Safe discharge in moderate Covid-19

Which patients with Covid-19 can be safely managed in the community?

PRIORITISE

PRognost**I**cation of **O**xygen **R**equ**I**remen**T** **I**n non-severe **S**ARS-CoV-2 inf**E**ction

Findings from a prospective cohort study in India

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on behalf of the PRIORITISE study group

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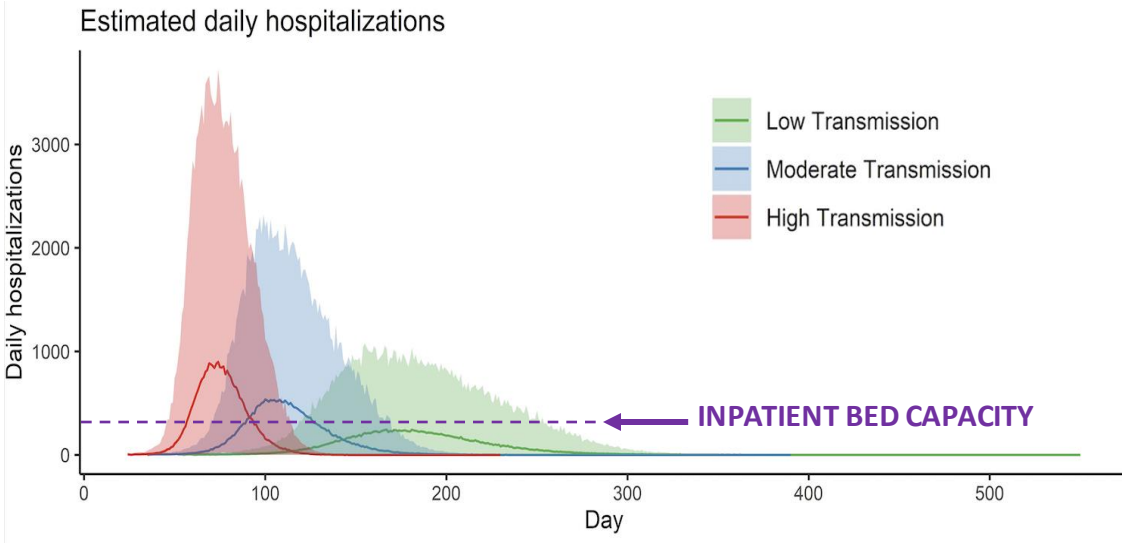
Rationale (mid-2020)

- **Most people** with Covid-19 **do not require hospitalisation**
- WHO estimate **~15% require oxygen** at some point
- Identifying patients not unwell at presentation but **at risk of deterioration** is difficult
- Bed capacity most limited where **safety-netting is hardest**

RESEARCH ARTICLE

The potential impact of COVID-19 in refugee camps in Bangladesh and beyond: A modeling study

Truelove et al., PLoS Med, 2020



- As many of the approaches used to prevent and respond to COVID-19 in the most affected areas so far will not be practical in humanitarian settings, novel and untested strategies to protect the most vulnerable population groups should be considered, as well as innovative solutions to fill health workforce gaps.

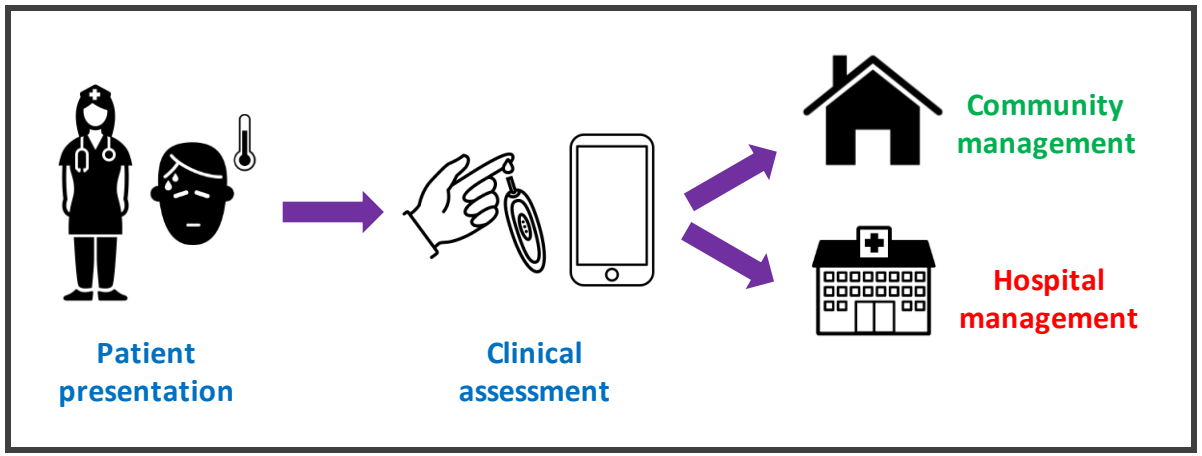
Hypothesis and objective

PRIMARY OBJECTIVE

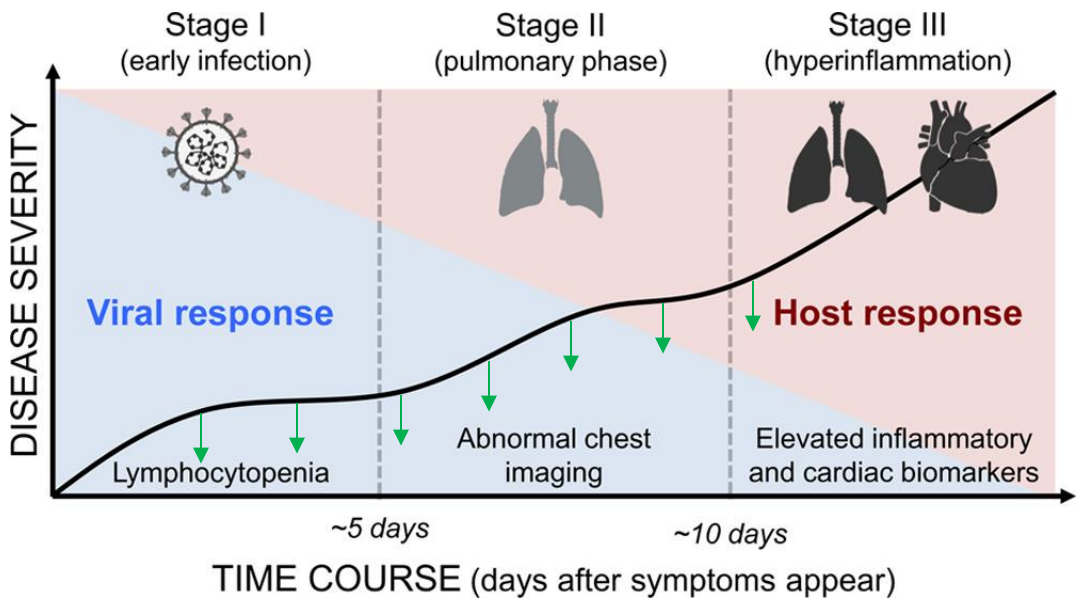
→ **prognostic tool** to help health workers **safely triage** patients presenting with moderate symptoms **away from the health facility** (rule-out)

FIELD-DEPLOYABLE

→ maximum **four predictors** and any **biomarker** must be **measurable with existing tests** practical for use in LMICs



Akhmerov and Marbán, Circ Res, 126, 1443-1455, 2020 (adapted from)



	I	IIa	IIb	III
Clinical presentation	Fever, headache cough, fatigue, myalgia, diarrhoea	SOB without hypoxia	SOB with hypoxia	ARDS, shock
Lab parameters	Lymphopenia, PT, D-dimer, CRP, LDH, ferritin, IL-6, AST, troponin, BNP			

Huang et al., Lancet, 395(10223), 497-506, 2020
Berlin et al., NEJM, 383, 2451-2460, 2020
Siddiqi et al., J Heart Lung Trans, 39(5), 405-407, 2020
Webb et al., Lancet Rheum, 2(12), E754-E763,2021

Participant enrolment

Screening

Consecutive adults with clinically-suspected Covid-19

Photo courtesy of Priyanka Gautam, CMC

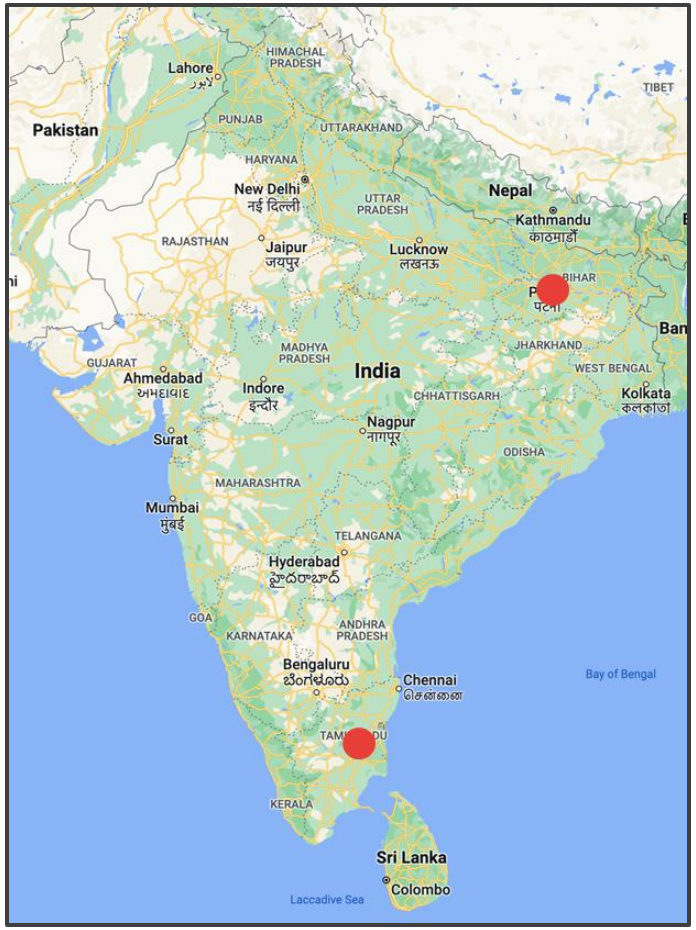
Inclusion criteria

1. Age ≥ 18 years
2. Lab-confirmed Covid-19
3. Systemic manifestation of SARS-CoV-2 infection:

   Breathing difficulty

   OR

   Fever **AND** chest pain OR abdominal pain OR loose stool OR severe myalgia



Exclusion criteria

1. Require O_2 at presentation (SpO_2 < 94% or RR > 30 or clinical decision to give O_2)
2. Previous lab-confirmed Covid-19
3. Documented vaccination

Baseline variables

Demographics: **age**, **sex**, anthropometrics

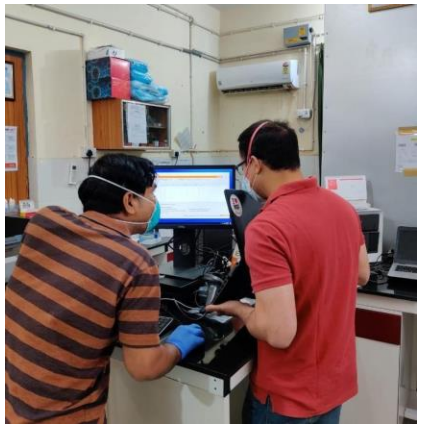
Vital signs: RR, **SpO_2**, HR, BP, temp, AVPU

Biomarkers: **NLR**, **CRP**, **PCT**, **D-dimer**, **suPAR**, **IL-6**, **sTREM-1**

FIND
Because diagnosis matters

CRP NycoCard™, Abbott

suPARnostic©, Virogates



Photos courtesy of
Vikash Kumar, MSF India

Primary endpoint

= Need for supplemental O_2

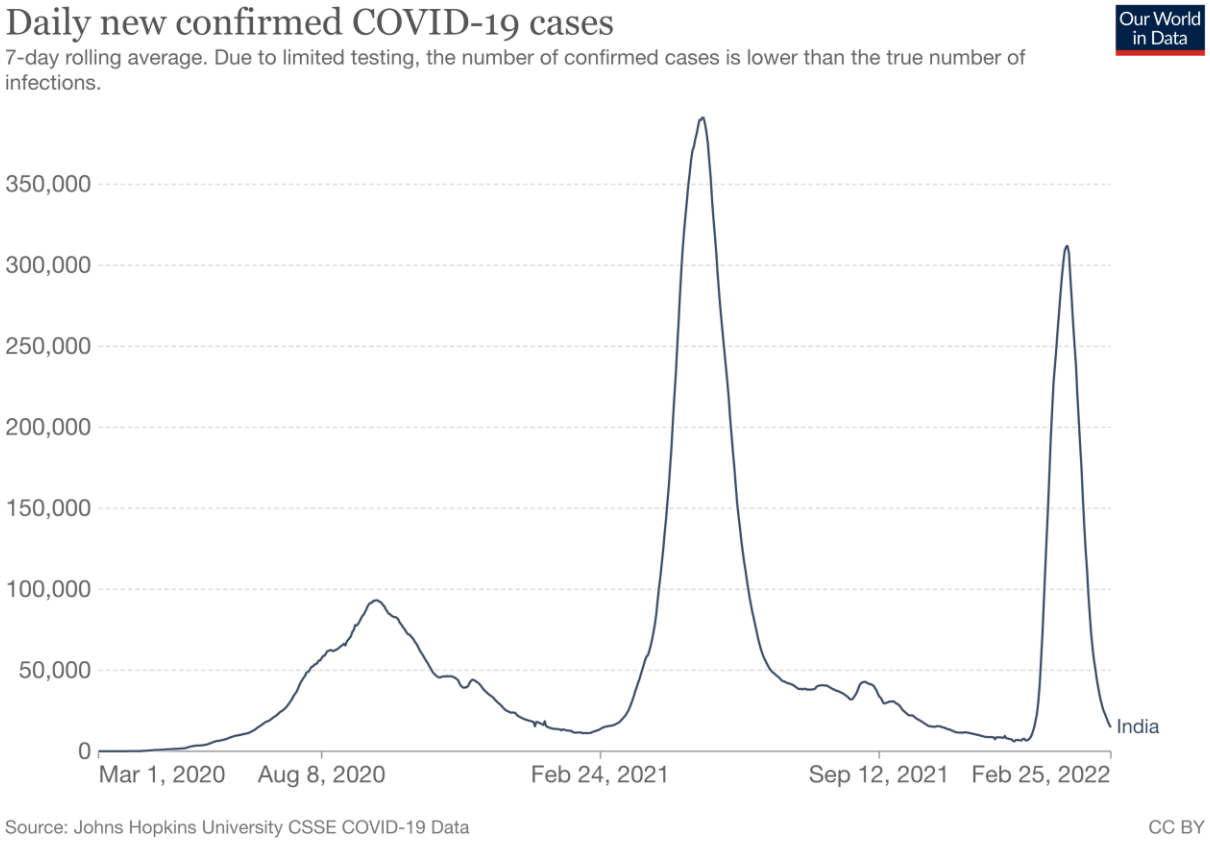
Assessed daily for admitted participants

D7 and D14 for everyone – telephone +/- recall

Composite endpoint:

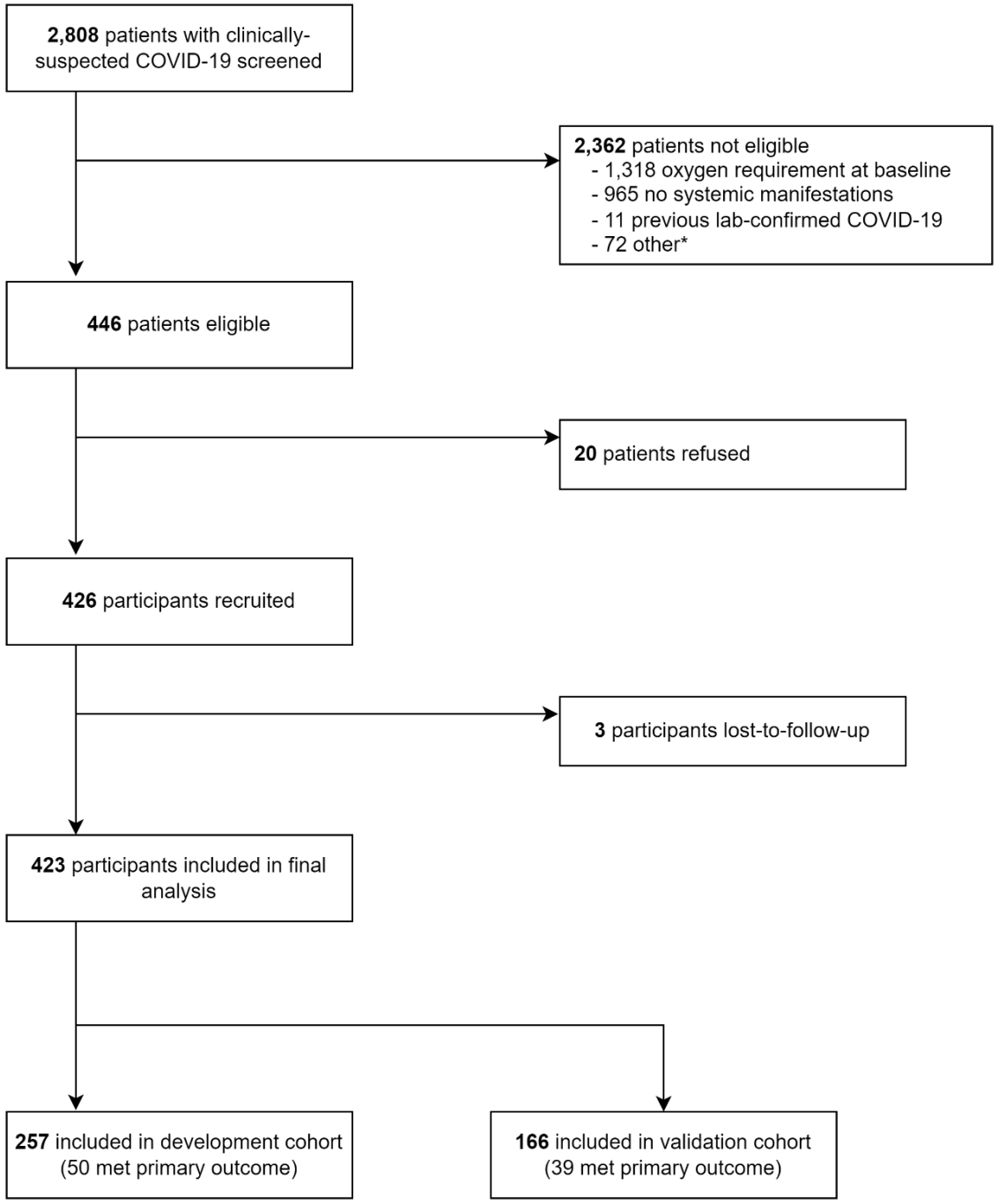
- SpO_2 < 94% or
- RR > 30 or
- Clinical indication to give O_2 (SpO_2/FiO_2 < 400) or
- Death

Recruitment



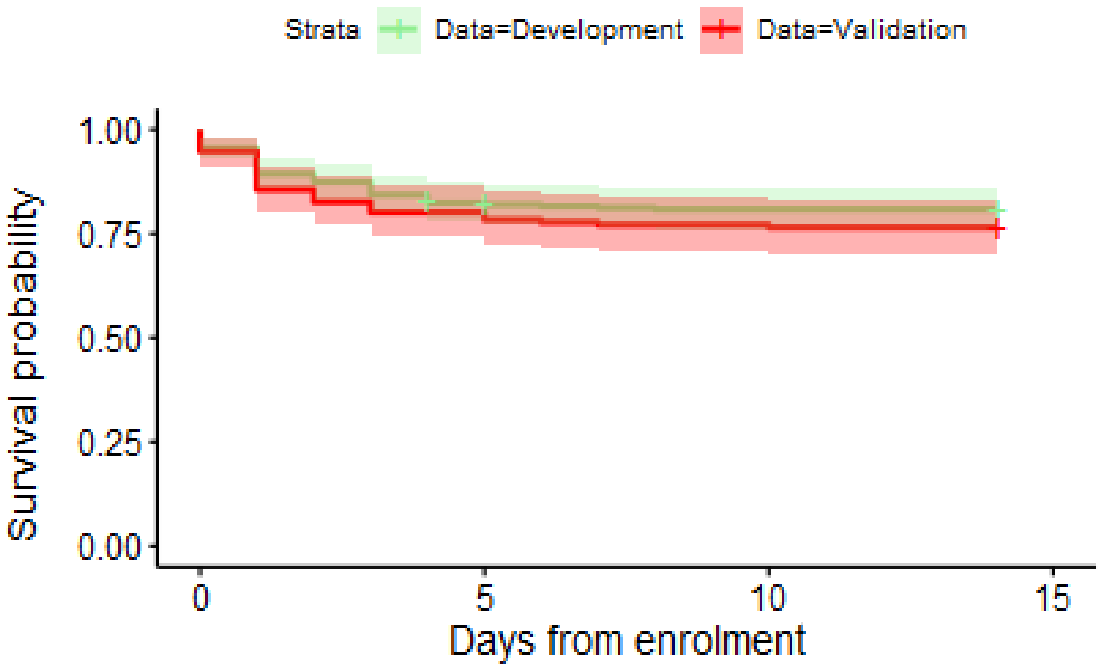
AIIMS, Patna (n = 125)

CMC, Vellore (n = 301)



Baseline characteristic	DEVELOPMENT COHORT			VALIDATION COHORT		
	Overall (n = 257)	Developed oxygen requirement		Overall (n = 166)	Developed oxygen requirement	
		No (n = 207)	Yes (n = 50)		No (n = 127)	Yes (n = 39)
Background						
Age (years)	**52.0** (40.0 to 61.0)	52.0 (40.0 to 60.0)	54.0 (42.2 to 62.0)	**54.0** (41.2 to 63.0)	55.0 (41.5 to 63.0)	54.0 (41.0 to 66.0)
Male sex	**72%** (185 / 257)	70% (144 / 207)	82% (41 / 50)	**61%** (101 / 166)	60 % (76 / 127)	64% (25 / 39)
Reported comorbidity	**64%** (165 / 257)	62% (128 / 207)	74% (37 / 50)	**70%** (117 / 166)	72% (91 / 127)	67% (26 / 39)
Vital signs						
Oxygen saturation (%)	**98.0** (96.0 to 99.0)	98.0 (97.0 to 99.0)	96.0 (95.2 to 98.0)	**98.0** (96.0 to 99.0)	98.0 (96.0 to 99.0)	96.0 (95.5 to 98.0)
qSOFA score ≥ 2	**5.1%** (13 / 257)	4.3% (9 / 207)	8.0% (4 / 50)	**9.6%** (16 /166)	7.9% (10 / 127)	15% (6 / 39)
Host biomarkers						
CRP (mg/l)	24.4 (3.9 to 88.9)	**17.9** (2.8 to 85.4)	**62.5** (19.7 to 134.4)	58.1 (17.2 to 147.1)	**42.5** (12.3 to 111.9)	**95.8** (52.8 to 176.9)
D-dimer (ng/ml)	725.0 (382.4 to 1,466.4)	**640.6** (329.7 to 1,234.9)	**1,201.7** (679.9 to 2,307.0)	968.2 (620.7 to 1,599.0)	**918.8** (579.0 to 1,454.9)	**1,148.1** (829.5 to 3,200.2)
IL-6 (pg/ml)	11.0 (4.9 to 36.2)	**8.7** (4.2 to 27.9)	**36.4** (18.4 to 70.7)	31.6 (13.9 to 63.0)	**24.4** (11.4 to 47.2)	**71.1** (39.4 to 98.9)
NLR	3.2 (1.9 to 4.9)	**2.9** (1.7 to 4.5)	**4.4** (3.2 to 7.2)	2.8 (1.8 to 5.4)	**2.5** (1.6 to 4.2)	**5.3** (2.7 to 7.0)
suPAR (ng/ml)	4.2 (3.1 to 5.8)	**4.0** (2.9 to 5.5)	**5.4** (4.0 to 6.8)	4.1 (3.1 to 5.6)	**3.8** (2.9 to 5.1)	**5.5** (3.9 to 6.7)

Progression to oxygen requirement



	Development (n = 257)	Validation (n = 166)	Overall (n=423)
Number meeting endpoint	**50**	**39**	**89**
Death	2	9	11
Mechanical ventilation	1	1	2
Non-invasive ventilation	5	10	15
FM and/or NC	32	17	49
No supplemental oxygen	10	2	12

- Most patients deteriorate in first 24h (75% by 48h; 85% by 5d)
- Similar rates / trajectories in both cohorts
- 1 patient who received O_2 did not meet endpoint
- 13% of patients who met endpoint did not receive O_2

MODEL = AGE + SEX + SpO_2 + ONE BIOMARKER

Model performance: rule-out (validation cohort; n = 166)

Probability of oxygen requirement (Cut Off)	Sensitivity (95% CI)	Negative Likelihood Ratio (95% CI)	Negative Predictive Value (95% CI)	Per 100 patients (23 patients who would require oxygen)				Incorrect to correct admissions (FP : TP)	Correct to incorrect discharges (TN : FN)
				Correct admissions (TP)	Incorrect admissions (FP)	Incorrect discharges (FN)	Correct discharges (TN)		
Clinical model									
10%	89.7 (75.8 to 97.1)	0.41 (0.15 to 1.08)	**88.9** (73.9 to 96.9)	21	58	2	19	3 to 1	**10 to 1**
15%	76.9 (60.7 to 88.9)	0.56 (0.31 to 1.04)	85.3 (73.8 to 93.0)	18	46	5	31	3 to 1	6 to 1
IL-6 model									
10%	100 (90.9 to 100)	0 (NA)	**100** (87.2 to 100)	23	61	0	16	3 to 1	**NA**
15%	92.3 (79.1 to 98.4)	0.21 (0.07 to 0.65)	93.9 (83.1 to 98.7)	21	49	2	28	2 to 1	**14 to 1**
NLR model									
10%	95.0 (82.7 to 99.3)	0.17 (0.04 to 0.68)	**95.0** (83.1 to 99.4)	22	54	1	23	2 to 1	**23 to 1**
15%	74.4 (57.9 to 86.9)	0.52 (0.29 to 0.91)	86.3 (76.3 to 93.2)	17	39	6	38	2 to 1	6 to 1
suPAR model									
10%	95.0 (82.7 to 99.4)	0.16 (0.04 to 0.61)	**95.4** (84.5 to 99.4)	22	52	1	25	2 to 1	**25 to 1**
15%	69.2 (52.4 to 82.9)	0.55 (0.34 to 0.90)	85.5 (76.1 to 92.3)	16	34	7	43	2 to 1	6 to 1

***** Routine MSF Epicentre data across 26 LMICs (Mar 20 – Nov 21) *****

→ 54% of patients (18,400/33,780) considered for admission with clinically-suspected Covid-19 eligible for assessment (moderates)

→ Potential to have saved ~5,000 admissions, at cost of 180 patients progressing to O_2 requirement

Acknowledgements

- **Study teams at CMC and AIIMS/MSF-Patna**
- **Lab teams at MSF-Patna, CMC, RMRI**
- **Data management and monitoring team at MORU**
- **External Advisory Panel**
- **FIND**

Thank you for listening :-)

Questions?

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Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America | hivma hiv medicine association | OXFORD

Facilitating Safe Discharge Through Predicting Disease Progression in Moderate Coronavirus Disease 2019 (COVID-19): A Prospective Cohort Study to Develop and Validate a Clinical Prediction Model in Resource-Limited Settings

MEDECINS SANS FRONTIERES

IF YOU HAVE DATA / SAMPLES FROM MODERATE PATIENTS AND ARE INTERESTED IN COLLABORATING ON AN EXTERNAL VALIDATION PLEASE GET IN TOUCH

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