ISARIC-4C: Lessons from 82 000 in-hospital patients with COVID-19

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Better health, better futures

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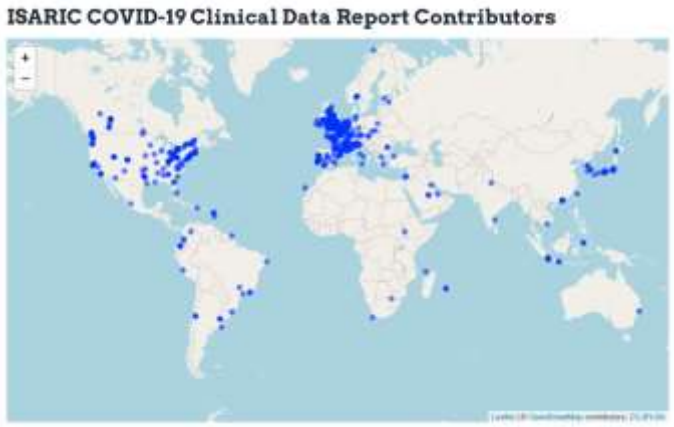
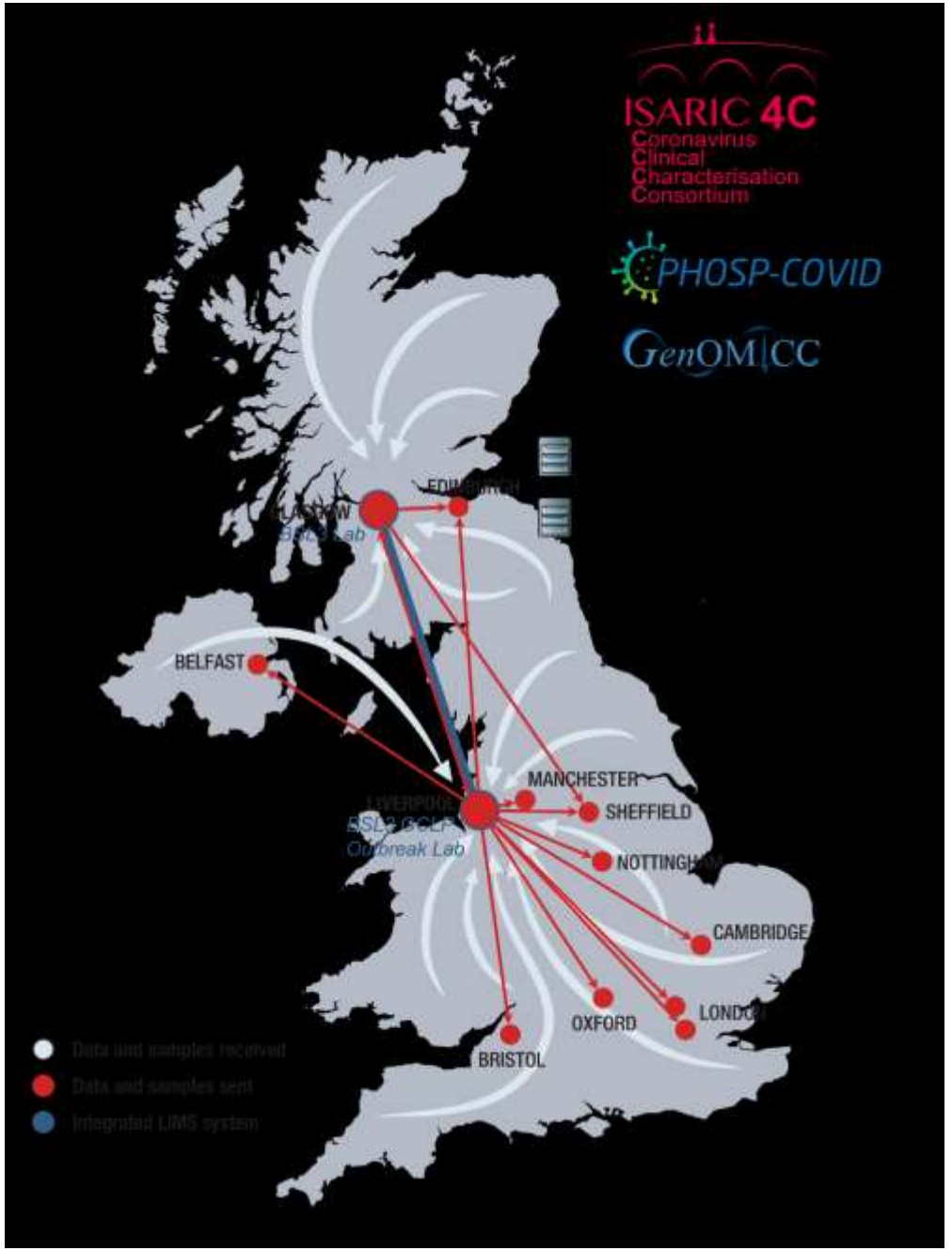
ISARIC 4C Coronavirus Clinical Characterisation Consortium

ISARIC-4C





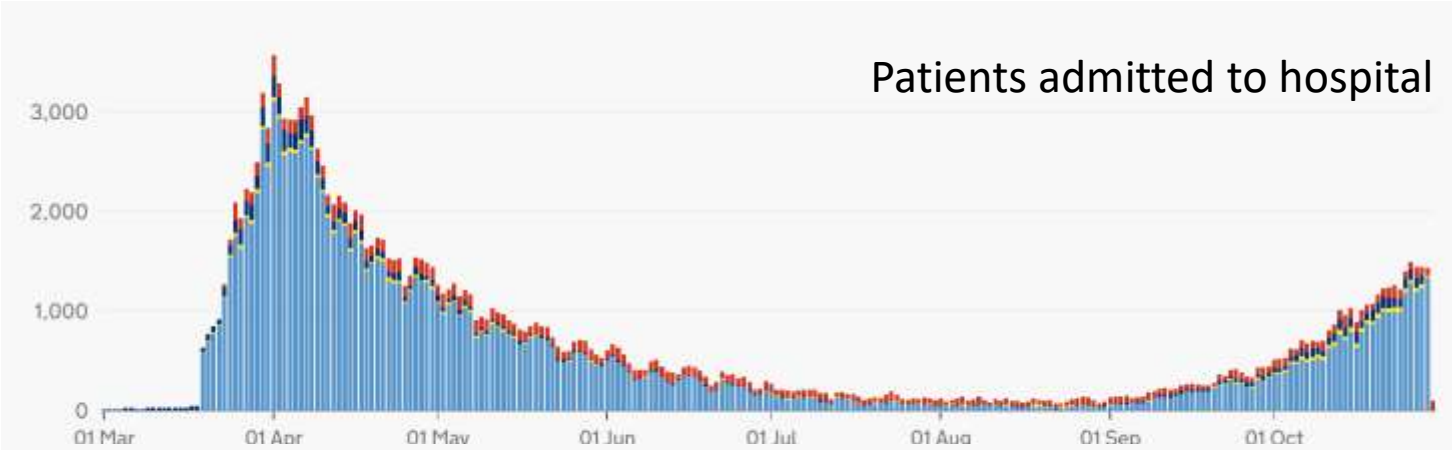
>90K patients
Largest in-hospital dataset

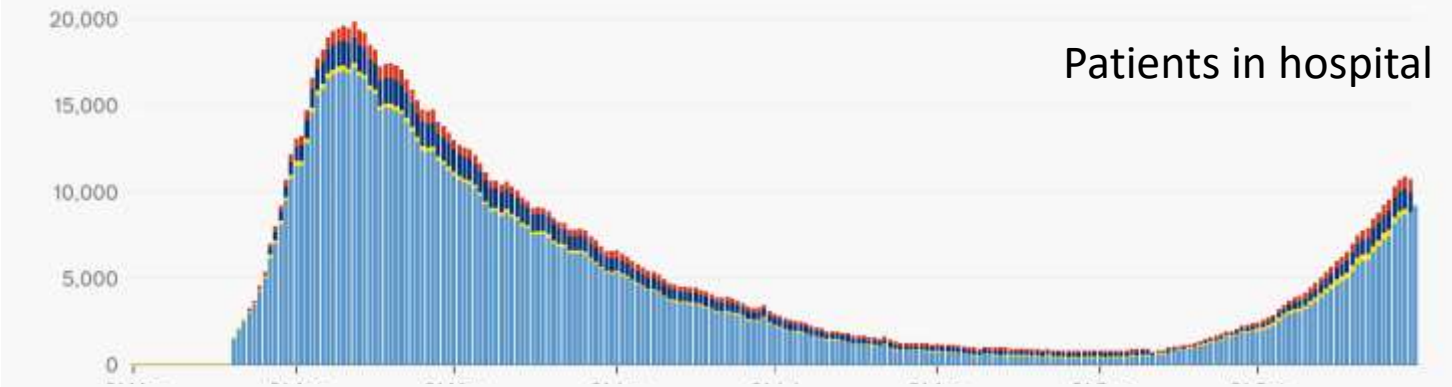
Summary

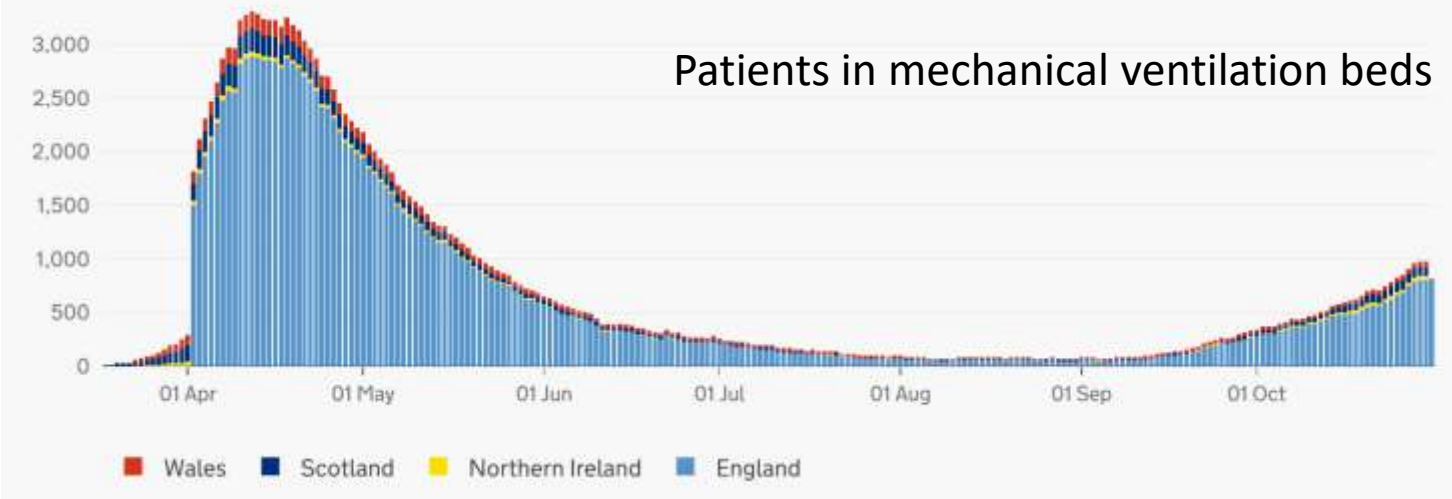
1. Characteristics of wave 1 vs. wave 2
2. Risk stratification of in-patients
3. Complications and sequelae of SARS-CoV-2 infection
4. Change in hospital mortality over duration of pandemic
5. Translating evidence into practice: Steroids and covid-19

Characteristics of wave 1 vs. wave 2

Current situation



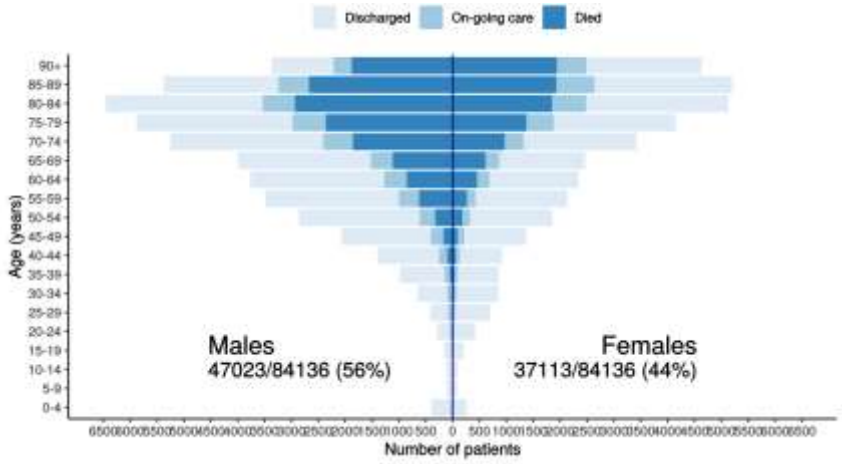




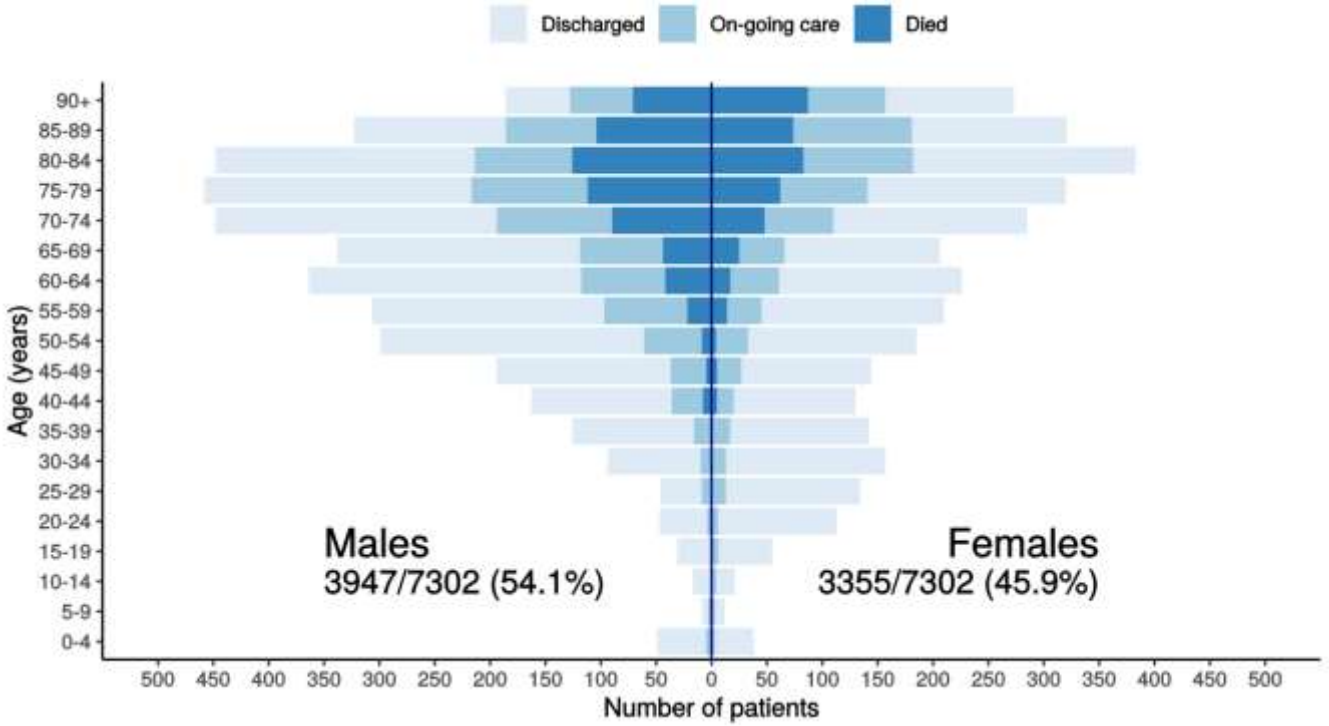
coronavirus.data.gov.uk

Age and sex

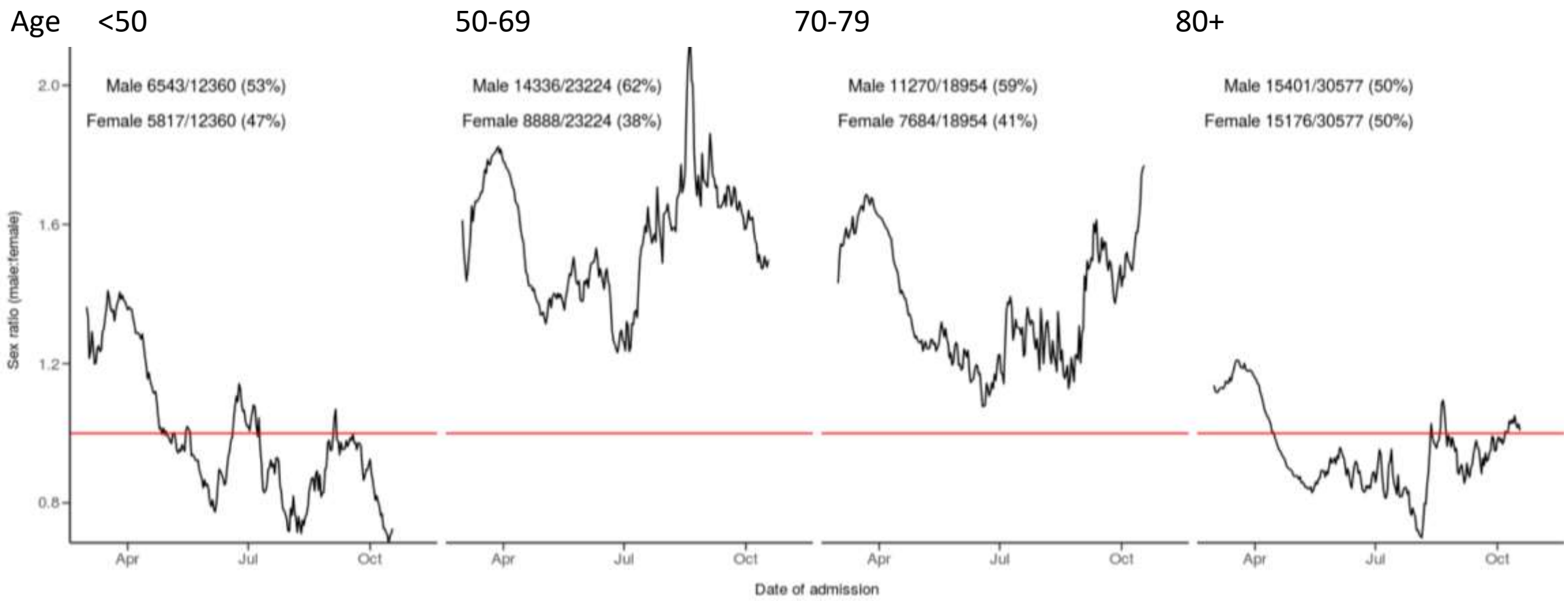
All



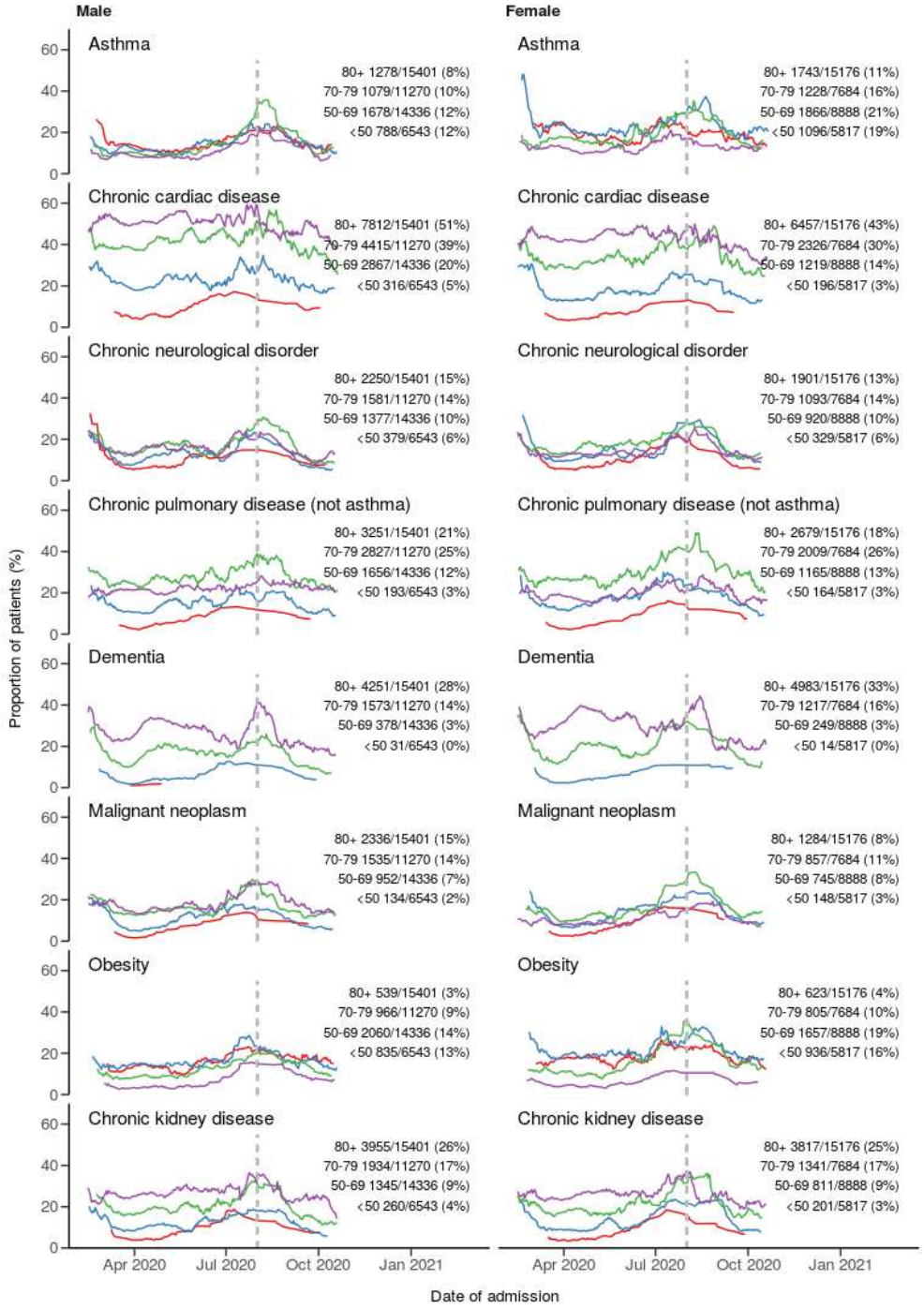
After 1st August



Sex ratio


Age <50
50-69
70-79
80+
Male 6543/12360 (53%)
Female 5817/12360 (47%)
Male 14336/23224 (62%)
Female 8888/23224 (38%)
Male 11270/18954 (59%)
Female 7684/18954 (41%)
Male 15401/30577 (50%)
Female 15176/30577 (50%)
Sex ratio (male:female)
2.0
1.6
1.2
0.8
Apr
Jul
Oct
Date of admission

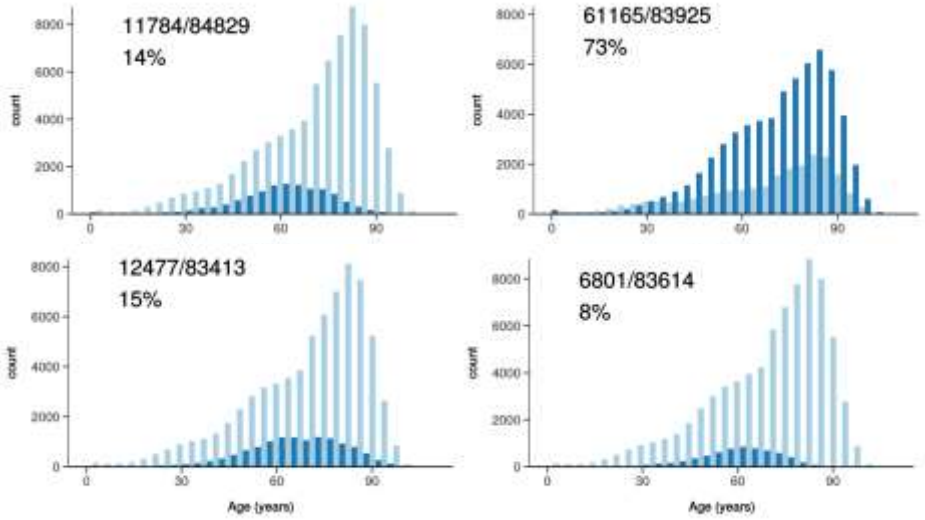
Comorbidities



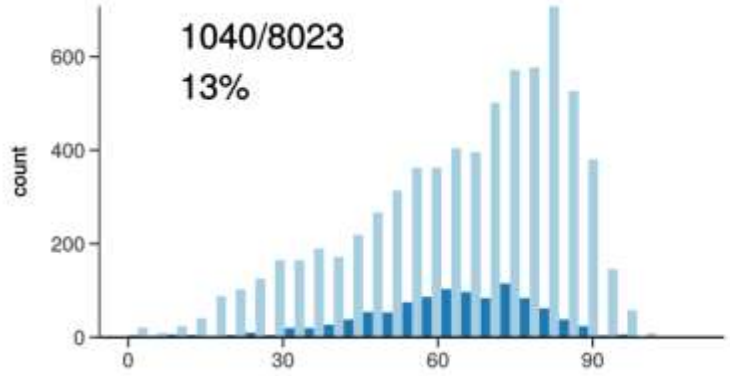
Age

— <50 — 50-69 — 70-79 — 80+

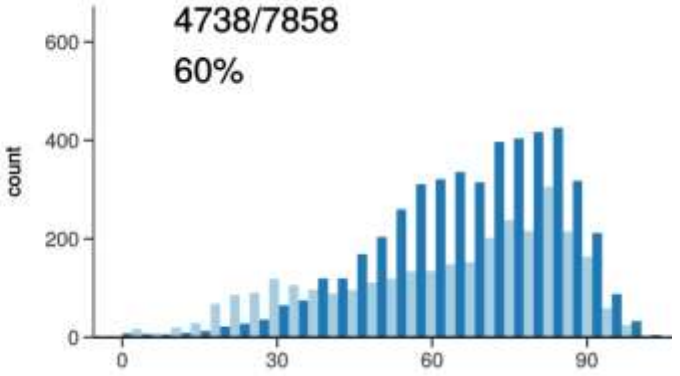
Management



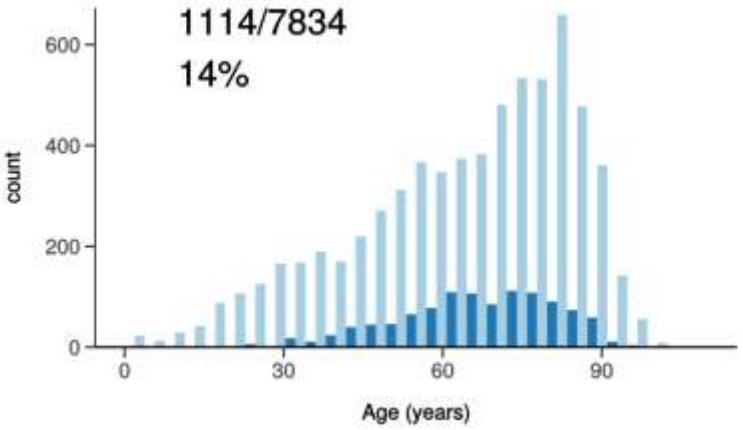
HDU/ICU



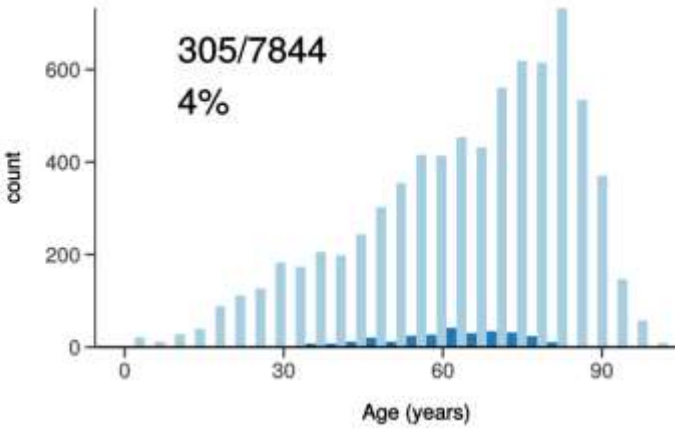
High flow oxygen



Non-invasive

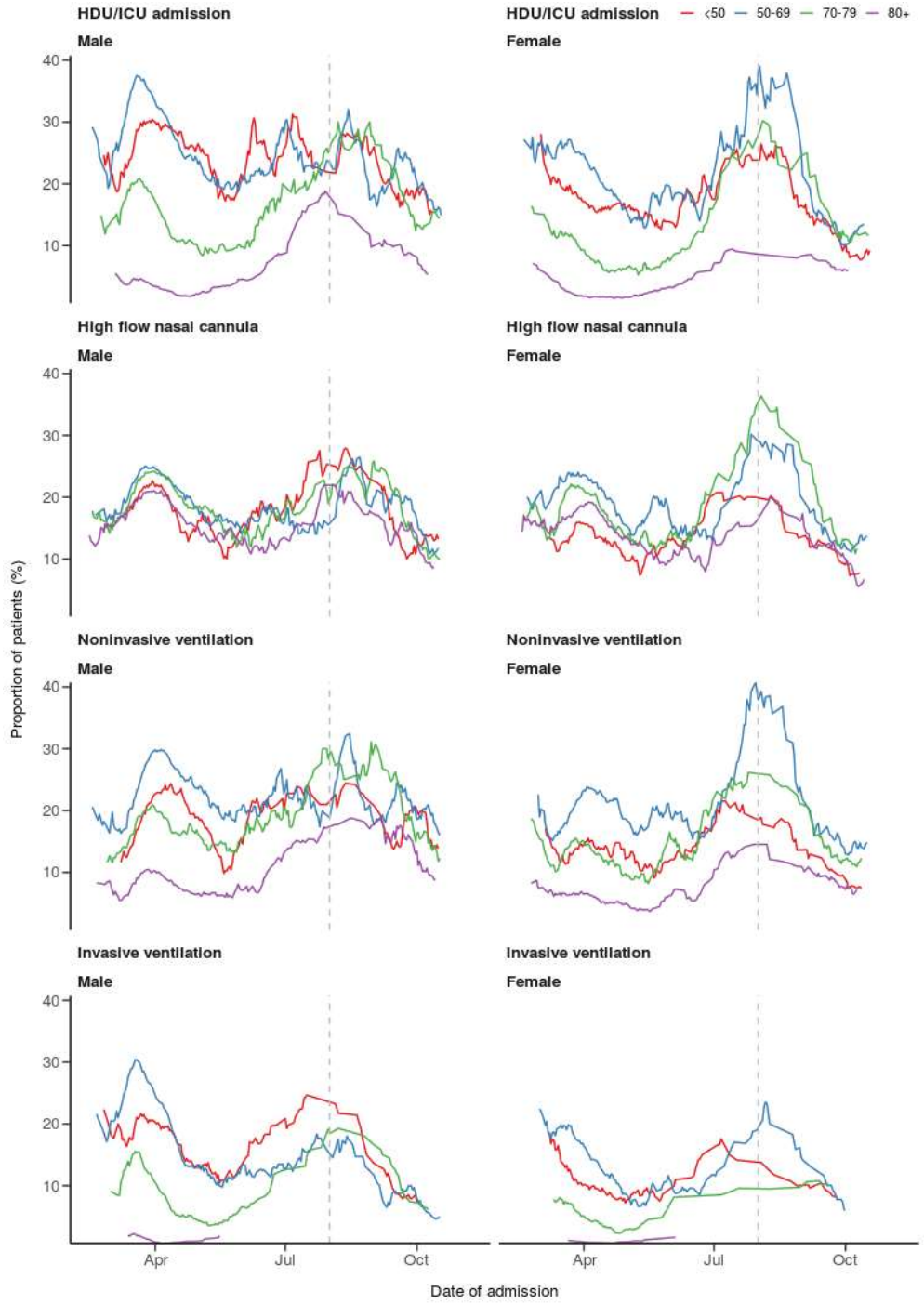


Invasive mechanical



No Yes

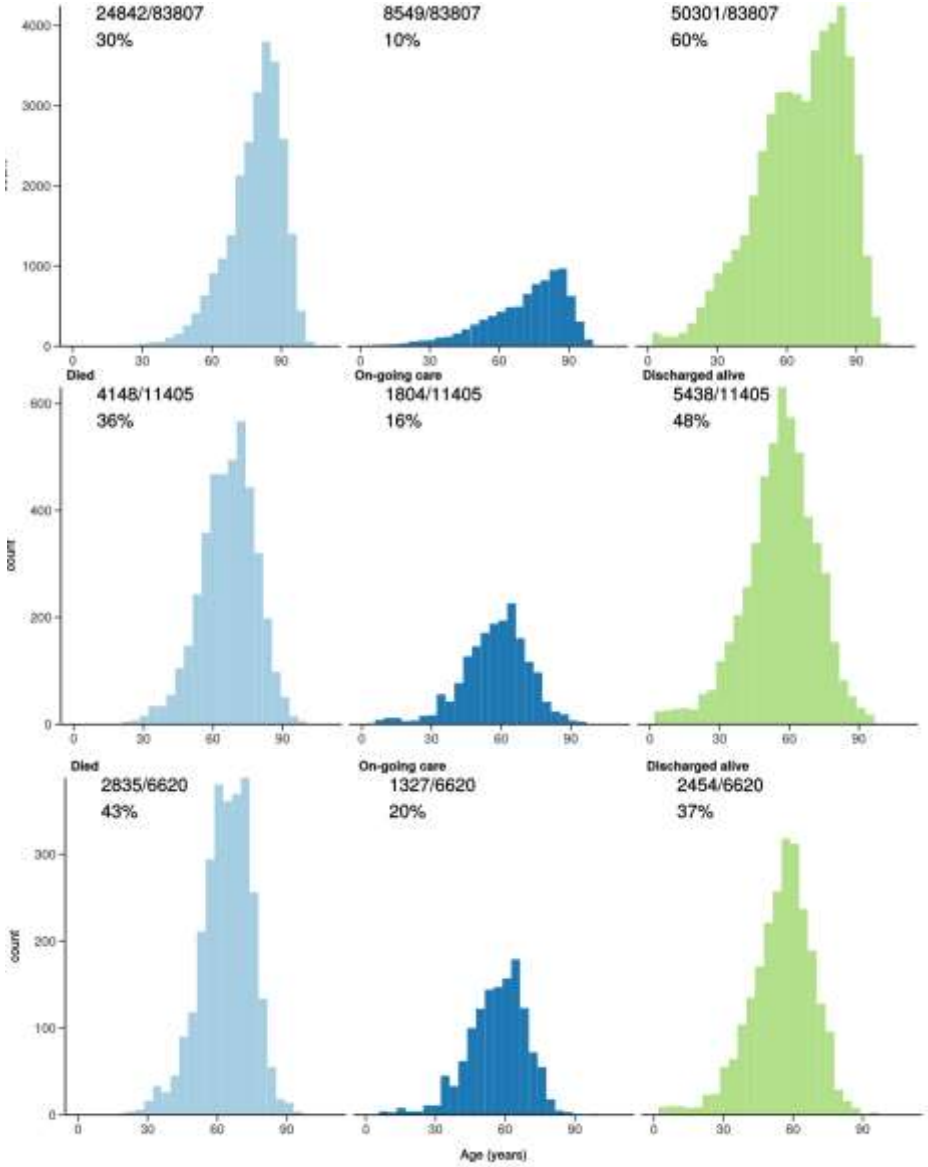
Management



Age

<50 50-69 70-79 80+

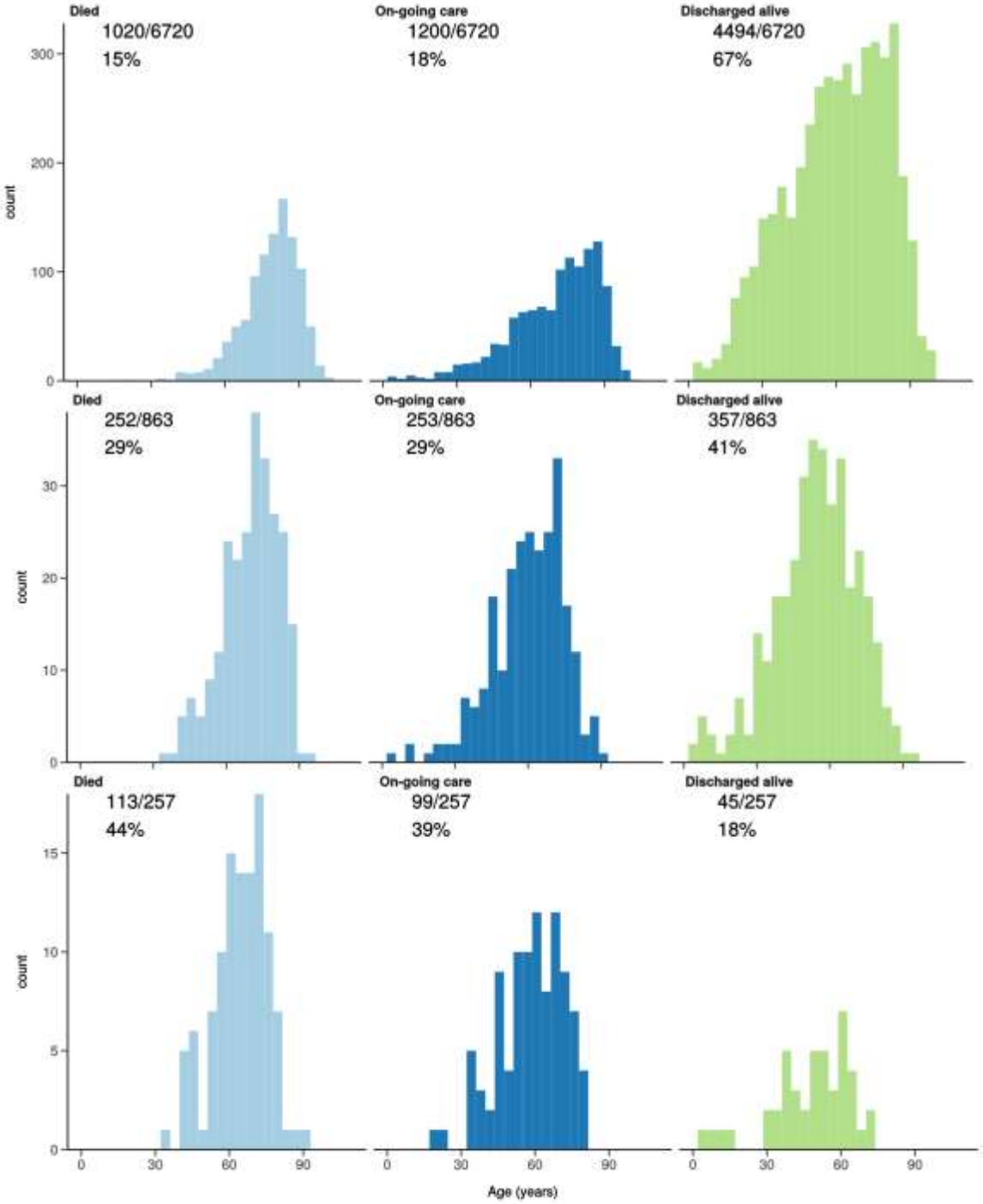
Outcomes



All patients

HDU/ICU

Invasive mechanical ventilation



Risk stratification of in-patients

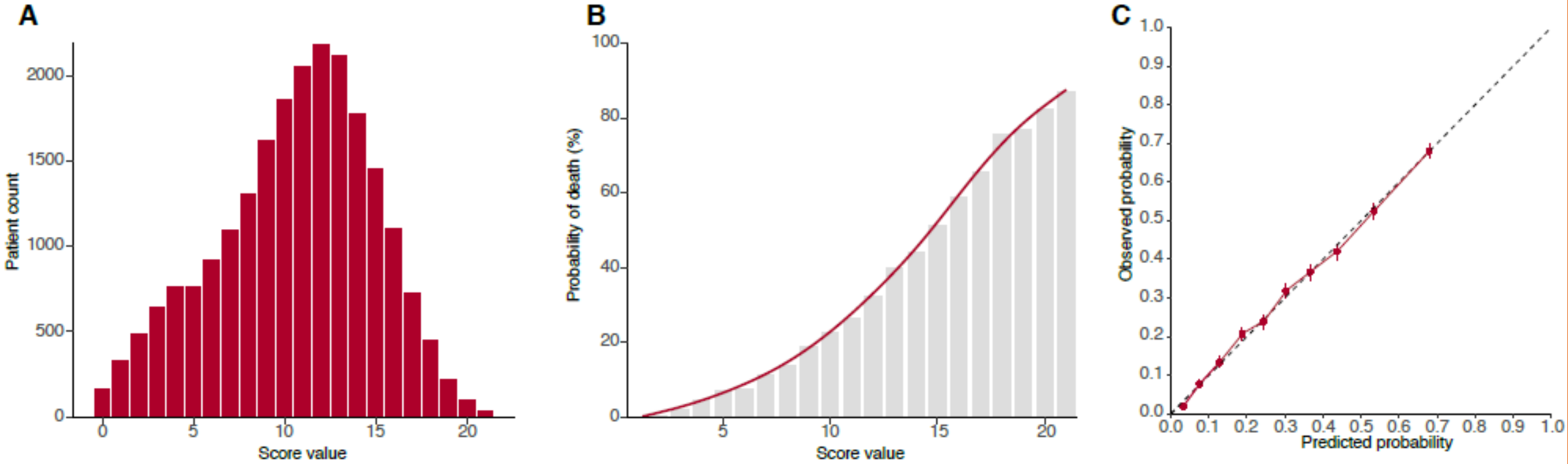
Risk stratification

4C mortality score
4C deterioration model

Variable		4C Mortality Score
Age (years)	<50	
	50-59	+2
	60-69	+4
	70-79	+6
	≥80	+7
Sex at birth	Female	
	Male	+1
Number of comorbidities*	0	
	1	+1
	≥2	+2
Respiratory rate (breaths/minute)	<20	
	20-29	+1
	≥30	+2
Peripheral oxygen saturation on room air (%)	≥92	
	<92	+2
Glasgow Coma Scale	15	
	<15	+2
Urea (mmol/L)	<7	
	7-14	+1
	>14	+3
CRP (mg/L)	<50	
	50-99	+1

Knight et al BMJ 2020

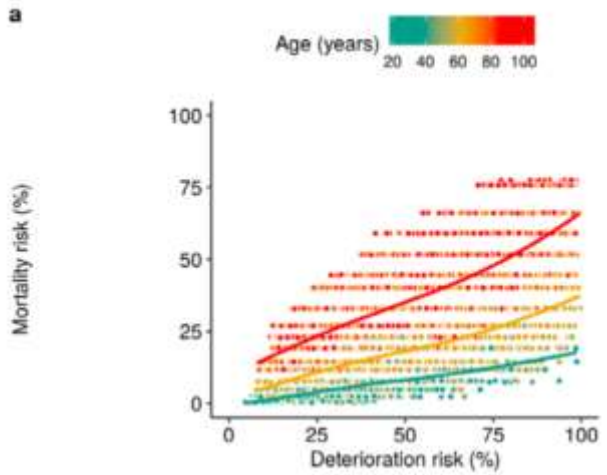
4C mortality score

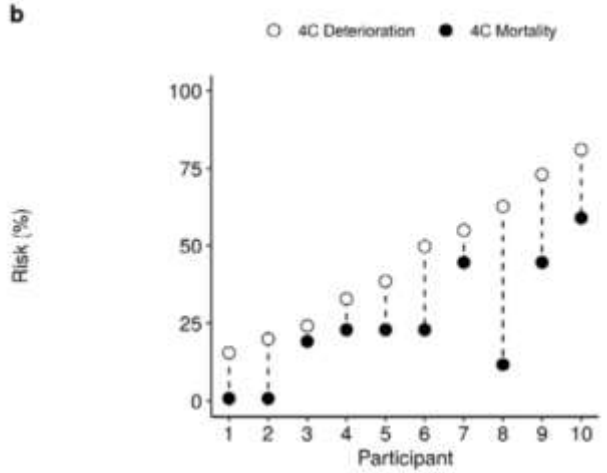


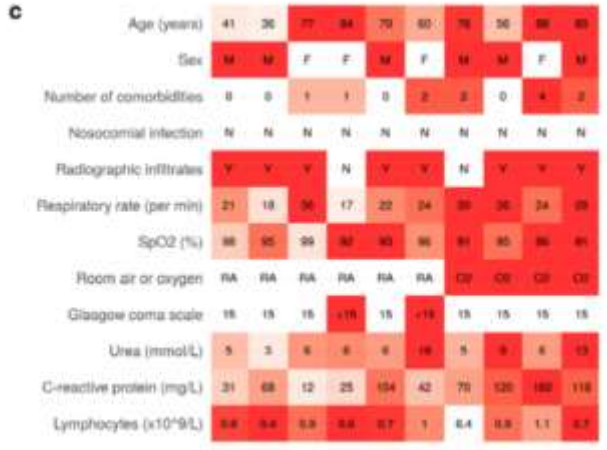
4C deterioration model

- +
- Lymphocyte count
- Radiological infiltrates
- Nosocomial infection

- 4C mortality
  - Simple score, high level risk of death
- 4C deterioration
  - Complex model, useful in younger age groups

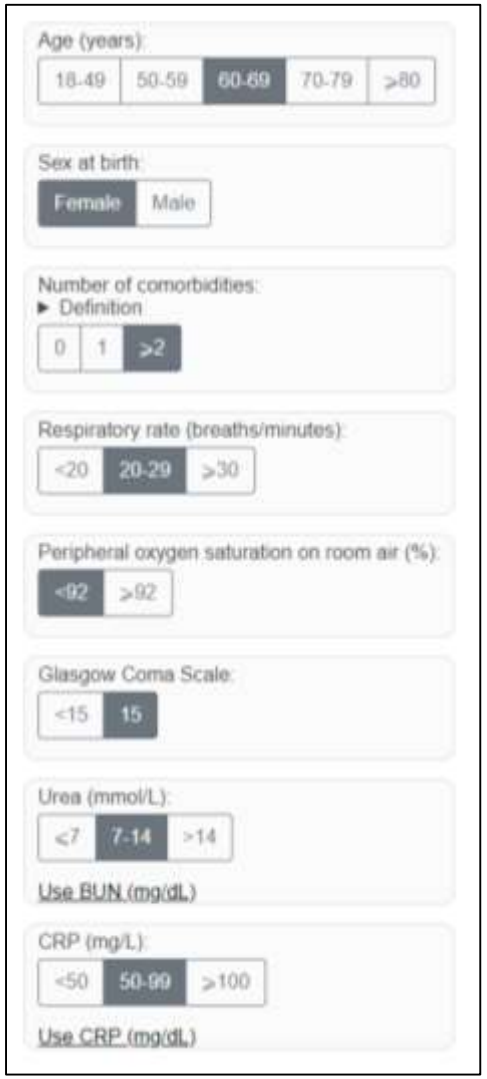


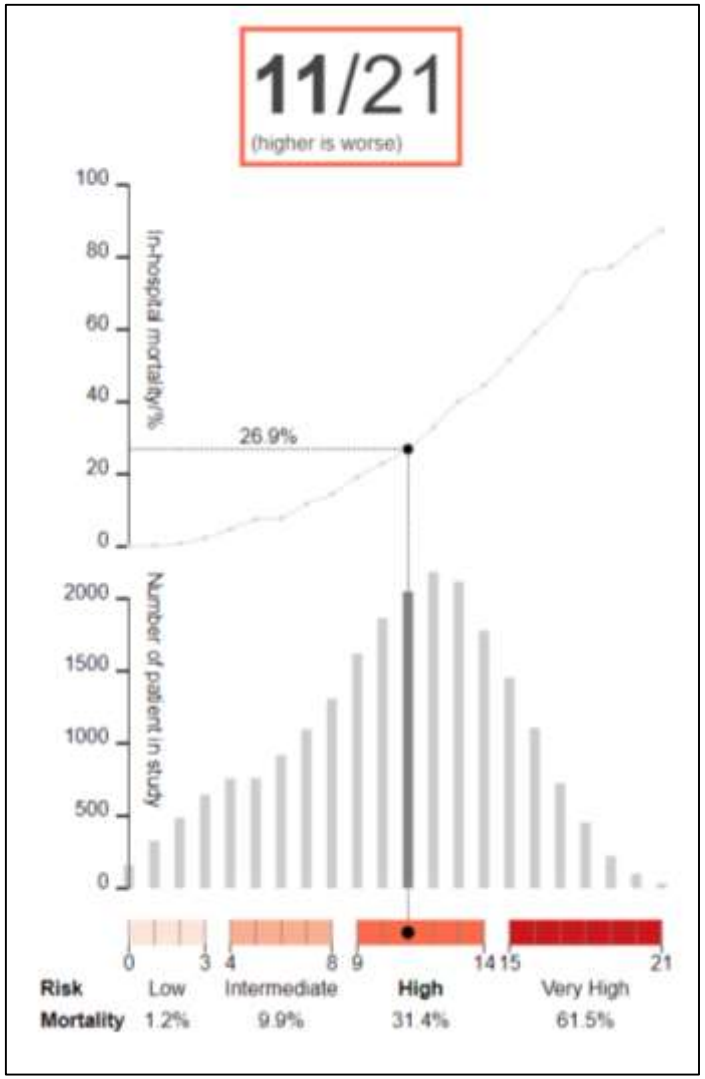




4C mortality score

- isaric4c.net/risk/

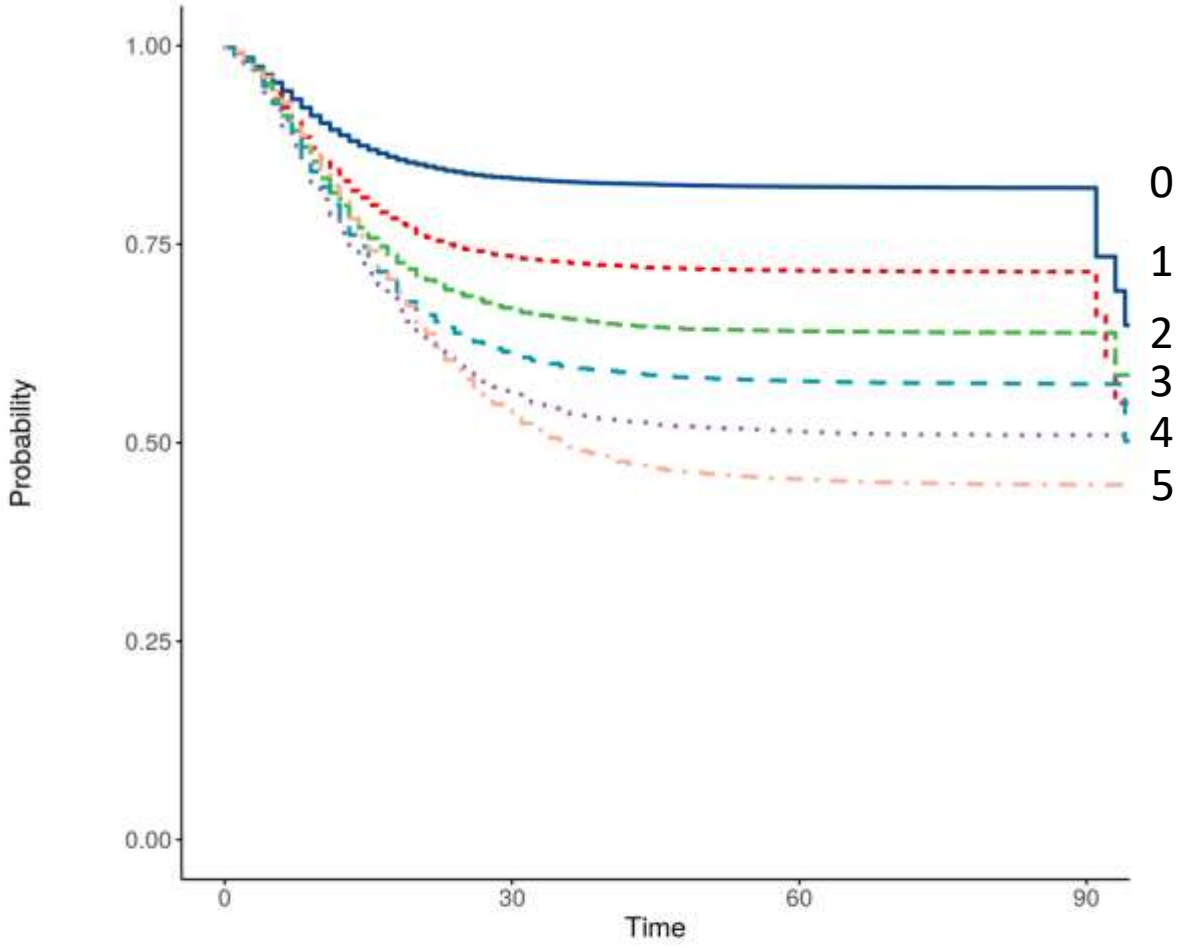




External validation

Complications and sequelae of SARS-CoV-2 infection

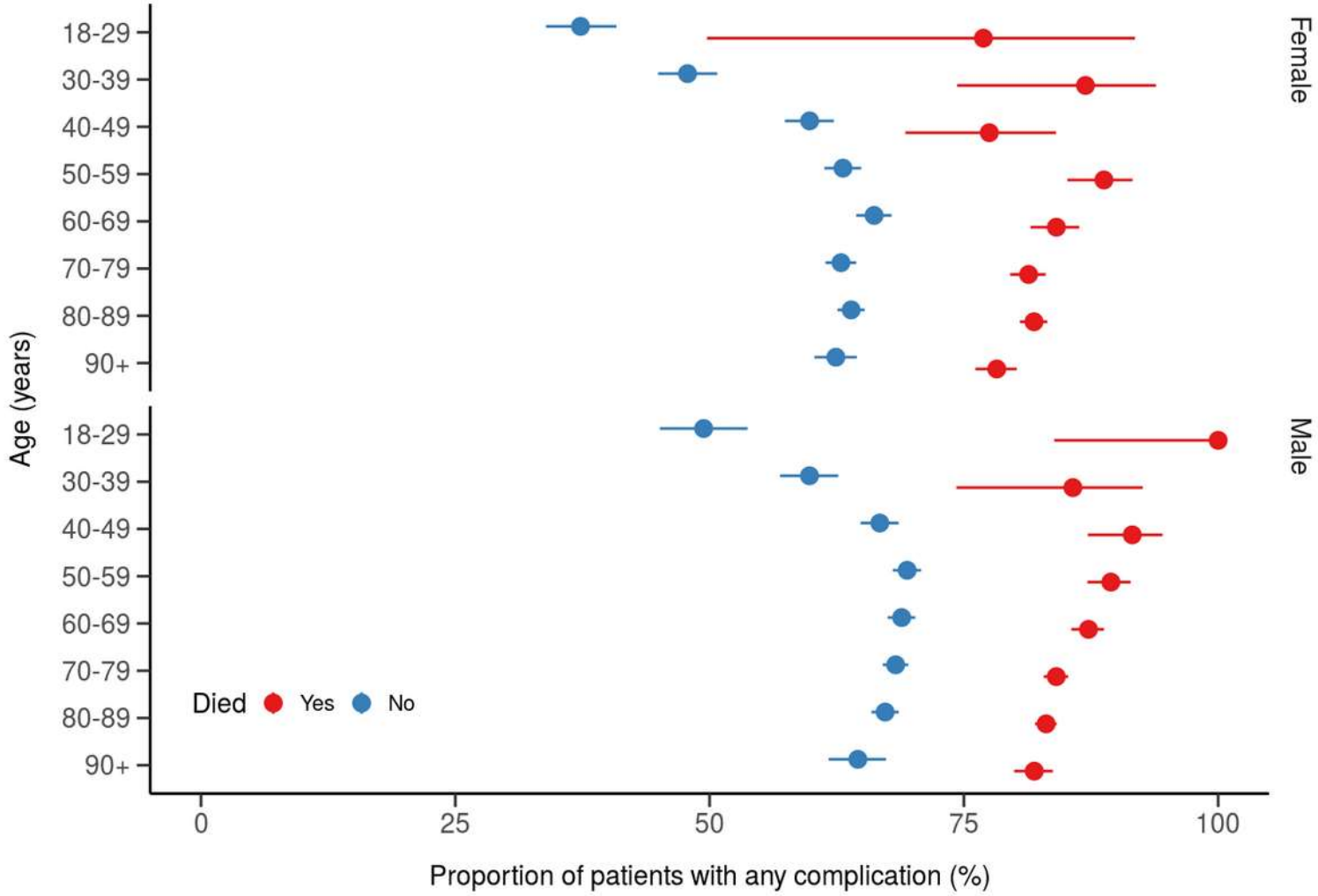
Complications and risk of death



Number at risk

n_comps_fct=0	20536	16921	16676	16641
n_comps_fct=1	19970	14640	14264	14231
n_comps_fct=2	11669	7795	7456	7431
n_comps_fct=3	6757	4146	3896	3869
n_comps_fct=4	3910	2210	2012	1992
n_comps_fct=5+	4873	2635	2210	2171

Complications by age and sex

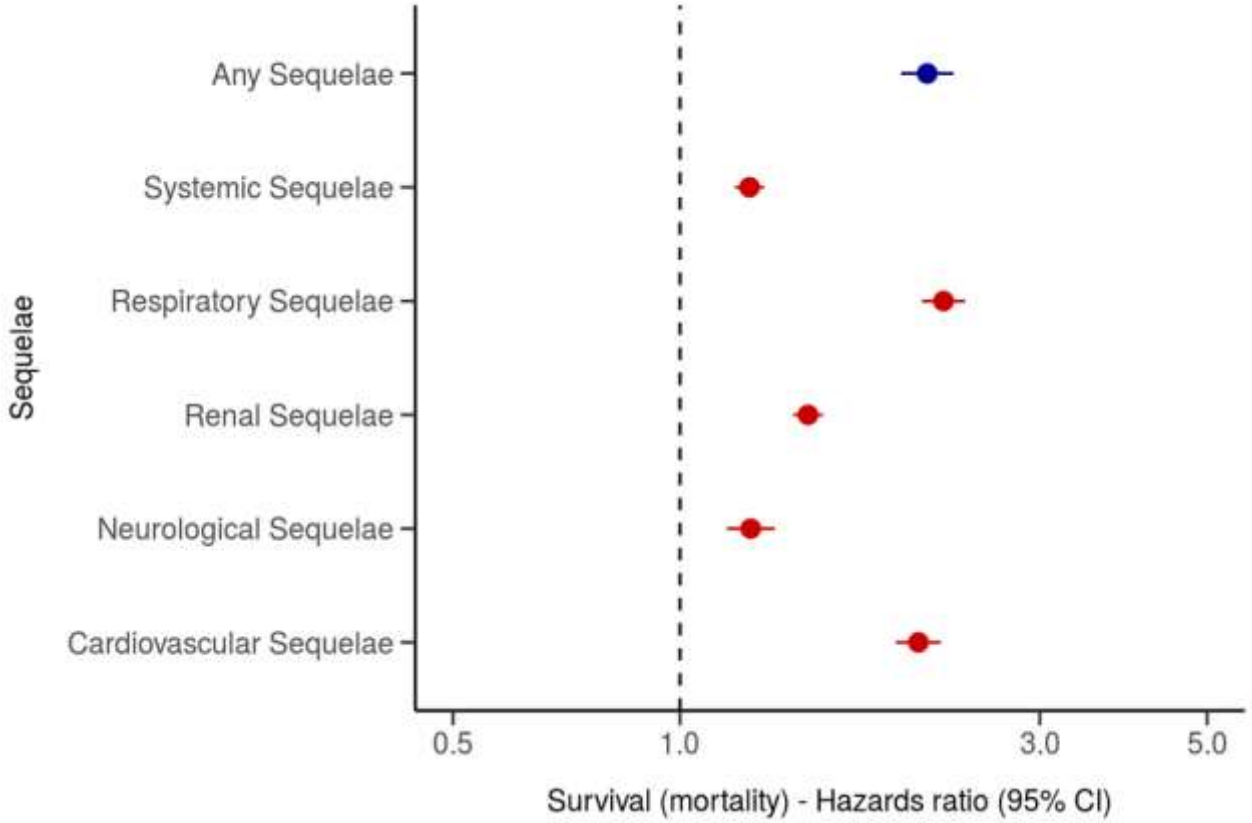


Complications by age and sex

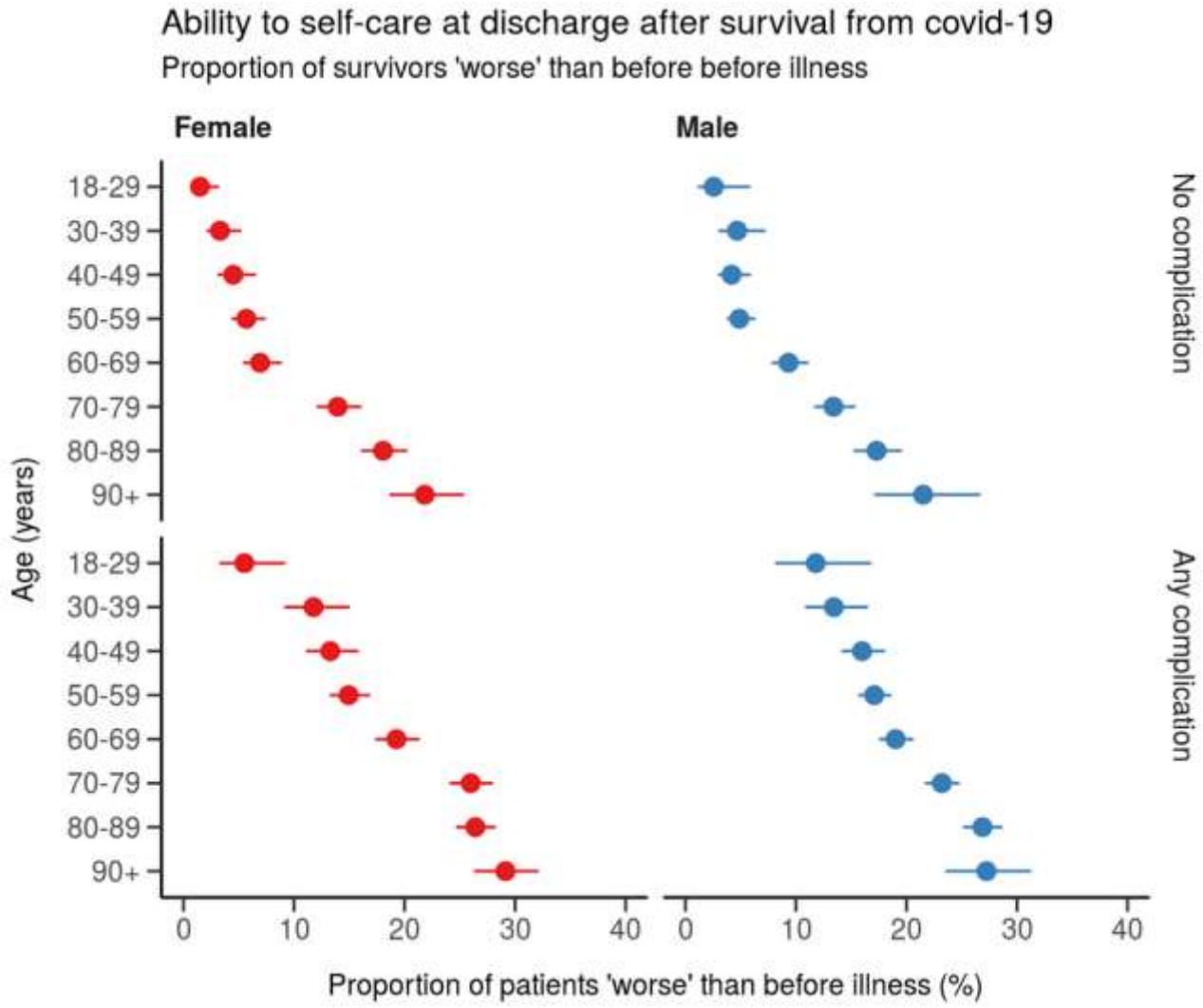
		Systemic	Renal	Cardiovascular	Neurological	Respiratory	Any complication
Total N (%)		11748 (19.2)	16240 (25.2)	8046 (13.2)	2674 (4.4)	37442 (60.1)	45723 (70.5)
Age on admission (years)	18-29	156 (12.5)	121 (9.3)	44 (3.5)	32 (2.6)	441 (35.0)	564 (43.2)
	30-39	354 (15.7)	317 (13.4)	112 (4.9)	75 (3.3)	1104 (48.3)	1308 (55.0)
	40-49	724 (17.2)	793 (18.0)	315 (7.5)	143 (3.4)	2556 (59.7)	2899 (65.6)
	50-59	1492 (19.4)	1926 (23.7)	770 (10.0)	312 (4.1)	4926 (62.8)	5710 (70.0)
	60-69	1980 (21.2)	2817 (28.5)	1263 (13.5)	430 (4.6)	6029 (63.2)	7189 (72.5)
	70-79	2707 (19.5)	3960 (27.1)	2005 (14.5)	619 (4.5)	8590 (60.9)	10617 (72.1)
	80-89	3218 (19.4)	4711 (26.9)	2570 (15.5)	797 (4.8)	10182 (60.2)	12889 (73.1)
	90+	1117 (18.8)	1595 (25.2)	967 (16.2)	266 (4.5)	3614 (59.2)	4547 (71.4)

Association between complications and morality

- Adjusted
  - Age, sex, comorbidity, deprivation

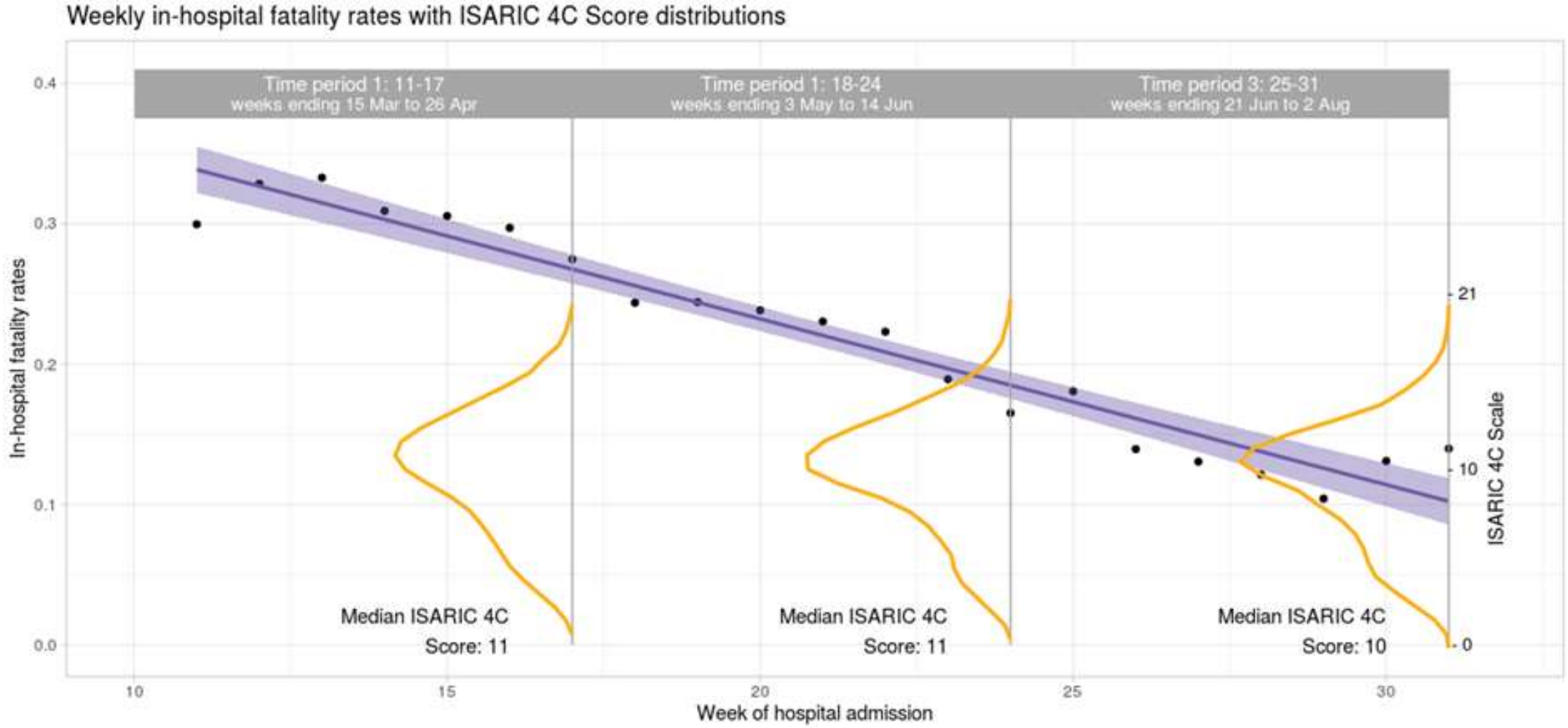


Ability to self-care at discharge



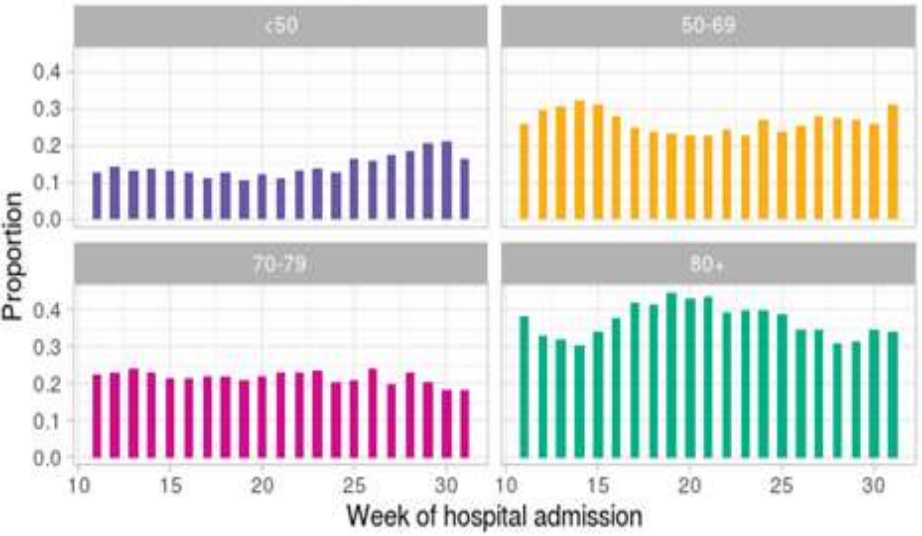
Change in hospital mortality over duration of pandemic

In hospital mortality over time

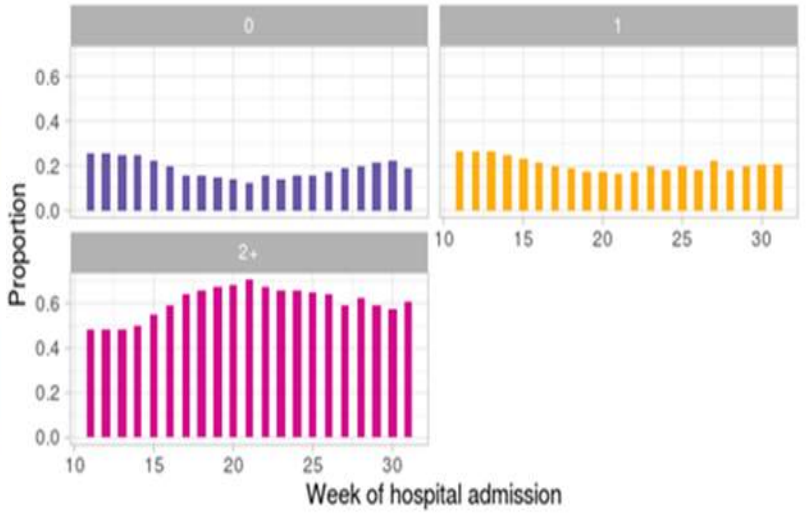


Changes in case-mix: Age, Comorbidity and Sex

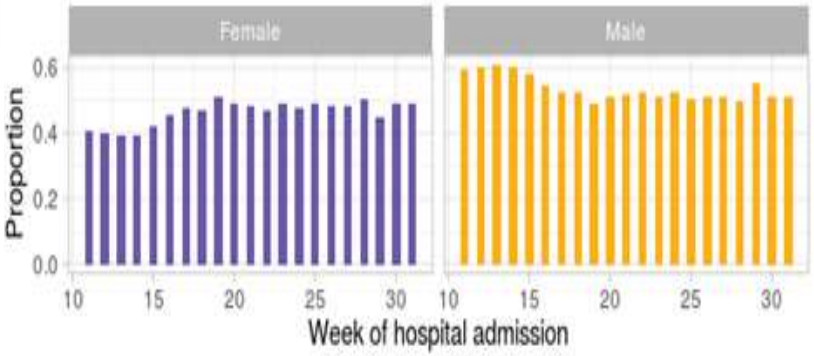
Age



Comorbidity count

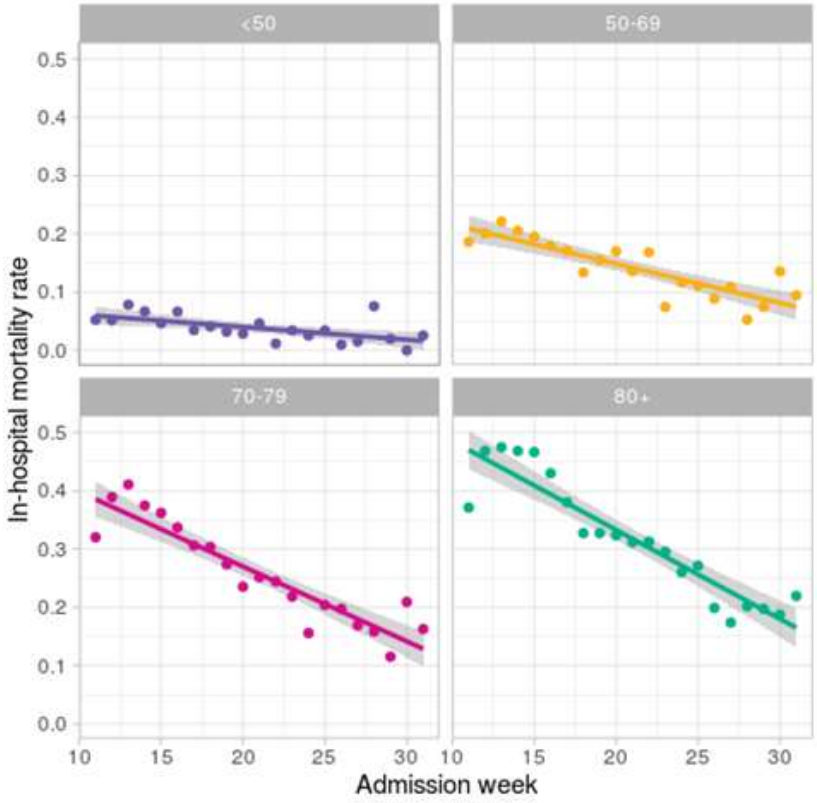


Sex

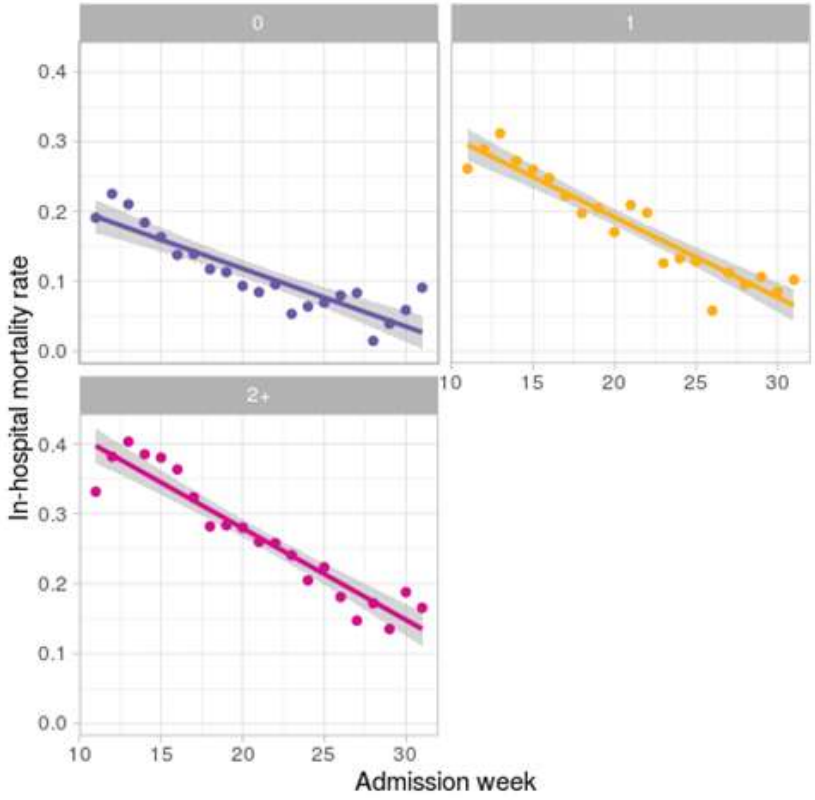


Age, Comorbidity, sex mortality over time

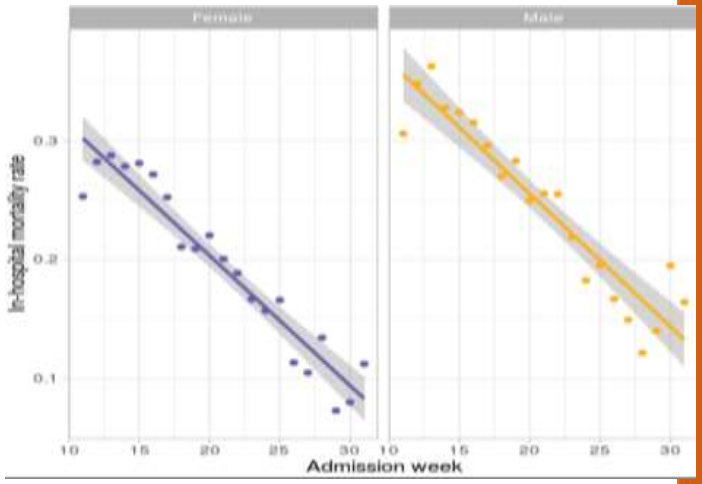
Age



Comorbidity count

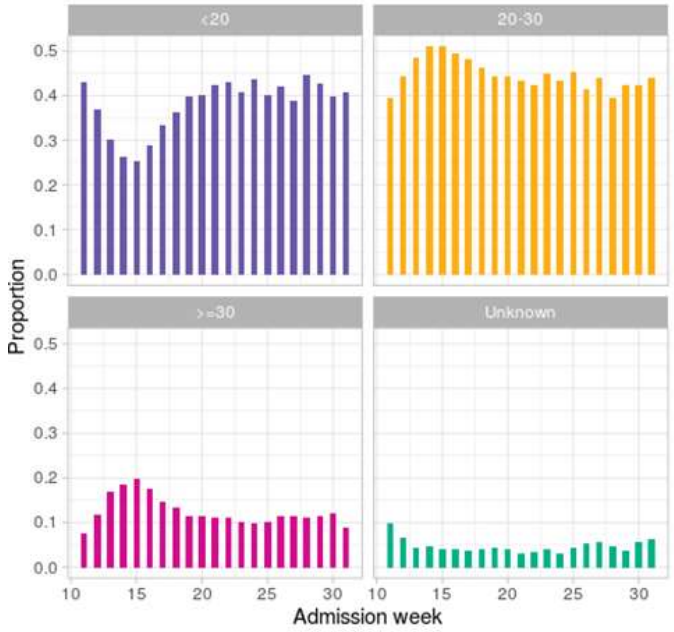


Sex

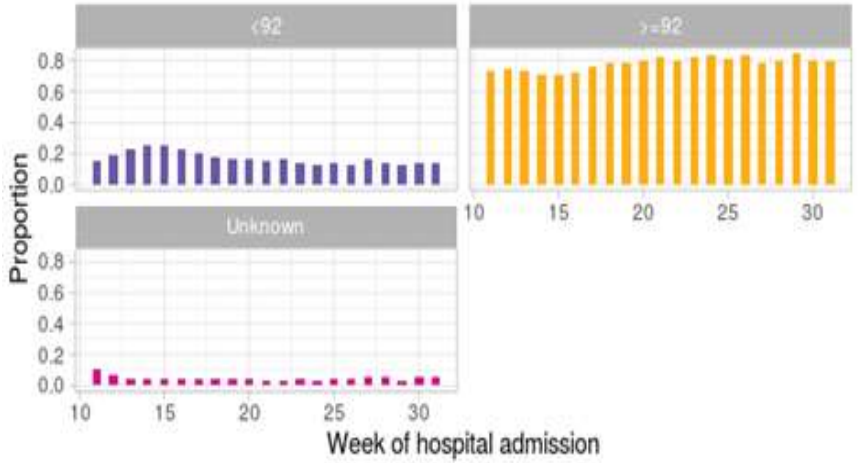


Illness severity at presentation

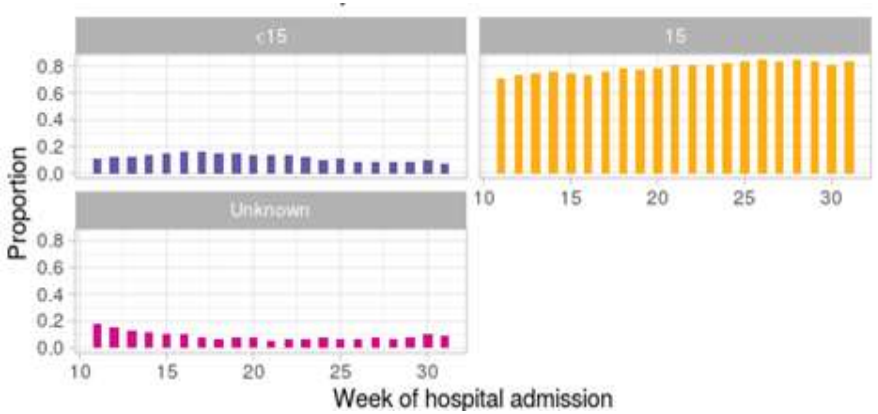
Respiratory rate



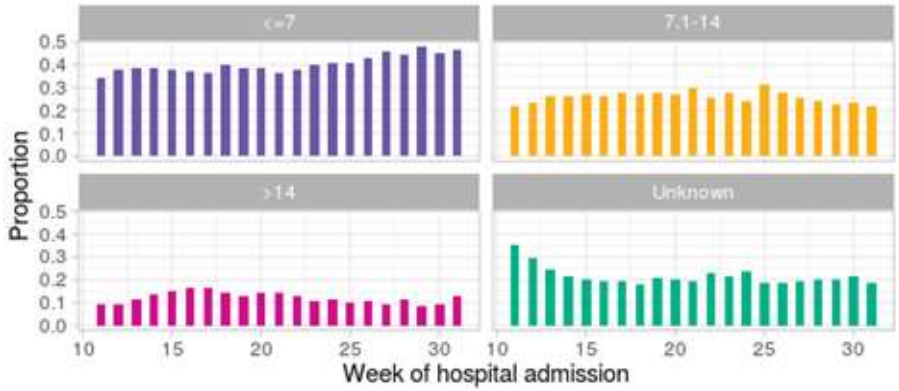
Oxygen



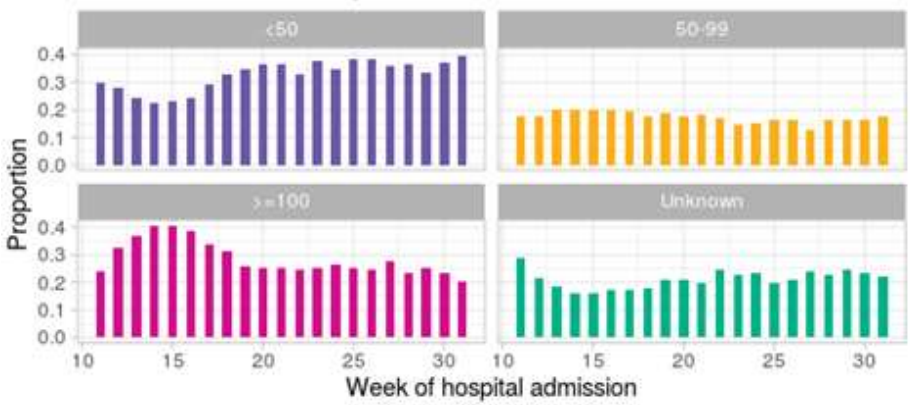
GCS



Urea

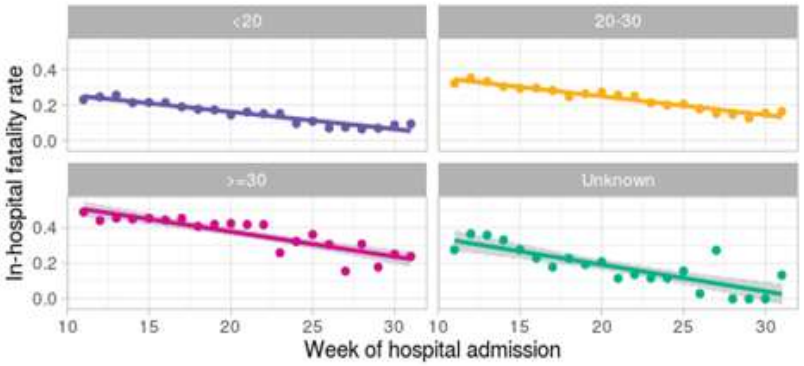


CRP

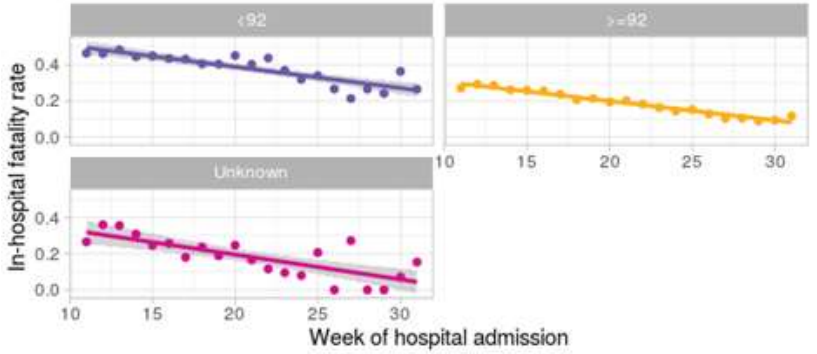


Illness severity at presentation

Respiratory rate



Oxygen



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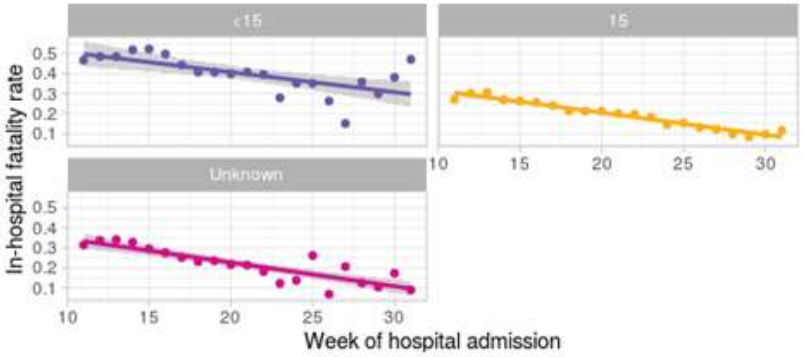

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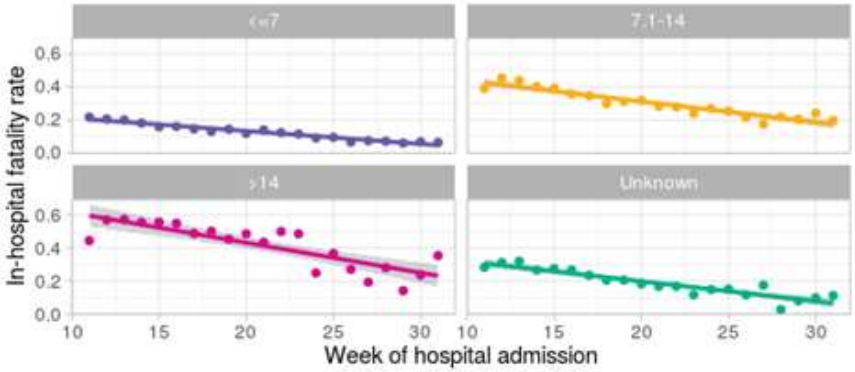
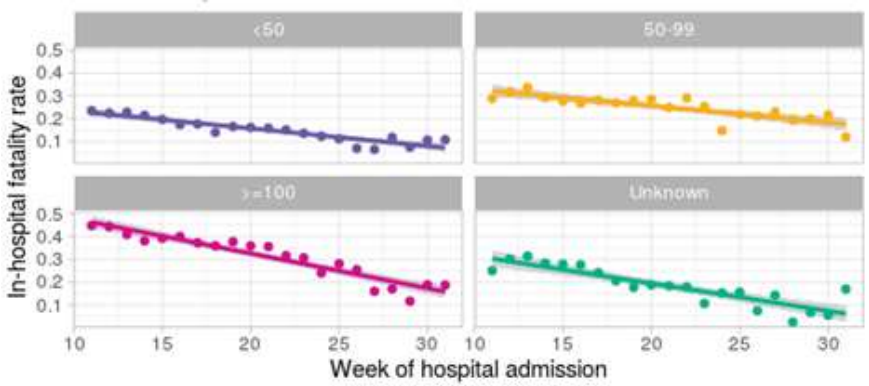
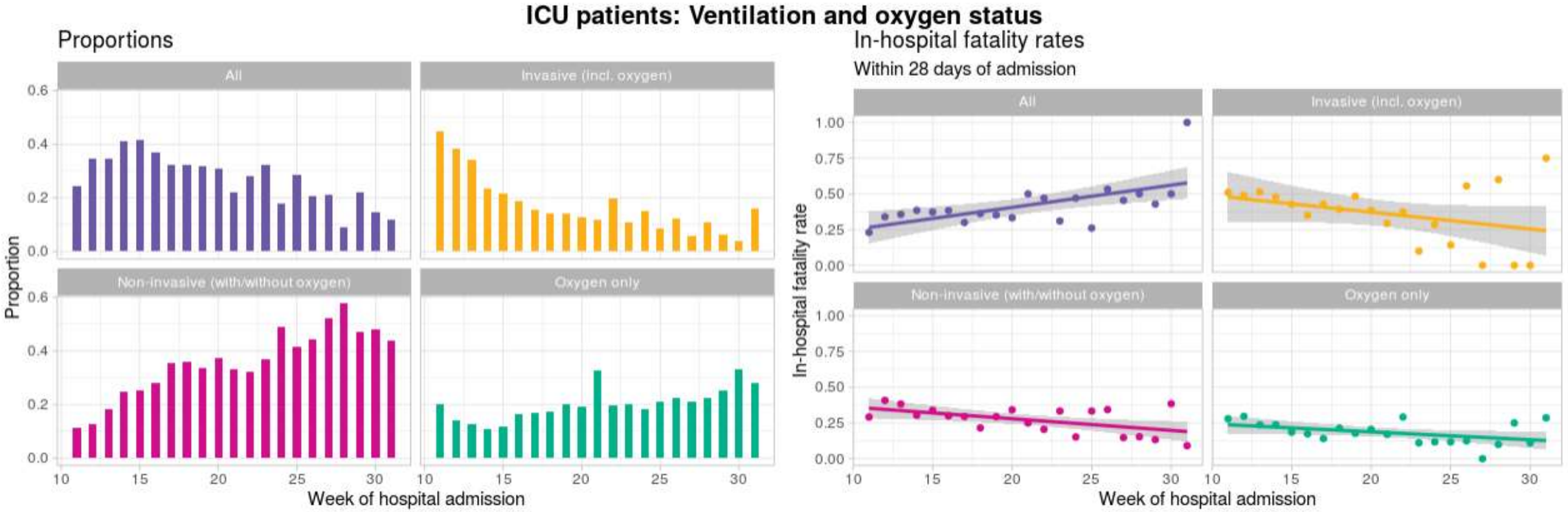


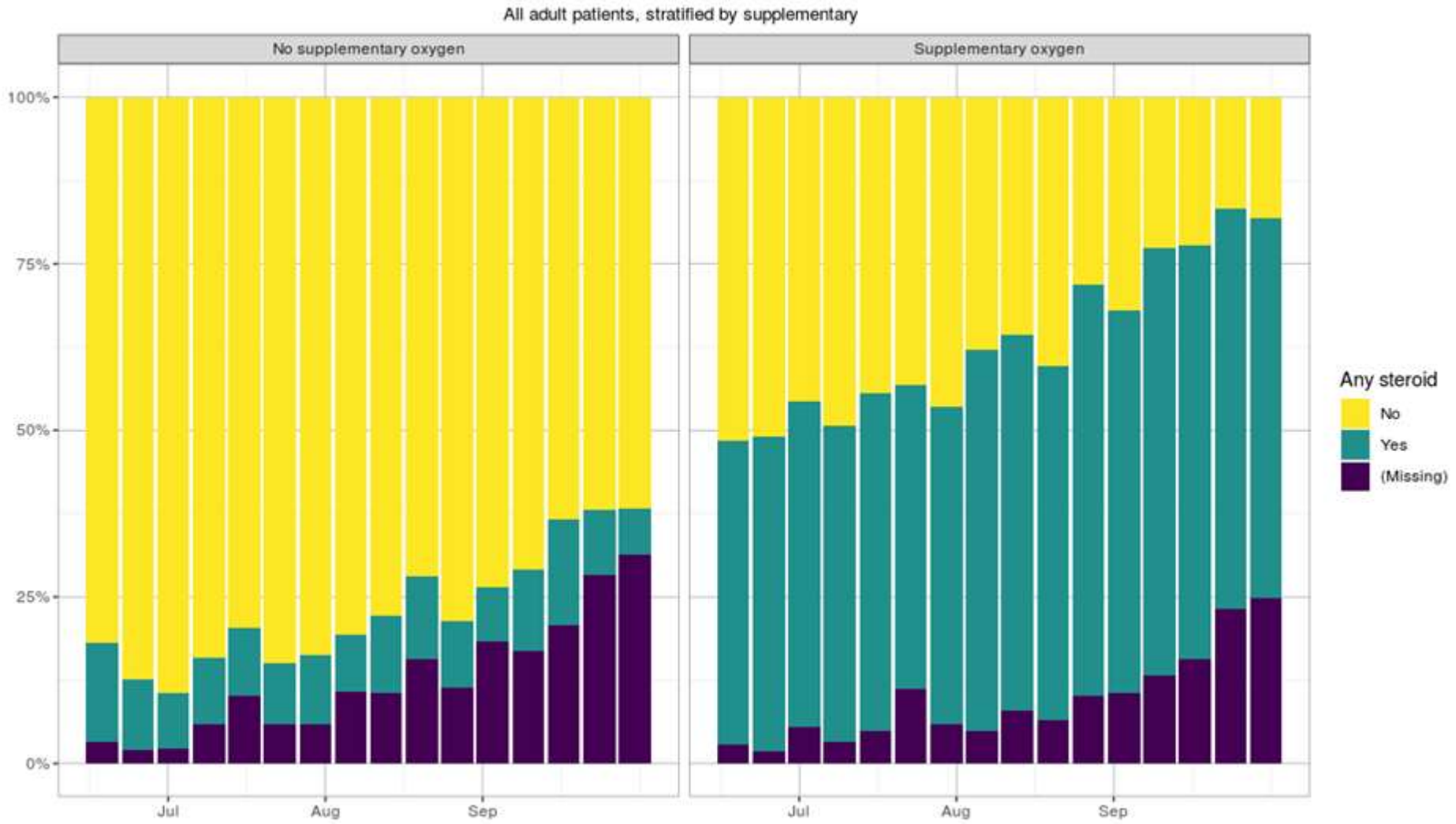
CRP



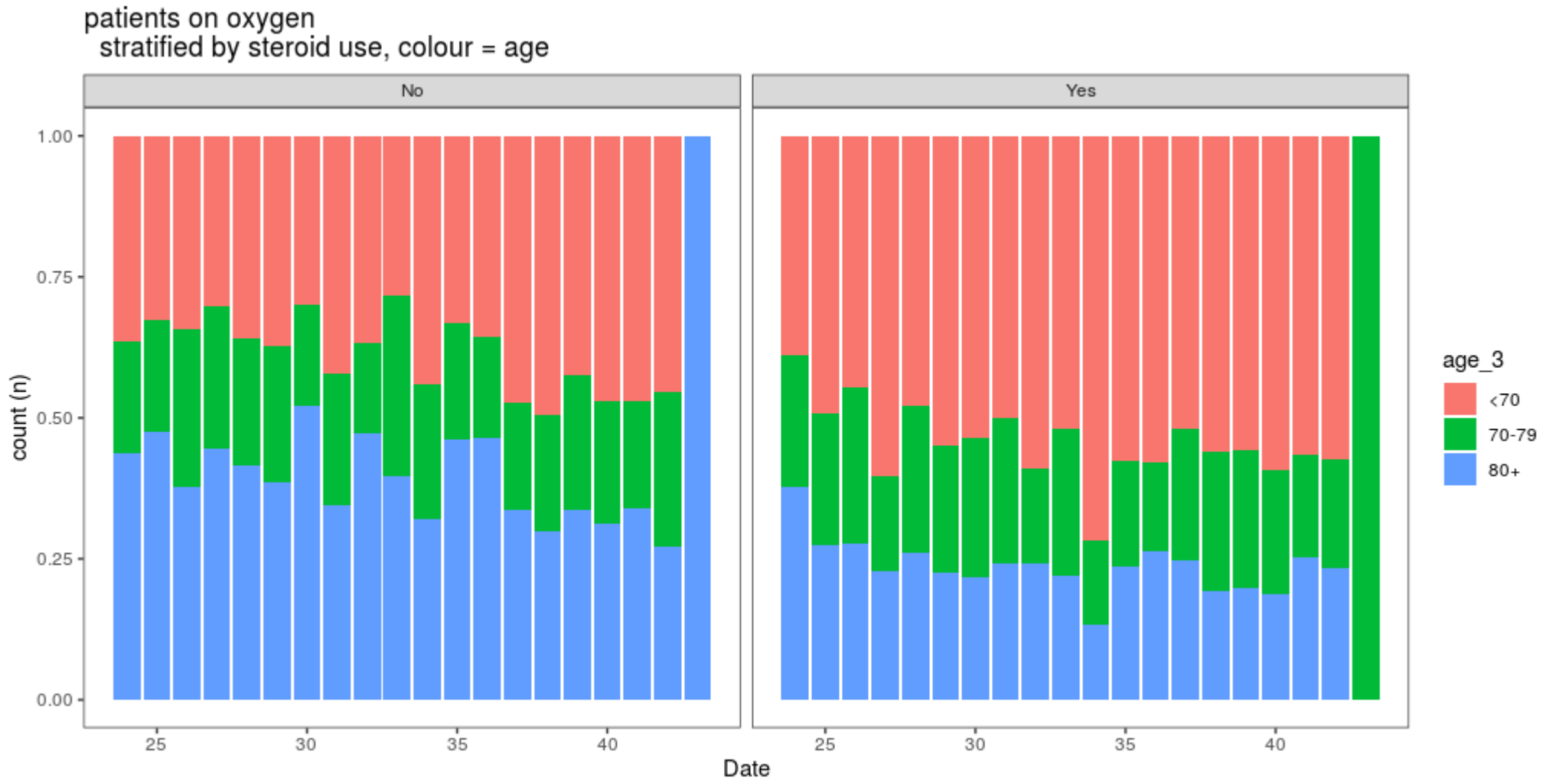
Respiratory support



Translating evidence into practice: Steroids and covid-19


All adult patients, stratified by supplementary
No supplementary oxygen
Supplementary oxygen
100%
75%
50%
25%
0%
Jul
Aug
Sep
Jul
Aug
Sep
Any steroid
No
Yes
(Missing)

Steroid use in patients on oxygen by age



Steroid use by comorbidity

	No steroid (n=1360, 34.8%	Any steroid (n=2130, 54.5%)	Dexamethasone (n=1914, 49.0%)	Hydrocortisone (n=125, 3.2%)	Methylprednisolone (n=35, 0.9%)	Prednisolone (n=295, 7.6%	Missing (n=416, 10.7%)
Chronic cardiac disease	468 (40.8)	546 (47.6)	477 (41.6)	41 (3.6)	8 (0.7)	105 (9.2)	133 (11.6)
Non-asthmatic chronic pulmonary disease	270 (35.4)	414 (54.3)	308 (40.4)	56 (7.3)	4 (0.5)	145 (19.0)	79 (10.4)
Asthma	144 (26.1)	348 (63.0)	298 (54.0)	38 (6.9)	4 (0.7)	78 (14.1)	60 (10.9)
Diabetes	244 (31.9)	442 (57.9)	398 (52.1)	27 (3.5)	6 (0.8)	67 (8.8)	78 (10.2)
Obesity	127 (24.6)	328 (63.6)	307 (59.5)	18 (3.5)	7 (1.4)	32 (6.2)	61 (11.8)
Chronic neurological disease	163 (40.9)	196 (49.1)	176 (44.1)	14 (3.5)	3 (0.8)	23 (5.8)	40 (10.0)
Dementia	210 (53.0)	145 (36.6)	122 (30.8)	11 (2.8)	2 (0.5)	21 (5.3)	41 (10.4)
Pre-adm immuno-suppressant	96 (21.2)	318 (70.4)	237 (52.4)	43 (9.5)	5 (1.1)	122 (27.0)	38 (8.4)

Where to next…?

- Characterise the second wave
  - Re-infection
  - Co-infection
- Changes in hospital mortality
- Asthma/CPD
- Phenotypes by symptoms
- Cytokine response
- GWAS
- Data linkages

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- For protocol, data sharing and sample access please visit https://isaric4c.net