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## Outline

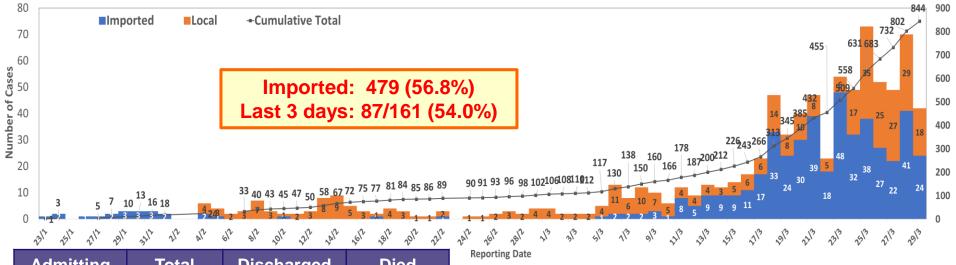
- Situation in Singapore
- NCID set up and ICU surge planning
- Profile of cases including ICU admissions
- Predictors/characteristics of CXR progression and critically ill patients
- Local treatment protocols
- Experience with Kaletra / IFN B-1B thus far



## **Local Situation Update**

#### **Total COVID-19 Cases by Reporting Date**





Admitting Hospital	Total (N=843)	Discharged (N=212)	Died (N=3)
NCID	553	143	2
NTFGH	51	15	0
SGH	51	15	1
NUH	45	15	0
CGH	39	3	0
SKH	35	10	0
KTPH	31	5	0
KKH	21	5	0
AH	7	2	0
MEH	6	0	0
GH	2	0	0
FPH	1	1	0
MAH	1	0	0

Characteristic	
Age, years (Median, Range)	39 (6 months – 86 years)
Male, n (%)	469 / 844 (56%)
Locally acquired, n (%)	365 (43%)

161 new confirmed COVID cases on 27-29

Mar

Linked: 41

☐ Unlinked: 33

☐ Imported: 88

National Public Health and Epi Unit

Updated 29 Mar 2020, 2200hrs

#### **About NCID**



The National Centre for Infectious Diseases (NCID) is a 330-bed purpose-built facility designed to strengthen Singapore's capacity and capability in infectious diseases and outbreak related prevention, surveillance, clinical management, outbreak readiness and response.

NCID houses clinical services, public health, research, training and education, and community engagement under one overarching structure.

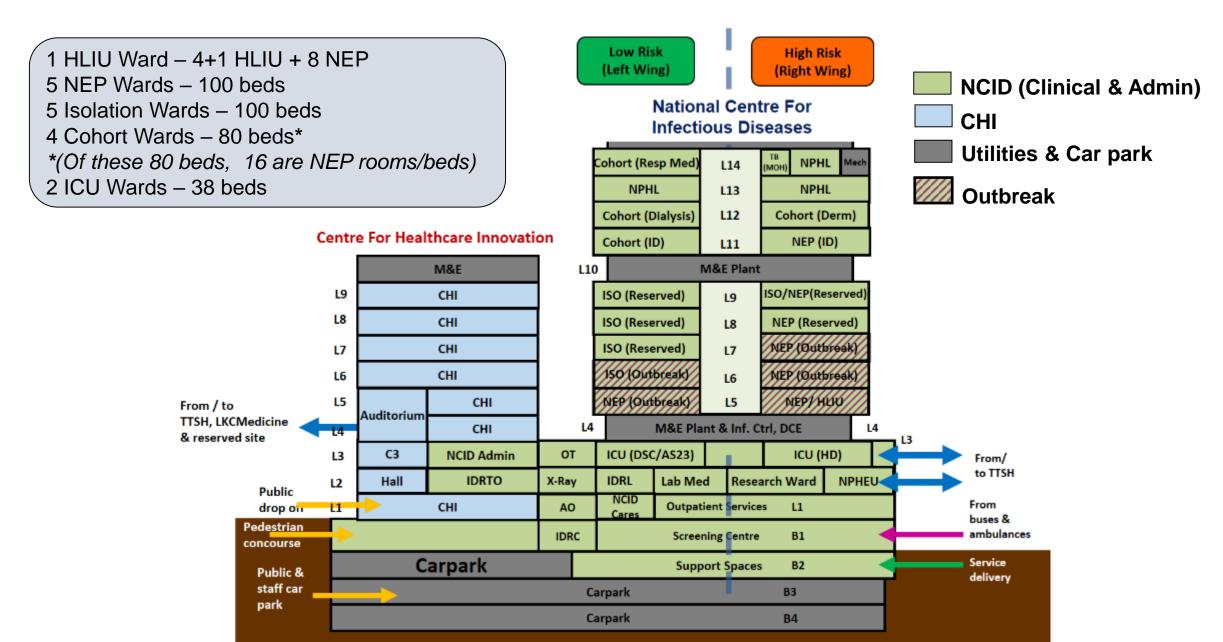
#### Mission

Protecting the people of Singapore from infectious diseases

#### Vision

Strong, trusted and united in keeping Singapore safe from infectious diseases

## NCID Building and Location of Services



## NCID Design Principles

**Capacity and Scalability** 



**64 Cohort beds** 

For general cases

Collated on-site with Tan Tock Seng Hospital (SARS 2003 Hospital), staff shared, provides additional surge capacity



100 Isolation beds

For non-ID patients requiring isolation



124 Negative Pressure (NEP) Beds

For airborne cases

Scalable design to increase number of beds to more than 500 beds

## ICU Decant and Conversion for Outbreak Patients





Event	Outbreak	Action for ICU	Non-ou	tbreak ICI	J Patients	(BAU, Ma	x bed occ	upancy)	ICU Grand
Event	Patients	Action for ICO	NICU	SICU	ccu	міси	3E (NCID)		Total
No Outbreak	0		14	11	8	10	10	53	53
1st outbreak case admitted to 3E	1	Isolated cases may not require decanting Start decanting 3E to 6B Reduce BAU	14	11	8	18	0	51	52
3E : 50% BOR	10	Start decanting 3F (if not done yet) Reduce BAU	12	10	8	16	0	46	56
3E : 100% BOR	20	Start admission to 3F	12	10	8	16	0	46	66
3E : 100% BOR 3F : 50% BOR	29	Start decanting 6B to 3A/B Reduce BAU Escalate to SMM for national ICU response	10	10	8	14	0	42	71
3E & 3F : 100% BOR	38	Start admission to 6B Reduce BAU	10	8	6	12	0	36	74
3E & 3F : 100% BOR 6B : 50% BOR	47	Reduce BAU	10	8	6	10	0	34	81
3E, 3F & 6B : 100% BOR	56		10	8	6	10	0	34	90

#### Notes:

- 1. Ward 3E: 20 ICU beds; Ward 3F, 6B, 6A, 3A, 3B: 18 ICU beds each; Ward 6C: 30 HDU beds; Ward 6D: 22 HDU beds.
- 2. 90 ICU beds maximum because of ICU manpower and resources.
- 3. 52 HDU beds because there are 30 HDU beds in Ward 6C and 22 HDU beds in Ward 6D.
- 4. Downscaling of ICU and HDU beds is a simulation. In an actual outbreak, the downscaling plan may differ.
- 5. Critical day is when there are 29 outbreak ICU patients (Ward 3E: 20 patients and Ward 3F: 9 patients).

## NCID Inpatient Status (accurate as of 29 Mar 2020, 1000hrs)



<b>Current COVID-19 Inpatients</b>	249
Supplemental O <sub>2</sub>	18
Critical care	
ICU	8
HDU	0

Total COVID-19 Inpatients (Including Discharged)	554
Require ICU	24 (4.3%)
ICU duration (excludes current ICU pts), median (range) n=16	9 (1-50) days
Symptom onset to ICU (n=23)	8 (1-21) days
Require O <sub>2</sub> supplementation	50 (9%)
Symptom onset to O <sub>2</sub> supplementation, median (range) n=52	8 (1-16) days

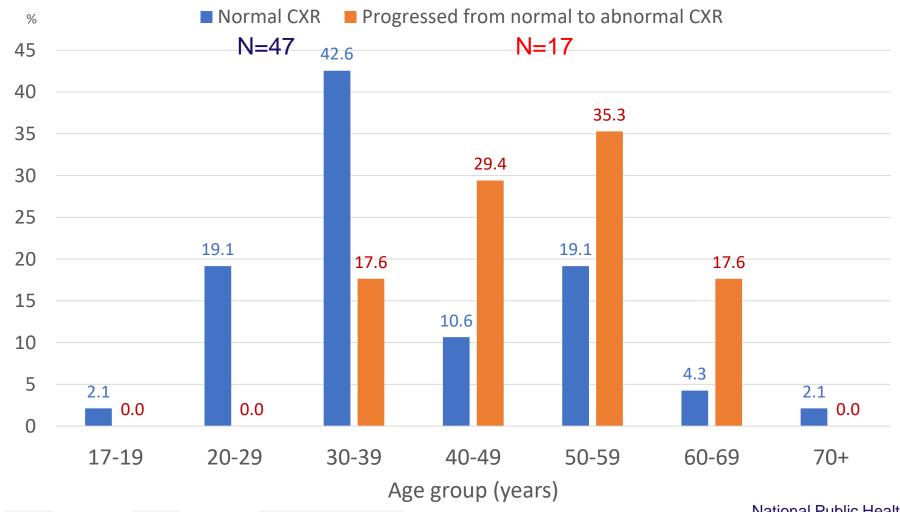
Discharged COVID-19 Patients	305
LOS for Patient discharged, median (range), n=126	12 (3-50) days
(2 patients were deceased)	
LOS for Patient decanted, median (range), n=179	7 (2-25) days

## **NCID** patients with 1<sup>st</sup> normal CXR



17/64 (27%) subsequently had an abnormal CXR

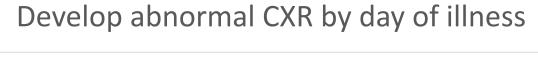
#### Age distribution of patients with 1st normal CXR

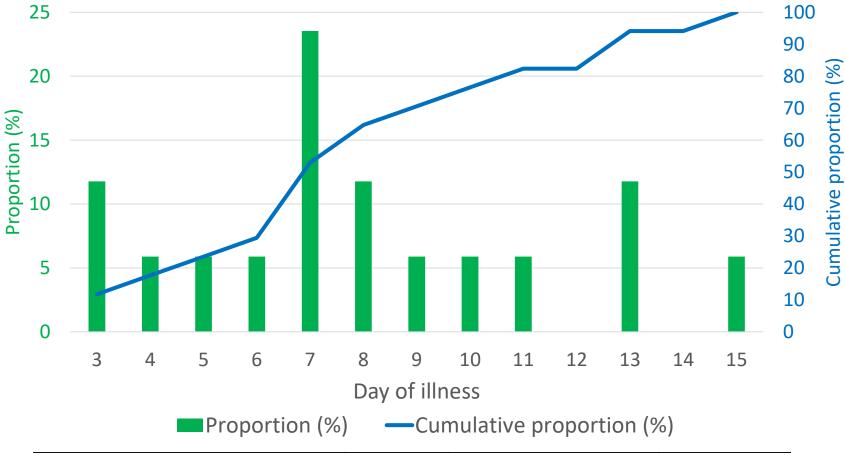


## **NCID** patients with 1st normal CXR



Subsequently develop abnormal CXR (by age group) [N=17]





Progression to abnormal CXR	Median	p75	p95	Max
Day of illness	7	10	13	15

# Clinical Features and Predictors of Severity in COVID-19 in ICU patients, Singapore (50 non-ICU vs 10 ICU)

- Ventilated patients were more likely to:
  - Be Older (52 years vs 43 yrs)
  - Report dyspnea (80% vs 16%)
  - Higher tempeatures (38.7 vs 37.6C)
  - Higher RR, Lower SpO2 (20.5 vs 18, SpO2 94 vs 98%)
  - Higher Neutrophil counts (5.3 versus 2.7 x 10^9/L)
- Logistic regression: RR (aOR 2.83, 95 CI 1.24-6.47); Neutrophil count (aOR2.39 95 CI 1.3-4.3) independent predictors of intubation (AUROC 0.928)
- Median duration of ventilation 6.5 days (IQR 5.5-13)
- Nationally, 2 patients were placed on ECMO so far.



#### Patient and treatment characteristics: Kaletra +/- Beta-Interferon 1B

	Total (n=43)
Mean age (range)	59 (30-86) years
Male (%)	31 (72%)
Mean time to kaletra initiation from onset of symptoms (range)	7 (1-15) days
Started kaletra therapy ≤7 days	21 (49%)
Mean duration of kaletra therapy (range) [n=34]	8.5 (2-15) days
Also on IFN	17 (40%)
Mean time to IFN initiation from onset of symptoms (range)	8 (1-15) days
Started IFN therapy ≤7 days (%)	8 (47%)
Mean no. of doses of IFN (range)[n=13]	3 (1-7)



#### Outcomes: Kaletra +/- Beta-Interferon 1B

	Total (n=43)
Mean hospital length of stay (range)[n=19]	15 (8-31) days
Required ICU/HD stay	25 (58%)
Mean ICU/HD length of stay (range)[n=20]	9 (1-28) days
Required supplemental oxygen	37 (86%)
Mean duration of Supplemental oxygen (range)[n=21]	9 (1-29) days
Required mechanical ventilation	16 (37%)
Mean duration of mechanical ventilation (range)[n=11]	11 (3-29) days
Required vasopressors	12 (28%)
Mean duration of vasopressors (range)[n=9]	4 (2-13) days
Mean time to defervescence (range)[n=36]	11 (2-24) days
Died	2



#### Adverse effects: Kaletra +/- Beta-Interferon 1B

	Total (n=43)
Any adverse effects	27 (63%)
GI intolerance (nausea, vomiting, diarrhoea)	11 (26%)
Abnormal LFTs (any grade)	23 (53%)
Time to onset of abnormal LFTs from start of therapy	4 (1-10)
Time to improvement of LFTs from end of therapy [n=16]	7 (0-22)
Other adverse effects Isolated Tspike attributed to IFN Thrombocytopenia possibly attributed to IFN Rash possibly attributed to kaletra	1 (2%) 2 (5%) 2 (5%)



#### Low versus High Risk of Disease Progression in COVID-19

#### **Low Risk**

- Age <30</li>
- No chronic comorbidities
- Reassuring Clinical Features
  - No dyspnoea
  - Respiratory rate ≤ 20 breaths/min
  - Normal SpO2 %
  - Not requiring oxygen therapy
- Normal Chest X ray
- Reassuring Laboratory results
  - CRP  $\leq$  60 mg/L
  - LDH < 550 U/L
  - Lymphocytes  $\geq 1 \times 10^9 / L$
  - Neutrophils ≤ 3 x 10<sup>9</sup>/L

## **High Risk**

- Age > 30, particularly >50
- Chronic comorbidities (chronic lung, heart or kidney disease, A1c >7.2%, immunosuppression)
- Concerning clinical features
  - Dyspnoea
  - Respiratory rate > 20 breaths/min
  - Abnormal SpO2 % (<95%)</li>
  - Requiring oxygen therapy
- Chest X ray with pneumonia
- Concerning Laboratory results
  - $CRP \ge 60 \text{ mg/L}$
  - LDH > 550 U/L
  - Lymphocytes < 1x 10<sup>9</sup>/L
  - Neutrophils >3 x 10<sup>9</sup>/L
  - Others: Worsening thrombocytopenia < 100x 10<sup>9</sup>/L, Ferritin > 300 ug/L, D-dimer > 1 ug/mL, Elevated troponin

#### **Definition of Severe COVID-19 Disease**

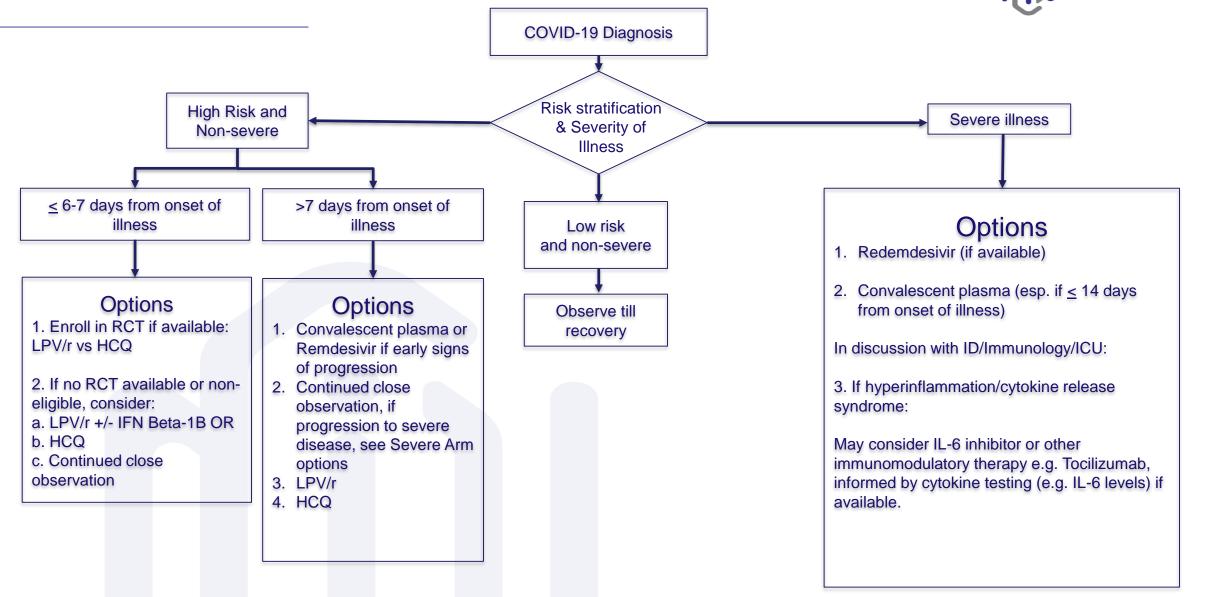


COVID-19 Infection with any one or more of the following features, attributable to SARS-CoV-2 infection:

- Dyspnea, RR >30 breaths/min, P/F ratio <300, Lung infiltrates</li>
   >50% of lung fields within 24-48 hours (WHO Criterion)
- Admission to an ICU
- Current receipt of mechanical invasive or non-invasive ventilation
- Current receipt of intravenous vasoactive medications to maintain mean arterial pressure >65 mmHg
- Myocarditis/myocardial dysfunction secondary to SARS-CoV-2

## **Proposed National Treatment Algorithm for COVID-19**





Note that algorithm may be updated/modified pending further clinical trial results

## Teamwork – Thank You

