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Self-reported olfactory loss associates with outpatient clinical course in Covid-19

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Abstract:

Background:

Rapid spread of the SARS-CoV-2 virus has left many health systems around the world overwhelmed, forcing triaging of scarce medical resources. Identifying indicators of hospital admission for Covid-19 patients early in the disease course could aid the efficient allocation of medical interventions. Self-reported olfactory impairment has recently been recognized as a hallmark of Covid-19 and may be an important predictor of clinical outcome.

Methods:

A retrospective review of all patients presenting to a San Diego Hospital system with laboratory-confirmed positive Covid-19 infection was conducted with evaluation of olfactory and gustatory function and clinical disease course. Univariable and multivariable logistic regression were performed to identify risk factors for hospital admission and anosmia.

Results:

A total of 169 patients tested positive for Covid-19 disease between March 3 and April 8, 2020. Olfactory and gustatory data were obtained for 128/169 (75.7%) subjects of which 26/128 (20.1%) required hospitalization. Admission for Covid-19 was associated with intact sense of smell and taste, increased age, diabetes, as well as subjective and objective parameters associated with respiratory failure. On adjusted analysis, anosmia was strongly and independently associated with outpatient care (aOR 0.09 95% CI: 0.01-0.74) while positive findings of pulmonary infiltrates and/or pleural effusion on chest radiograph (aOR 8.01 95% CI: 1.12-57.49) was strongly and independently associated with admission.

Conclusions:

Normosmia is an independent predictor of admission in Covid-19 cases. Smell loss in Covid-19 may associate with a milder clinical course.

Introduction:

The rapid worldwide spread of the Covid-19 pandemic has placed an unprecedented strain on hospitals and healthcare systems.[1] SARS-CoV-2, the virus mediating Covid-19, continues to affect individuals of all ages, ranging from asymptomatic to fatal infection.[2–7] Recent examples of overwhelmed healthcare systems underline the urgent need for developing strategies to predict early symptoms and disease trajectory with biomarkers and clinical prognosticators.[8] A cost-effective method of early risk stratification of disease severity would enable improved medical decision-making, rapid and severity-appropriate intervention, and facilitate the allocation of limited medical resources. Under such a paradigm, patients found to carry markers associated with severe manifestations of Covid-19 would be considered high-risk and monitored closely for further escalation of care. Meanwhile, those displaying markers associated with low-risk disease could be recommended to self-monitor under quarantine conditions, allowing health systems to conserve scarce resources for impending Covid-19 case surges or the care of non-Covid-19 patients.

Olfactory and gustatory dysfunction have recently been found to be associated with Covid-19 infection.[9–12] The growing number of internet searches inquiring about loss of smell strongly correlates with the increased prevalence of Covid-19.[13] In ambulatory populations, patients who present with influenza-like symptoms and anosmia are 6-10 times more likely to test positive for Covid-19 infection.[9,10] Indeed, 59-86% of outpatient Covid-19 positive patients self-reported olfactory loss.[9,10,12] Notably, self-reported anosmia in Covid-19-positive hospitalized patients has also been identified as a common symptom, but is consistently reported at lower rates in this population (5-35%).[11,14,15] Although limited quantitative olfactory data exist in either outpatient or inpatient contexts, early findings in inpatients with Covid-19 suggest that only

28% self-reported smell loss and a minority (25%) demonstrated complete anosmia, despite some degree of measurable olfactory dysfunction in almost all subjects.[11] In contrast, in an outpatient managed cohort of Covid-19 subjects, the self-reported severity and incidence of olfactory dysfunction was high, with most patients reporting a profound and complete loss of smell (0 of 10).[9] Comparing the prevalence of self-reported smell loss between mild or ambulatory cases and moderate to severe inpatient cases of Covid-19 may provide insights into an individual's disease prognosis. This study sought to investigate the association between self-reported anosmia and hospital admission during the course of Covid-19.

Materials and Methods:

Study Design and Population

A retrospective analysis of all adult subjects presenting to the UC San Diego Health System (Jacobs and Hillcrest Medical Centers) with confirmed polymerase chain reaction (PCR)-positive testing for the SARS-CoV-2 viral nucleic acid from nasopharyngeal swabs. Demographic data (Table 1) along with subjective and objective clinical data (Table 2) were obtained from review of electronic medical records (EMR), specifically encounters pertaining to Covid-19 diagnosis. Self-reported sense of smell and taste during time of illness were compared to pre-morbid levels as dichotomous variables (loss of smell/taste vs. normal/baseline). Specifically, we first retrospectively queried the EMR for assessments on olfactory/gustatory function in the encounters related to Covid-19. If self-reported olfactory/gustatory function data was not available in the EMR, we emailed or called patients to inquire about the status of olfactory and gustatory function ("Have you had any smell loss during this period of illness compared to before?" and "Have you had any taste loss during this illness compared to before?"). Chest

radiograph findings were categorized as 'negative' if no findings were present and defined as 'positive' if presence of pulmonary infiltrates and/or pleural effusions were reported on final read by the attending radiologist. This study was approved by the Institutional Review Board of University of California San Diego (IRB #200485).

Statistical Analysis

Statistical analysis was conducted with Stata 15.1 software (StataCorp, College Station, TX). The primary outcome was hospital admission. The secondary outcome was anosmia. Descriptive comparisons stratified by hospital admission and anosmia were conducted using a chi-squared (χ^2) test for categorical data and two-way student's t-test for continuous variables. The threshold for statistical significance was set at $p < 0.05$. Multivariable logistic regression models were built to identify independent patient characteristics associated with hospital admission as the dependent variable. Logistic regression was also performed with anosmia as the dependent variable. Inclusion criteria for factor inclusion in multivariable models were set a priori and included variables with the strongest magnitudes of association and lowest probability of type I error on univariable logistic regression. A maximum of 8 variables were included to minimize potential model overfitting. Given the known colinear relationship between anosmia and dysgeusia, analyses focused on anosmia alone. Similarly, analyses involving decision to admit and decision to obtain a chest radiograph focused on decision to admit; these variables were thus also considered colinear. Although anosmia is not plausibly dependent upon hospital admission, hospital admission was kept in the multivariable model investigating associations with anosmia as a marker for overall disease severity. Distribution medians with interquartile ranges (IQR), odds ratios (OR, univariable logistic regression), adjusted odds ratios (aOR,

multivariable logistic regression), and 95% confidence intervals (CI) were reported with corresponding probabilities of type-I error (p-value).

Results:

Clinical Characteristics

A total of 169 patients tested positive for Covid-19 infection between March 3, 2020 and April 8, 2020. Smell and taste data were available for 128 subjects (75.7%) who were included in the final study cohort. Patients without smell and taste data included those who were deceased (3/169, 1.7%) or intubated (6/169, 3.5%) at the close of data collection, were recently hospitalized with incomplete admission data (4/169, 2.4%), or could not be reached or declined to participate in the study and had no smell or taste information recorded in the medical record (28/169, 16.6%). The demographics and baseline clinical characteristics of the study participants are described in Table 1. Table 2 reports the cohort's subjective and objective clinical findings at presentation.

A total of 26/128 (20.1%) patients were admitted for management of Covid-19. Patients who were admitted were significantly less likely to report anosmia/hyposmia (26.9% vs 66.7%, $p < 0.001$) and dysgeusia (23.1% vs 62.7%, $p<0.001$) than those who were managed outpatient. Beyond the symptoms of anosmia/hyposmia and dysgeusia, age (median 53.5 years [IQR: 40-65] vs 43.0 years [IQR: 34-54], $p=0.009$), diabetes (30.1% vs 5.9%, $p = 0.001$) were associated with admission. Clinical subjective and objective characteristics associated with respiratory failure at the time of presentation were also associated with admission (Table 2). Specifically, admitted patients more frequently reported dyspnea (76.9% vs 43.1%, $p = 0.002$) and sputum production (30.8% vs 11.8%, $p = 0.03$), and exhibited elevated respiratory rate (median 19

[IQR: 18-23] vs 18 [IQR: 16-18], p< 0.001) and body temperature (median 99.8 [IQR: 99.0-101.4] vs 98.6 [IQR: 98.3-99.0], p < 0.001). Both the decision to obtain a chest radiograph (92.3% vs 34.3%, p < 0.001) as well as the presence of positive findings (88.5% vs 14.7%, p < 0.001) were more commonly found in the patients who were ultimately admitted. Further data profiling the admitted cohort, but not applicable to comparisons with an outpatient cohort, is included in Table S1.

Regression Analysis

On univariable logistic regression anosmia/hyposmia was found to be inversely related to hospital admission in Covid-19 patients; patients reporting anosmia/hyposmia were five-fold more likely to be managed in the outpatient setting (OR: 0.20, 95% CI: 0.06-0.64). Other factors associated with hospital admission included age (OR: 1.04, 95% CI: 1.01-1.07), diabetes mellitus (OR: 6.67, 95% CI: 2.06-21.55), dyspnea (OR: 4.39, 95% CI: 1.63-11.86), sputum production (OR: 3.21, 95% CI: 1.81-9.70), temperature (OR: 2.33, 95% CI: 1.52-3.59), heart rate (OR: 1.04, 95% CI: 1.01-1.07), respiratory rate (OR: 1.04, 95% CI: 1.01-1.07), whether chest radiograph was performed (OR: 21.94, 95% CI: 4.90-98.36), and chest radiograph findings positive for infiltrates and/or pleural effusion (OR: 20.91, 95% CI: 4.13-105.81; Table 3, left).

Multivariable logistic regression adjusting for factors associated with admission on univariable analysis demonstrated that self-reported intact olfactory function and positive chest radiograph findings were the only factors independently associated with hospital admission. Notably both smell loss and positive findings on chest radiograph showed clinically significant association strengths. Patients with anosmic/hyposmic Covid-19 were more than ten-fold less likely to be

admitted than those with normosmic Covid-19 (aOR: 0.09, 95% CI: 0.01-0.74). Patients with positive findings on chest radiograph were eight times more likely to be admitted (aOR: 8.01, 95% CI: 1.12-57.49), consistent with an expected clinical indicator of pulmonary disease and potentially impending respiratory failure requiring hospital admission (Table 3, right).

A multivariable analysis of independent predictors of anosmia revealed that anosmia was negatively associated with sputum production (aOR: 0.26, 95%: 0.08-0.91). Hospital admission status was included in the model as a surrogate control for disease severity and, as was demonstrated in the primary analysis, showed a strong inverse relationship to anosmia/hyposmia (aOR: 0.26, 95% CI: 0.07-0.96) (Table 4, right).

Discussion:

Given the rapidly increasing number of Covid-19 cases that threaten to overwhelm healthcare systems, strategies to risk stratify patients and early determination of disease severity are urgently needed. Clinical characteristics associated with critical illness and mortality from Covid-19 have been reported. A meta-analysis of clinical characteristics of over 40,000 Covid-19 patients from Wuhan found that patients with severe disease requiring intensive care were more likely to have comorbidities of hypertension (OR 2.36), respiratory system disease (OR 2.46) and cardiovascular disease (OR 3.42) compared to patient not requiring intensive care.[16] Similar observations were made in Italy, with hypertension and coronary artery disease being more prevalent in the severely ill Covid-19 patients.[17] Of critically ill patients, risk factors for mortality included increased age as a predictor of inpatient death (OR 1.1, or 10% increase with each additional year of age)[18] along with markers of end-organ failure.[17,18]

In addition to investigating markers of critical illness, it is important to consider characteristics that may help stratify mild and moderate infections in early-stage Covid-19. Here we present a novel clinical characteristic to help stratify mild from moderate disease early in SARS-CoV-2 infection. Patients reporting loss of smell were ten times less likely to be admitted for Covid-19 (OR 0.09, 95% CI: 0.01-0.74) compared to those without loss of smell. Furthermore, anosmia/hyposmia was not associated with any other measures typically related to the decision to admit, suggesting that smell loss is truly an independent correlate and may serve as a marker for milder manifestations of Covid-19.

Our study's findings are consistent with those of other studies evaluating both inpatient and outpatient self-reported olfactory dysfunction.[9–12,14,15] Moein and colleagues reported very high rates of measured olfactory dysfunction (98%) on quantitative analysis of Covid-19 inpatients, but only 25% demonstrated complete anosmia and 35% self-reported smell loss.[11] This discrepancy between quantitative and self-reported olfactory dysfunction is thought to be related to a general unawareness or under-reporting of hyposmia.[19] In the Covid-19 inpatient population, decreased awareness of chemosensory dysfunction may also be influenced by the presence of more severe symptoms such as respiratory distress. Despite this mismatch, we believe that our study's findings differentiating the incidence of smell loss between Covid-19 inpatients and outpatients are valuable, as self-reported loss may more closely reflect profound or functional anosmia. While the present study did not specifically investigate degree of smell loss, our previous study demonstrated that those who reported smell loss typically suffered from its complete absence (0 out of 10 on a 0-10 scale).[9] Although quantitative testing is more sensitive in detecting olfactory dysfunction, self-reporting of anosmia is relatively accurate (90%).[19] Thus, our study suggests that milder cases of Covid-19 may be heralded by profound

anosmia and higher self-reporting, compared to the undetected or mild hyposmia associated with moderate to severe Covid-19 cases. Further objective olfactory testing of both outpatient and inpatient cohorts is required to clarify if quantitative differences in the severity of olfactory dysfunction correlate with differences in self-reported loss.

Assessment of smell may not only aid in the diagnosis of Covid-19 infection during pre-test screening, but also help guide the post-test triaging of patients at all levels. Patients with influenza-like symptoms concerning for Covid-19 infection but without anosmia should be more vigilant and present earlier for evaluation and management. Although in this particular study, we did not ask subjects the timing of smell loss onset in relationship to their other symptoms, it has previously been shown that 33-60% of anosmic Covid-19 patients reported smell loss either before or at the same time of other symptoms.[9,12,15] Of the self-reported anosmic/hyposmic inpatients, 12 of 20 (60%) noted onset of smell loss prior to admission while 91% experienced taste loss before admission, which we suspect may be a profound anosmia impairing the odorant component of flavor.[15] Furthermore, epidemiologic studies found that the average time from symptom onset to admission was 11 days.[18] This data, taken together, suggest that profound anosmia is a relatively early manifestation while admission tends to occur relatively late in the disease process. Although smell loss may not yet be manifested for all patients at the time of their evaluation by a healthcare professional, it still may be a useful early indicator in the majority of patients. If the findings reported here remain consistent in independent cohorts, anosmia/hyposmia could be considered as a clinical marker inversely related to disease severity. As such, anosmia/hyposmia could be included in the clinical assessment of disease severity and potentially aid in the allocation of limited medical interventions. Just as APGAR scores are an effective means to rapidly assess and triage at-risk newborns,[20] a future Covid-19

risk stratification model may have a potential to improve resource allocation and thereby save lives. Further research is needed to shed light on clinical findings, upon which a model based on disease severity as shown in Figure 1 could be built. While the presented hypothetical model is not intended to substitute for nuanced, patient driven clinical decision making, it may in the future serve as a general model to organize decision making and risk stratification. Further study and validation of all risk factors will evolve as the pandemic progresses, but anosmia is emerging early as an important clinical component of both Covid-19 diagnosis and potentially outcome as well.

Beyond the immediate practical applications of anosmia in addressing the pandemic, these findings potentially hint at some characteristics of the pathophysiology of the infection. The site and dosage of the initial viral burden, along with the effectiveness of the host immune response are all potentially important variables in determining the spread of the virus within an individual and ultimately the clinical course of infection. A focused, small upper airway SARS-CoV-2 viral load may be associated with a less fulminant infection, decreasing the risk of overwhelming the host immune response and subsequently, decreasing the risk of respiratory failure and hospitalization. This hypothesis, is in essence the concept underlying live vaccinations, where low dosage and distant site of inoculation generates an immune response without provoking a severe infection.[21]

Similarly, anosmia may be a biomarker of the magnitude of a host's innate immune response to SARS-CoV-2 infection. Although the mechanism of olfactory loss remains unclear, radiographic imaging of a single case of isolated anosmia and Covid-19 infection shows bilateral olfactory cleft obstruction consistent with local inflammation.[22] This finding may be consistent with a

greater local immune response in the infection of patients presenting with anosmia leading to an olfactory loss secondary to local infection and edema and perhaps a milder overall clinical course. Indeed, early, pre-peer review analyses of transcriptome data suggest that the candidate receptors mediating cellular entry of SARS-CoV-2, ACE2 and TMPRSS2, are expressed on olfactory epithelial support cells and not on olfactory sensory neurons.[23,24] Taken together, data demonstrating that SARS-CoV2 infects olfactory epithelia and causes highly localized inflammation of the olfactory cleft suggest that Covid-19-related olfactory dysfunction may result in a conductive olfactory loss. Such a phenomenon would be consistent with relatively rapid recovery of olfactory function with the resolution of viral infection in most patients, consistent with previously reported clinical findings.[9] In addition, these preliminary findings may be consistent with a greater local immune response in patients presenting with anosmia that may be indicative of a milder overall clinical course. The inverse association of anosmia and sputum production (OR 0.26) in the present study suggest that anosmic Covid-19 are less likely to have a symptom associated with more severe lower airway inflammatory response. While these are tantalizing hypotheses of the underlying pathophysiology currently only supported by piecemeal, circumstantial molecular and clinical findings, significant investigations into SARS-CoV-2 infection of airway mucosa and the host immune response are required to begin elucidating the underlying pathophysiology of the present study's clinical observations.

Additionally, further studies are warranted to validate our clinical findings. Limitations include the use of self-reported anosmia/hyposmia, particularly in those who reported anosmia after being informed of Covid-19 diagnosis. This group is most susceptible to recall bias. Therefore, findings herein and elsewhere based on self-reported anosmia after Covid-19 diagnosis should be validated in future studies with quantitative testing of olfaction. In other disease processes

there is discrepancy between self-reported anosmia and measured anosmia.[25] Furthermore, the design of the questions posed to the subjects in this particular study did not specifically assess the severity of smell loss, but only if there was a loss of smell during their illness. Thus, in this analysis, we cannot draw a distinction between hyposmia and anosmia. However, our prior study did assess severity of smell loss and those who reported smell loss typically recalled complete functional anosmia.[9] Our study has also achieved a higher response rate from ambulatory Covid-19 patients, some of whom were unable to be evaluated for olfactory function due to their clinical status. As a result, our data does not inform any potential relationship between anosmia and critical illness requiring intensive care monitoring and intubation, or mortality. Notwithstanding these limitations, in the absence of objective olfactory testing, self-reported anosmia retains robust associations with specific Covid-19-related disease features.

Our report is among the minority of reports focusing on mild to moderate Covid-19 in which we attempt to elucidate clinical features to differentiate between patients with mild disease who could be managed at home and 'moderately' sick patients who require admission and may be at risk of further clinical deterioration. Prospective studies are required to better determine the extent to which anosmia informs overall disease trajectory. Most early data have focused on severely ill patients[16–18], but as the pandemic approaches plateau and eventually passes its peak, the clinical characteristics of the moderately sick patient are important to identify and administer early intervention before a subset succumbs to critical, potentially fatal infection. Further research is required to validate the association between olfactory function and hospitalization risk in patients with Covid-19, which may include prospective, longitudinal, and larger multi-institutional studies.

Conclusion:

The current study has identified a strong inverse association between Covid-19-related anosmia and a critical branch point in management of Covid-19: the decision to commit to hospital admission. Patients admitted for Covid-19 were ten times less likely to report anosmia. These findings have important immediate practical applications to the lay public as well as healthcare workers and healthcare systems looking to efficiently risk stratify patients to efficiently provide appropriate medical and non-medical interventions. The association between olfactory dysfunction and clinical outcomes also carries important implications for future investigations seeking to understand the ability of SARS-CoV-2 virus to overwhelm the host immune response.

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Tables and legends:

Table 1: Baseline characteristics. Comparison of demographic and baseline clinical characteristics in admitted and ambulatory Covid-19-positive subjects.

	Variable		Covid19-positive Admitted n=26 n (%)	Covid19-positive Ambulatory n=102 n (%)	p-value*
Baseline characteristics	Age, years	Median (IQR)**	53.5 (40-65)	43 (34-54)	0.0093
	Gender	Male	9 (34.6)	52 (51)	0.14
		Female	17 (65.4)	50 (49)	
	Race	White	8 (30.8)	50 (49)	0.29
		Black	3 (11.5)	5 (4.9)	
		Hispanic	7 (26.9)	21 (20.6)	
		Asian	4 (15.4)	7 (6.9)	
		Other/mixed	4 (15.4)	13 (12.8)	
		Unknown/missing	0	6 (5.9)	
	BMI (kg/m2)	Median (IQR)**	28.4 (25.7-31.2)	25.9 (23.1-29.7)	0.11
	Tobacco use	Never smoker	22 (84.6)	79 (77.5)	0.87
		Current/recent smoker	4 (15.4)	13 (12.8)	
		Unknown/missing	0	10 (9.8)	
Past medical history	Hypertension	No	19 (73.1)	81 (79.4)	0.18
		Yes	7 (26.9)	15 (14.7)	
		Unknown/missing	0	6 (5.9)	
	Diabetes mellitus	No	18 (69.2)	90 (88.2)	0.001
		Yes	8 (30.8)	6 (5.9)	
		Unknown/missing	0	6 (5.9)	
	COPD	No	26 (100)	92 (90.2)	0.29
		Yes	0	4 (3.9)	

		Unknown/missing	0	6 (5.9)	
	Asthma	No	23 (88.5)	86 (84.3)	0.87
		Yes	3 (11.5)	10 (9.8)	
		Unknown/missing	0	6 (5.9)	
	Sinusitis***	No	26 (100)	91 (89.2)	0.24
		Yes	0	5 (4.9)	
		Unknown/missing	0	6 (5.9)	
	Cardiovascular disease	No	23 (88.5)	91 (89.2)	0.25
		Yes	3 (11.5)	5 (4.9)	
		Unknown/missing	0	6 (5.9)	
	Chronic kidney disease	No	24 (92.3)	94 (92.2)	0.15
		Yes	2 (7.7)	2(2.0)	
		Unknown/missing	0	6 (5.9)	
	Cancer	No	25 (96.2)	91 (89.2)	0.78
		Yes	1 (3.8)	5 (4.9)	
		Unknown/missing	0	6 (5.9)	
	HIV/other immunosuppression	No	24 (92.3)	82 (80.4)	0.41
		Yes	2 (7.7)	13 (12.8)	
		Unknown/missing	0	7 (6.9)	
	Obstructive sleep apnea	No	25 (96.2)	93 (91.2)	0.86
		Yes	1 (3.8)	3 (2.9)	
		Unknown/missing	0	6 (5.9)	
	Stroke	No	23 (88.5)	96 (94.1)	0.001
		Yes	3 (11.5)	0	
		Unknown/missing	0	6 (5.9)	

Notes:

*p-values determined by chi-square test unless otherwise specified, unknowns excluded in statistical testing

**student's two-way t-test

***chronic rhinosinusitis or currently experiencing acute episode of rhinosinusitis

Table 2: Covid-19-associated clinical findings. Comparison of subjective and objective clinical findings in admitted and ambulatory Covid-19-positive subjects.

	Variable		Covid19-positive Admitted n=26 n (%)	Covid19-positive Ambulatory n=102 n (%)	p-value*
Subjective clinical findings	Days symptomatic prior to Covid-19 test	Median (IQR)**	4 (2-7)	5.5 (3-8)	0.39
	Anosmia/hyposmia	No	19 (73.1)	34 (33.3)	<0.001
		Yes	7 (26.9)	68 (66.7)	
	Dysgeusia	No	19 (73.1)	31 (30.4)	<0.001
		Yes	6 (23.1)	64 (62.7)	
		Unknown/missing	1 (3.8)	7 (6.9)	
	Fatigue	No	5 (19.2)	33 (32.4)	0.19
		Yes	21 (80.8)	69 (67.6)	
	Diarrhea	No	12 (46.2)	68 (66.7)	0.054
		Yes	14 (53.8)	34 (33.3)	
	Fever	No	4 (15.4)	34 (33.3)	0.074
		Yes	22 (84.6)	68 (66.7)	
	Cough	No	1 (3.8)	15 (14.7)	0.14
		Yes	25 (96.2)	87 (85.3)	
	Dyspnea	No	6 (23.1)	58 (56.9)	0.002
		Yes	20 (76.9)	44 (43.1)	
	Sputum production	No	11 (42.3)	53 (51.9)	0.03
		Yes	8 (30.8)	12 (11.8)	
		Unknown/missing	7 (26.9)	37 (36.3)	
	Sore throat	No	17 (65.4)	56 (54.9)	0.34
		Yes	9 (34.6)	46 (45.1)	

	Headache	No	13 (50.0)	53 (51.9)	0.86
		Yes	13 (50.0)	49 (48.1)	
	Rhinorrhea	No	25 (96.2)	86 (84.3)	0.11
		Yes	1 (3.8)	16 (15.7)	
	Nasal obstruction/thick discharge	No	22 (84.6)	71 (69.6)	0.13
		Yes	4 (15.4)	31 (30.4)	
Objective clinical findings	Temperature	Median (IQR)**	99.8 (99-101.4)	98.6 (98.3-99)	<0.001
	Heart rate	Median (IQR)**	95.5 (83-106)	83 (75-96)	0.004
	Respiratory rate	Median (IQR)**	19 (18-23)	18 (16-18)	<0.001
	Blood oxygen saturation	Median (IQR)**	96 (94-98)	98 (95-100)	0.77
	Total leukocyte count	Median (IQR)**	6.5 (5.7-9.4)	4.9 (3-5.4)	0.012
	Lymphocyte count	Median (IQR)**	1.1 (0.6-13)	1.8 (0.9-24)	0.41
	Serum creatinine	Median (IQR)**	0.8 (0.6-1.0)	0.9 (0.8-0.9)	0.34
	Serum AST	Median (IQR)**	44 (28-68)	34 (27-51)	0.14
	Serum ALT	Median (IQR)**	32 (20-82)	31 (23-44)	0.15
	Serum lactate	Median (IQR)**	1.9 (1.5-2.2)	1.4 (1.1-1.9)	0.43
	Chest Radiograph performed	No	2 (7.7)	64 (62.7)	<0.001
		Yes	24 (92.3)	35 (34.3)	
		Unknown/missing	0	3 (2.9)	
	Chest Radiograph findings***	Negative	2 (7.7)	20 (19.6)	<0.001
		Positive	23 (88.5)	15 (14.7)	
		No chest radiograph	1 (3.8)	67 (65.7)	

Notes:

*p-values determined by chi-square test, unless otherwise specified, unknowns excluded in statistical test

**ttest

***positive findings include pulmonary infiltrates and/or pleural effusion

Table 3: Clinical characteristics associated with admission for Covid-19. Associations of baseline demographics and clinical findings of Covid-19 individuals with hospital admission were determined using univariable (reporting odds ratios) and multivariable (reporting adjusted odds ratios) logistic regression models. Abbreviations: OR, odds ratio; aOR, adjusted odds ratio.

	Dependent variable: admission	Univariable Regression OR (95% CI)	p-value	Multivariable Regression aOR (95% CI)	p-value
Baseline characteristics	Age, years	1.04 (1.01-1.07)	0.012	0.97 (0.90-1.04)	0.39
	Sex, Male (ref: Female)	1.96 (0.80-4.81)	0.14		
	Race (ref: White)	1.17 (0.92-1.48)	0.2		
	BMI (kg/m2)	1.07 (0.98-1.17)	0.11		
	Tobacco use	1.10 (0.33-3.73)	0.87		
Past medical history	Hypertension	1.99 (0.71-5.56)	0.19		
	Diabetes mellitus	6.67 (2.06-21.55)	0.002	4.23 (0.34-52.52)	0.26
	COPD	--	--		
	Asthma	1.12 (0.29-4.41)	0.87		
	Sinusitis	--	--		
	Cardiovascular disease	2.37 (0.53-10.67)	0.26		
	Chronic kidney disease	3.92 (0.52-29.25)	0.18		
	Cancer	0.73 (0.08-6.52)	0.78		
	HIV/other immunosuppression	0.53 (0.11-2.49)	0.42		
	Obstructive sleep apnea	1.24 (0.12-12.44)	0.86		
	Stroke	--	--		
Subjective clinical findings	Anosmia/Hyposmia	0.20 (0.06-0.64)	0.007	0.09 (0.01-0.74)	0.025
	Fatigue	2.01 (0.70-5.80)	0.19		
	Diarrhea	2.33 (0.97-5.59)	0.057		
	Fever	2.75 (0.88-8.62)	0.083		

	Cough	4.31 (0.54-34.25)	0.17		
	Dyspnea	4.39 (1.63-11.86)	0.003	0.49 (0.08-3.13)	0.45
	Sputum production	3.21 (1.81-9.70)	0.039		
	Sore throat	0.64 (0.26-1.58)	0.34		
	Headache	1.08 (0.46-2.56)	0.86		
	Rhinorrhea	0.22 (0.03-1.70)	0.15		
	Nasal obstruction/thick discharge	0.42 (0.13-1.30)	0.13		
Objective clinical findings	Temperature	2.33 (1.52-3.59)	<0.001	2.40 (0.95-6.05)	0.063
	Heart rate	1.04 (1.01-1.07)	0.007	0.96 (0.90-1.04)	0.35
	Respiratory rate	1.46 (1.16-1.86)	0.002	1.34 (0.95-1.88)	0.09
	Blood oxygen saturation	0.99 (0.95-1.04)	0.77		
	Total leukocyte count	1.50 (1.06-2.14)	0.023		
	Lymphocyte count	0.98 (0.93-1.03)	0.41		
	Serum creatinine	0.45 (0.09-2.33)	0.34		
	Serum AST	1.02 (0.99-1.05)	0.16		
	Serum ALT	1.02 (0.99-1.04)	0.18		
	Serum lactate	5.41 (0.26-111.36)	0.27		
	Chest Radiograph performed	21.94 (4.90-98.36)	<0.001		
	Chest Radiograph findings	20.91 (4.13-105.81)	<0.001	8.01 (1.12-57.49)	0.039

Table 4: Clinical characteristics associated with Covid-19-associated anosmia.

Associations of baseline demographics and clinical findings of Covid-19 subjects with anosmia were determined using univariable (reporting odds ratios) and multivariable (reporting adjusted odds ratios) logistic regression models.

	Dependent variable: Anosmia	Univariable Regression OR (95% CI)	p-value	Multivariable Regression aOR (95% CI)	p-value
Baseline characteristics	Age, years	0.97 (0.95-0.99)	0.017	0.99 (0.96-1.03)	0.75
	Sex, ref: Female	0.75 (0.37-1.51)	0.42		
	Race, ref: White	0.93 (0.76-1.14)	0.47		
	BMI (kg/m2)	1.03 (0.95-1.11)	0.52		
	Tobacco use	1.06 (0.37-3.01)	0.91		
	Admission	0.18 (0.07-0.48)	0.001	0.26 (0.07-0.96)	0.043
Past medical history	Hypertension	0.44 (0.17-1.13)	0.09		
	Diabetes mellitus	0.52 (0.17-1.59)	0.25		
	COPD	0.24 (0.02-2.34)	0.22		
	Asthma	1.21 (0.37-3.95)	0.75		
	Sinusitis	3.09 (0.34-25.50)	0.32		
	Cardiovascular disease	1.26 (0.29-5.51)	0.76		
	Chronic kidney disease	0.24 (0.02-2.34)	0.22		
	Cancer	1.52 (0.27-8.60)	0.78		
	HIV/other immunosuppression	0.62 (0.21-1.84)	0.39		
	Obstructive sleep apnea	0.74 (0.10-5.39)	0.76		
	Stroke	0.36 (0.03-4.11)	0.41		
Subjective clinical findings	Fatigue	0.55 (0.25-1.23)	0.15		
	Diarrhea	0.65 (0.32-1.35)	0.25		
	Fever	0.55 (0.25-1.23)	0.15		
	Cough	0.83 (0.28-2.44)	0.74		

	Dyspnea	0.82 (0.41-1.67)	0.59		
	Sputum production	0.26 (0.08-0.80)	0.019	0.26 (0.08-0.91)	0.034
	Sore throat	1.11 (0.54-2.26)	0.78		
	Headache	1.43 (0.70-2.87)	0.34		
	Rhinorrhea	1.01 (0.36-2.85)	0.98		
	Nasal obstruction/thick discharge	2.59 (1.10-6.13)	0.03	2.44 (0.16-7.89)	0.14
Objective clinical findings	Temperature	0.73 (0.52-1.04)	0.08		
	Heart rate	0.98 (0.96-1.01)	0.15		
	Respiratory rate	0.88 (0.75-1.02)	0.08		
	Blood oxygen saturation	0.99 (0.94-1.04)	0.62		
	Total leukocyte count	0.87 (0.69-1.10)	0.24		
	Lymphocyte count	0.99 (0.94-1.04)	0.75		
	Serum creatinine	0.34 (0.04-2.62)	0.30		
	Serum AST	1.01 (0.98-1.03)	0.63		
	Serum ALT	1.00 (0.99-1.01)	0.98		
	Serum lactate	0.42 (0.08-2.07)	0.29		
	Chest Radiograph performed	0.45 (0.22-0.93)	0.03		
	Chest Radiograph findings	0.38 (0.13-1.14)	0.08		

Figure caption:

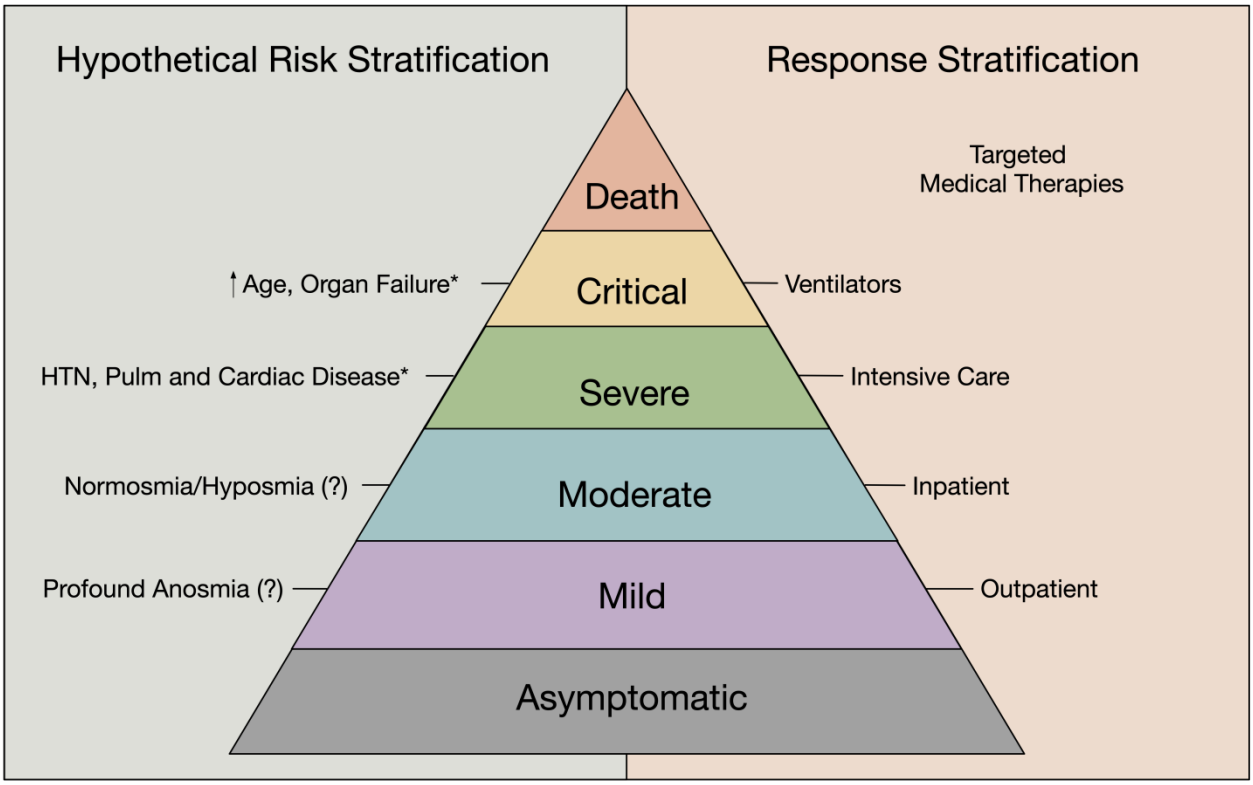

Figure 1: Presentation of a hypothetical model suggesting that effective risk and response stratification of all levels of Covid-19 disease severity may assist in efficient allocation of limited resources. *Risk factors for severe and critical disease based on early reports on the Covid-19 pandemic (references 16-18).

Supplemental materials:

Table S1: Characteristics of admitted Covid-19 patients

Variable		Covid19-positive Admitted n=26 n (%)
Remdesivir	No	13 (50.0)
	Yes	7 (26.9)
	Unknown/missing	6 (23.1)
Hydroxychloroquine	No	12 (46.2)
	Yes	1 (3.8)
	Unknown/missing	13 (50.0)
Vasopressors	No	10 (38.5)
	Yes	7 (26.9)
	Unknown/missing	9 (34.6)
Antibiotics	No	5 (19.2)
	Yes	17 (65.4)
	Unknown/missing	4 (15.4)
Intubation/Mechanical vent	No	17 (65.4)
	Yes	9 (34.6)
Disposition	Death	1 (3.8)
	Intensive care	4 (15.4)
	Ward	7 (26.9)
	Discharged	13 (50.0)
	Outpatient	1 (3.8)
	Unknown/missing	0