

THE ASSOCIATION OF CHRONIC DISEASES WITH COVID-19 OUTCOMES AND ITS ROLE ON RISK PERCEPTION: NATIONWIDE COVID-19 DATABASE & ONLINE COMMUNITY-BASED SURVEY

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Abstract

Background: COVID-19 is a viral respiratory disease, which became a global threat to public health. Further understanding of the epidemiology of this virus and on the risk perception of the community may better inform health authorities for targeted interventions to reduce the impact and spread of COVID-19.

Objective: In this study we aimed to examine the association between chronic diseases and worse outcomes following COVID-19 infection, and to explore its role on the self-perception of risk for worse COVID-19 outcomes.

Methods: This study draws from 2 databases: 1) The nationwide database of all confirmed COVID-19 cases in Portugal, extracted in 28th of April 2020 (n=20,293); and 2) the community-based survey “COVID-19 Barometer”, which contains data on health status, perceptions and behaviors during the first wave of COVID-19 (n=171,087). We assessed the association of relevant chronic diseases (i.e. respiratory, cardiovascular, renal disease, diabetes, and cancer) with death and ICU use following COVID-19 infection, and identified determinants of self-perception of risk for severe COVID-19 disease using logistic regression models.

Results: Respiratory, cardiovascular, and renal diseases were associated with mortality and ICU use among patients hospitalized due to COVID-19 infection (ORs [95%CI]: 1.48 [1.11-1.98]; 3.39 [1.80-6.40]; 2.25 [1.66-3.06]). Diabetes and cancer are associated with such outcomes but only when considered the full sample of COVID-19 infected cases in the country (ORs: 1.30 [1.03-1.64]; 1.40 [1.03-1.89], respectively). Older age and male sex were both associated with mortality and ICU use. The prevalence of at least one of the analyzed health conditions is high in the country's population, particularly on those aged 65 years old or over (19.6% and 44.6%, respectively). Self-awareness of risk for severe COVID-19 disease in the country's population is 23.9%, which is markedly increased on older people (46.4%), those with at least one chronic disease (51.7%), or those under both conditions (67.7%). All the analyzed diseases were associated with self-perception of high risk in the population.

Conclusions: Our study results demonstrate the association of some prevalent chronic diseases with increased risk of worse COVID-19 outcomes. It also brings further understanding on the current population risk perception for COVID-19 severe disease and useful insights into factors influencing it, in particular morbidity. Hence, this study may aid health authorities to better adapt measures to the real needs of the population and to identify those more vulnerable requiring further education and awareness on due preventive measures. Clinical Trial: NA

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Original Manuscript

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ABSTRACT

BACKGROUND: COVID-19 is a viral respiratory disease, which became a global threat to public health. Further understanding of the epidemiology of this virus and on the risk perception of the community may better inform health authorities for targeted interventions to reduce the impact and spread of COVID-19.

OBJECTIVES: In this study we aimed to examine the association between chronic diseases and worse outcomes following COVID-19 infection, and to explore its role on the self-perception of risk for worse COVID-19 outcomes.

METHODS: This study draws from 2 databases: 1) The nationwide database of all confirmed COVID-19 cases in Portugal, extracted in 28th of April 2020 (n=20,293); and 2) the community-based survey “COVID-19 Barometer”, which contains data on health status, perceptions and behaviors during the first wave of COVID-19 (n=171,087). We assessed the association of relevant chronic diseases (i.e. respiratory, cardiovascular, renal disease, diabetes, and cancer) with death and ICU use following COVID-19 infection, and identified determinants of self-perception of risk for severe COVID-19 disease using logistic regression models.

RESULTS: Respiratory, cardiovascular, and renal diseases were associated with mortality and ICU use among patients hospitalized due to COVID-19 infection (ORs [95%CI]: 1.48 [1.11-1.98]; 3.39 [1.80-6.40]; 2.25 [1.66-3.06]). Diabetes and cancer are associated with such outcomes but only when

considered the full sample of COVID-19 infected cases in the country (ORs: 1.30 [1.03-1.64]; 1.40 [1.03-1.89], respectively). Older age and male sex were both associated with mortality and ICU use. The perception of risk for severe COVID-19 disease in the country's population is 23.9%, which is markedly increased on older people (46.4%), those having at least one chronic disease (51.7%), or those under both conditions (67.7%). All the analyzed diseases were associated with self-perception of high risk in the population.

CONCLUSIONS: Our results demonstrate the association of some prevalent chronic diseases with increased risk of worse COVID-19 outcomes. It also brings further understanding on the community's risk perception for COVID-19 serious disease. Hence, this study may aid health authorities to better adapt measures to the real needs of the population and to identify those more vulnerable requiring further education and awareness on due preventive measures.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a viral respiratory disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which has become a global threat to human health [1-2]. By early December, over 68 million SARS-CoV-2 infections and over 1.5 million deaths have been reported worldwide [3].

Several studies have reported that chronic conditions, such as respiratory and cardiovascular diseases, are associated with worse outcomes following infection [1,4-8]. Given the rapid spread and high mortality rate of COVID-19 among those with a more vulnerable health status, soon it became clear the urgent need to expand research to elucidate the epidemiology of the novel virus, namely the identification of risk factors for severe illness or death [9].

In addition, there is ample evidence that perceived susceptibility to the severity of the disease is an important predictor of preventive behavior [10]. In accordance with theories of decisions about health behavior [11-14], engagement on preventive behaviors are shaped by the awareness and perception of risk, particularly on those more vulnerable to severe disease [13,15-17]. Preventive behaviors, such as curfew, social distancing, handwashing and mask wearing, are so far the most effective way to fight the spread of COVID-19 and due consequences [18-19]. Therefore, it is imperative to research risk perception in the community, given that such understanding may inform targeted interventions, including communication and health education strategies, aimed at minimizing the impact and spread of COVID-19.

Thus, the objectives of this study were: 1) to examine the association between chronic diseases and worse outcomes following COVID-19 infection (i.e. death and intensive care unit [ICU] use); and 2)

to understand its role on the self-perception of risk for worse COVID-19 outcomes.

METHODS

Databases

This study draws on two data sources:

1) **COVID-19 Database:** The official database of COVID-19 cases in Portugal, which contains anonymized data from the Directorate-General of Health (DGS), including all confirmed cases of COVID-19 notified to the National Epidemiological Surveillance System (SINAVE) extracted in April 28 2020 (n=20,293 laboratory confirmed cases of COVID-19). SINAVE is an electronic platform through which clinicians are obliged to notify all suspected and confirmed cases of COVID-19, and includes information on clinical findings and pre-existing conditions. Notifications trigger an epidemiological investigation by the Local Public Health Services, where a Public Health Physician (health authority in the area of residence of the case) validates the case. At a later stage the Regional Public Health Department and finally DGS conducts a final validation of case information. Outcome data are completed primarily at the local level, but can be updated at the Regional and National level (DGS). We compared the characteristics of these COVID-19 cases against a nationwide representative sample from the National Health Survey (*Inquérito Nacional de Saúde*, INS – Appendix 1) [20].

2) **COVID-19 Barometer:** we develop a community-based survey “COVID-19 Barometer”, which contains data on health (including mental health), healthcare utilization, perception of risk, and social experiences of over 180,000 individuals (≥ 16 years old) in Portugal during its first wave of COVID-19. Potential participants were invited to participate through existing contact networks and mailing lists (including large databases of students, teachers, researchers, staff and other collaborators of the ENSP-NOVA and other institutions nationwide), digital social networks, and social media promotion. The study was also promoted to vulnerable groups through partnerships with third sector organizations, including patient associations, public health doctors and other healthcare professional groups. Data were collected using a structured, closed-ended questionnaire administered online through the Microsoft Forms software program. The questionnaire was developed based on the Portuguese National Health Survey (INS) regarding the sociodemographic characteristics of respondents, health status and healthcare utilization [20]. Specific questions about COVID-19 were created by the authors and based on the COVID-19 Rapid Quantitative Assessment Tool of WHO, whenever possible [21]. The questionnaire was pretested to verify response times, to ensure comprehensibility and to solve operational errors. We used the latest available responses from each

participant, obtained during the time period between 21st of March 2020 and 23rd of May 2020 (n=171,087).

Measures

In this study, we considered the following main chronic diseases, which, according to the available evidence, are potential risk factors for COVID-19: respiratory, cardiovascular, renal disease, diabetes, and cancer.

Regarding the case definition for the main outcome in the DGS database, we analyzed a composite COVID-19 outcome of death and ICU use. At the time of the analysis there was a delay in the notification of death and thus considered a better choice to focus on a broader major outcome.

In the COVID-19 Barometer database, we surveyed the respondent's perception of risk for severe disease in case of COVID-19 infection with the following question: "To what extent do you consider to be at risk of developing serious illness or complications, if you become infected with COVID-19?" We then created a dichotomous variable with a value one for "high risk" category and zero otherwise (i.e. "moderate risk", "low risk", "no risk", "don't know").

Statistical Analysis

The analysis included two main steps: First, logistic regression models were used to assess the association of the analyzed diseases with death/ICU, adjusting for age (categorized in 6 groups with reference 0-50 and then 10 years age groups until >90), sex, region, and other relevant comorbidities available in the database, such as HIV. Two models were developed: one for all COVID-19 cases and another one with the subgroup of hospitalized COVID-19 patients, to better understand the association of morbidity with worse intrahospital COVID-19 outcomes, thereby limiting the potential bias arising from the higher likelihood of hospitalization of any given COVID-19 case solely based on the decider's knowledge of the pre-existence of a chronic disease (as further discussed below).

Second, descriptive analysis standardized for the distribution of the Portuguese population (by sex and age group using the direct method), and a logistic regression model was used to assess the level of self-perception of severe disease in the population and potential influencing factors, mainly the selected morbidity. We adjusted the model for age, sex, region, education (grouped into three major levels according to the highest qualification completed: basic or no education, secondary school, and university), other relevant comorbidities, smoking, self-reported health and mental status (both grouped into two major levels: "very good"/"good"/"moderate", and "poor"/"very poor"), high risk professional or living with one (including, healthcare professionals, security forces and customer-facing positions), living alone, and confidence in the NHS response. All these factors were chosen based on the database data availability and on the plausibility of influencing the analyzed outcome.

The model was built by means of a manual stepwise technique (backward elimination). In the descriptive analysis, additional results for those aged 65 years and above were also provided given that it is a common cut-off age criteria for added COVID-19 risk [22].

All statistical analyses were carried out using Stata version 13.1. In the descriptive analysis, the significance of the study variables was tested using Student's t-test or the Chi-square test, where appropriate. The significance level for all analysis was fixed at 5%, and confidence intervals were set at 95% (95%CI).

Ethical Considerations

Data was shared by DGS with the National School of Public Health under a partnership for COVID-19 research. Ethical Committee of the National School of Public Health approved the project (Approval: CE/ENSP/CREE/2/2020). Anonymity of participants and confidentiality of data on all used databases were guaranteed. Informed consent was obtained from all participants.

RESULTS

The Association of Chronic Diseases with COVID-19 Outcomes

The average age of all COVID-19 infection cases was 52.1 years old (men: 51.7 and women: 52.4; $P=.03$). 14.6% were hospitalized, 1.3% were admitted to an ICU and 2.5% died (3.6% for ICU or death). Among those hospitalized, the average age was 68.9 years old (men: 67.6 and women: 70.3; $P<.001$). More women were infected (58.7%), both amongst those bellow (59.2%) and above 65 years old (57.4%). However, male gender was more frequently found in cases requiring hospitalization (52.4%) and among those who died/ICU use (54.9%; $P<.001$). Male gender was associated with worse outcomes (Table 1). There was also an association between death/ICU use and respiratory, cardiovascular, renal disease, diabetes and cancer. Although, when analyzing specifically those who were admitted in the hospital, merely lung, cardiovascular, and kidney disease were associated with this composite outcome (Table 1).

Table 1 – Multivariable Logistic Regression to Assess the Association of Chronic Diseases with Severe Outcomes (Death or ICU use) following COVID-19 Infection.

	All INFECTED (n=20,203)	HOSPITALISED (n=2,958)
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	Univariable Logistic Regression OR (95% IC)	Multivariable Logistic Regression OR (95% IC)	Univariable Logistic Regression OR (95% IC)	Multivariable Logistic Regression OR (95% IC)
AGE (ref <50)	5.14 (3.27-8.08) ^b	5.03 (3.20-7.93) ^b	2.48 (1.53-4.03) ^b	2.52 (1.54-4.13) ^b
50-59				
60-69	14.81 (9.74-22.40) ^b	12.36 (8.15-18.76) ^b	3.31 (2.13-5.14) ^b	3.21 (2.04-5.02) ^b
70-79	35.65 (23.98-52.99) ^b	24.70 (16.48-37.01) ^b	3.85 (2.53-5.86) ^b	3.58 (2.32-5.53) ^b
80-89	50.58 (34.33-74.52) ^b	35.72 (24.04-53.08) ^b	5.20 (3.45-7.84) ^b	4.90 (3.20-7.50) ^b
90	52.47 (34.72-79.30) ^b	41.58 (27.22-63.53) ^b	5.05 (3.18-8.03) ^b	4.78 (2.95-7.75) ^b
Female	0.57 (0.49-0.66) ^b	0.56 (0.48-0.66) ^b	0.83 (0.69-0.99) ^b	0.78 (0.64-0.95) ^c
Respiratory Disease	4.74 (3.76-5.97) ^b	2.42 (1.89-3.10) ^b	1.65 (1.25-2.17) ^b	1.48 (1.11-1.97) ^c
Cardiovascular Disease	24.08 (13.51-42.90) ^b	8.66 (4.61-16.27) ^b	3.99 (2.16-7.36) ^b	3.39 (1.80-6.39) ^b
Renal Disease	11.71 (9.06-15.12) ^b	4.19 (3.17-5.53) ^b	2.68 (2.00-3.60) ^b	2.25 (1.66-3.06) ^b
Diabetes	3.33 (2.68-4.14) ^b	1.30 (1.03-1.64) ^c	1.12 (0.87-1.45) NS	0.95 (0.73-1.25) NS
Cancer	3.08 (2.31-4.10) ^b	1.40 (1.03-1.89) ^c	0.95 (0.68-1.32) NS	0.90 (0.64-1.27) NS
Other Comorbidity	4.33 (3.54-5.30) ^b	2.32 (1.86-2.89) ^b	1.31 (1.03-1.66) ^c	1.24 (0.96-1.60) NS
Any Major Comorbidity	6.62 (5.69-7.72) ^b	^a	1.86 (1.54-2.24)	^a

^aCofactor not included in the model due to high variance inflation factor (VIF>5) to avoid multicollinearity.

Any Major Comorbidity: Respiratory, cardiovascular, renal disease, diabetes or cancer. Other Comorbidity: includes other diseases collected in the official database of COVID-19 cases.

^bp<.001

^cp<.05

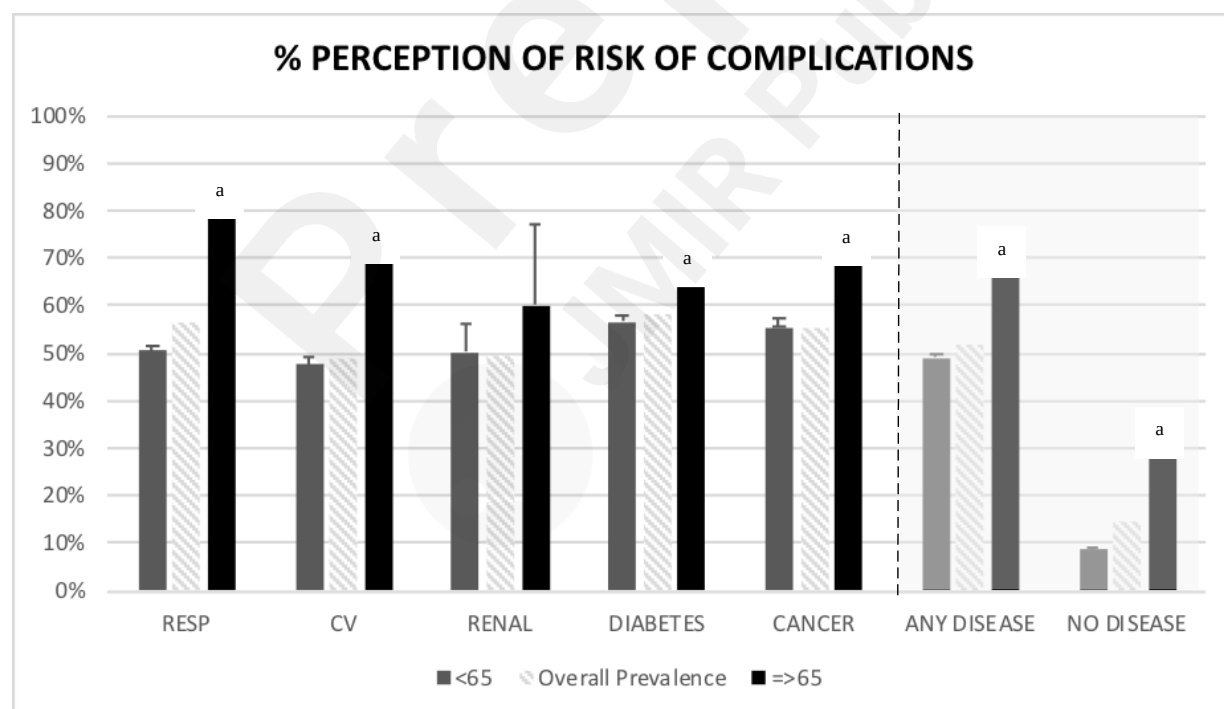
When comparing the COVID-19 Database with a nationwide representative sample from the Health Interview Survey it is noticeable that, across all the analyzed groups, there is a higher proportion of oldest people (≥ 65 years old) on those infected with COVID-19 than the overall country's

population (Respiratory: 60.0% vs. 48.3%; Cardiovascular: 91.5% vs. 69.8%; Renal: 78.8% vs. 53.2%; Diabetes: 65.5% vs. 59.3%; and at least one of these underlying health conditions: 64.7% vs. 54.0%, respectively). This asymmetry was particularly evident for renal and cardiovascular diseases (variation of 48.1% and 31.1%, respectively). A lower proportion of women was found in the COVID-19 Database versus the country's population (group with at least one of the underlying health conditions: 48.7% vs. 57.1%, respectively).

The Role of Chronic Diseases on the Risk Perception

We found that 23.9% of the COVID-19 Barometer participants (n=171,087) considered to be at high risk to develop severe disease in case of COVID-19 infection. This self-perception of risk was significantly higher among those aged above 65 years old (46.4%) and on those suffering from any of the analyzed diseases (51.6%. Figure 1). For those on both conditions that proportion rise to 67.7%. Across all subgroups, the oldest people suffering from respiratory diseases presented the highest self-perceived risk (78.5%), followed by cardiovascular (69.6%) and cancer (69.0%) on the same age-group (≥ 65); while those at younger ages (<65) and not suffering from any of the analyzed illnesses presented the lowest value (8.9%. Figure 1).

Figure 1 – Age-specific and Standardized Prevalence of Self-Perceived Risk to Develop Severe Disease Following COVID-19 Infection (n=171,087).



In the multivariable logistic regression, we observed a strong association between chronic diseases and self-perceived risk (Table 2), particularly for cancer (OR: 8.57; 95%CI: 5.73-12.81), respiratory

disease (OR: 8.25; 95%CI: 7.21-9.44), and diabetes (OR: 6.17; 95%CI: 4.58-8.31). Increasing age was also associated with self-perceived high risk, but it became non-significant for the oldest age levels in the multivariable model, likely due to small sample size on those age-groups (Appendix 2). Females, lower education, smoking and worse health status were also associated with self-perceived risk of severe COVID-19 disease (Table 2).

Table 2 – Logistic Regression to Assess the Association of Chronic diseases with Self-Perceived Risk to Develop Severe Disease Following COVID-19 Infection (n=11,247).

	Univariable Logistic Regression OR (95% IC)	Multivariable Logistic Regression OR (95% IC)
AGE (ref <50)		
50-59	1.84 (1.78 -1.90) ^c	1.74 (1.46-2.07) ^c
60-69	3.82 (3.68-3.96) ^c	2.64 (2.14-3.26) ^c
70-79	6.98 (6.57-7.41) ^c	3.85 (2.81-5.37) ^c
80-89	8.25 (6.68-10.17) ^c	1.35 (0.45-3.66) NS
>90	9.19 (3.50-24.14) ^c	3.72 (0.34-47.06) NS
Female Gender	0.88 (0.86-0.90) ^c	1.17 (1.02-1.33) ^d
Education (ref. Basic /No educ)		
Secondary School	0.68 (0.65-0.72) ^c	0.88 (0.73-1.06) NS
University	0.53 (0.51-0.56) ^c	0.77 (0.64-0.93) ^d
Respiratory Disease	7.20 (6.98-7.43) ^c	8.25 (7.21-9.44) ^c
Cardiovascular Disease	5.67 (5.43-5.94) ^c	4.92 (3.69-6.55) ^c
Renal Disease	5.83 (4.62-7.37) ^c	3.99 (2.67-5.98) ^c
Diabetes	6.93 (6.56-7.33) ^c	6.17 (4.58-8.31) ^c
Cancer	6.79 (6.37-7.22) ^c	8.57 (5.73-12.81) ^c
Any Major Comorbidity	9.70 (9.43 -9.97) ^c	^a
Other Comorbidity	1.96 (1.89-2.04) ^c	3.29 (2.81-3.86) ^c
Smoking	1.17 (1.05-1.31) ^d	1.28 (1.12-1.45) ^c
Worse Health Status	8.24 (7.49-9.05) ^c	2.85 (2.09-3.90) ^c

Worse Mental Status	1.44 (1.25-1.65) ^c	^b
High Risk Professional or Living with one	0.99 (0.96-1.02) NS	^b
Living Alone	1.26 (1.21-1.30) ^c	^b
No Social Support	1.62 (1.56-1.69) ^c	^b
Lower Confidence in the NHS	1.13 (1.10-1.16) ^c	^b

^a Cofactor not included in the model due to high variance inflation factor ($VIF > 5$) to avoid multicollinearity.

^b Cofactor excluded in the stepwise method (backward elimination with $P > .05$)

Any Major Comorbidity: Respiratory, cardiovascular, renal disease, diabetes or cancer. Other Comorbidity: includes other diseases collected in the community-based survey "COVID-19 Barometer".

^c $p < .001$

^d $p < .05$

DISCUSSION

We found a significant association between respiratory, cardiovascular, renal disease, diabetes and cancer with coronavirus-related mortality and ICU use, which was stronger for respiratory, cardiovascular, and renal disease, when analyzing only those COVID-19 cases requiring hospitalization. The overall self-reported prevalence of these illnesses in the country's population is 19.6%. However, more importantly, it affects almost half of those aged 65 years old or over (44.6%), a population *per se* vulnerable to COVID-19, namely because of age-related frailty and immune system decline (Appendix 1) [23]. In our study, we also found that among this group at the highest risk, approximately two thirds (67.7%) are self-aware of such hazard; while it drops to about half for individuals above 65 years old, but not suffering from any relevant chronic condition (46.4%). Morbidity seems in fact to be the strongest determinant of risk perception given the results of the multivariable regression. Furthermore, the inclusion of self-reported health status in the model did not affect these results, which suggests that this perception of risk is not so much altered by how the patient actually feels, but rather by the knowledge itself of having the chronic disease. This is corroborated with low (in some cases even absent) association of morbidity with self-perceived risk of infection (*data not shown*). The plausible risk of COVID-19 severe disease, and not so much the risk of infection, posed by several chronic diseases, particularly among the elderly, was abundantly communicated by the media, medical societies, public health institutes, Health Authorities and patient organizations. Therefore, it is not surprising that older patients suffering from the analyzed illnesses are particularly concerned with the risk of developing severe disease following COVID-19, despite how active or controlled the disease is, or even how well one feels.

Our study also found that other factors may contribute to self-perception of higher risk. Old-age

seems to be associated with increased perception of risk, which is in line with other studies. For instance, a survey in US has shown that older adults perceive larger risks of dying if getting COVID-19 [24]. Female gender seems also associated with higher self-perception of risk. This finding is aligned with other evidence showing that women tend to be more aware of their health status and seek healthcare more proactively than men [25-27]. Interestingly, we found in the analysis of the COVID-19 database that women are less prone to die or to require ICU in case of infection than men (despite more cases of infection among women, likely due to more older women in the Portuguese population), which is in line with what has been reported elsewhere [29,30], probably owing to other risk factors unequally distributed by gender, which are not being taken in consideration in this analysis. Finally, this finding is consistent with results from past surveys, which found the association between female gender and adoption of preventive behaviors during a pandemic respiratory disease [31-35]. Recently, two surveys performed in the US showed that women are more knowledgeable about COVID-19 and engage more than men in COVID-19 preventive behaviors [36,37].

Higher education was associated with further concern regarding the risk of severe COVID-19 disease. This is also aligned with other surveys and with available data, which consistently show that education is linked with health literacy, awareness and preventive behaviors [38,39]. On the other hand, the literature shows that lower education is associated with greater risk of morbidity [40-42]. We thus foresee opportunities for patient education regarding COVID-19 threat targeting disadvantage communities with a lower level of education, aggravated by lower income and reduced access to care, thereby mitigating the health inequities which are reportedly emphasized by COVID-19 [43].

It is worth noting that smokers were more likely to self-perceive high risk as well. Soon it became clear that smokers are more susceptible to coronavirus complications and that was thoroughly communicated in the media, thereby prompting a higher concern among smokers [44].

Several literature reports have documented the increased risks caused by comorbidities in patients infected with SARS-CoV-2 related virus, such as the avian influenza [45-47], SARS-CoV [48,49], and MERS-CoV infection [50,51]. The most common health conditions with poorer prognosis included respiratory diseases [15,16], cardiac diseases [15,16], renal diseases [16], diabetes [18], hypertension [16], Error: Reference source not found and cancer [15]. Initial reports from China suggested that these comorbidities would also play a negative role in the prognosis of the novel coronavirus infections [52-54], promptly health authorities and public health institutes, such as the Centers for Disease Control and Prevention, to act and declare these comorbidities as relevant risk

factors [22]. However, some contradictory data was released meanwhile from other geographies and/or alternative methodological approaches, including adjustment for potential confounders, like age and gender. For instance, Wang B and colleagues conducted a metanalysis, which highlighted hypertension, diabetes, chronic obstructive pulmonary disease (COPD), cardiovascular disease and cerebrovascular disease as major risk factors for COVID-19, while ruling out cancer and renal disease [55]. On the other hand, other authors have claimed that cancer and renal disease are risk factors as well [56-58]. This inconsistency on the available knowledge urges for further evidence on the relationship between morbidity and COVID-19 outcomes, as recently highlighted on a call for COVID-19 research [59].

Our data clearly shows an independent association between respiratory, cardiovascular, and renal disease with COVID-19 worse outcomes. Chronic diseases share several standard features with infectious disorders, such as the proinflammatory state, and the attenuation of the innate immune response, which may make individuals more susceptible to disease complications [60]. This is particularly true for cardiovascular diseases and an extensive discussion of this relationship with COVID-19 has been described elsewhere [61]. On the other hand, renal disease dysfunction causes reduced lymphocyte numbers and function, creating an immunodeficiency state, predisposing the individual to severe infections [62]. When it comes to pre-existence of respiratory diseases, such as COPD, the patient's lung function is damaged and thus less resistant to the virus and more disposed to develop serious disease. This link has been presented elsewhere [27,64-67].

Our findings are not so convincing concerning diabetes and cancer, since the multivariable model which specifically focused on those hospitalized (less influenced by Berkson's bias, as discussed below) provided non-significant results for these pathologies. As mentioned above, this is aligned with some previous results [20], but not with others [24]. Error: Reference source not found We cannot rule out that lack of statistical power may undermine our results.

Limitations & Strengths

This study is hampered by some limitations that need to be stated. First, the analysis is based on self-reported data, which might be subject to recall bias and misclassification bias (e.g. chronic diseases not clinically confirmed in the Barometer survey and differences in the case definitions of the analyzed databases). Furthermore, it is possible that underreporting might have taken place among those who consult less and/or are less aware of their own chronic condition (e.g. low educated groups with lack of health literacy and awareness). Secondly, COVID-19 database is prone to Berkson's bias

[68] given that any patient infected with COVID-19 and suffering from a chronic disease is more likely to be hospitalized than another infected case not suffering from any chronic disease, which might lead to spurious association between the risk factors under study and major COVID-19 outcomes. Furthermore, guidelines were issued recommending hospitalization of COVID-19 cases when some comorbidities were present, thereby worsening the Berkson's bias [69]. This highlights how important was the specific analysis of the subgroup of hospitalizations we performed in this study. Thirdly, disease severity and staging were not taken into consideration, given that there was no such information in the datasets. Lastly, the Barometer survey was subjected to the volunteer bias (e.g. more engaged and informed citizens adhered to the survey), thereby compromising the external validity of the analysis; and to social desirability bias. Although this sort of bias has been found to be lower in anonymous online surveys than in telephone or in-person surveys [70], we cannot rule out the possibility that some respondents reported more risk awareness than others due, in part, to social desirability [71]. We applied direct age and sex standardization to improve the external validity of these results.

This study has several strengths too. It uses individual observations from two nationwide databases, including the official database with all COVID-19 cases in Portugal and a nationwide population-based survey that reached over 170 thousand people, which to our knowledge makes it the world's largest community-based survey performed on COVID-19 so far.

Policy Implications

Our results encourage authorities to protect those citizens at the highest risk to develop severe COVID-19 disease, as well as to promote knowledge and health literacy among those who despite their increased risk are not fully aware of it. In particular, older and uneducated men – a population group with insufficient awareness, which should definitely be targeted by health policies aiming to fight the pandemic threat effectively. Such policies should customize communication and foster preventive behaviors. Risk perception of pandemics can predict compliance with preventive measures and tendency to seek treatment or vaccination [72]. So far, measures of social distancing and responsible behavior have proven successful in preventing the spread of the disease, as well as its worse consequences [73]. Knowing how risk is perceived is essential for preparing an effective plan for risk communication, and may be predictive of the public's response [74,75]. As already mentioned, available literature shows that people with increased perception of risk are more likely to be engaged in protective behaviours [13,15-17].

Conclusions

Our study results demonstrate the association of some prevalent chronic diseases with increased risk of worse COVID-19 outcomes. It also brings further understanding on the community's risk perception for COVID-19 serious disease. Hence, this study may aid health authorities to better adapt measures to the needs of the population and to identify those more vulnerable requiring further education and information on due preventive measures.

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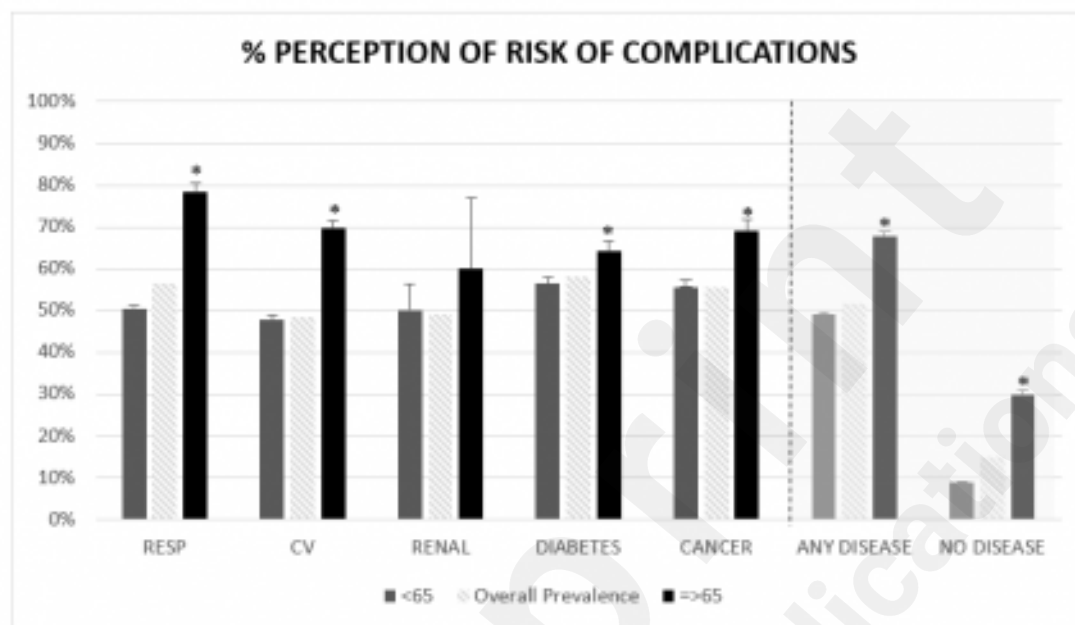
Supplementary Files

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Figures

Age-specific and Standardized Prevalence of Self-Perceived Risk to Develop Severe Disease Following COVID-19 Infection.



Multimedia Appendixes

Prevalence of Chronic Diseases in the Country's Population.

URL: <https://asset.jmir.pub/assets/b38b953754a09fb8ddd2a55f04ea8316.docx>

Patient characteristics.

URL: <https://asset.jmir.pub/assets/061f6ccb21336608e65016f57c823d53.docx>

