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Comments

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Abstract This paper demonstrates that once we control for comorbidity factors, age has a minor effect on COVID-19 mortality. This has implications for the treatment of current and recovered COVID-19 patients, including health screenings of recovered COVID-19 patients, triage decisions for patients in critical care, and prioritization of vaccinations when one is developed. The coronavirus epidemic in Italy has strained hospital resources, including ICU beds and ventilators for those experiencing acute respiratory failure. Studies of COVID-19 in China [1], Italy [2], and the United States [3] show that fatality rates increase rapidly with age, especially beyond age 60. The same studies and others also show that fatalities increase substantially with comorbidity factors, such as heart disease, hypertension, diabetes, stroke, and liver disease [1, 4, 5]. These morbidity factors are known to increase rapidly with age [6, 7, 8]. Among the elderly the higher incidence of heart disease, diabetes, hypertension, and other comorbidity factors lead to their increased mortality from COVID-19. If it is primarily comorbidity factors that lead to death with COVID-19 patients and not age, then patient treatment will be more effective if physicians are aware that these factors lead to much greater risk than age does.

Introduction

We examine 124,352 cases of COVID-19 and 14,859 deaths from COVID-19 in Italy through April 6, 2020. Based on estimates of the prevalence of comorbidity factors in Italy by age group and

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on the frequency of COVID-19 cases and mortality rates for age groups from [8], we estimate the percentage of patients with and without morbidity factor that would be expected to die, first assuming that those with and without comorbidity factors are equally likely to die. Subsequently, we use a maximum likelihood estimate to get mortality probabilities for people in each age group, with and without comorbidity conditions. COVID-19 patients with comorbidity conditions are 7.4 times as likely to die than those without a comorbidity condition. For example, an Italian COVID-19 patient between 70 and 79 years old with no comorbidity factor has about a 3.7% chance of death, whereas a 70 to 79 year-old patient with a comorbidity condition has a 27.5% chance of death.

Health care decisions will be improved when age as a risk factor, and other critical risk factors are better understood and quantified, both for the immediate surge of critically ill COVID-19 patients, and for those that are likely to follow in future outbreaks. As medical resources become strained during the epidemic, it will be important to take account of the probabilities of survival for patients with different medical histories.

Analysis

Table 1 in [4] shows that 61.9% of the fatal cases of COVID-19 in Italy through April 6, 2020 had 3 or more of the comorbidity factors. Another 20.5% had 2 of these factors, and 14.4% had one factor. Only 3.3% had no factor. This last statistic is important. If age alone were an independent factor that leads to high mortality, then – we will demonstrate in this paper – there would be many more deaths among those who are elderly but otherwise healthy. In other words, the 3.3% frequency of no comorbidity factors among the deceased would be approximately 20.0% if a patient with no comorbidity condition was as likely to die as a patient with one or more comorbidity condition.

The first table in [9] (Tabella 1) shows that 21,613 of 124,352 COVID-19 cases in Italy through 4 p.m. on April 6, 2020 were among people age 70 to 79. From the 7th table in [8] (Tavola 7), we can infer that about 19.8% of those people have no comorbidity condition, so we estimate that there are 4,279 healthy people between 70 and 79 who were among the COVID-19 cases. We take death rates for the age groups from the first table in [9] (Tabella 1). We consider the

hypothesis that healthy people in each age group are as likely to die as those with 1 or more comorbidity condition. This hypothesis will lead us to the conclusion that there should be approximately 6.1 times as many people with no comorbidity factors as the number that are shown in Table 1 in [4].

If healthy people between the ages of 70 and 79 are as susceptible to death from COVID-19 as those in their age group who have comorbidity conditions, then their death rate should be 22.71%, like their age group. Our estimate of 4,279 healthy people between 70 and 79 times this death rate produces an estimate of 972 deceased healthy people between 70 and 79 years old. Now we repeat this analysis for the remaining age groups and fill out Table 1. We estimate that across all age groups, if the healthy and the unhealthy are as likely to die, there would be 2,970 deceased healthy victims of COVID-19 for the data through April 6.

Table 1: Column E shows the number of the 124,352 total cases that would be healthy people (i.e., no comorbidity factor) in their age group and would die from COVID-19.

	A	B	C	D	E
Age group	% healthy	Number of cases in age group	Estimated number of healthy in age group (C = A x B)	Death rate from COVID-19 for age group	Estimated contribution of healthy to death total (E = C x D)
80+	13.9%	25,119	3,492	29.78%	1040
70 – 79	19.8%	21,613	4,279	22.71%	972
60 – 69	30.2%	20,406	6,163	8.45%	521
50 – 59	54.6%	24,320	13,279	2.33%	309
40 – 49	69.7%	16,202	11,293	0.84%	95
30 – 39	78.4%	8,980	7,040	0.38%	27
20 - 29	81.1%	5,662	4,592	0.12%	6
0 - 19	89.8%	2,050	1,841	0.05%	1
TOTALS		124,352			2,970

We now carry out a similar calculation in Table 2, but we consider here those people who have one or more comorbidity factor. This calculation estimates that there would be 11,888 people with one or more comorbidity factor who died by April 6, 2020.

Table 2: Column E shows the percentage of the 124,352 cases in each age group that would die who have one or more comorbidity factor.

	A	B	C	D	E
Age group	% with at least one comorbidity	Number of cases in age group	Estimated number of unhealthy in age group (C = A x B)	Death rate from COVID-19 for age group	Contribution of unhealthy to death total (E = C x D)
80+	86.1%	25,119	15,095	29.78%	6,441
70 – 79	80.2%	21,613	13,098	22.71%	3,936
60 – 69	69.8%	20,406	10,493	8.45%	1,204
50 – 59	45.4%	24,320	9,339	2.33%	257
40 – 49	30.3%	16,202	3,625	0.84%	41
30 – 39	21.6%	8,980	1,370	0.38%	7
20 - 29	18.9%	5,662	728	0.12%	1
0 - 19	10.2%	2,050	135	0.05%	0
TOTAL		124,352			11,888

As a check, total predicted deaths are 14,858. The total number of deaths from Tabella 1 in [9] where we get our total number of cases and our lethality factors for age groups (Column D) is 14,859.[3]

Our hypothesis that healthy people in each age group have the same probability of dying from COVID-19 leads us to the conclusion that of our estimated 14,858 deceased, 2,970 or 20.0% should have no comorbidity factor. The discussion preceding Table 1 in [4] states that among "patients dying in-hospital for whom it was possible to analyse clinic charts" only 3.26% had no comorbidity factor. Consequently, the hypothesis that the probability of dying is the same for all people in an age group regardless of their comorbidity factors leads to the conclusion that there would be about 6.1 times as many deaths among those with no comorbidity factor than what we see in the sample of deceased persons in Table 1 in [4].

This analysis can be augmented by assuming different probabilities of mortality for those with and without comorbidity factors. If we multiply every element in Column D in Table 1 by 0.1632 we would get 484 deaths among those with no comorbidity factor. If we multiple every element in Column D, Table 2 by 1.2091 we would get 14,374 deaths among those with one or more comorbidity factor. We would then have 484/14,858 = 3.26% of the deceased having no comorbidity factor, which matches the percentage

[3] The split between those with and without comorbidity conditions comes from tables of chronic pathologies in [8]. The difference between the number of predicted deaths and the actual deaths arises from any difference between the survey of the population and the characteristics of the population of people who contracted COVID-19. These differ by about 0.01%, which suggests that the surveys are good and the people who contract COVID-19 are quite representative of the population.

of the deceased with no comorbidity factor in Table 1 in [4]. Thus, the best estimate of the probabilities of death for age groups and comorbidity status are those in Table 3.

Table 3: These mortality probabilities produce fatalities in each age group that match total fatalities and match the frequency of comorbidities found in the first table in [4].

	20 - 29	30 – 39	40 – 49	50 – 59	60 – 69	70 – 79	80+
No comorbidity factor	0.0%	0.1%	0.1%	0.4%	1.4%	3.7%	4.9%
One or more factor	0.1%	0.5%	1.0%	2.8%	10.2%	27.5%	36.0%

From this we conclude that age is most likely only a moderate factor leading to COVID-19 mortality. Of course, healthy elderly patients are not dying in large numbers from COVID-19, so triage decisions that ignore the elderly healthy are not likely to lead to large numbers of deaths within this group. These patients are likely to recover, but they are likely to recover more quickly and with less physical damage if they are provided the same treatment as younger people. They also are unlikely to require critical care for much longer than a healthy young person, since like the healthy young, they are recovering. For these reasons, we believe that triage and other critical care decisions should be made more with regard to comorbidity factors than with regard to a patient's age.

Data limitations and potential extensions

The probabilities of death for COVID-19 patients by age and by comorbidity status are constrained across the two conditions (patients with and patients without a comorbidity factor) to have the same proportions. We cannot separately identify the probability of death in an age group. We can only increase or decrease the probabilities for the entire age profile to comport with the death frequency that we have from the subsample of the deceased for whom full clinical charts were available. Important research questions can be examined if the reporting agencies, such as the Italian Ministry of Health and the Centers for Disease Control make more detailed data available to researchers.

The general data reporting problem is that most agencies and researchers report marginal distributions, such as the probability of death for people in an age group or the probability of death for people with a comorbidity factor. Many important research questions require the joint distribution. What are the frequencies of death for people with a comorbidity factor in each age group, and what are the frequencies of death for people with no comorbidity factor in each age group. These frequencies would allow us to see directly how much the chance of death increases with age and how much it increases with the presence of one or more comorbidity. Even more granular data would allow researchers to evaluate

death frequencies for people with different combinations of comorbidities. Data are held by agencies that are unable to address all the critical questions that acute care physicians could use to make more effective decisions about the use of their resources at this critical time. This paper uses data to disentangle the two most important factors that influence mortality from COVID-19: comorbidity factors and age. A database with multiple factors would allow researchers to examine many other critical questions, perhaps most importantly, which specific comorbidity factors – and combinations of factors – are leading to high mortality among COVID-19 patients.

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