Ricerca clinica sullaCovid-19: lo studio GeroCovid e GeroVax

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Roma

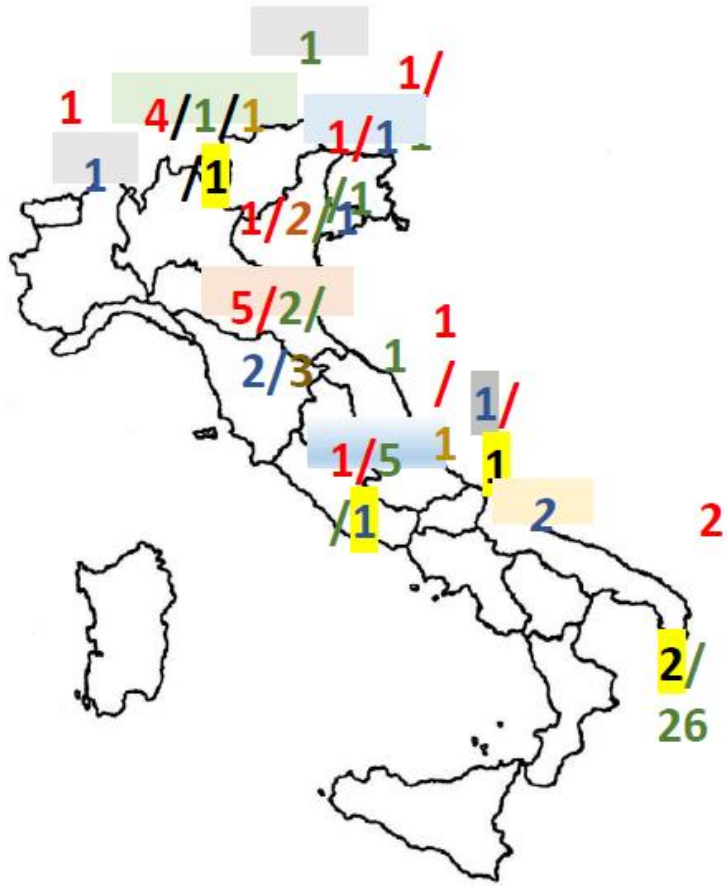
Make the Health System resilient to pandemic!

Acute care	It should account upon as needed quantitative and qualitative modulation
Architectural standards	The «all on one» paradigm does not work. Provide dedicated areas for treating contagious patients safely.
Home care	Absolutely unplanned to fight a pandemic in a double perspective: to guarantee continuity of care to non contagious patients; to limit the burden of contagious patients on the acute care system.
Epidemiologic surveillance	To make the network able to detect new events timely

SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

GeroCovid

GeroCovid Observational
76 Italian Investigational Sites



Acute Wards	16
Long-term Care	38
Geriatric Clinic Outpatients	8
Memory Clinics	10
Home-Care	4

BLUE COMPANION E-HEALTH PROJECTS

Activity dates:

- ✓ e-registry opened on April 2020
- ✓ Prospective and retrospective cases
- ✓ New observations from March 1st to December 31st, 2020
- ✓ 6-month follow-up subset closed on June 30th, 2021
- ✓ On-going VAX subset

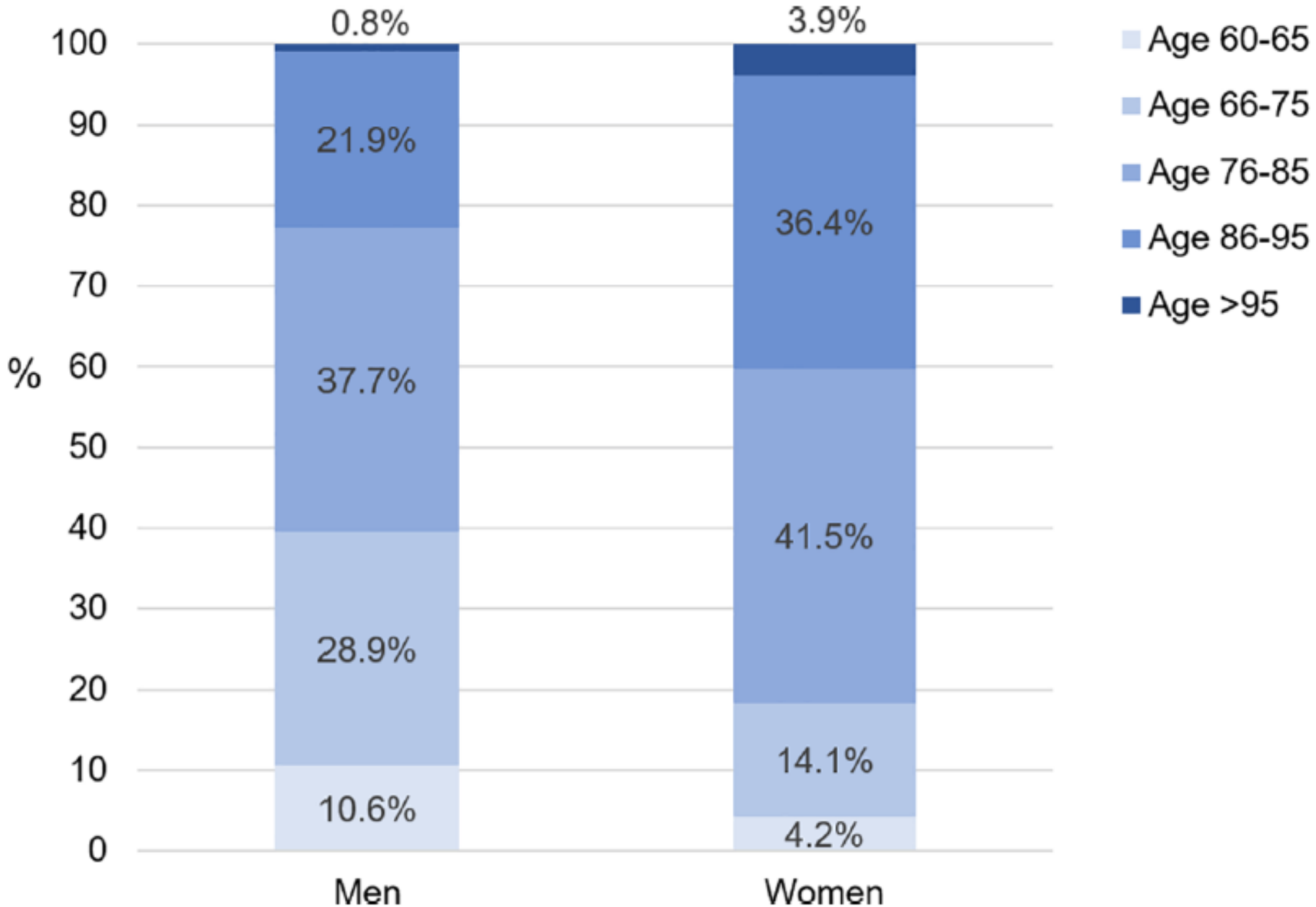
GeroCovid Observational:
Recruitment of cases per type of centre

34,2%	1232	COVID-specialised hospital
1,2%	43	Intensive Care (repurposed)
16,9%	608	Geriatric Unit / Outpatients
19,1%	690	Memory Clinic - Alzheimer's Outpatient (CDCD)
6,5%	235	Nursing-Home (RSA Anziani)
4,2%	153	Medicalized Nursing-home (RSA Medicalizzata)
10,4%	376	Hospital at Home (Assistenza Domiciliare Integrata)
4,8%	174	Retirement Home (Casa di Riposo)
0,5%	17	Specialized Alzheimer's Unit (Nucleo Alzheimer) (Nursing Home)
1,3%	47	Assisted Living (Casa Protetta)
0,7%	27	Follow-up Rehab (Centro di Riabilitazione Estensiva)
0,1%	2	Doctors' House / GPs (Medici di base)
100,0%	3604	

Hospital infrastructures ***52,3%***

At-home ***19,1%***

Long Term Care Facilities ***28,5%***


100
90
80
70
60
50
40
30
20
10
0
%
0.8%
21.9%
37.7%
28.9%
10.6%
3.9%
36.4%
41.5%
14.1%
4.2%
Men
Women
Age 60-65
Age 66-75
Age 76-85
Age 86-95
Age >95

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Original article

Assessing the impact of COVID-19 on the health of geriatric patients: The European GeroCovid Observational Study

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Protect non Covid-19 patients!

Gerontology

Clinical Section: Brief Report

Gerontology
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Management of Older Outpatients during the COVID-19 Pandemic: The GeroCovid Ambulatory Study

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Tests used

- Mini-Mental State Examination (MMSE)
- Activities of Daily Living (ADL)
- Instrumental ADL (IADL)
- Cumulative Illness Rating Scale (CIRS)
- 5-items Geriatric Depression Scale for mood (GDS)
- Euro Quality of Life (EuroQoL-5D)

Table 1. Outpatient and home-based health services provided before and during the lockdown period

Health services provided	December 2019–February 2020	March 2020–May 2020	% change
Video calls	12	662	+5416.7
Urgent visits	20	64	+220
Ambulatory visits	167	18	−89.2
Home visits	175	46	−73.7
Total	374	790	+111.2

Table 3. Changes in the evaluated scales after 3 months in the sample of geriatric outpatients ($n = 90$)

Scales	T0 (baseline)	T1 (90 days)	*p* value
ADL	2.27±1.65	1.98±1.72	0.001
IADL	1.71±2.19	1.61±2.31	0.083
MMSE	15.59±7.83	14.49±7.96	<0.001
GDS-5 items	1.64±1.40	1.76±1.50	0.101
CIRS	4.08±0.82	4.08±0.82	1.000
EuroQoL	42.22±11.88	40.0±12.45	0.005

Gerontology 2021 Jun 28;1-6. doi: 10.1159/000516969

Conclusions

- Our study suggests that contacts through telephone and video consultations are likely associated with an overall health status preservation of geriatric outpatients
- **24.4% out of the assessed patients suffered from cognitive and BPSD worsening, and 17.7% out of them complained of anxiety and insomnia worsening, while other studies, lacking standardized contact procedures, found up to 60% incidence/worsening of BPSD in people affected with dementia following quarantine**
- Patients and their caregivers felt reassured from being able to get a prompt response through video consultation whenever things were going wrong
- The remote monitoring allowed facing supervening needs timely and effectively. For instance, for patients reporting behavioral changes and/or anxiety and insomnia, video consultation allows timely pharmacologic and nonpharmacological/behavioral interventions
- Although the size of the population and the lack of a control group make these results preliminary in nature, they offer interesting insights to be tested and validated in larger samples

UNIVERSITÀ DEGLI STUDI DI PADOVA
DIPARTIMENTO DI MEDICINA - DIMED

Benessere psicologico in anziani con deterioramento cognitivo durante la quarantena: risultati preliminari dello studio GeroCovid.

(GeroCOVID – Sez. Territorio 1)

Front. Med., 22 September 2021

https://doi.org/10.3389/fmed.2021.715294

Dott.ssa A. Coin

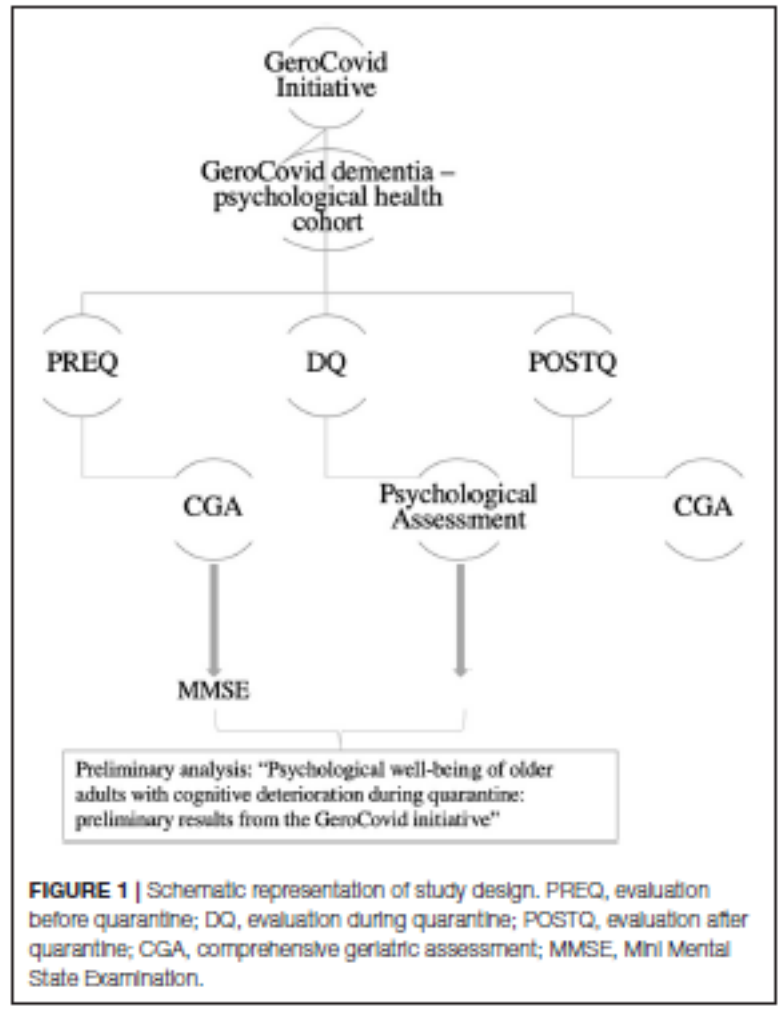

FIGURE 1 | Schematic representation of study design. PREQ, evaluation before quarantine; DQ, evaluation during quarantine; POSTQ, evaluation after quarantine; CGA, comprehensive geriatric assessment; MMSE, Mini Mental State Examination.

METODI

1. **Osservazione PRE- Covid**
2. **Contatto telefonico in itinere**
3. **Valutazione POST- Covid**

METODI

1. Osservazione PRE- Covid

3. Valutazione POST- Covid

Valutazione geriatrica multidimensionale:

- Funzioni cognitive: **Mini Mental State Examination** (**MMSE** – Folstein 1975);
- Stato funzionale: - **Activity of Daily Living** (**ADL** – Katz et al.. 1970)
  - **Instrumental Activity of Daily Living** (**IADL** – Lawton et al.. 1969);
- Stato nutrizionale: **Mini Nutritional Assessment Short Form** (**MNA**-SF – Rubenstein et al.. 2001);
- Disturbi del comportamento e umore: - **Neuro Psychiatric Inventory** (**NPI** – Cummings et al.. 1994);
  - **Geriatric Depression Scale** (**GDS** – Sheikh et al.. 1986);
- Fragilità: **Frailty Questionnaire** (**FRAIL** – Morley et al.. 2012);
- Solitudine e isolamento sociale: University of California. Los Angeles. **Loneliness Scale** (**UCLA** 3-items Loneliness Scale - Hughes et al.. 2004). **Social Isolation Scale** (Shankar et al.. 2013).

METODI

2. Contatto telefonico in itinere

Strumenti testistici:

- Stress e strategie di coping: **- Scala dello Stress Percepito** (PSS- 10 – Cohen 1983).
  - Caregiver Burden Inventory (CBI – Caserta et al.. 1996).
  - COPE (Carver. 1997);
- Disturbi del comportamento e dell'umore: **Depression Anxiety Stress Scales-21** (DASS-21 – Bottesi et al.. 2015);
- Riserva Cognitiva: **Cognitive Reserve Index questionnaire** (CRIq – Nucci et al.. 2012).

TABLE 3 | Linear regression models on the association between pre-quarantine MMSE and patients' psychological well-being and caregivers' burden during quarantine.

	β coefficient (95% confidence interval), p-value							
PREQ MMSE	**DASS total score**	**PSS total score**	**COPE ∑3**	**COPE ∑4**	**CBI ∑ 1–5**	**CBI ∑ 6–10**	**CBI ∑ 11-14**	**CBI total score**
Total score								
Per each 1-point increase	−0.7 (−1.3; −0.04) $p = 0.04$	−0.7 (−1.1; −0.4) $p < 0.001$	0.3 (0.1; 0.6) $p = 0.006$	0.3 (0.2; 0.5) $p < 0.001$	−0.7 (−1.0; −0.4) $p < 0.001$	−0.5 (−0.8; −0.2) $p = 0.001$	−0.3 (−0.5; −0.1) $p = 0.01$	−1.7 (−2.6; −0.8) $p < 0.001$
Categorical variable								
≥25	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]	[ref]
23–24	4.2 (0.3; 8.1) $p = 0.04$	3.2 (0.9; 5.5) $p = 0.007$	−0.6 (−2.0; 0.9) $p = 0.42$	−0.9 (−2.1; −0.2) $p = 0.12$	1.2 (−0.8; 3.2) $p = 0.24$	1.4 (−0.6; 3.4) $p = 0.17$	0.5 (−1.0; 1.9) $p = 0.55$	3.3 (−3.3; 10.0) $p = 0–32$
<23	4.4 (0.6; 8.2) $p = 0.02$	4.1 (1.9; 6.3) $p < 0.001$	−1.8 (−3.2; −0.5) $p = 0.009$	−1.7 (−2.8; −0.6) $p = 0.002$	3.2 (1.3; 5.1) $p = 0.001$	2.3 (0.4; 4.2) $p = 0.02$	0.9 (−0.5; 2.3) $p = 0.22$	6.7 (0.8; 12.7) $p = 0.03$

Models are adjusted for age, sex, education, social environment, depression, use of antipsychotics, number of chronic diseases. DASS, Depression Anxiety Stress Scales; PSS, Perceived Stress Scale; COPE, coping strategies inventory; ∑3 = sum of the items 2, 6, 12, 16, 23, 24 indicating positive attitude; ∑4 = sum of the items 3, 5, 9, 13, 20 indicating orientation to problem. CBI, Caregiver Burden Inventory. ∑ [1–5] = sum of the items from 1 to 5 indicating time spent for assistance; ∑ [6–10] sum of the items from 6 to 10 indicating social involvement ∑ [11–14] sum of the items from 11 to 14 indicating physical involvement; ∑ [15–19] sum of the items from 15 to 19 indicating relational involvement; PREQ MMSE, pre-quarantine Mini-Mental State Examination.

Il decadimento cognitivo più severo si è rivelato indipendentemente associato con punteggi più elevati alla DASS e al PSS, oltre che a meno efficaci strategie di coping ($p<0.05$).

Non essere socialmente protetti correla con un maggior punteggio alla scala DASS ($p<0.05$) ma la contempo con la maggiore adozione di alcuni comportamenti, soprattutto religiosi, per fronteggiare la situazione stressante (non mostrati).

Il funzionamento cognitivo è inoltre inversamente associato al CBI particolarmente nei soggetti socialmente protetti (conviventi con i caregivers).

CONCLUSIONE: L'impatto della quarantena sul benessere psico-affettivo di individui con MCI e demenza, nonchè lo stress dei loro caregiver, varia in accordo con il funzionamento cognitivo PREQ, laddove persone con una compromissione più severa mostrano esiti psicologici peggiori legati al COVID-19. **La possibilità di vivere con il caregiver o di ricevere più di 2 visite a settimana risulta fattore protettivo per ansia e depressione**.

Do not criminalize nursing homes! (Malara A et al…)

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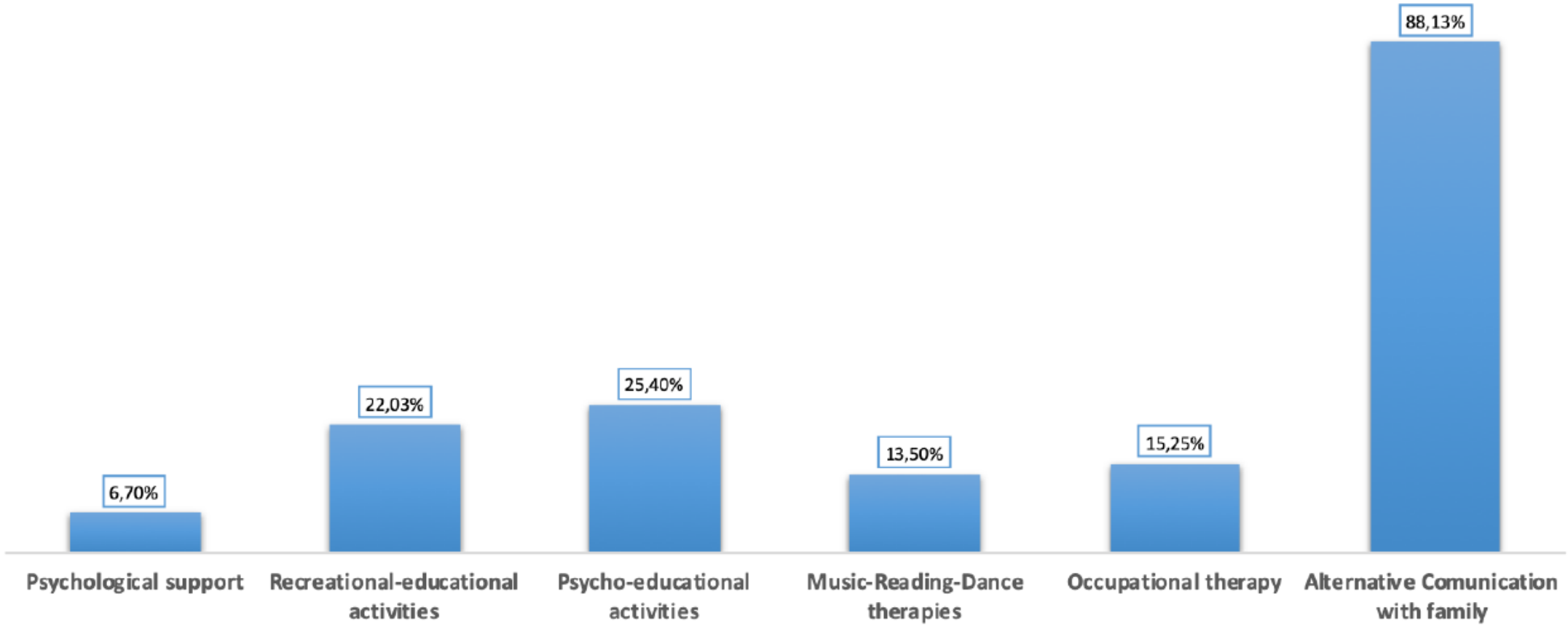
GeroCovid LTCFs: Infection containment interventions

- ✓ Universal use of PPE
- ✓ Restriction of visitation
- ✓ Social distancing
- ✓ Implementation of additional sanitizing
- ✓ Creation of COVID-19 isolation area
- ✓ Limited non-essential procedures
- ✓ Daily Resident and Staff check Body Temperature
- ✓ Daily Resident and Staff SPO2 check
- ✓ Staff education relating to preventive strategies
- ✓ Residents and Staff Virological Surveillance

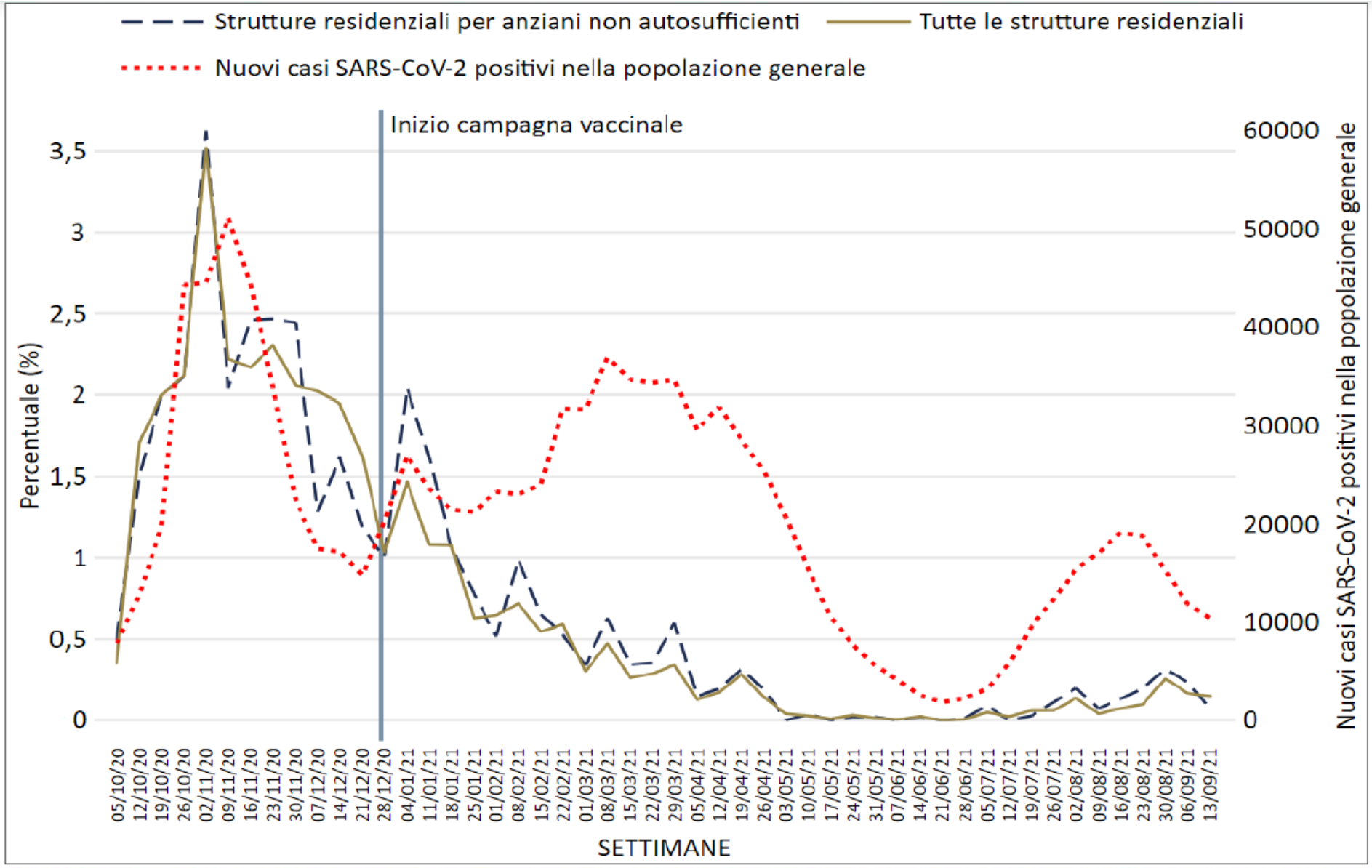
Strategies to improve mood of patients in GeroCovid LTCFs during COVID-19 outbreak



Le RSA a livello nazionale

Incidenza settimanale SARS-CoV-2 positivi in residenza

Sorveglianza ISS



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The Covid-19 in Italian Long-Term Care Facilities: GeroCovid LTCFs Observational Study

Alba Malara[1], Marianna Noale[2], Angela Marie Abbatecola[3], Gilda Borselli[4], Stefano Fumagalli[5], Pietro Gareri[6], Enrico Mossello[5], Caterina Trevisan[7], Stefano Volpato[8], Fabio Monzani[9], Alessandra Coin[5], Giuseppe Bellelli[10], Chukwuma Okoye [9], Susanna Del Signore[12], Gianluca Zia[12], Raffaele Antonelli Incalzi[13] and GeroCovid-LTCFs Group*

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GeroCovid LTCFs:Pattern onset symptoms

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The 29.6% of SARS-CoV-2 positive residents did not report an symptom and 70.4% reported at least one symptom

Table 2. Symptoms of older adults within the GeroCovid LTCFs study, by SARS-CoV-2 positive or negative swabs results

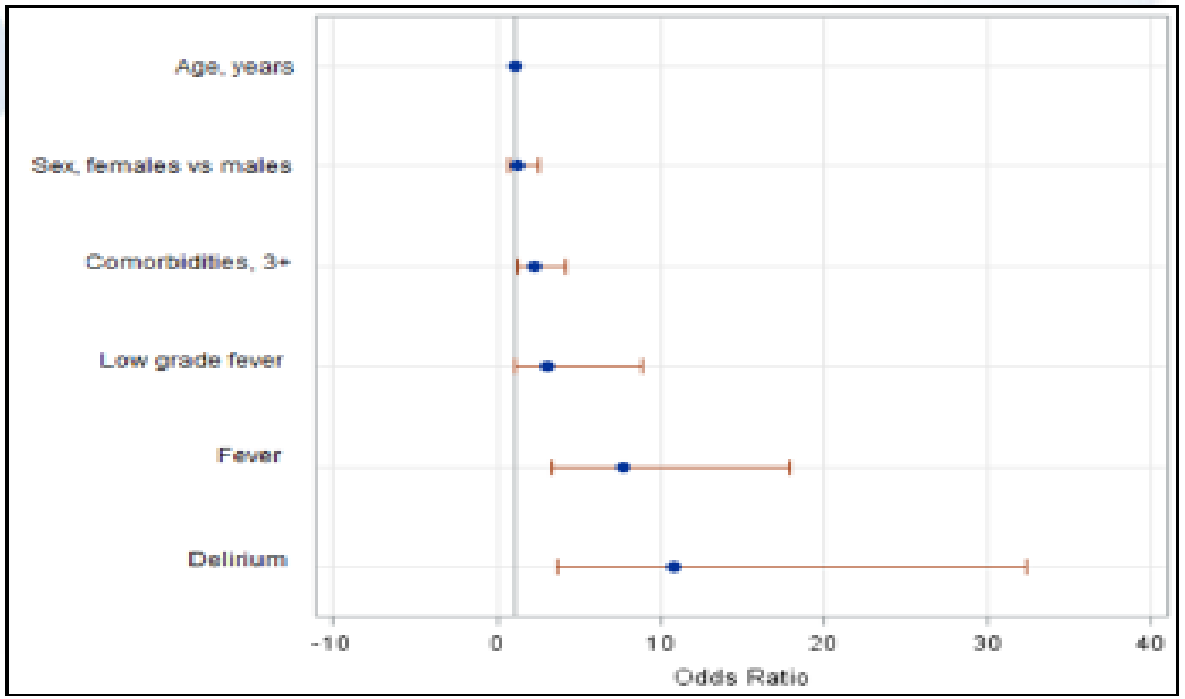
	SARS-CoV-2 + (n=179*)	SARS-CoV-2 - (n=324*)	P value
No symptoms, n (%)	53 (29.6)	203 (62.7)	<.001
At least one symptom, n (%)	126 (70.4)	121 (37.3)	<.001
Fever, n (%)	70 (39.1)	21 (6.5)	<.001
Low-grade fever, n (%)	64 (36.2)	8 (2.5)	<.001
Pharyngodynia, n (%)	1 (1.3)	3 (1.0)	1.00
Cough, n (%)	21 (12.4)	16 (5.0)	.003
Sneezing, n (%)	4 (2.3)	6 (1.9)	.72
Dyspnoea, n (%)	46 (26.1)	18 (5.7)	<.001
Low oxygen saturation after walking, n (%)	2 (2.0)	6 (2.1)	1.00
Low oxygen saturation at rest (<=90%), n (%)	37 (29.6)	15 (4.9)	<.001
S 02 %, mean±SD	95 (93, 96)	97 (96, 98)	<.001
Weakness/Prostration, n (%)	52 (32.1)	41 (12.7)	<.001
Fall or fainted, n (%)	1 (0.9)	7 (2.3)	.69
Muscles aching, n (%)	10 (6.6)	13 (4.1)	.24
Delirium, n (%)	49 (41.2)	7 (2.3)	<.001
Conjunctivitis, n (%)	3 (1.8)	5 (1.6)	1.00
Loss of smell (if new), n (%)	0 (0.0)	0 (0.0)	
Loss of taste, n (%)	3 (2.2)	2 (0.6)	.17
Anorexia, n (%)	30 (27.0)	20 (6.6)	<.001
Nausea/vomiting, n (%)	12 (7.2)	4 (1.3)	.004
Diarrhea, n (%)	36 (21.6)	12 (3.8)	<.001
Raynaud syndrome, n (%)	4 (3.5)	0 (0.0)	.005
Cutaneous symptoms, n (%)	6 (5.1)	2 (0.7)	.007
Sudden worsening of health status, n (%)	43 (35.0)	5 (1.6)	<.001
Aphasia/dysnomia, n (%)	1 (1.0)	6 (2.0)	.68
Cognitive Impairment, n (%)	27 (30.0)	49 (16.3)	.004
Diuresis contraction, n (%)	17 (14.2)	5 (1.6)	<.001
Urines of faeces incontinence, n (%)	5 (4.5)	47 (15.9)	.002
Unable to ask questions, n (%)	3 (4.4)	24 (9.2)	.21
Unable to fill a self-evaluation questionnaire, n (%)	7 (10.6)	35 (13.6)	.52
Number of symptoms, median (Q1, Q3)	2 (0, 6)	0 (0, 2)	<.001
Number of symptoms, n (%)			<.001
0	53 (29.6)	203 (62.7)	
1	25 (14.0)	36 (11.1)	
2+	101 (56.4)	85 (26.2)	

Abbreviations: SD, Standard Deviation; Q1, Quartile 1; Q3, Quartile 3

The most common symptoms in SARS-CoV-2 positive residents:

- ✓ Delirium (41.2%)
- ✓ Fever (39.1%)
- ✓ Low grade fever (36.2%)
- ✓ Sudden worsening of health status (35%)
- ✓ Weakness/prostration (32.1%)
- ✓ Low oxygen saturation at rest (SpO2<92%) (29.6%)
- ✓ Anorexia (27.0%)
- ✓ Dyspnea (26.1%)
- ✓ Diarrhea (21.6%)
- ✓ Diuresis contraction (14.2%).

Figure 1. Association between clinical features and positive swab test (stepwise selection)



Logistic regression model with stepwise selection procedure (sle=0.15; sls=0.20), adjusted for age, sex and comorbidity (defined as having 3+ chronic diseases). Symptoms reported by at least 5% of study participants (including fever, low-grade fever, cough, dyspnea, low oxygen saturation at rest, weakness/prostration, delirium, anorexia, diarrhea, sudden worsening of health status, diuresis contraction, urines or faeces incontinence, unable to ask questions, unable to fill a self-evaluation questionnaire) were considered as possible independent variables.

Conclusions: The residents often present an asymptomatic or pauci-symptomatic course of SARS Cov-2. Among onset symptom, the delirium is was the most frequent clinical expression of the infection.

Keywords. Covid-19; Long Term Care Facilities;

References: [1] *Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. N Engl J Med. 2020;382(22):2081-90.https://doi.org/10.1056/ NEJMoa2008457 PMID: 32329971*

Nel setting per acuti

Studio 1
Eterogeneità nella presentazione clinica di Covid-19 nell'anziano

Covid-19 as a paradigmatic model of the heterogeneous disease presentation in older people: data from the GeroCovid Observational study

Caterina Trevisan, Francesca Remelli, Stefano Fumagalli, Enrico Mossello, Chukwuma Okoye, Giuseppe Bellelli, Alessandra Coin, Alba Malara, Pietro Gareri, Fabio Monzani, Susanna Del Signore, Gianluca Zia, Raffaele Antonelli Incalzi, Stefano Volpato, and the GeroCovid acute ward working group

[*under review*]

Nel setting per acuti

Studio 1
Eterogeneità nella presentazione clinica di Covid-19 nell'anziano

Metodi:

Popolazione: **981 pazienti di età 78.3±9.39 anni (49.4% F), ricoverati per COVID-19**

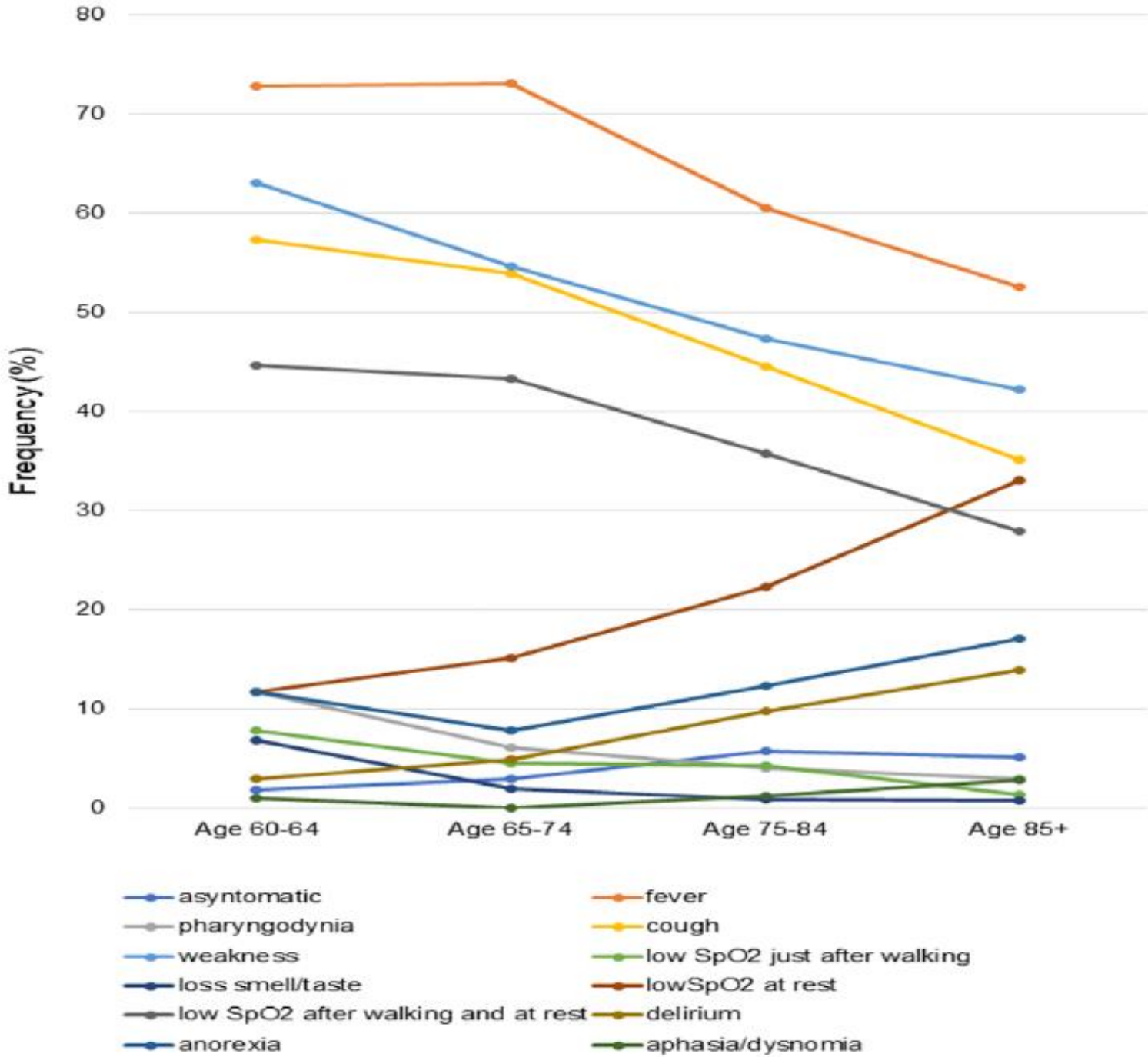
Variabili raccolte: segni/sintomi di COVID-19 ad esordio di malattia, dati sociodemografici, comorbilità, stato cognitivo, e livello di mobilità (da documentazione medica)

Outcomes: degenza prolungata (≥16 giorni) e mortalità intraospedaliera

Analisi statistica:

Identificazione di clusters di segni/sintomi: clustering gerarchico agglomerativo

Valutazione di segni/sintomi singoli o clusters rispetto a degenza prolungata e mortalità: regressione logistica binaria e regression di Cox


80
70
60
50
40
30
20
10
0
Frequency(%)
Age 60-64
Age 65-74
Age 75-84
Age 85+
asyntomatic
fever
pharyngodynia
cough
weakness
low SpO2 just after walking
loss smell/taste
lowSpO2 at rest
low SpO2 after walking and at rest
delirium
anorexia
aphasia/dysnomia

Nel setting per acuti

Studio 2

Dinamicità nell'andamento clinico di COVID-19 nel paziente anziano: risultati dallo studio multicentrico GeroCovid Observational

Caterina Trevisan, Riccardo Calvani, Ilaria Parrotta, Francesco Tonarelli, Alberto Zucchelli, on behalf of the Young Epidemiologist SIGG (YES), and the GeroCovid acute ward working group

[*work in progress*]

Nel setting per acuti

Studio 2

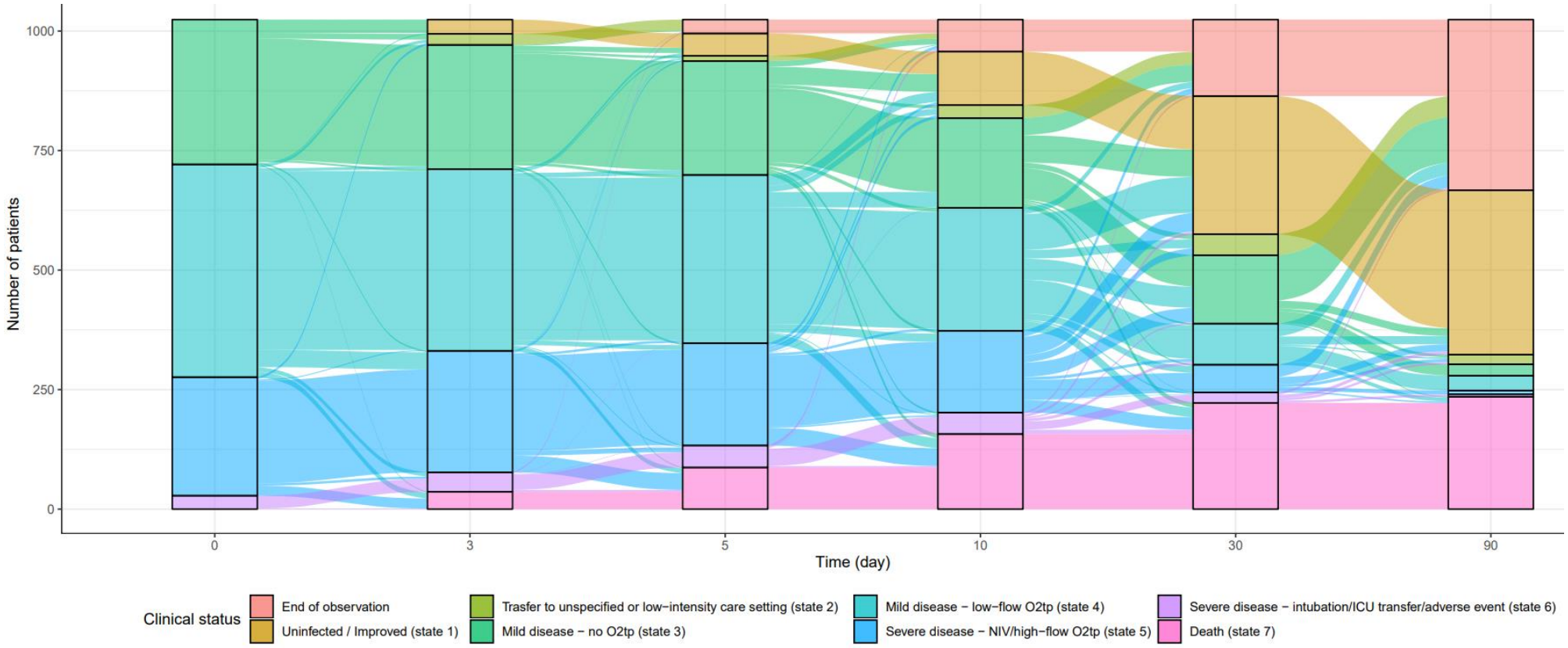
Dinamicità nell'andamento clinico di COVID-19 nel paziente anziano: risultati dallo studio multicentrico GeroCovid Observational

Risultati: Probabilità di transizione da/a

- **State 1**, hospital discharge with clinical improvement/stability
- **State 2**, mild disease – no O2-therapy
- **State 3**, mild disease – low-flow O2-therapy
- **State 4**, severe disease – high-flow O2-therapy or NIV
- **State 5**, severe disease – intubation/organ support/ ICU transfer
- **State 6**, transfer to unspecified/low-intensity care setting
- **State 7**, death

From	5-day transition's probability (%) to						
	State 1	State 2	State 3	State 4	State 5	State 6	State 7
State 2	46	25.3	3.4	2.7	1.2	12.4	8.9
State 3	27.7	11.4	22.7	8.3	2.3	10.2	17.4
State 4	21.3	5.6	3.2	18	2.9	11.5	37.5
State 5	28	3.8	5.7	1.7	18.3	10	32.4
	10-day transition's probability (%) to						
State 2	59.5	7	1.8	1.5	0.7	16.3	13.2
State 3	41.7	6	5.9	3.7	1.3	15.1	26.2
State 4	29.4	2.9	1.6	3.7	1.2	14.9	46.3
State 5	36.9	2.4	2.5	1.2	3.6	13.1	40.3
	30-day transition's probability (%) to						
State 2	65.7	0.1	0	0	0	18.2	15.9
State 3	50.3	0.1	0.1	0.1	0	18.1	31.4
State 4	33.8	0.1	0	0	0	16.5	49.6
State 5	41.6	0.1	0	0	0	14.7	43.6
	90-day transition's probability (%) to						
State 2	65.8	0	0	0	0	18.2	15.9
State 3	50.4	0	0	0	0	18.1	31.4
State 4	33.9	0	0	0	0	16.5	49.6
State 5	41.6	0	0	0	0	14.7	43.7

Alluvial plot for the transitions of older patients with COVID-19 between different clinical states since hospital admission (time 0)



Nel setting per acuti

Studio 2
Dinamicità nell'andamento clinico di COVID-19 nel paziente anziano: risultati dallo studio multicentrico GeroCovid Observational

Conclusioni:

- COVID-19 nell'anziano presenta elevata dinamicità con peggioramenti/miglioramenti clinici che si possono manifestare fino a 30 giorni dall'esordio, influenzati da fattori sociodemografici e mobilità pre-ricovero.

- In anziani con presentazioni COVID-19 severe e necessità di supporto d'organo o ventilazione meccanica si è osservato una migliore prognosi rispetto ai richiedenti ossigenoterapia ad alti flussi o NIV
  → selezione all'accesso alle cure intensive?

Osservazioni di farmacologia clinica

COVID-19 and Atrial Fibrillation in Older Patients: Does Oral Anticoagulant Therapy Provide a Survival Benefit?—An Insight from the GeroCovid Registry

Stefano Fumagalli[1] Caterina Trevisan[2] Susanna Del Signore[3] Giulia Pelagalli[1] Stefano Volpato[4] Pietro Gareri[5] Enrico Mossello[1] Alba Malara[6] Fabio Monzani[7] Alessandra Coin[2] Giuseppe Bellelli[8] Gianluca Zia[3] Raffaele Antonelli Incalzi[9] for the GeroCovid Working Group*

Endpoint

The aim of this study was to identify the factors associated with mortality in older COVID-19 patients with atrial fibrillation (AF) —anamnestic or diagnosed at ward admission — focusing on the role of preadmission and in-hospital OAC therapy

Methods

- Retrospective analysis of the ≥60 years patients enrolled by the 16 centres participating to the "GeroCovid acute wards" section of the registry
- Enrolment period: March 1st – June 9th, 2020 (first wave of the pandemics)
- This cohort is highly representative of the real-world scenario of COVID-19 at an advanced age

Thrombosis and Haemostasis, 2021

Osservazioni di farmacologia clinica

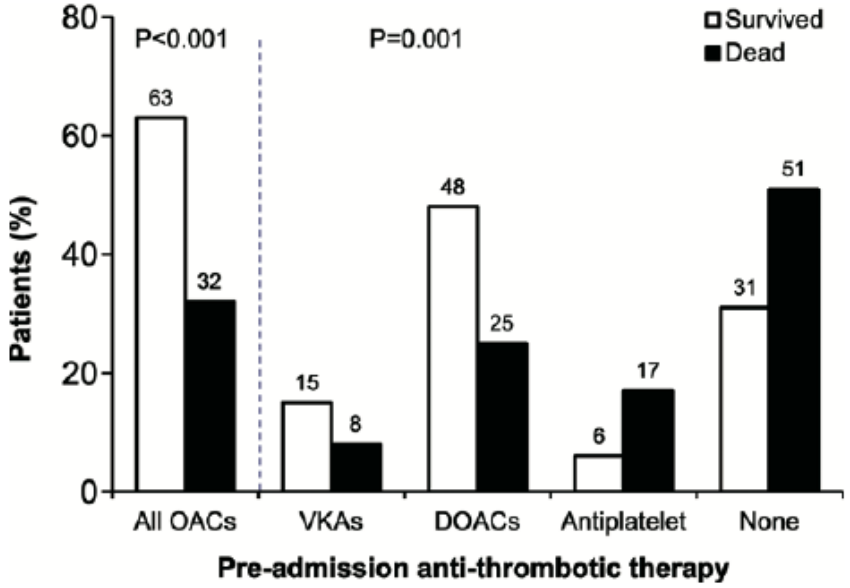
COVID-19 and Atrial Fibrillation in Older Patients: Does Oral Anticoagulant Therapy Provide a Survival Benefit?—An Insight from the GeroCovid Registry

Stefano Fumagalli[1] Caterina Trevisan[2] Susanna Del Signore[3] Giulia Pelagalli[1] Stefano Volpato[4] Pietro Gareri[5] Enrico Mossello[1] Alba Malara[6] Fabio Monzani[7] Alessandra Coin[2] Giuseppe Bellelli[8] Gianluca Zia[3] Raffaele Antonelli Incalzi[9] for the GeroCovid Working Group*

Results

- 806 patients were evaluated (age: 78±9 years; men: 50.7%)
- AF prevalence: 21.8% (N=176); CHA_2DS_2-VASc: 4.1±1.5
- Use of anticoagulants: 51.7% (N=91; VKAs: 12.5%; DOACs: 39.2%)

Figure. In-hospital vital status of AF patients with COVID-19 by use of antithrombotic agents at ward admission



- The use of OACs before hospitalization was higher in patients who survived
- Antiplatelet therapy was more common in those who died

Thrombosis and Haemostasis, 2021

La disabilità modula il rischio AF-relato nella Covid-19

Aging Clinical and Experimental Research
https://doi.org/10.1007/s40520-021-02008-5

ORIGINAL ARTICLE

Atrial fibrillation and COVID-19 in older patients: how disability contributes to shape the risk profile. An analysis of the GeroCovid registry

Stefano Fumagalli[1] · Caterina Trevisan[2] · Susanna Del Signore[3] · Giulia Pelagalli[1] · Carlo Fumagalli[1] · Andrea Herbst[1] · Stefano Volpato[4] · Pietro Gareri[5] · Enrico Mossello[1] · Alba Malara[6] · Fabio Monzani[7] · Chukwuma Okoye[7] · Alessandra Coin[2] · Giuseppe Bellelli[8] · Gianluca Zia[3] · Andrea Ungar[1] · Anette Hylen Ranhoff[9] · Raffaele Antonelli Incalzi[10] · for the GeroCovid Working Group

In-hospital mortality was higher in AF patients (36.9 vs. 27.5%; OR = 1.55, 95% CI = 1.09–2.20; $p = 0.015$). A decision tree analysis showed that, in AF subjects, preserved functional status at admission was the most important factor associated with survival. In patients without AF, baseline COVID-19 severity was the most relevant variable related to clinical prognosis.

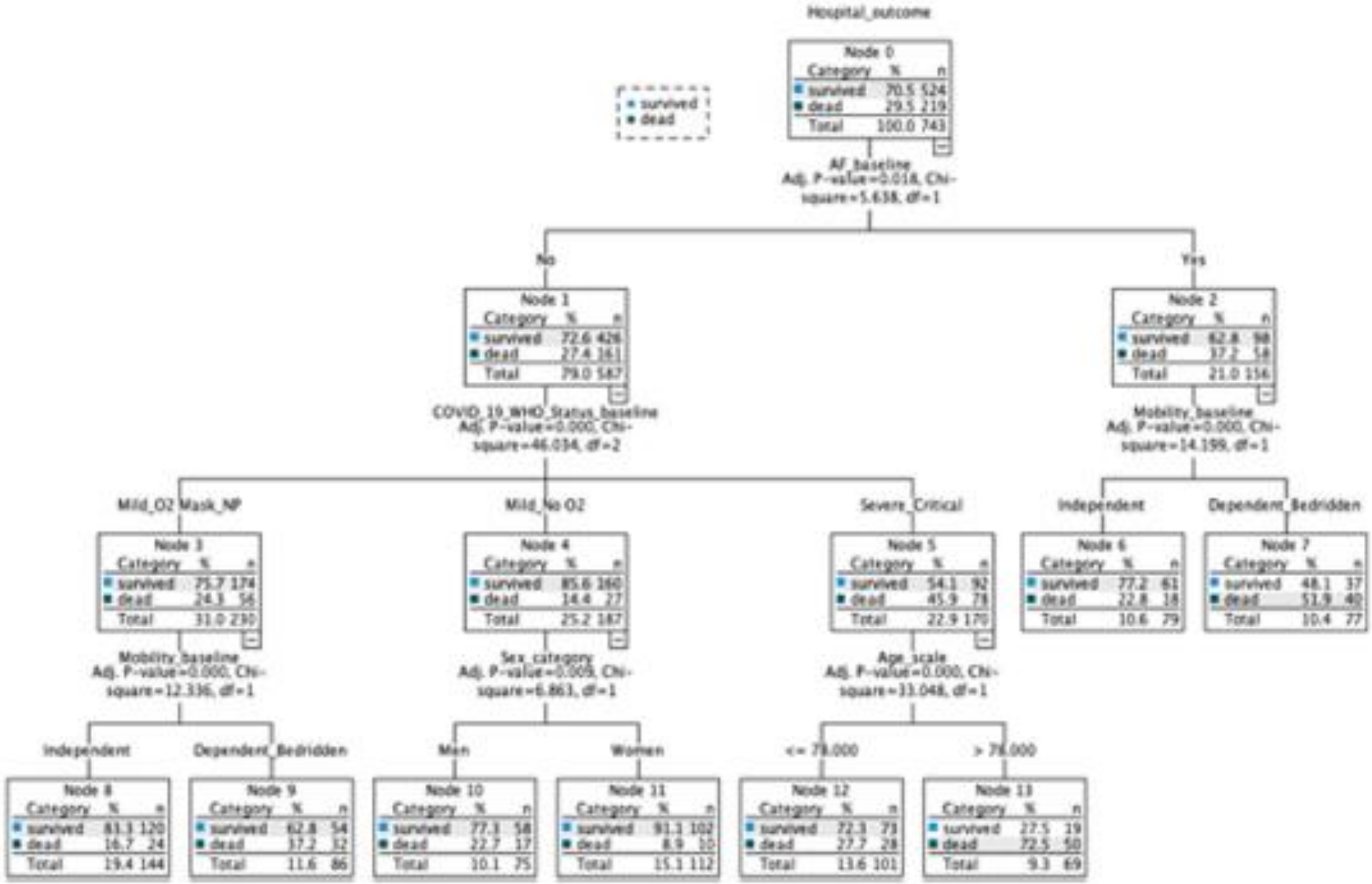
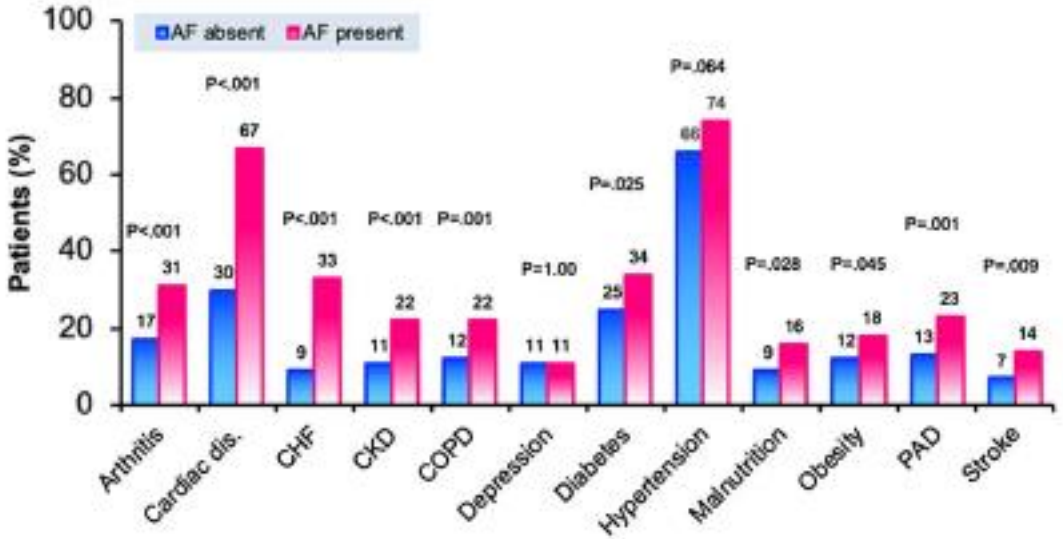


Fig. 2 Tree-based classification model for in-hospital mortality in the GeroCovid population assuming AF at baseline as the first clustering node. *AF* atrial fibrillation, *Age_scale* age, *COVID_19_WHO_Status_baseline* WHO classification of severity of COVID-19, *Mild_No O2* mild disease with no oxygen support needed, *Mild_O2 Mask_NP* mild disease with low-flow oxygen support (oxygen mask or nasal prongs) needed, *Severe_Critical* disease needing high-flow oxygen support, non-invasive or invasive mechanical ventilation, or organ support

Per inciso: AF e comorbidità

Fig. 1 Prevalence of comorbid conditions by AF status in the GeroCovid population. *CHF* signs and symptoms of chronic heart failure, *CKD* chronic kidney disease, *COPD* chronic obstructive pulmonary disease, *dis.* disease, *PAD* peripheral artery disease



Peculiari reperti HRCT nell'anziano con Covid-19

Okoye et al. BMC Geriatrics (2022) 22:166
https://doi.org/10.1186/s12877-022-02837-7

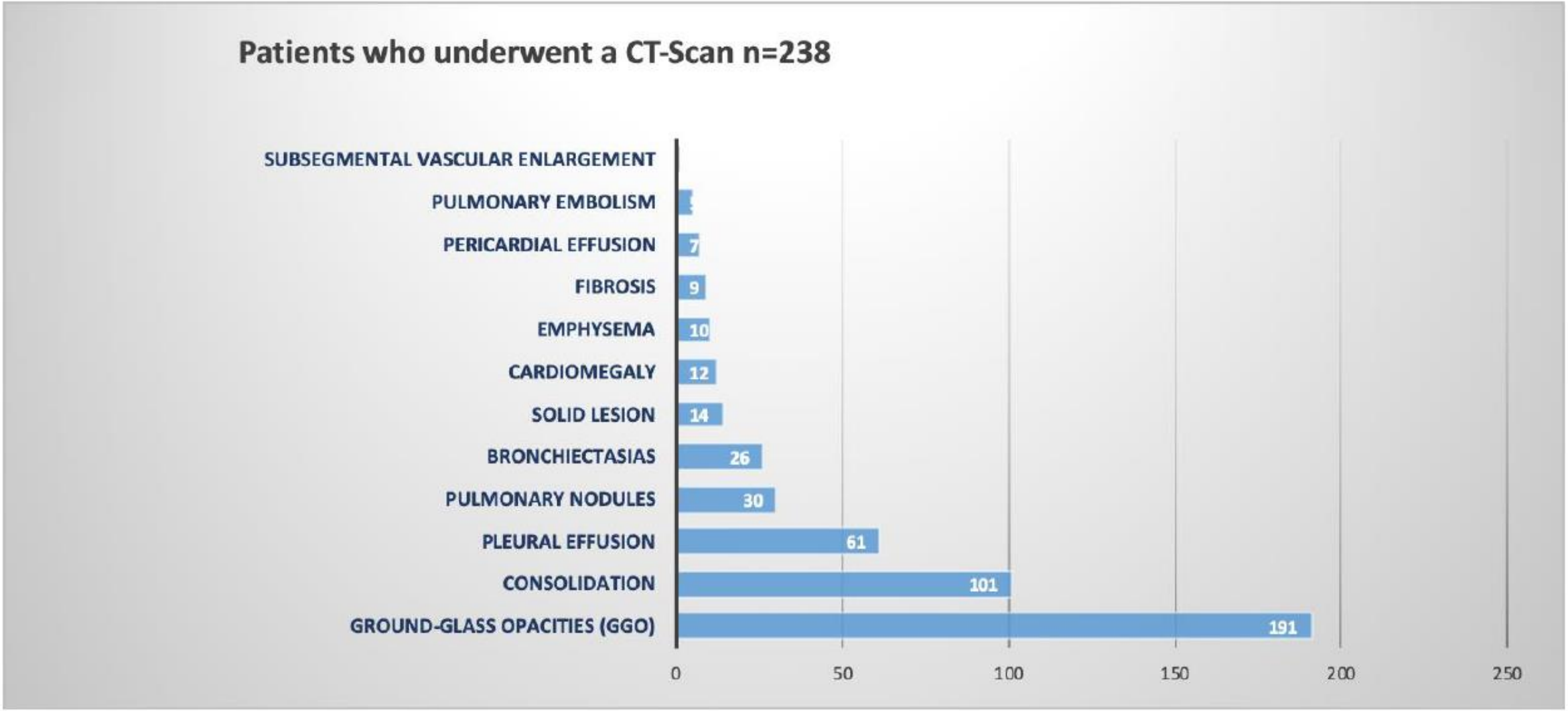
BMC Geriatrics

RESEARCH Open Access

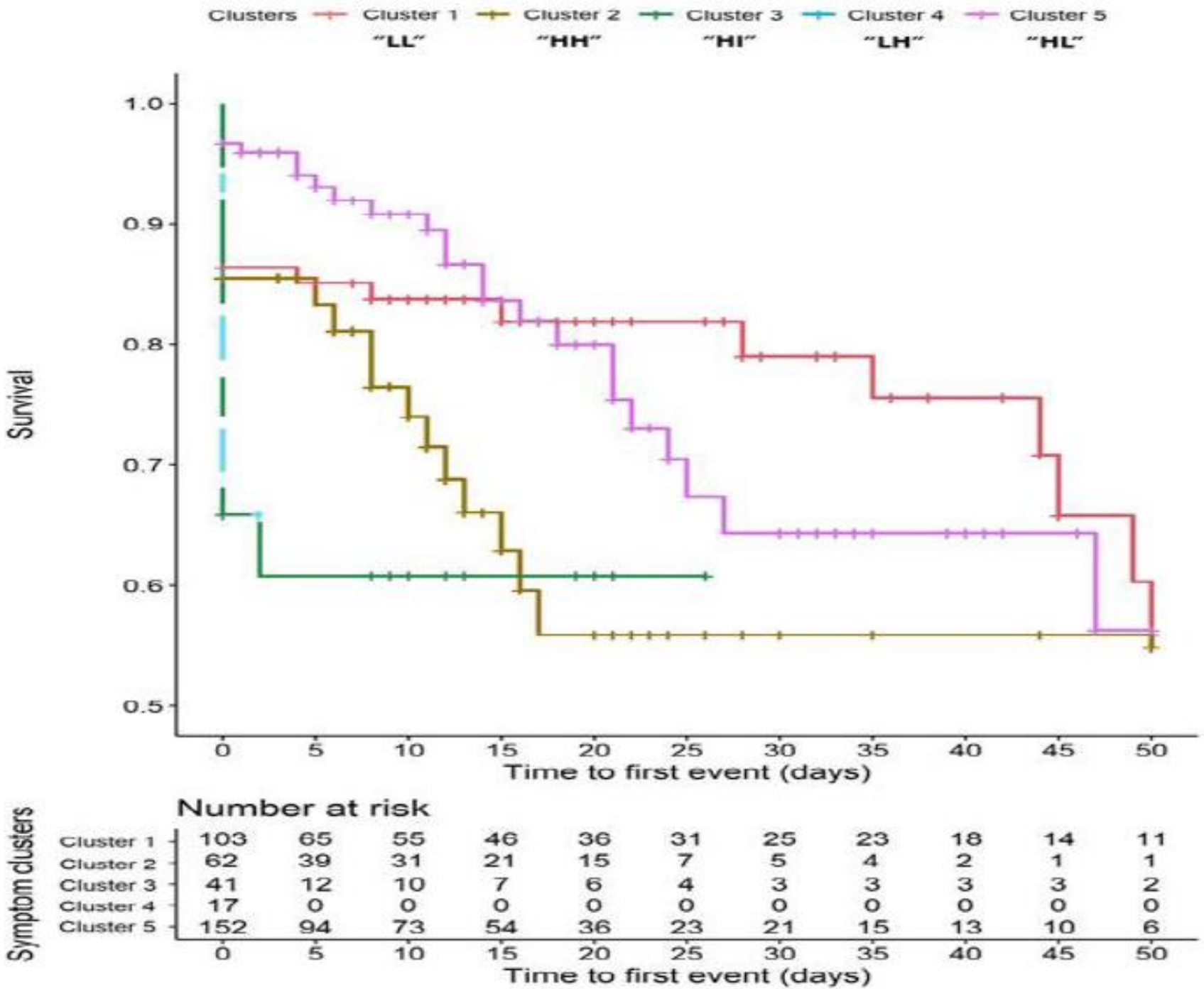
Computed tomography findings and prognosis in older COVID-19 patients

Chukwuma Okoye[1], Panaiotis Finamore[2*], Giuseppe Bellelli[3], Alessandra Coin[4], Susanna Del Signore[5], Stefano Fumagalli[6], Pietro Gareri[7], Alba Malara[8], Enrico Mossello[6], Caterina Trevisan[4], Stefano Volpato[9], Gianluca Zia[5], Fabio Monzani[1] and Raffaele Antonelli Incalzi[2]

HRCT in Covid19: the contribution by GeroCovid



Cluster 1 showed a low prevalence of both GGO and pleural effusion ("LL"), Cluster 2 a high prevalence of both the previous findings ("HH"), Cluster 3 a high prevalence of GGO and intermediate prevalence of pleural effusion ("HI"), Cluster 4 a low prevalence of GGO and high of pleural effusion ("LH") and Cluster 5 a high prevalence of GGO and low of pleural effusion ("HL"). Clusters were similar in terms of consolidation, except for Cluster 4 ("LH") showing a low prevalence. More details on CT-scan findings by clusters are reported in e-Table 3.



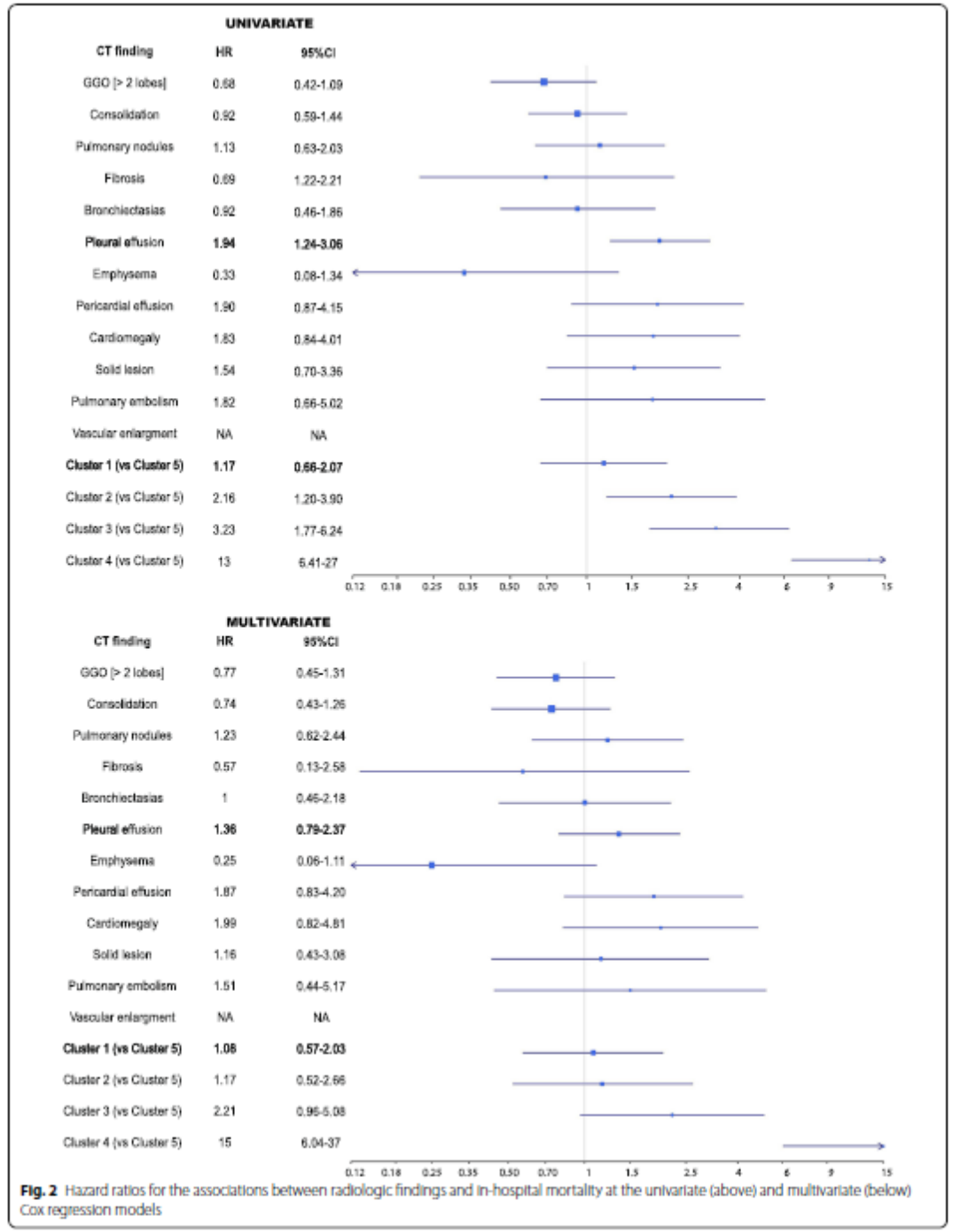


Fig. 2 Hazard ratios for the associations between radiologic findings and in-hospital mortality at the univariate (above) and multivariate (below) Cox regression models

Conclusions:

- GGO is the most common CT pulmonary alteration in older and multimorbid COVID-19 inpatients, however its absence does not exclude the diagnosis, particularly in the oldest old.

- The prevalence of pleural effusions, bronchiectasis, and pulmonary nodules is higher than in the studies carried out in younger cohorts of hospitalized patients with COVID-19.

- Pleural effusion at admission qualifies as a marker of disease severity.

- The fact that only cluster 4 “LH” qualifies as an independent risk factor suggests that pleural effusion plays a major prognostic role in the older patients.

Pleural effusion, an unusual, but dready prognostic finding in Covid19 (Feng Y et al. Am J Respir Crit Care Med 2020; 201: 1380–1388)

Table 6. Chest Computed Tomography Findings on Admission of 476 Patients with COVID-19

		Disease Severity			
	All (*N* = 476)	**Moderate (*n* = 352)**	**Severe (*n* = 54)**	**Critical (*n* = 70)**	***P* Value**
Bilateral lungs involved	373/442 (84.4)	266/327 (81.3)*	53/54 (98.1)	54/61 (88.5)	0.04
Lung lobes involved, median (IQR)	5 (3–5)	5 (3–5)	5 (5–5)	5 (5–5)	<0.001
Consolidation	87/442 (19.7)	68/327 (20.8)	13/54 (24.1)	6/61 (9.8)	0.098
Ground-glass opacity	425/442 (96.2)	311/327 (95.1)	53/54 (98.1)	61/61 (100)	0.137
Linear opacity	129/442 (29.2)	88/327 (26.9)	19/54 (35.2)	22/61 (36.1)	0.206
Pleural effusion	25/442 (5.7)	10/327 (3.1)†	4/54 (7.4)	11/61 (18)	<0.001
Pleural thickening	238/442 (53.8)	176/327 (53.8)	32/54 (59.3)	30/61 (49.2)	0.567

Definition of abbreviations: COVID-19 = coronavirus disease; IQR = interquartile range.

P values denote *post hoc* comparisons between the moderate, severe, and critical groups. Data are shown as no./total no. (%) unless otherwise noted.

*$P < 0.05$, comparison between the severe group and the moderate group.

†$P < 0.05$, comparison between the critical group and the moderate or severe group.

Vaccine 39 (2021) 2325–2327

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Commentary

Are vaccines against COVID-19 tailored to the most vulnerable people?

Raffaele Antonelli Incalzi [a], Caterina Trevisan [b,*,1], Susanna Del Signore [c,1], Stefano Volpato [d], Stefano Fumagalli [e], Fabio Monzani [f], Giuseppe Bellelli [g], Pietro Gareri [h], Enrico Mossello [e], Alba Malara [i], Alessandra Coin [b], Gianluca Zia [c], Anette Hylen Ranhoff [j]

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[b] *Geriatrics Division, Department of Medicine (DIMED), University of Padua, Italy*
[c] *Bluecompanion Ltd, London, UK*
[d] *Department of Medical Science, University of Ferrara, Ferrara, Italy*
[e] *Geriatric Intensive Care Unit, Department of Experimental and Clinical Medicine, University of Florence, Italy*
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[g] *School of Medicine and Surgery, University of Milano-Bicocca and Acute Geriatric Unit, San Gerardo Hospital, Monza, Italy*
[h] *Center for Cognitive Disorders and Dementia - Catanzaro Lido, ASP Catanzaro, Italy*
[i] *Scientific Committee of National Association of Third Age Residences (ANASTE) Calabria, Lamezia Terme (Catanzaro), Italy*
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Table 1
Health-related eligibility criteria influencing geriatric representation in the clinical trials for vaccines against COVID-19.

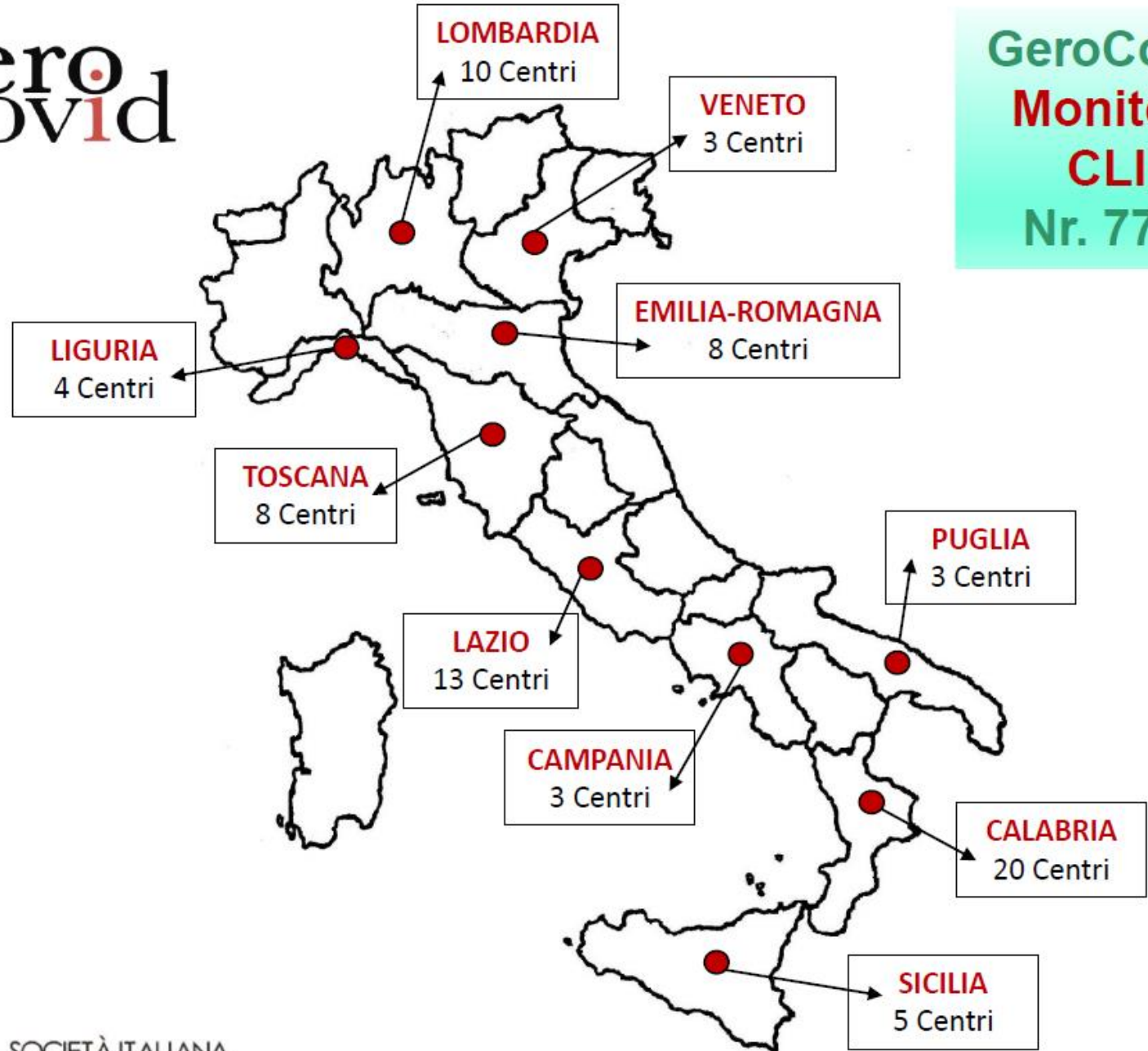
	Pfizer/BionTech [4]	Moderna [5]	Oxford-AstraZeneca [7]
Age classes	42.2% with age > 55 years	24.8% with age ≥65 years	15.9% with age >55 year (10.9% from 56 to 70 years, and 5% >70 years)
Inclusion criteria	- Healthy participants who, through medical history, physical examination, and clinical judgment of the investigator are eligible for inclusion in the study. - Individuals with preexisting stable disease (i.e. disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment).	Healthy adults or adults with pre-existing medical conditions who are in stable condition (i.e. not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment).	Healthy adults or adults with comorbidities assessed as mild or moderate and well controlled by the Investigator.
Exclusion criteria	- Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study. - Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.	- Acute illness or fever 72 h prior to or at screening. - Immunosuppressive or immunodeficient state.	- Severe or uncontrolled conditions, e.g. cardiovascular, respiratory, gastrointestinal, liver, renal diseases, endocrine, autoimmune/ rheumatological disorders, neurological illness, immunosuppression, and cancer. - Chronic use of anticoagulants. - Psychiatric conditions (including dementia or cognitive impairment), or psychiatric history. - Any other comorbidities deemed severe or uncontrolled as determined by the clinical judgement of the Investigator. In case of uncertainty regarding the nature or severity of the comorbidity (e.g. new medical diagnosis; new symptom, disorder or finding that are currently under investigation; recent change or deterioration in a symptom, disorder or finding) the participant may be excluded, at the discretion of the investigator. - Clinical Frailty Scale ≥4 (vulnerable and frail), only for participants aged ≥65 years.

GeroCovid Vax

Sponsor:	AIFA
Coordinatore:	ISS
Partners:	SIGG, Campus Biomedico, Blue Companion
Partecipanti:	77 RSA in 10 Regioni

GeroCovid

GeroCovid VAX
Monitoraggio CLINICO
Nr. 77 Centri



SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

BLUE COMPANION E-HEALTH PROJECTS

Scopo

1. valutare sicurezza ed efficacia clinica della vaccinazione anti-SARS-CoV-2 (**Monitoraggio Clinico**);
2. identificare la durata della protezione indotta dalla vaccinazione attraverso il monitoraggio dell'andamento del titolo anticorpale e della risposta cellulo mediata (**Monitoraggio immunologico**)

Studio ancillare 1
Monitoraggio titolo anticorpale

600 residenti

GeroCovid

GeroCovid VAX
Monitoraggio SIEROLOGICO
Nr. 29 Centri

SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

BLUE COMPANION E-HEALTH PROJECTS

Studio ancillare 1

Tempo 0

immediatamente prima della vaccinazione

Tempo 1

A distanza di 1 mese dalla seconda dose di vaccino (circa 2 mesi dal tempo 0)

Tempo 2

A distanza di 6 mesi dall' inizio vaccinazione

(circa 6 mesi dal tempo 0)

Tempo 3

a distanza di 12 mesi dall' inizio vaccinazione

(circa 12 mesi dal tempo 0)

Terza dose

Studio ancillare 2
Immunità cellulo-mediata

In un sottocampione di 40 residenti sarà valutata anche la risposta immunitaria cellulo mediata (CMI). La CMI sarà valutata a distanza di 6 e 12 mesi dalla vaccinazione. Saranno arruolati 40 residenti stratificati in base alla presenza della risposta anticorpale (20 con positività delle IgG anti S e 20 senza positività delle IgG anti S). La valutazione dell'immunità cellulo-mediata in due momenti (6 e 12 mesi) consentirà di valutare la variazione nel tempo di tale parametro.

JGG JOURNAL OF GERONTOLOGY AND GERIATRICS

JGG Online First 2021;Nov 30
doi: 10.36150/2499-6564-N440

Disentangling the impact of COVID-19 infection on clinical outcomes and preventive strategies in older persons: an Italian perspective

Angela Marie Abbatecola[1,2], Raffaele Antonelli Incalzi[2,3], Alba Malara[2,4], Annapina Palmieri[5], Anna Di Lonardo[5], Gilda Borselli[2], Marcello Russo[1], Marianna Noale[6], Stefano Fumagalli[7], Pietro Gareri[8], Enrico Mossello[7], Caterina Trevisan[9], Stefano Volpato[2,10], Fabio Monzani[2,11], Alessandra Coin[7], Giuseppe Bellelli[2,12], Chukwuma Okoye[11], Susanna Del Signore[13], Gianluca Zia[13], Elisa Bottoni[14], Carmine Cafariello[15], Graziano Onder[5], GeroCovid Observational[16], GeroCovid Vax Group[17]

Table I. General characteristics of GeroCovid Observational and GeroCovid Vax Studies.

	GeroCovid Observational	GeroCovid Vax
Age	≥ 60 years of age	≥ 60 years of age
	- with COVID-19 - no COVID-19	- no COVID-19
Study Aims	• assess changes in COVID risk profile	• assess the safety of COVID-19 vaccines
	• assess the impact on physical, cognitive, psychological & behavioral status in non COVID-19 participants	• assess adverse side effects following vaccine inoculation
	• assess clinical & functional outcomes following COVID-19 hospitalization	• assess clinical & functional changes over time following vaccination
		• assess COVID-19 following vaccination
		• assess efficacy (monitor immune response)
	• identify significant measures in homecare & outpatient services	
	• identify measures in LTC to prevent & protect against COVID-19	
Settings	Acute wards, outpatient clinics (memory, post hospitalization from COVID-19), Homecare assistance, LTC (assisted living, retirement homes, NHs)	LTC (NH, Retirement home)
Functional, cognitive, comorbidity parameters	ADL, IADL, CIRS, MMSE, GDS, physical activity	ADL, IADL, CIRS, MMSE, GDS, physical activity
Frailty anamnestic parameters	Frailty criteria [20-21]	Frailty criteria [20-21]
Biochemical parameters	Blood/urine analyses	Blood samples
Drug use monitoring	ATC classification	ATC classification
Outcome	Type of outcome [18] *(infection, death, hospitalization, changes in clinical, cognitive & functional parameters)*	Adverse events *(infection, death, hospitalization, other) immune response*
Data entry method	E-registry (BlueCompanion, France) [11]	E-registry (BlueCompanion, France) [11]

ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; GDS: Geriatric Depression Scale; LTC: Long-Term Care; MMSE: Mini-Mental State Examination

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Monitoring COVID-19 vaccine use in Italian long term care centers: The GeroCovid VAX study

Angela Marie Abbatecola [a,b,*], Raffaele Antonelli Incalzi [b,c], Alba Malara [b,d], Annapina Palmieri [e], Anna Di Lonardo [e], Giorgio Fedeli [e], Paola Stefanelli [e], Gilda Borselli [b], Marcello Russo [a], Marianna Noale [f], Stefano Fumagalli [g], Pietro Gareri [h], Enrico Mossello [g], Caterina Trevisan [i,j], Stefano Volpato [b,j], Fabio Monzani [b,k], Alessandra Coin [i], Giuseppe Bellelli [b,l], Chukwuma Okoye [k], Susanna Del Signore [m], Gianluca Zia [m], Elisa Bottoni [n], Carmine Cafariello [o], Graziano Onder [e], GeroCovid Vax Working Group

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[i] *Geriatrics Division, Department of Medicine (DIMED), University of Padua, Italy*
[j] *Department of Medical Science, University of Ferrara, Italy*
[k] *Geriatrics Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy*
[l] *School of Medicine and Surgery, University of Milano-Bicocca and Acute Geriatric Unit, San Gerardo Hospital, Monza, Italy*
[m] *Bluecompanion Ltd, Londra, UK*
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[o] *Geriatrics Outpatient Clinic and Territorial Residences, Italian Hospital Group, Rome, Italy*

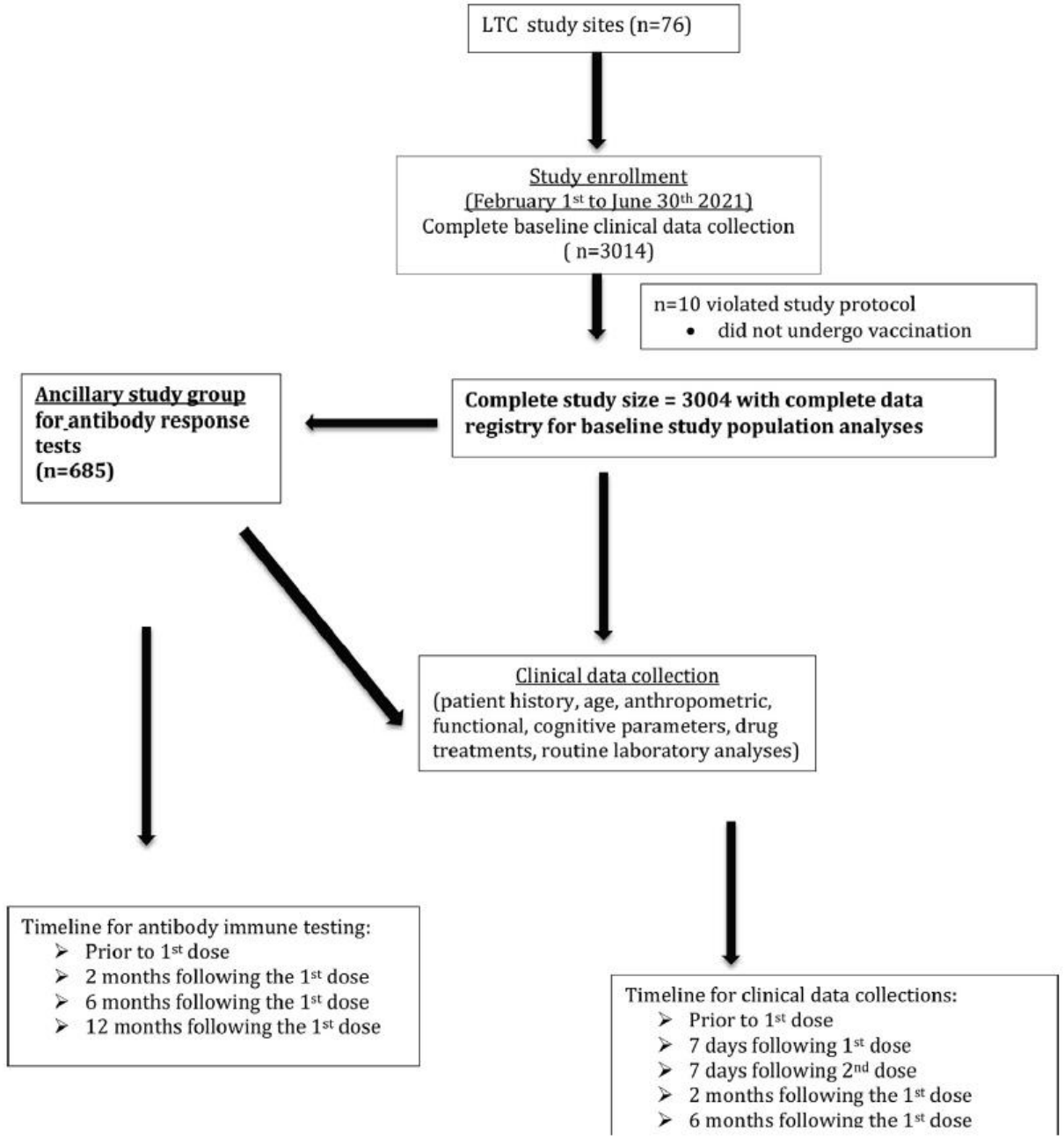
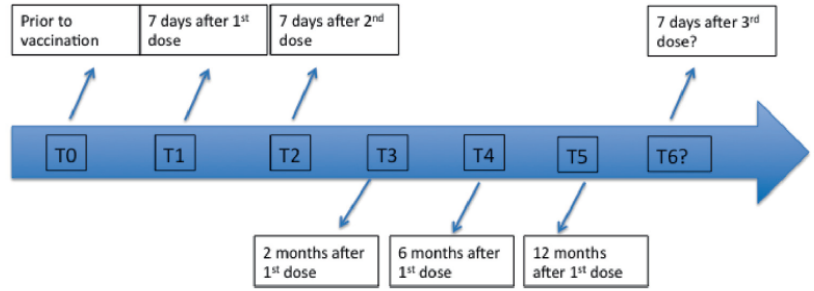


Fig. 1. Participant recruitment and follow-up flow diagram.



Data collection parameter	Scale
Functional, Cognitive Comorbidity parameters	ADL (9), IADL (10), CIRS (14), MMSE (11), GDS (13), Mobility function (see methods)
Frailty anamnestic parameters	Frailty criteria (12)
Biochemical Parameters	Blood samples/urine analyses
Drug use monitoring	ATC classification
Outcome	Adverse events (COVID-19 infection, death, hospitalization, other) Immune response
Data entry method	E-registry (BlueCompanion, France)

ADL=Activities of Daily Living; IADL=Instrumental Activities of Daily Living; GDS= Geriatric Depression Scale; LTC= Long-Term Care; MMSE= Mini-Mental State Examination

Fig. 2a. Timeline description for Clinical GeroCovid Vax data collection and parameters at each observation follow up.

Humoral immune response

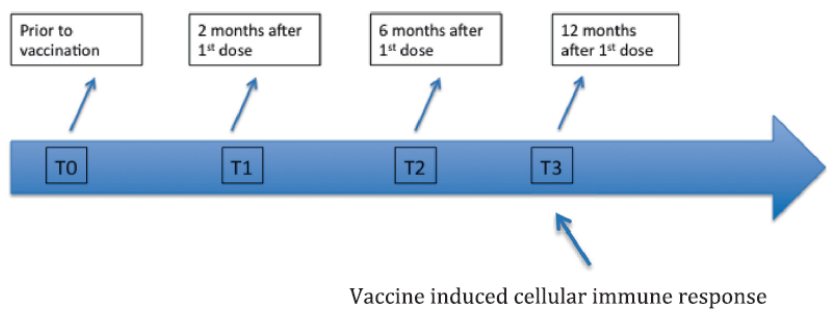
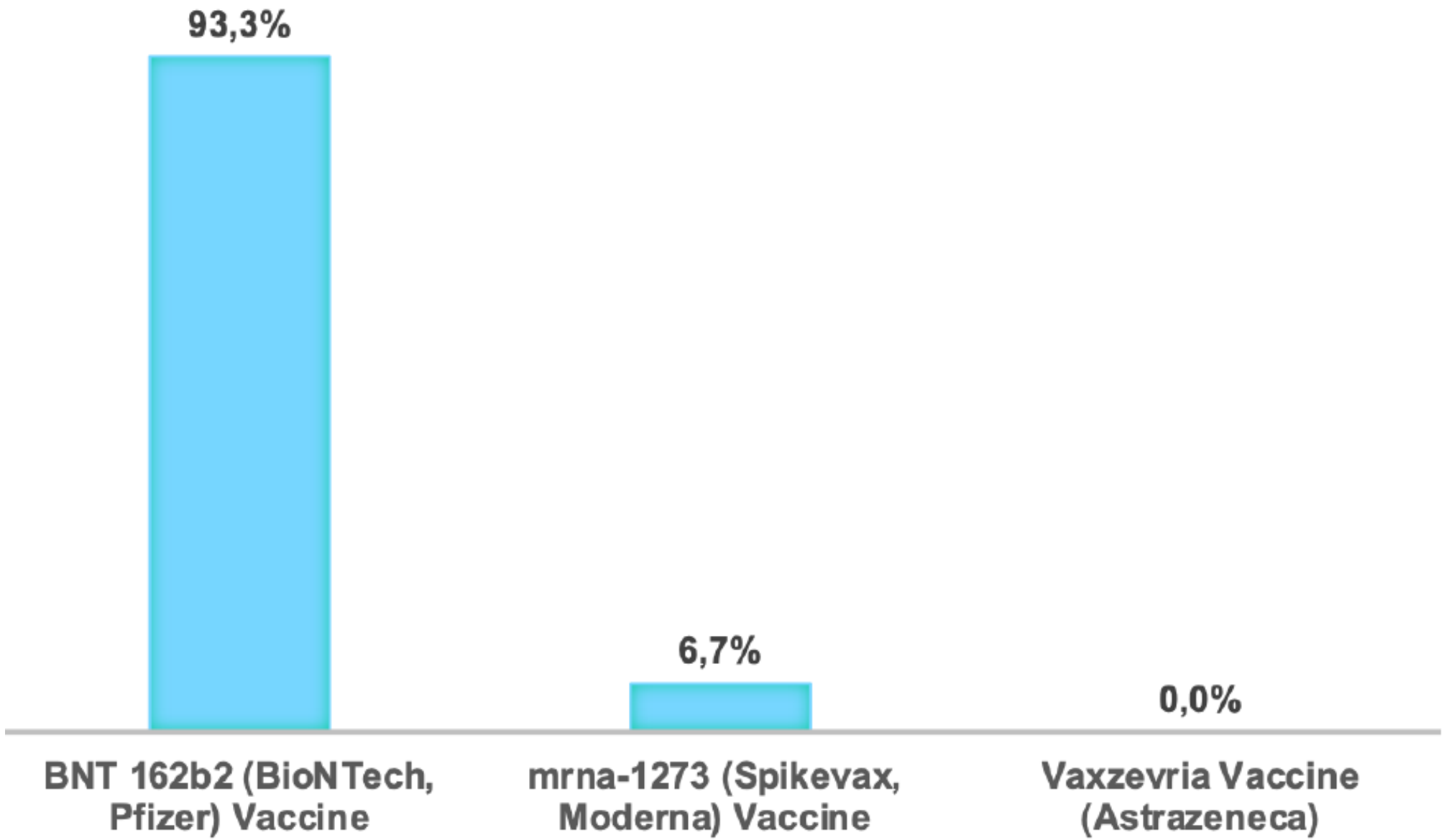


Fig. 2b. Timeline description.

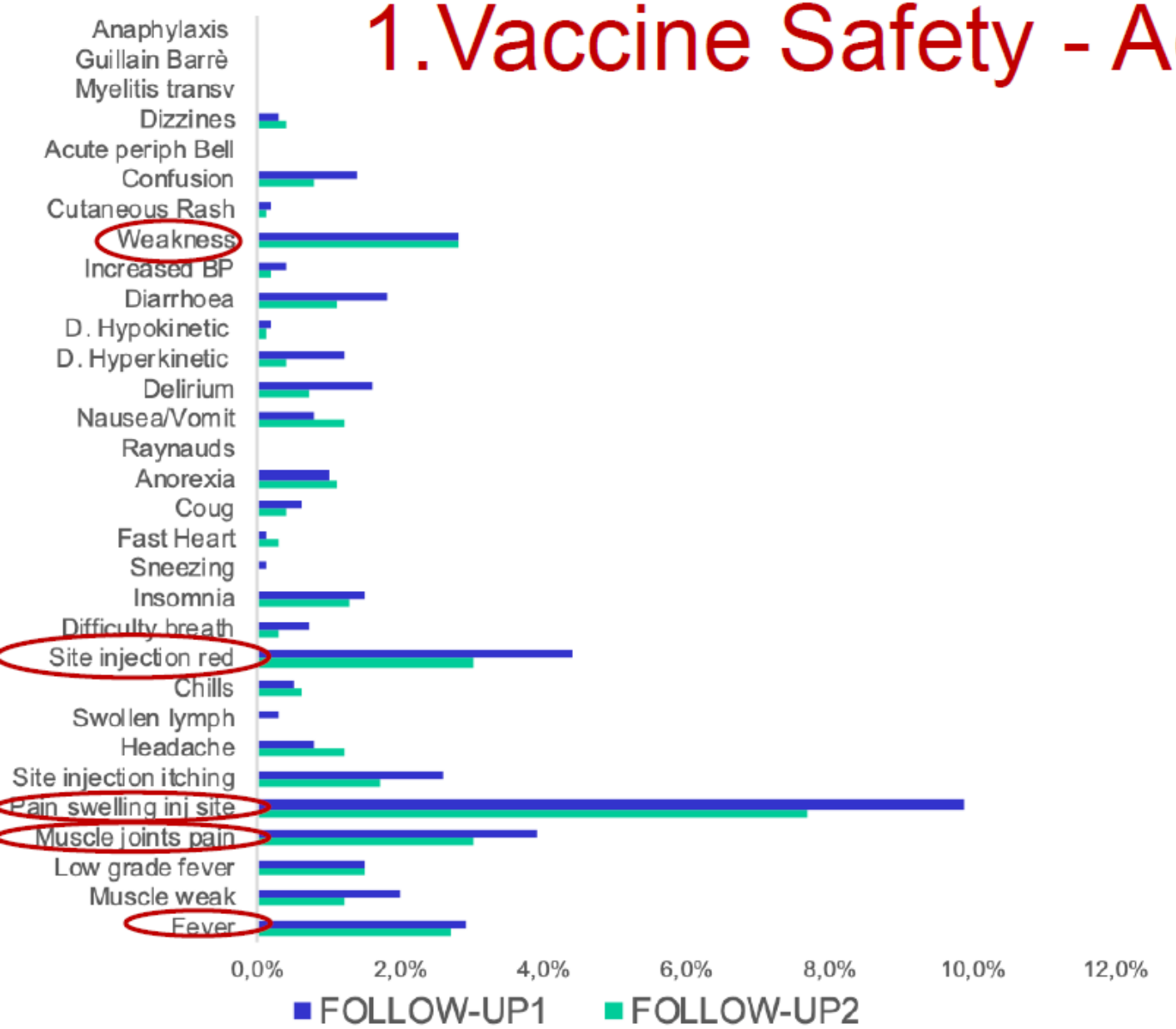
SARS-CoV-2 Type Vaccine

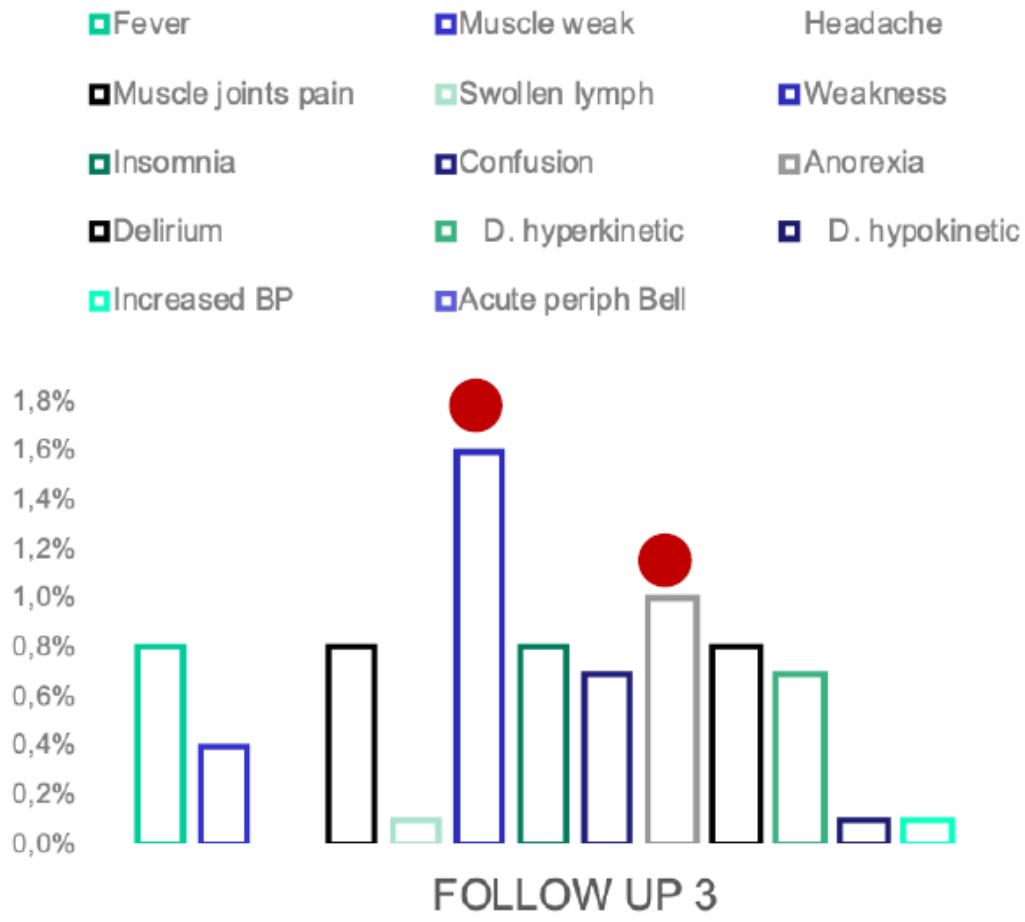


Sample characteristics

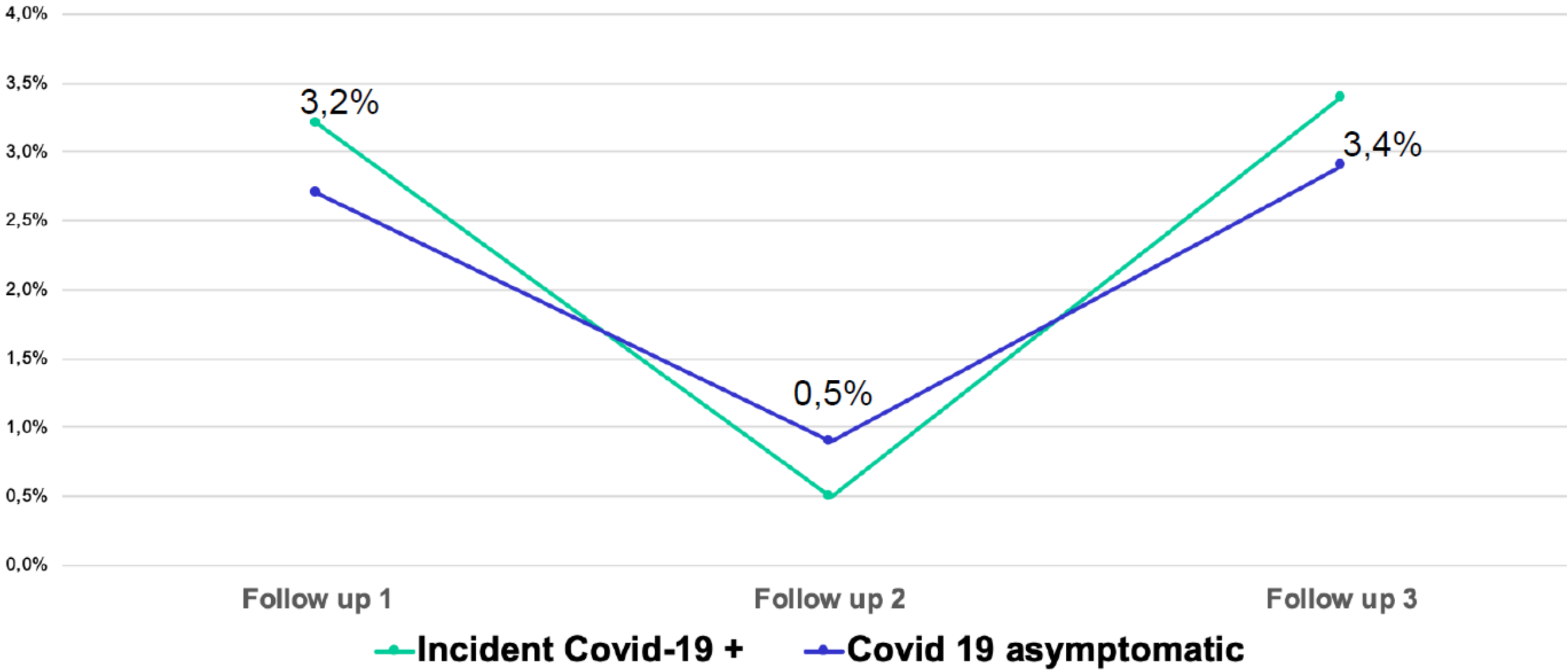
- ✓ Women: 71,1%
- ✓ White Race: 87,4%
- ✓ Age mean: 83,35 ± 9,15
- ✓ Number Chronic Diseases: 5,34 ± 2,48
- ✓ Mobility > Walk indep/cane/walker: 58,0%
  - > Move with wheelchair: 26,6%
  - > Bed Ridden: 6,6%
- ✓ Previous Covid-19 Residents: 30,3%

1.Vaccine Safety - Adverse Reactions



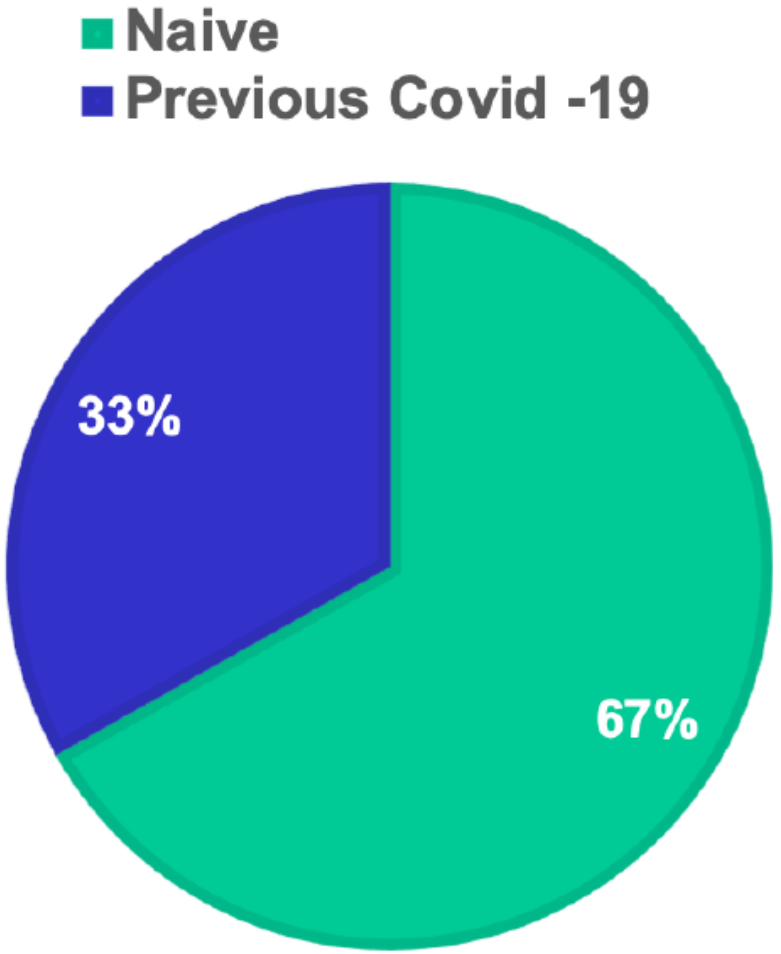


2. Vaccine Efficacy- New Covid-19 cases



Gerovax Ancillary Study 1

- ✓ Women: 68,5%
- ✓ Age mean: 82,35 ± 9,56
- ✓ White Race: 97,3%
- ✓ Number Chronic Diseases: 4,91 ± 2,34
- ✓ Mobility > Walk indep/cane/walker: 50,9%
  - > Move with wheelchair: 27,7%
  - > Bed Ridden: 8,5%
- ✓ Cognitive Disorders: 66,5%



- ✓ The 82.6% among naïve and 19,5% among previous Covid-19 received the 2nd dose

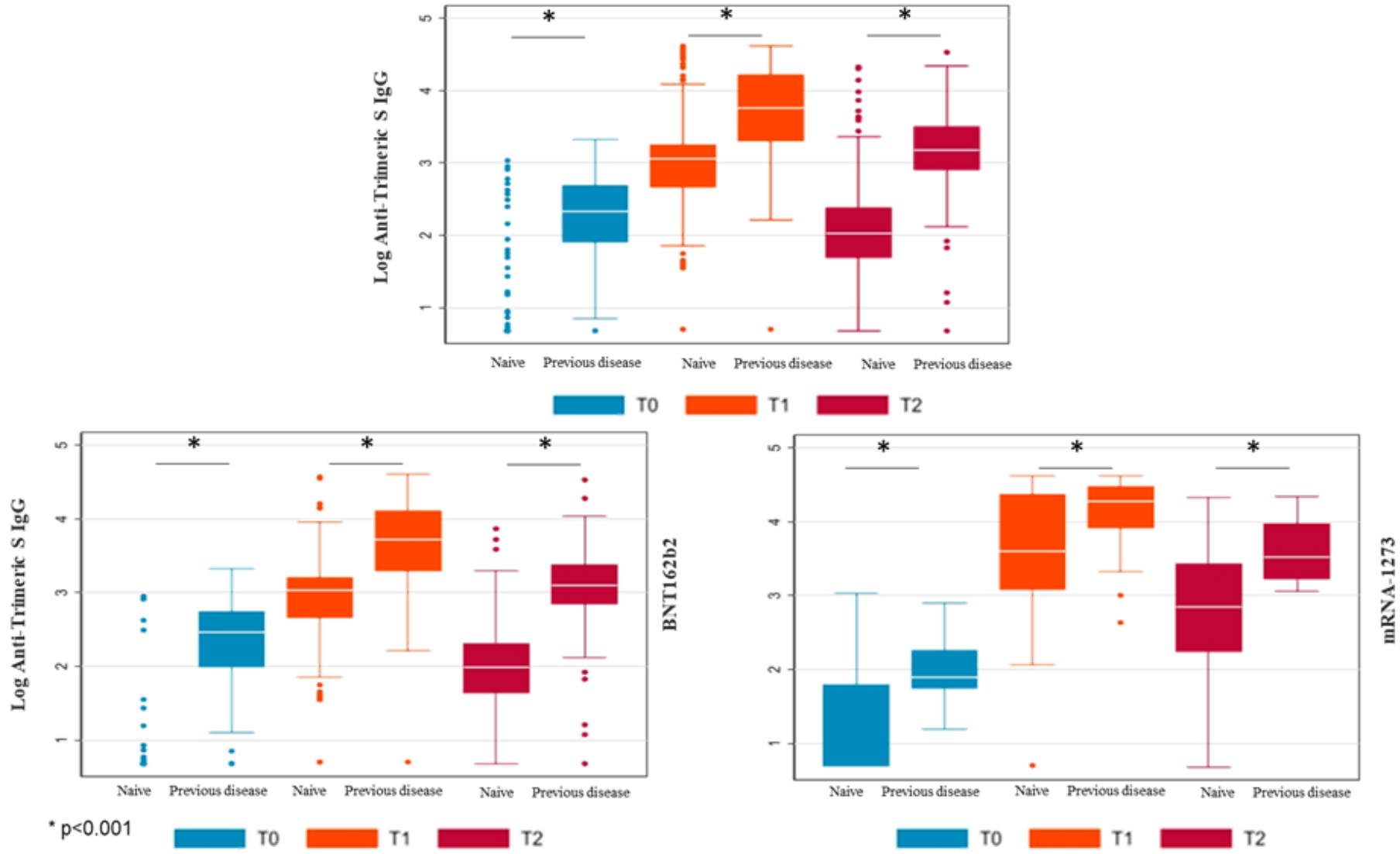


Figure 1. SARS-CoV-2 trimeric S IgG antibody concentration (log-transformed values) before vaccination (T0), 2 months (T1) and 6 months (T2) after first dose of vaccine according to prior SARS-CoV-2 infection. Data are presented for the whole sample (upper panel, n=395), for mRNA-1273 (n=51, lower left panel) and BNT162b2 vaccines (n=344, lower right panel).

Preliminary Results

- ✓ No serious adverse reactions were reported in the sample examined
- ✓ The short and long-term adverse reactions, associated with the anti SARS CoV-2 vaccine, were mainly mild or moderate
- ✓ Anti-S Ab response was significantly higher in previous Covid-19 residents.
- ✓ Older age, female sex and vaccine doses number, seem to be associated with a greater anti-S Ab response in residents with previous Covid-19
- ✓ Older age, female sex, and higher number of chronic diseases seem to be associated with a greater anti-S Ab response in naïve individuals
- ✓ After an increase in anti-S Ab response at T1, we observed a decline at the 6-month assessments indipendently to all determinants evaluated.

GeroCovid VAX/ Observational

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THANK YOU FOR YOUR ATTENTION

Definitions

- **Efficacy** is the ability of an intervention to produce an effect. In medicine is the ability of an intervention or a drug to produce a desired effect in ideal conditions.
- **Effectiveness** is the ability to achieve a desired result. In medicine, effectiveness investigates how a treatment works in practice and not in a RCT or laboratory study.

The real patient is different from the ideal one

COMPLEXITY

- Multimorbidity
- Polypharmacy
- Functional status
  - Cognitive
  - Physical
  - Mood
- Incontinence
- Malnutrition
- Falls
- Osteoporosis

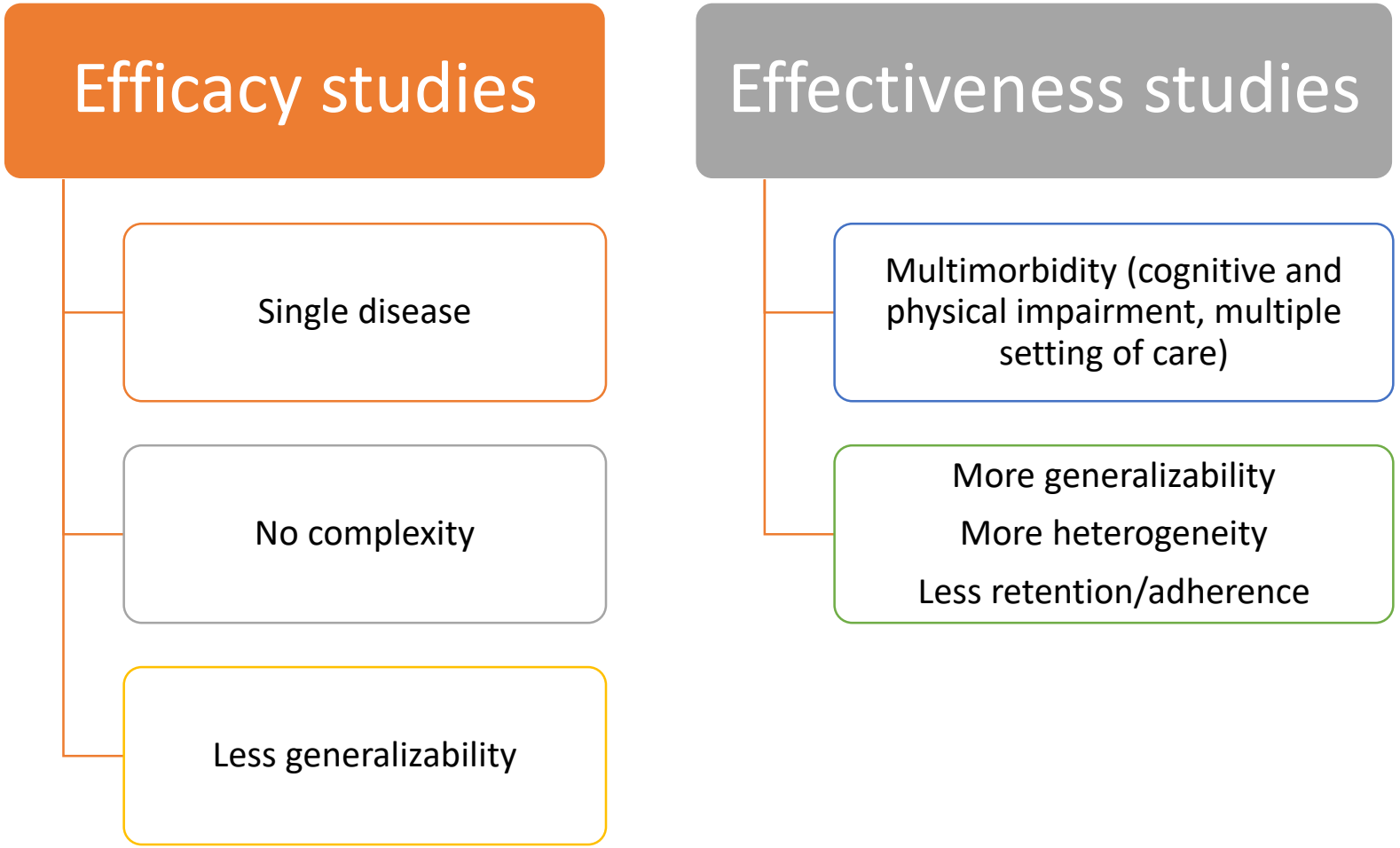
Comparative Effectiveness Research and Patients with Multiple Chronic Conditions

Mary E. Tinetti, M.D., and Stephanie A. Studenski, M.D.

Researchers have largely shied away from the complexity of multiple chronic conditions — avoidance that results in expensive, potentially harmful care of unclear benefit.

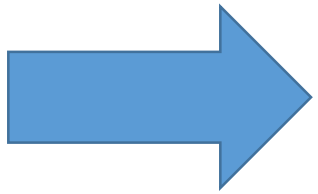
N ENGL J MED 364;26 NEJM.ORG JUNE 30, 2011

Study populations



Heterogeneity

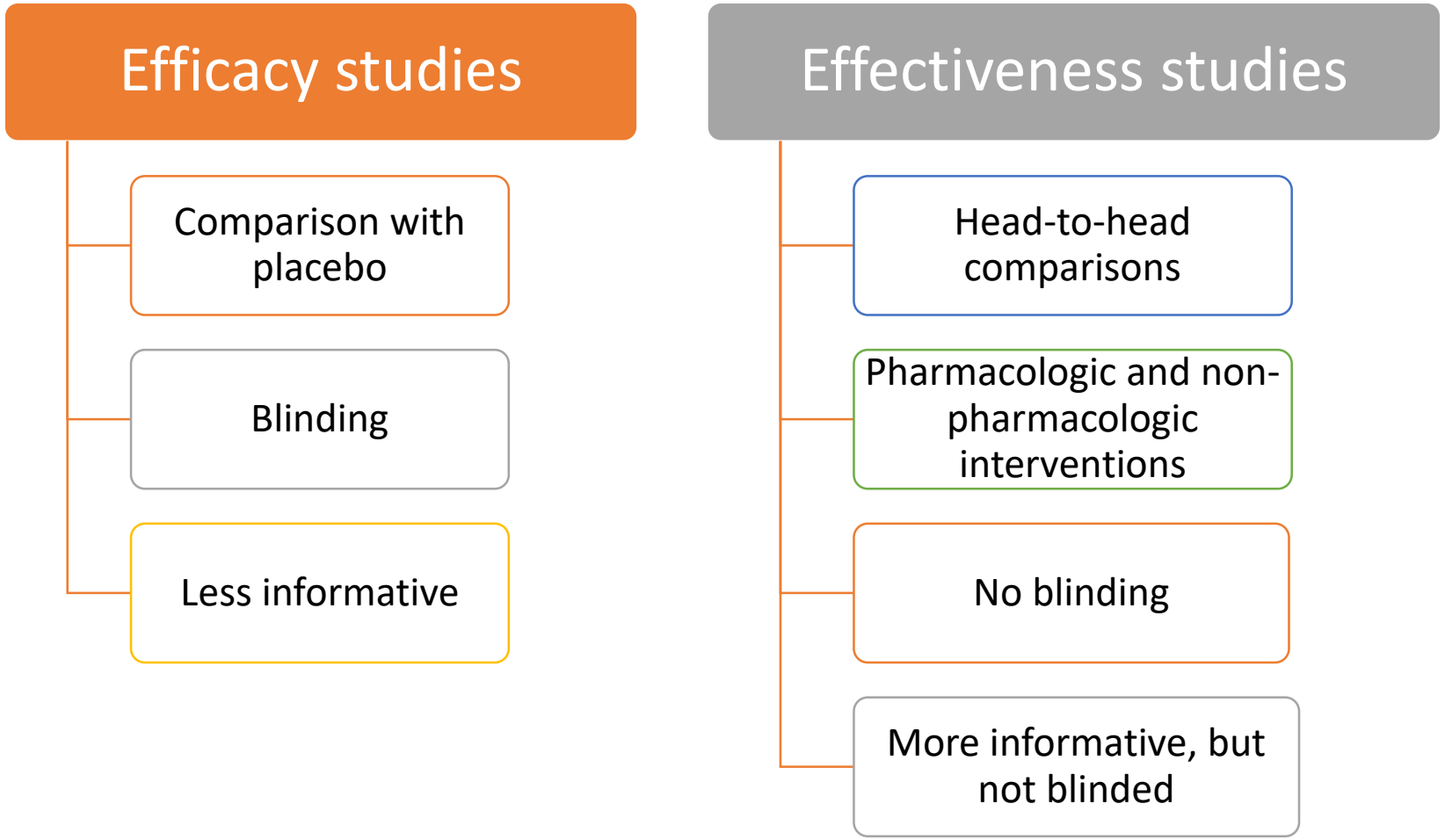
- Heterogeneity is caused by:
  - Initial risk level for selected outcomes
  - Response to treatment
  - Risk of adverse event



Strata analysis: evaluating treatment in homogeneous groups

Tinetti & Studenski, NEJM 2011

Intervention and study design



Intervention and design for effectiveness studies

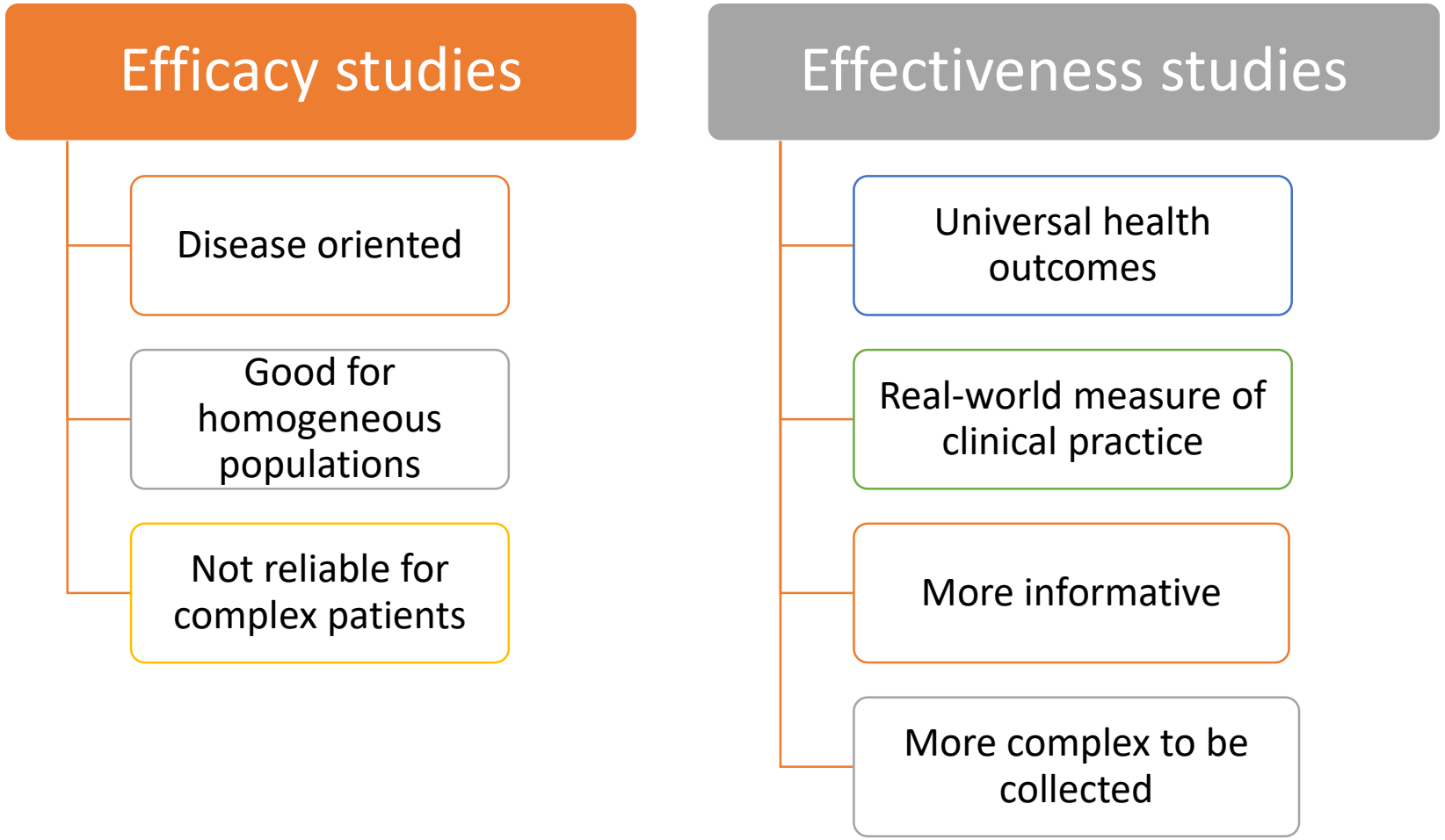
- To investigate treatments for associated disease in which the treatment of a disease may exacerbate or improve the other one;
- To test interventions that can simultaneously affect multiple diseases;
- To test combinations of pharmacological and non-pharmacological interventions;
- To compare models of care

Blinding and outcomes issue

- The combination of non-blinded interventions and subjective clinical outcomes (self- assessed) may lead to potential bias: the expectations of the patient may influence subjective outcome reporting
- Effectiveness studies have greater strength when they include both objective outcome (survival, hospitalization, etc) and subjective measures (quality of life, etc).

Ware et al, NEJM 2011

Outcomes


Efficacy studies
Disease oriented
Good for homogeneous populations
Not reliable for complex patients
Effectiveness studies
Universal health outcomes
Real-world measure of clinical practice
More informative
More complex to be collected

Evidence “biased” geriatric medicine

- Older patients with comorbid conditions are frequently excluded from clinical trials, and evidence coming from these studies is only partly applicable to this population.
- This bias also affects clinical practice guidelines that are based on evidence coming from randomized trials and meta-analyses.
- Guidelines are generally disease-focused, thus raising the difficulties for applying them in older patients with comorbid conditions. Indeed, a guideline-driven therapeutic approach in such patients often results in adverse drug-drug or drug-disease interactions in the presence of complex polypharmacy regimens.
- **Antimicrobial trials including older complex patients are urgently needed.**

Conclusioni

- L’epidemia Covid-19 ha imposto un rapido reindirizzamento della ricerca clinica ed epidemiologica.
- E’ necessario ripensare: metodi di ricerca, setting e popolazioni, scopi.
- Le relative acquisizioni dovrebbero essere funzionali alla programmazione sanitaria e all’implementazione del PNRR.
- Senza un’integrazione tra monitoraggio clinico e sorveglianza epidemiologica si rischia di ignorare eventi ad alto impatto sanitario.
- Servono competenze e professionalità mediamente ignorate.