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More than 50 Long-term effects of COVID-19:

a systematic review and meta-analysis

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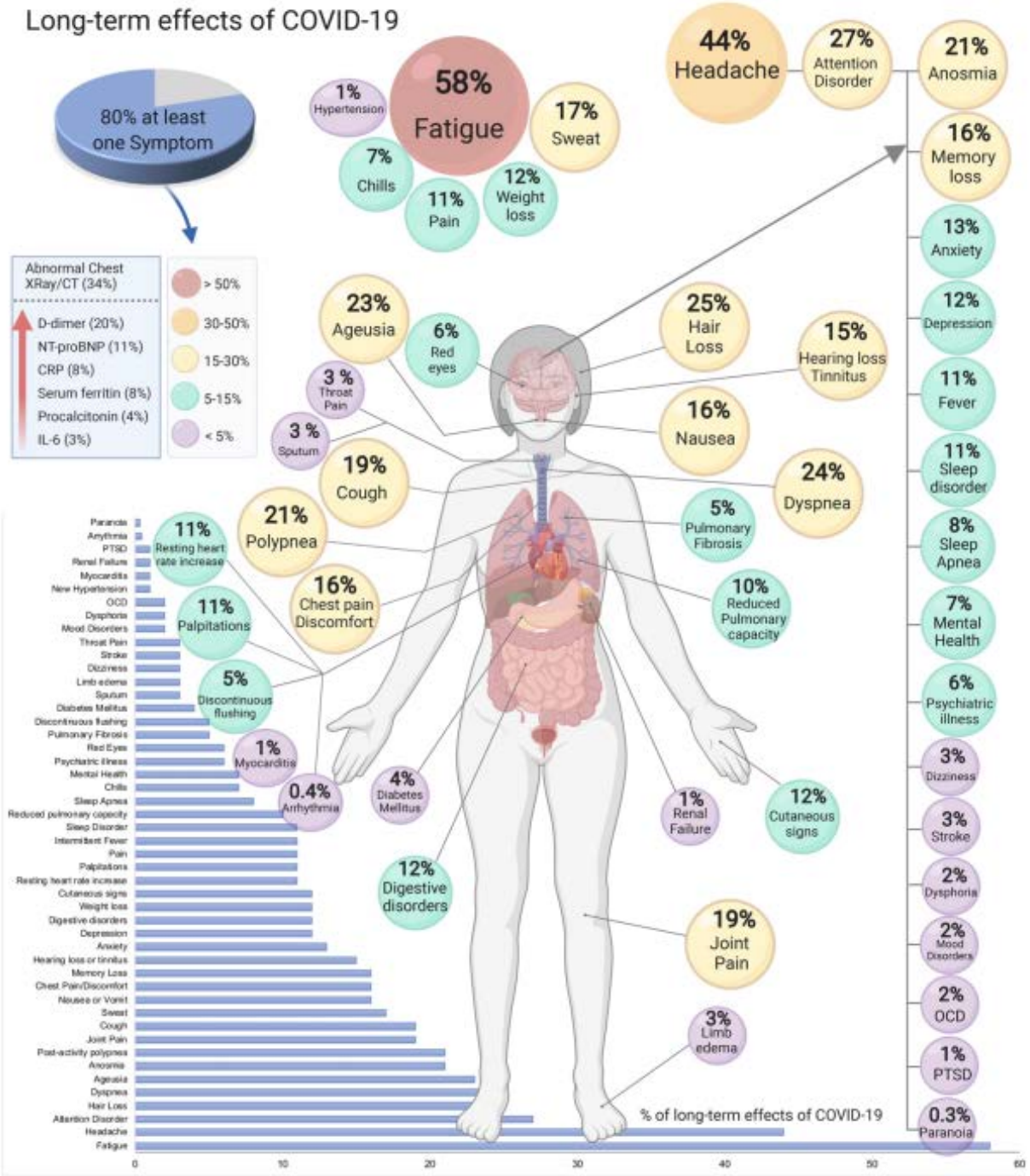
Long-term effects of COVID-19
80% at least one Symptom
Abnormal Chest XRay/CT (34%)
D-dimer (20%)
NT-proBNP (11%)
CRP (8%)
Serum ferritin (8%)
Procalcitonin (4%)
IL-6 (3%)
> 50%
30-50%
15-30%
5-15%
< 5%
1% Hypertension
58% Fatigue
17% Sweat
7% Chills
11% Pain
12% Weight loss
44% Headache
27% Attention Disorder
21% Anosmia
16% Memory loss
13% Anxiety
12% Depression
11% Fever
11% Sleep disorder
8% Sleep Apnea
7% Mental Health
6% Psychiatric illness
3% Dizziness
3% Stroke
2% Dysphoria
2% Mood Disorders
2% OCD
1% PTSD
0.3% Paranoia
23% Ageusia
6% Red eyes
3 % Throat Pain
3 % Sputum
19% Cough
21% Polypnea
16% Chest pain Discomfort
11% Palpitations
5% Discontinuous flushing
1% Myocarditis
0.4% Arrhythmia
11% Resting heart rate increase
25% Hair Loss
15% Hearing loss Tinnitus
16% Nausea
24% Dyspnea
5% Pulmonary Fibrosis
10% Reduced Pulmonary capacity
4% Diabetes Mellitus
1% Renal Failure
12% Cutaneous signs
12% Digestive disorders
19% Joint Pain
3% Limb edema
Paranoia
Arrythmia
PTSD
Renal Failure
Myocarditis
New Hypertension
OCD
Dysphoria
Mood Disorders
Throat Pain
Stroke
Dizziness
Limb edema
Sputum
Diabetes Mellitus
Discontinuous flushing
Pulmonary Fibrosis
Red Eyes
Psychiatric illness
Mental Health
Chills
Sleep Apnea
Reduced pulmonary capacity
Sleep Disorder
Intermittent Fever
Pain
Palpitations
Resting heart rate increase
Cutaneous signs
Weight loss
Digestive disorders
Depression
Anxiety
Hearing loss or tinnitus
Memory Loss
Chest Pain/Discomfort
Nausea or Vomit
Sweat
Cough
Joint Pain
Post-activity polypnea
Anosmia
Ageusia
Dyspnea
Hair Loss
Attention Disorder
Headache
Fatigue
0
10
20
30
40
50
60
% of long-term effects of COVID-19

Where are we? Therapeutics

Good Quality Evidence

In favor

- **Monoclonal Antibodies vs S-protein**
- **Remdesivir**
- **Dexamethasone**
- **Anticoagulation**
- **Proning**

Against:

Lopinavir/rito

Hydroxychloroquine

Azithromycin

Low Quality or Mixed Evidence

- Convalescent Plasma
- IL-6 inhibitors (Tocilizumab, Sarilumab)
- Baricitinib
- Favipiravir/Umifenovir
- Ivermectin
- Fluvoxamine
- Hyper immune IG
- Interferon beta-1-a
- Dipiridamole
- Sitagliptine

Tocilizumab, una de cal y otra de arena

REMAP-CAP (IL-6 Receptor Inhibitor Arm)

- Design: International, multifactorial, adaptive platform trial
- Analysis of IL-6 receptor inhibitor (Tocilizumab 8mg/kg vs Sarilumab 400mg vs SOC) (open label)

  (93.3% received Steroids, 29.9% 2nd dose of Toci)

  Inclusion: 24h of commencing organ support in ICU COVID+ patients
  (28.8% HFNC, 41.5% NIV, 29,5% MechVent)
- Primary Model: ordinal scale combining in-hosp. Mortality and days free of organ support at 21d
- Enrollment: 353 Toci, 48 Sari, 402 SOC

Preprint doi: https://doi.org/10.1101/2021.01.07.21249390

REMAP-CAP

Intervention	Support Free Days (Hospital Mortality)	Odds ratio for support free days	Odds Ratio for Hospital Survival
Tocilizumab	10 days (28%)	1.64 (1.25-2.14)	1.64 (1.14-2.35)
Sarilumab	11 days (22.2%)	1.76 (1.17.2.91)	2.01 (1.18-4.71)
Standard of Care	0 days (35.8%)	Ref.	Ref.

Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial

Viviane C Veiga,[1,2] João A G G Prats,[1] Danielle L C Farias,[1] Regis G Rosa,[2,3] Leticia K Dourado,[4]

- RCT 1:1 Tocilizumab 8mg/kg
- Inclusion: 18y, SARSCoV2 RTPCR+, pulmonary infiltrates,
  Supplemental O2 or Mech Vent (<24h)
  Increased Markers (at least 2: D-dimer, Ferritin, DHL, CRP)
- Primary Outcome: Clinical Status at 15 days (several other secondary outcomes)
- Enrolled: 129 (65 Toci, 64 SOC)
- **Study stopped by DSMB: increased number of deaths in the TOCI arm at 15 days**

Cite this as: *BMJ* 2021;372:n84
http://dx.doi.org/10.1136/bmj.n84

Accepted: 11 January 2021

Table 1 | Baseline characteristics of patients with severe or critical coronavirus disease 2019 and assigned to tocilizumab plus standard care or standard care alone. Values are numbers (percentages) unless stated otherwise

Characteristics	Tocilizumab group (n=65)	Control group (n=64)
Mean (SD) age (years)	57.4 (15.7)	57.5 (13.5)
Men	44 (68)	44 (69)
Mean (SD) days from symptom onset to randomisation	10.0 (3.1)	9.5 (3.0)
Comorbidities:		
Hypertension	30 (46)	34 (53)
Diabetes	22 (34)	20 (31)
Obesity	15 (23)	16 (25)
Heart failure	4 (6)	3 (5)
Myocardial infarction	4 (6)	3 (5)
Chronic obstructive pulmonary disease	2 (3)	2 (3)
Asthma	4 (6)	1 (2)
Chronic kidney disease	5 (8)	1 (2)
Solid malignancy	4 (6)	5 (8)
Haematological malignancy	1 (1)	0 (0)
Previous drug use		
Clinical status on seven level ordinal scale:		
4: Admitted to hospital, receiving supplemental oxygen	39 (60)	28 (44)
5: Admitted to hospital, receiving non-invasive ventilation or high flow oxygen through nasal cannula	15 (23)	26 (41)
6: Admitted to hospital, receiving mechanical ventilation	11 (17)	10 (16)

Table 2 | Primary and secondary outcomes. Values are numbers (percentages) unless stated otherwise

Outcomes	Tocilizumab group (n=65)	Control group (n=64)	Effect estimate	Effect size (95% CI)	P value
Primary endpoint					
Receiving mechanical ventilation or died at day 15*	18 (28)	13 (20)	Odds ratio 1-5 *v* 6-7	1.54 (0.66 to 3.66)	0.32
Secondary endpoints					
Mortality up to 28 days	14 (21)	6 (9)	Odds ratio	2.70 (0.97 to 8.35)	0.07
In-hospital mortality	14 (21)	6 (9)	Odds ratio	2.70 (0.97 to 8.35)	0.02
Mean (SD) SOFA score:					
Day 8	4.1 (3.9)	3.4 (3.0)	Mean ratio	1.20 (0.87 to 1.64)	0.26
Day 15	4.3 (3.6)	4.3 (3.6)	Mean ratio	0.99 (0.65 to 1.49)	0.95

NIH | COVID-19 Treatment Guidelines

For patients who are within 24 hours of admission to the intensive care unit (ICU) and require invasive or noninvasive mechanical ventilation or high-flow oxygen (>0.4 FiO_2/30 L/min oxygen flow), there are insufficient data to recommend either for or against the use of tocilizumab or sarilumab for the treatment of COVID-19.

For patients who do not require ICU-level care or are admitted to the ICU but do not meet the above criteria, the Panel **recommends against** the use of **tocilizumab** or **sarilumab** for the treatment of COVID-19, except in a clinical trial **(BIIa)**.

https://www.covid19treatmentguidelines.nih.gov/whats-new/

¿Es la combinación de dos monoclonales capaz de disminuir las hospitalizaciones en COVID leve a moderardo?

Blaze 1: Bamlanivimab vs. Bam+Etesenimab vs. Placebo in **Mild to Moderate** COVID-19

- 5 arm Double Blind, Study n=613, PCR+ plus 1 mild-mod symptoms <3d of their PCR test
- Primary End Point: Viral load at day 11
- Secondary End Points: VL at other time points, Symptom and Cliical Outcome (hospitalization)

Study Arm	Viral Load day 11	Hospitalization (%)
Bam 700mg	-3.72	1.0%
Bam 2800mg	-4.08	1.9%
Bam 7000mg	-3.49	2.0%
Bam 2800mg+Etesenimab 2800mg	-4.37	0.9%
Placebo	-3.80	5.8%

JAMA Published online Jan 21 2021

THE EFFECTIVENESS OF THE FIRST DOSE OF BNT162b2 VACCINE IN REDUCING SARS-CoV-2 INFECTION 13-24 DAYS AFTER IMMUNIZATION: REAL-WORLD EVIDENCE

Gabriel Chodick, PhD[1,2] *, Lilac Tene, MSc [1], Tal Patalon, MD[1], Sivan Gazit, MD[1], Amir Ben Tov, MD [1], Dani Cohen [#], PhD [2], Khitam Muhsen, PhD[# 2]

Findings

Data of 503,875 individuals (mean age 59·7 years SD=14·7, 47·8% males) were analysed, of whom 351,897 had 13-24 days of follow-up. The cumulative incidence of SARS-CoV-2 relative risk reduction (RRR) was calculated in weighted-average daily incidence of SARS-CoV-2 infection from 43·41-per-100,000(SE=12·07) in days 1-12 to 21·08-per-100,000(SE=6·16) in days 13-24 following immunization

A 51.45 RRR in days 13-24 after 1st dose compared to 1-12 d post-1st dose

medRxiv preprint doi: https://doi.org/10.1101/2021.01.27.21250612;

Title: Decreased SARS-CoV-2 viral load following vaccination

Matan Levine-Tiefenbrun[1,*], Idan Yelin[1,*,+], Rachel Katz[2], Esma Herzel[2], Ziv Golan[3], Licita Schreiber[3], Tamar Wolf[3], Varda Nadler[3], Amir Ben-Tov[2,4], Jacob Kuint[2,4], Sivan Gazit[2], Tal Patalon[2], Gabriel Chodick[2,4], Roy Kishony[1,5,+]

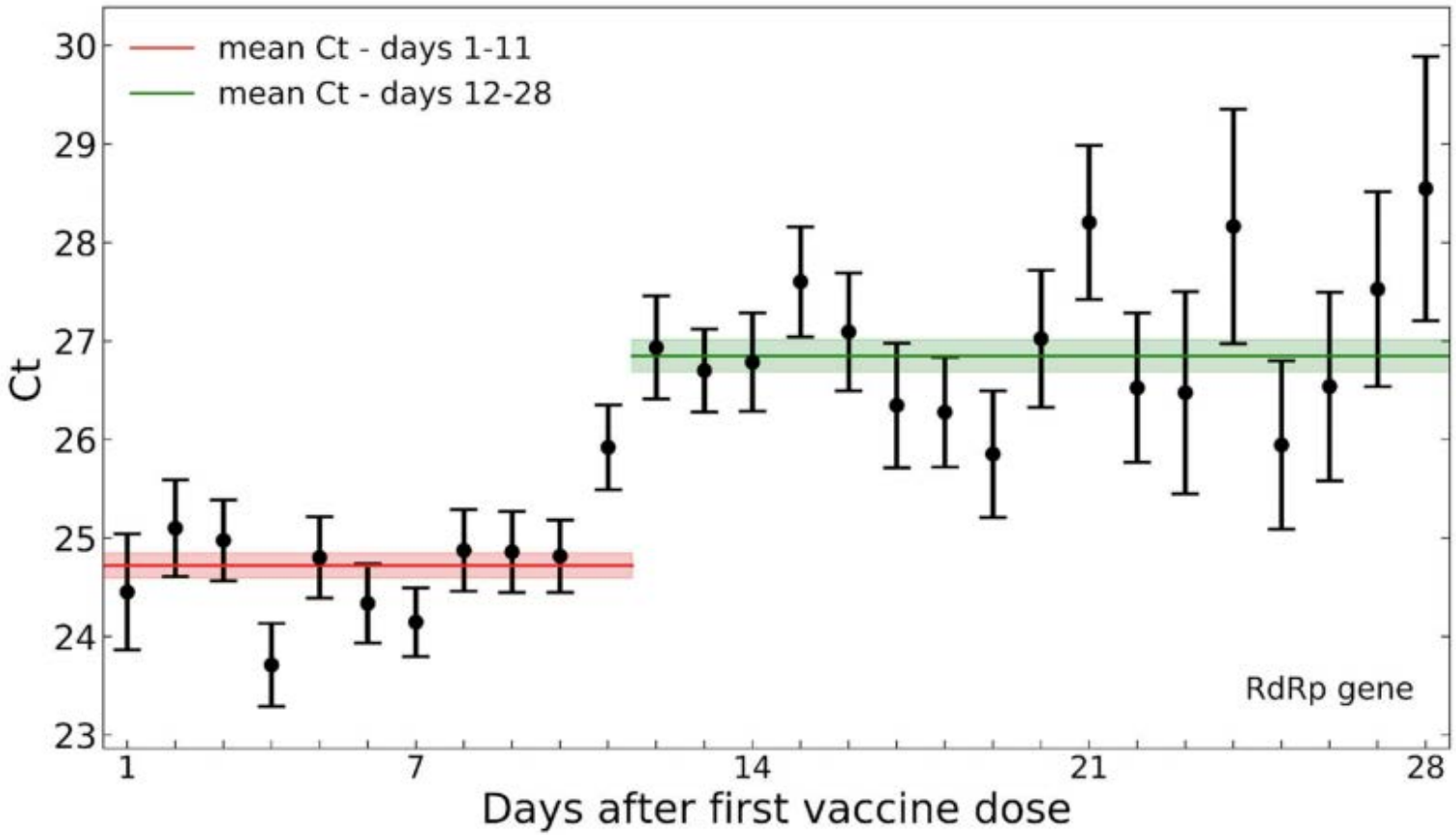

Figure 1. Decreased SARS-CoV-2 viral load after 12 days post-vaccination. Mean Ct values of the RdRp gene for positive tests following vaccination are plotted by the post-vaccination day in which the sample was taken. Error bars indicate the standard error of the mean. For gene E and N see Extended Data Fig. 1.

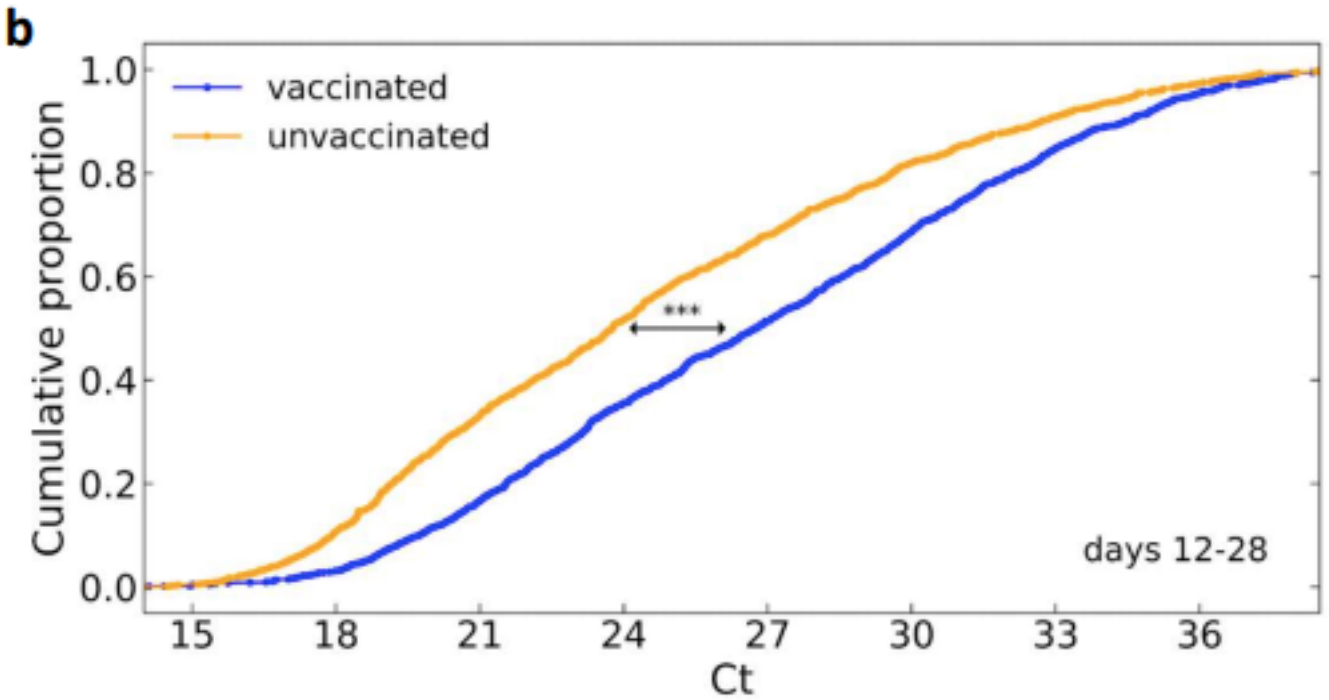

Figure 2. Comparison of SARS-CoV-2 viral loads among vaccinated and unvaccinated patients. a-b, The distribution of Ct values of the RdRp gene as determined for positive samples taken 1-11 days post-vaccination (a, n=1,755, blue) and 12-28 days post-vaccination (b, n=1,142, blue) with their respective demographically-matched control groups (orange, *** - P-value < 10^{-8}, Mann-Whitney). **c,** Coefficient for the association of Ct of the RdRp gene with

Prospective cohort of fluvoxamine for early treatment of COVID-19

David Seftel MD [1,2], David R Boulware MD MPH [3]

Abstract:

We report a real-world experience using fluvoxamine for coronavirus disease 19 (COVID-19) in a prospective cohort in the setting of a mass outbreak. Overall, 65 persons opted to receive fluvoxamine 50mg twice daily and 48 declined. Incidence of hospitalization was 0% (0/65) with fluvoxamine and 12.5% (6/48) with observation alone. At 14 days, residual symptoms persisted in 0% (0/65) with fluvoxamine and 60% (29/48) with observation.

Table 1. Demographics and Outcomes in Prospective COVID-19 Cohort.

Group	Fluvoxamine N=65	No Therapy N=48	P-value [a]
Men	50 (59%)	35 (41%)	.66
Age, years	44 ±15	43 ±15	.74
Age >65 years	5 (7%)	2 (4%)	
Age 50-64 years	17 (26%)	15 (31%)	
Days for PCR confirmation	3.7 ±1.3	3.4 ±1.4	.25
Disease Status at time of testing			.064
Asymptomatic	25 (38%)	28 (58%)	
Mild	33 (37%)	24 (19%)	
Moderate [b]	16 (25%)	11 (23%)	
Chronic comorbidity	16 (25%)	18 (38%)	.15
Diabetes	11 (17%)	4 (8%)	
Hypertension, treated	11 (17%)	17 (35%)	
Lung Disease	2 (3%)	1 (2%)	
Hospitalized within 14 days	0	6	.005
ICU care and/or Death	0	2	--

Gracias