85-89	17.6	[13.7	22.6]	17.8	1.95
90-94	32.	[24.2	42.2]	31.6	.90
95-99				56.2	.24
100+				60.	.02
				100.	100.

TABLE I. **Comparison of infection fatality rates (IFR).** The first column reproduces the age-dependent IFR from Levin et al. [2] evaluated at the center of the age group alongside 95% confidence interval bounds. The second column list the IFR values used in the analysis, which are calculated using eq. (2). The right half displays the predicted and observed percentage of deaths in each age group, cumulatively summing over all preceding age groups. For the estimated percentage for Germany, the age-specific IFR from the 3rd column is multiplied with the fraction of population in the age group. The observation refers to deaths in weeks 31-40 [1]. The observed fraction of deaths was almost twice as large as the estimated one in the age group up to 60 years (last two columns), reflecting that the virus spread more among the younger people than expected. These columns also show that 5.23 % (10.1%) of all deaths are expected among the age group up to 60, thus almost 95 % (90 %) of all deaths are expected to originate from the age groups 60+ assuming age-independent (or age-dependent) spreading.

Period	Number of		IFR _{eff} (in percent)	CFR
	Cases	Deaths		
Jul	14163	122.5	.86	1.0
Aug	32273	156.3	.48	.39
early Sep	30476	214.4	.70	.6
late Sep	28064	270	.96	-

TABLE II. **Comparison of predicted and deaths.** Predicted and observed deaths are associated with the assumed date of reporting of the infection 2 weeks earlier, as described in section II 0.c. Both the effective IFR based on age structure of cases and the CFR based on observed deaths is calculated. Predicted and observed deaths are within 20% of each other. *late Sep* starts 2020/09/21 containing two weeks and *early Sep* contains the first three weeks of September. For comparison: $\text{IFR}_{\text{Levin}}^{\text{DE}} = 1.61[1.29; 2.02]$ would be observed as CFR if infections were evenly distributed across the population and no infections remained undetected.

simple assumption by using at least 3 weeks of data (table II).

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HAUPTTEXT

Eine zweite Welle von SARS-CoV-2 breitet sich derzeit in Dutzenden von Ländern aus. Diese zweite Welle manifestiert sich zwar stark in neuen gemeldeten Fällen, aber im Vergleich zur ersten Welle weniger in der Zahl der Todesfälle. In Deutschland sind in den letzten drei Monaten die gemeldeten Neuinfektionen um das Fünf- bis Zehnfache angestiegen, während die Zahl der Todesfälle kaum zugenommen hat (FIG. 2, unten). Diese Diskrepanz nährte Spekulationen, dass der Anstieg der gemeldeten Fälle nicht auf eine zweite Welle, sondern nur auf umfassendere Tests zurückzuführen sei. Unsere Analysen zeigen jedoch, dass diese scheinbare Diskrepanz weitgehend durch die Altersstruktur der Infizierten erklärt werden kann. Da sich die Ausbreitung offensichtlich nun erneut auf ältere Altersgruppen ausweitet, prognostizieren wir in absehbarer Zeit einen deutlichen Anstieg der Todesfälle.

Wir haben diese offensichtliche Diskrepanz anhand von altersstrukturiert Fall- und Todeszahlberichten [1] und der altersabhängigen Infektionssterblichkeitsrate (ISR) untersucht. Die ISR steigt für jeweils 20 Lebensjahre um einen auf 10 geschätzten Faktor und liegt im Alter von 82 Jahren bei etwa 10% ($\pm 2,3\%$) [2, 3]. Mit dieser ISR können wir die COVID-19-assoziierten Todesfälle basierend auf den gemeldeten Fällen prognostizieren. Diese Vorhersagen (farblich) decken sich in jeder Altersgruppe gut mit den tatsächlich beobachteten Todesfällen (schwarz, FIG. 2, rechts). Selbst die absoluten Zahlen stimmen überein, was auf einen niedrigen Anteil unbeobachteter SARS-CoV-2-Infektionsketten hindeutet.

Diese altersabhängige Analyse löst die scheinbare Diskrepanz zwischen den gemeldeten Neuinfektionen und Todesfällen auf: Der Anstieg der gemeldeten Neuinfektionen wird hauptsächlich von den jüngeren Generationen (jünger als 60 Jahre) verursacht, die nur wenig zu den absoluten Todesfällen beitragen (FIG. 2, rechts). Erst seit Anfang September beginnen die gemeldeten Fälle in den älteren Generationen (≥ 60 Jahre) zu steigen, dafür allerdings massiv. Dies deutet darauf hin, dass die vulnerablen Altersgruppen nicht mehr gut geschützt sind. Dieses Unvermögen, ältere Menschen zu schützen, zeigt sich auch in einer um den Faktor vier erhöhten Rate positiver Tests bei nahezu konstanten Testzahlen [4].

Die Übertragung auf ältere Generationen, die wir hier beobachten können, wird umso wahrscheinlicher, wenn die Anzahl der Neuinfektionen so hoch ist, dass die Kapazitäten für Testung und Kontaktnachverfolgung überschritten werden: Es dauert zu lange, bis Testergebnisse vorliegen, wodurch sich eine steigende Anzahl an Infektionsketten der Kontaktverfolgung entziehen kann. Diese Überschreitung der Kapazitäten stellt einen Kipppunkt dar, jenseits dessen immer mehr SARS-CoV-2-Träger unbemerkt bleiben und so das Virus unbeabsichtigt übertragen - auch auf Risikopersonen [5–7].

Die Altersgruppen 60+ waren im Sommer 2020 offenbar vergleichsweise gut geschützt: Hätte sich das Virus

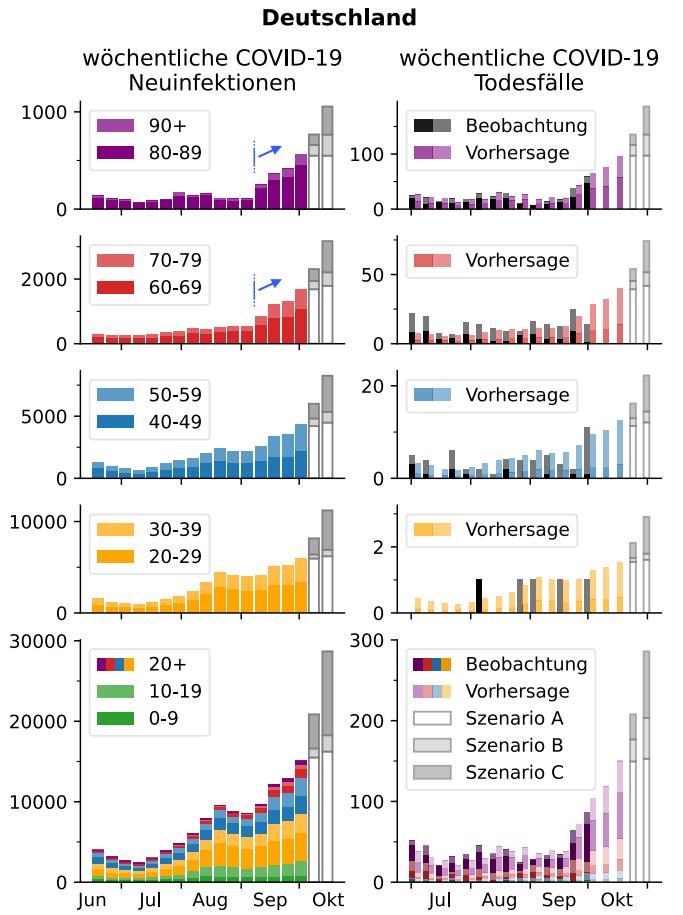


FIG. 2. Die Anzahl der wöchentlichen COVID-19-Fälle (links) sowie die Anzahl der vorhergesagten und tatsächlichen COVID-19-assoziierten Todesfälle werden für jede Altersgruppe (rechts) dargestellt. Die Vorhersage der Anzahl der Todesfälle anhand der Fallzahlen (farblich) stimmt mit den gemeldeten Todesfällen (schwarz) in jeder Altersgruppe gut überein. Für diese Vorhersage wurde die altersabhängige Infektionssterblichkeitsrate [2] verwendet. Trotz eines Anstiegs der berichteten Fälle über alle Altersgruppen seit Mitte Juli (unten) begannen die Fälle in den älteren Altersgruppen erst im September zu steigen (blaue Pfeile). Infolgedessen wird erwartet, dass sich bald auch ein Anstieg der Todesfälle zeigt (rechts). Die Prognoseszenarien A, B, C (grau) sagen einen weiteren Anstieg der Fallzahlen und Todesfälle voraus. Der jüngste Anstieg der Fallzahlen in den älteren Jahrgängen zusammen mit dem Gesamtanstieg der Fälle weist klar auf die Entwicklung einer unkontrollierten Ausbreitung und den Beginn einer zweiten Welle hin.

in allen Altersgruppen gleich verbreitet, wären zwischen 1,3 % und 2,0 % der Infizierten gestorben. Die Fallsterblichkeitsrate (FSR) lag zeitweise jedoch nur bei 0,39 % (siehe Tabelle III). Jetzt, mit der stark zunehmenden Zahl an Infektionen bei älteren Menschen (FIG. 2), wird die FSR höchstwahrscheinlich bald ansteigen. Dies deutet darauf hin, dass ein Schutz der Risikopersonen möglich ist, solange die Fallzahlen niedrig sind, aber vermutlich

Zeitraum	Infektionen	Anzahl der Tode		ISR _{eff}	FSR (in Prozent)
		Vorhersage	Beobachtet		
Jul	14163	122,5	146	0,86	1,0
Aug	32273	156,3	127	0,48	0,39
Sept früh	30476	214,4	184	0,70	0,6
Sept spät	28064	270	-	0,96	-

TABLE III. Vergleich der vorhergesagten und beobachteten Todesfälle. Vorhergesagte und beobachtete Todesfälle beziehen sich auf das zwei Wochen zuvor angenommene Meldedatum der Infektion und werden hier entsprechend früher eingeordnet. Auf den altersstrukturierten Fallzahlen wird die effektive Infektionssterblichkeit (ISR) berechnet, während sich die Fallsterblichkeit (FSR) als Vergleich der beobachteten Fallzahlen und Todesfälle ergibt. Die Vorhergesagten und beobachteten Todesfälle liegen innerhalb von 20% voneinander. *Sept spät* startet am 21.09.2020 und beinhaltet zwei Wochen, während *Sept früh* die ersten drei September Wochen enthält. Zum Vergleich: ISR_{Levin}^{DE} = 1,61 [1,29; 2,02] würde beobachtet werden, wenn Infektionen gleichverteilt über die komplette Population und ohne unentdeckte Infektionen stattfinden würden.

versagt, wenn die Inzidenz steigt.

Für die kommenden zwei Wochen sagen wir auf Grund der bereits gemeldeten Fälle voraus, dass sich die Zahl der wöchentlichen Todesfälle fast verdoppeln wird. Vorhersagen jenseits von zwei Wochen sind schwierig, da die Zahl der Todesfälle von den noch nicht gemeldeten Neuinfek-

tionen abhängt. Um dieser Unsicherheit Rechnung zu tragen, zeigen wir drei Zukunftsszenarien auf, bei denen die gemeldeten Fälle (A) aus der geschätzten Verteilung innerhalb und zwischen den verschiedenen Altersgruppen abgeleitet oder (B, C) auf der Grundlage der letzten fünf Wochen extrapoliert werden, und zwar einfach mittels linearer Fortschreibung (B) oder unter Annahme eines exponentiellen Wachstums (C). Die Vorhersagen dieser Szenarien liegen zwischen 150 und 300 wöchentlichen Todesfällen Anfang November; jedoch könnte die Anzahl an Todesfällen sogar noch schneller ansteigen, wenn eine zweite Welle ungebremst eintritt.

Bisher hat die potentielle zweite Welle in Deutschland die Krankenhäuser noch nicht überfordert, aber bereits jetzt werden die Testkapazität und die Kapazität für eine Kontaktnachverfolgung überschritten. Wenn diese beiden wichtigen Kontrollmaßnahmen nicht mehr funktionieren, ist die bisher erfolgreiche Bekämpfung der Pandemie in Deutschland insgesamt ernsthaft gefährdet. Um die Kontrolle wieder herzustellen und den Kippunkt bei Überschreitung der Testkapazität und der Kapazität zur Kontaktnachverfolgung zu vermeiden, müssen die Fallzahlen gesenkt werden. Sollte dies nicht gelingen, erfordern die Eindämmung der Ausbreitung und der Schutz gefährdeter Menschen spätestens dann restriktivere Maßnahmen, wenn es sich abzeichnet, dass die Krankenhauskapazität ausgeschöpft ist.