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COVID-19 RAPID GUIDELINE

Organisation and management in low resource countries

ABSTRACT

This guideline covers the wide range of global efforts to counter the COVID-19 pandemic, aiming to outline options for delivery of care.
In noting the wide variation in testing, triage, management and vaccination (summarised in Table 1.[1–5]), we seek to identify opportunities for rapid transformational change particularly in countries with stretched resources and less well-developed healthcare systems.
The infographics should enable easy translation, education, and dissemination among both the healthcare population and the public.

Keywords
COVID-19; low resource countries; clinical guidance

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Organisational delivery

The COVID-19 pandemic, now totalling 160 million cases and over 3 million deaths, has overwhelmed even the most well-developed healthcare systems.[6,7] At the outset in early 2020, the U.K. government's phased approach matched that of many European countries. 4 phases were described: Contain (test, trace and isolate), Delay (restrictions to social interaction supported by emergency legislation), Research (which reaped significant rewards) and Mitigate (re-prioritisation of healthcare resources from elective programs to COVID response). Most moved rapidly from containment to delay, seeking effective interventions to reduce the R0 of SARS-CoV-2. These included limitations to social interaction ('lockdown', social distancing, masks), large scale testing of the population, contact tracing with isolation of symptomatic patients together with close contacts and border controls with ever increasing travel restrictions.[1,8,9] Countries employed these measures with differing levels of scrutiny, timing, rigor and emphasis with consequent outcomes noted in Table 1.[10,11]

Many island states fared comparatively well. New Zealand, an exemplar of care, delivered a long national lockdown supported by a very early, uncompromising border control policy. The resultant

caseload was extraordinarily low and absolute mortality effectively suppressed. To date New Zealand has reported 2,644 cases and 26 deaths.[12] Their success was under-pinned by accurate data capture, an appreciation of how cases entered the country and a willingness to seize the opportunity to block all routes of entry. Prompt identification that 58% of infections were imported lead to a rapid transition from alert level of 4 to 1 within 5 days and complete travel restriction.[13,14]

China used regional lockdowns with widespread clinical assessments and laboratory-based screening, Fangcang shelters (field hospitals with infection control measures) followed by purpose-built COVID hospitals and rehabilitation facilities. China and Singapore's focus on index case isolation, large scale population screening, stringent lockdown regimen and assured high levels of adherence also proved successful and demonstrates the art of the possible in other countries with challenged resources and vast populations.[15,16] Europe and the UK used phased intermittent national lockdowns, regional lockdowns, track, trace and isolate programs and travel restrictions to manage infection.

However, recent UK data has suggested relatively poor adherence to both lockdown and Track, Trace and Isolate rules, particularly among younger adults with low incomes and this despite government measures to mitigate for loss of income during the required isolation period, emphasising the importance of compliance in any national program of this type.[17,18] Furthermore, the extent, speed, quality and adherence to local and international travel restrictions in Europe have also drawn significant scrutiny in the debate over how our responses could have been improved.

The ability to successfully isolate at home exposes the differential impact of COVID-19 across varying cultures and socio-economic groups. Where large families live together in smaller homes, in high population density areas or where dependence on a daily income is required, this intervention becomes increasing difficult to deliver effectively.

The organisation of clinical care for COVID patients evolved at pace during wave 1. In addition to hospital management, Italy, France, USA, and the UK used home-based care programmes overseen by specialist teams (e.g. COVID virtual hospitals, oximetry monitoring at home) with improved, supported index patient isolation and management.[2,5,19] Hospitals diverted resources to expanding level 2 and 3 care for acutely ill patients, retrained staff and developed clinical pathways to standardise care in relation to treatment escalation, ventilation strategies and therapeutics.[20–22] Field hospitals were built in many countries using existent large public venues but were used to a variable extent usually because of staff shortages. In the UK, NHSE promoted regional collaboration to support *stressed* hospitals with high caseloads, especially where ICU bed occupancy was high.

Without doubt, the rapid deployment of vaccine programs preferentially rolling through high-risk groups has been one of the most effective strategies in pandemic control. 'Real world' data from Israel with the Pfizer-Biontec vaccine not only demonstrated case load suppression, falling mortality but also reduced viral transmission.[23,24] However, once infection is established, countries that failed to employ lockdown strategies have noted much higher infection rates making pandemic control difficult, requiring the division of finite resource between caring for the ill and vaccinations, with delays in the latter. [25]

This review aims to highlight successful strategies and opportunities for countries still struggling with the COVID pandemic.

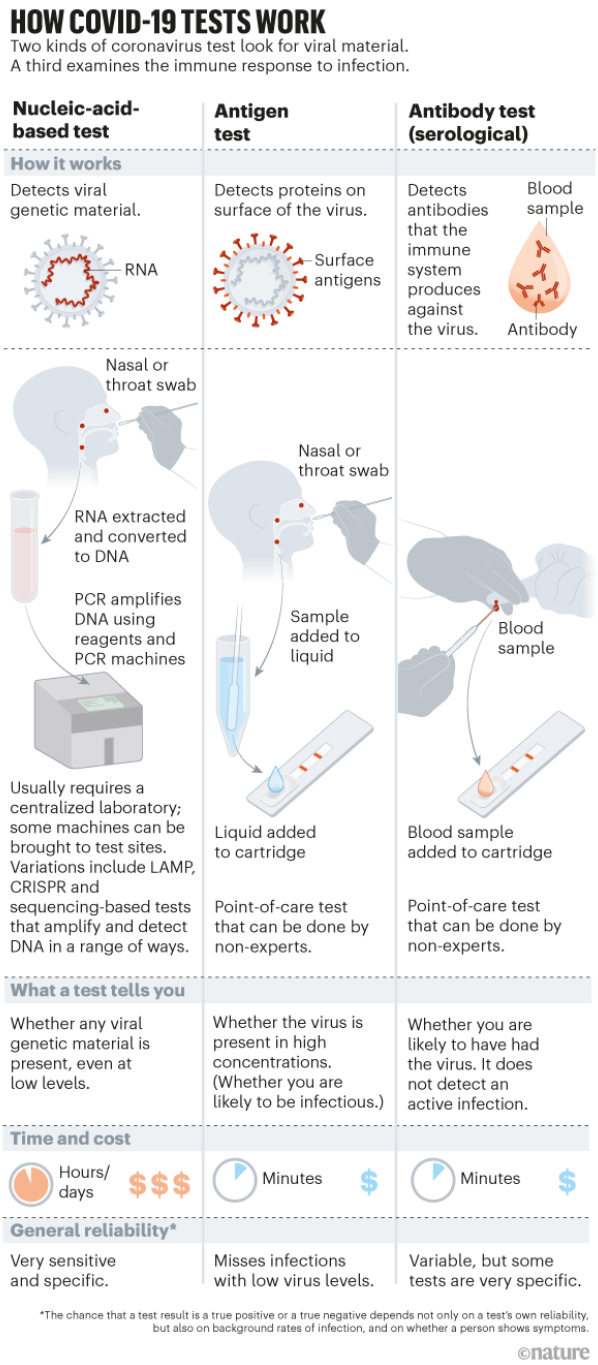


Figure 1: How COVID-19 tests work[26]

Confirmation of acute infection

There are 2 main techniques used to demonstrate the presence of SARS-CoV-2 (figure 1). Nasopharyngeal swabs which are sent for laboratory PCR analysis can detect the viral RNA and give a good indication regarding current infection and infectivity. This is the most sensitive and specific method.[26]

A more cost-effective and widely available alternative is rapid antigen tests. Individuals can self-test and get a result within 15 minutes regarding current infection, but they offer lower accuracy and may miss cases with lower viral loads.

Confirmation of previous infection

Point of care serum antibody tests also give a quick result but are not suitable to demonstrate acute infection. They test for IgG and IgM (and in some cases IgA) against SARS-CoV-2 and can give an indication regarding an individual's infection status as well as possible immunity.

Of note the viral RNA PCR analysis can give information regarding the genetic subtype of SARS-CoV-2, which is a significant advantage over the other methods of testing.

Table 1: Organisational delivery and key outcomes in a selected number of countries affected by the COVID-19 pandemic.

Organisational delivery	China	Singapore	Italy	UK	US	NZ	S Africa	Israel
Population (m)	1,439	5	60	68	332	9	59	9
Ro reduction measures	Lockdown	Lockdown Border control	Lockdown	Lockdown	Partial lockdown	Lockdown Border shutdown	NA	Lockdown Border shutdown
Test types	Clinical diagnosis PCR- lab based. Antibody	PCR lab based	PCR-lab based	PCR- lab based. Lateral flow PCR	PCR-lab based	PCR-lab based	PCR-lab based	PCR-lab based
Sites of testing	Home visits Hospital	Home visits Screening Drive through Hospitals	Hospital	Home Drive through Community hubs Hospital	Home Postal swabs Hospital	Screening Hospital	Hospital	Hospital
Triage	Hospital	Hospital	Hospital	Hospital	Hospital	Hospital	NA	Hospital
Models of care: Home Virtual hospitals Field hospitals Hospitals	Home FangCang Nightingale hospitals COVID hospitals	Home Hospital	Home Hospital	Home Virtual hosp Nightingale Hospital	Home Virtual hospitals Hospital	Home Hospital	Home Hospital	Home Hospital
Risks of each model **Home based care**	Family infections	Family cluster	Can isolate	Can isolate	Can Isolate	Can isolate	Family/community infections	Can isolate
Field hospitals **Hospitals**	Patient isolation, care, and escalation	Not required	Not required	Minimally used	Minimal use	Not required	NA	Not required
	Not enough beds for the pandemic	Not required	Inadequate hospital beds	Reduced all other work	Inadequate beds	Not required	Inadequate beds	Inadequate beds
Vaccination (population immunised) – one dose. (May 2021)	NA	24%	28%	52.3%	46%	4.4%	0.7%	60%
No of documented infections	90,783	61,403	4,116,287	4,437,217	33,515,308	2,643	1,597,724	838,957
Deaths	4,636	31	123,031	127,609	596,179	26	54,825	6,378
Total cases/1million population	63	10,425	76,574	65,070	20,479	528	26,652	91,215
Viral variants	Parent	Parent	Parent	Parent B1.1.7 (Kent)	Parent	Parent	Parent B 1.351.	Parent
Waves	1	1	2	2	2	0	2	1
Model that may be useful to low resource countries	Yes	No	No	No	No	No	Yes	No

Patient risk-stratification

The setting of care for patients is dependent on their level of need. It is noted that 85% of patients are asymptomatic or mildly symptomatic and can be managed at home or in a low care setting such as a Field Hospital or shelter, staffed by lesser trained healthcare and support workers. The aim of care is mostly supportive with low levels of oxygen supplementation being the maximum level of care. Table 2 shows the WHO severity scale where patients who score 1- 4 can be managed at home or in a shelter.[27] Patients with a WHO grade of 5 or more require hospital management. Good triage using this score will enable appropriate use of critical hospital resources.

Table 2: WHO severity scale with management options[27]

Patient State	Descriptor	Score	Triage
Uninfected	Uninfected; no viral RNA detected	0	Home/ Shelter based care
Ambulatory mild disease	Asymptomatic; viral RNA detected Symptomatic; independent Symptomatic; assistance needed	1 2 3	
Hospitalised: moderate disease	Hospitalised; no oxygen therapy	4	
	Hospitalised; oxygen by mask or nasal prongs	5	Shelter with Oxygen
Hospitalised: severe diseases	Hospitalised; oxygen by NIV or high flow Intubation and mechanical ventilation, pO/FiO_2, ≥150 or $SpO_2/FiO_2 \geq 200$ Mechanical ventilation pO_2/FiO_2 < 150 (SpO_2/FiO_2 <200) or vasopressors Mechanical ventilation pO_2/FiO_2 <150 and vasopressors, dialysis or ECMO	6 7 8 9	Hospital based Care
Dead	Dead	10	

A plethora of in-patient prognostication scores were developed and validated for COVID-19 to support the range of clinical pathways within hospitals (Table 3).
Crucially and uniquely, the published early prognostication tool 'SOARS' (a clinical score based on 5 markers: Stroke, Obesity, Age, Respiratory rate and Saturations) supports decision making at hospitals' entry point.[28] When used together with 'virtual hospitals' and home-based monitoring, this tool effectively and safely streams patients into community-based care and should be a consideration where beds, ventilators, oxygen and drugs are in short supply.[29] Additional benefits of this approach included reassuringly low mortality rates (in the home-cared group) and very low re-admission rates in comparison to patients discharged without this additional support. An example of the utility of this score within a pathway is provided in Figure 2.

Other scores have been developed to give an estimate of mortality associated with each case; not only using physiological parameters and patient demographics, but also incorporating hospital-based investigations.[30] These are designed and validated for patients admitted to hospital and are therefore not applicable to community settings or emergency departments.

Virtual hospitals or wards have been successfully employed in the U.K. and elsewhere. In principle, these place the patient at home with daily review by experienced clinicians (doctors or other healthcare professionals) and most are supported by home-based monitoring with oximetry. They provide an alternative pathway for new patients presenting to hospitals, but also facilitate early discharges. Patients can also be stratified into low/high risk groups according to the age, with lower risk patients directed towards a less resource-heavy home care option called oximetry@home, which places the onus on the patient to monitor and respond to their evolving clinical status.[31]

Table 3: Triage scores: Prognostication tools at different stages of presentation

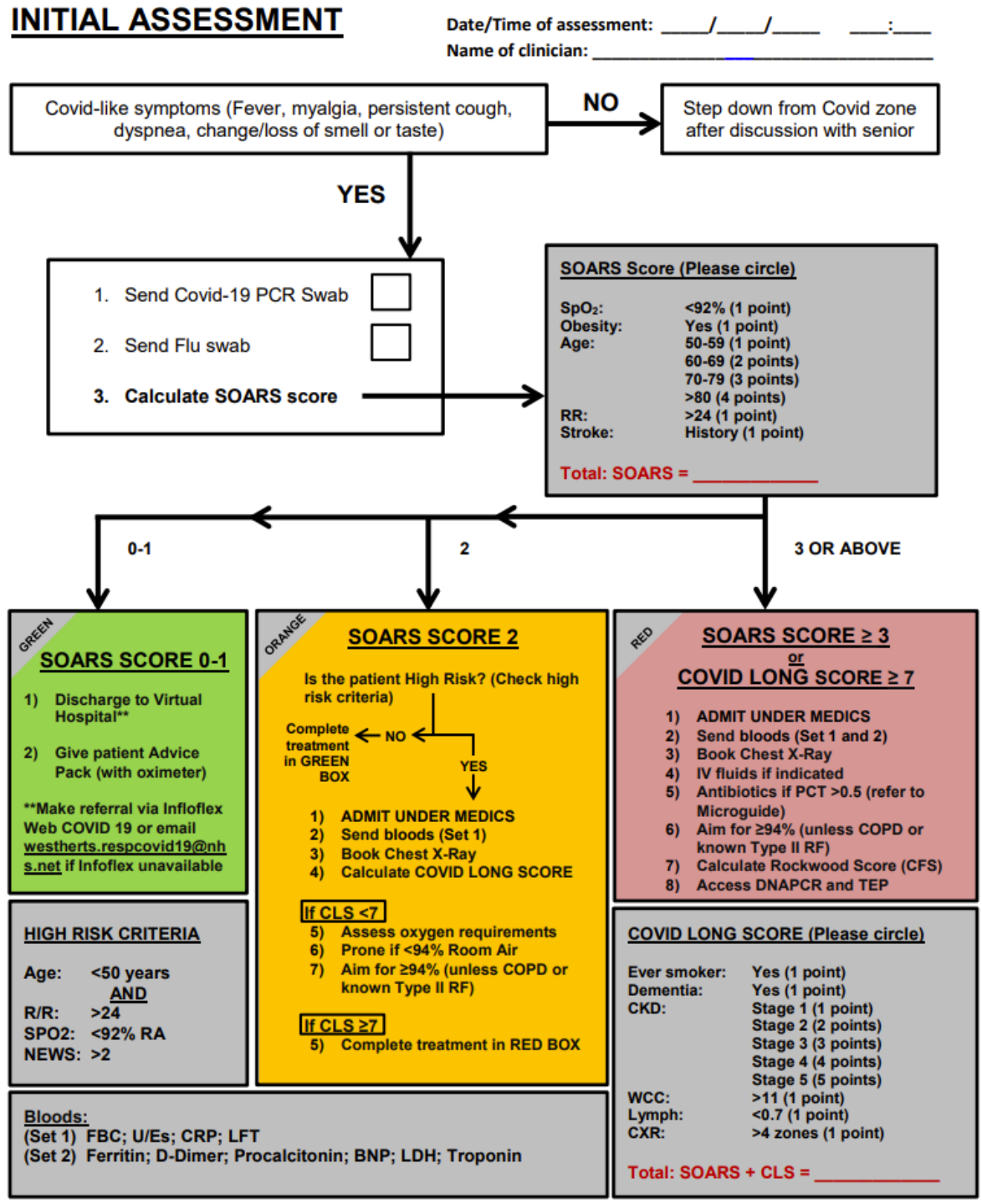
Pre-infection COVID-19 prognostic tool. Assesses comorbidities without effect of infection	**Infection: Clinical assessment without bloods** (SOARS, Thorax 2021)[28] Assess safety for discharge and need for hospitalisation	**Infection: Clinical with bloods** (ISARIC 4C mortality score), BMJ 2020[30] Assess severity with hospitalisation	**Infection, hospitalised Needs to be ventilated** ROX for HFNO[32] Failed oxygenation with CPAP Quick COVID-19 severity index

Models of care

The WHO and various organisation have provided models of care that can be developed to ensure the organisational delivery of services to a population. Figure 3 shows the WHO recommended model and Figure 4, a suggested model that may be considered for low resource countries with high populations such as India.

Figure 3 (WHO appendix 1): Domiciliary/Virtual Hospital/FangCang shelters/Nightingale Hospitals/ Hospitals: COVID and non, mixed (WHO Appendix 1).

Figure 2: Example of a pathway in the UK



SOARS score mortality								
0	1	2	3	4	5	6	7	8
1.4%	5.3%	5.9%	23.4%	35.4%	53.9%	72.5%	78.6%	>78.6%

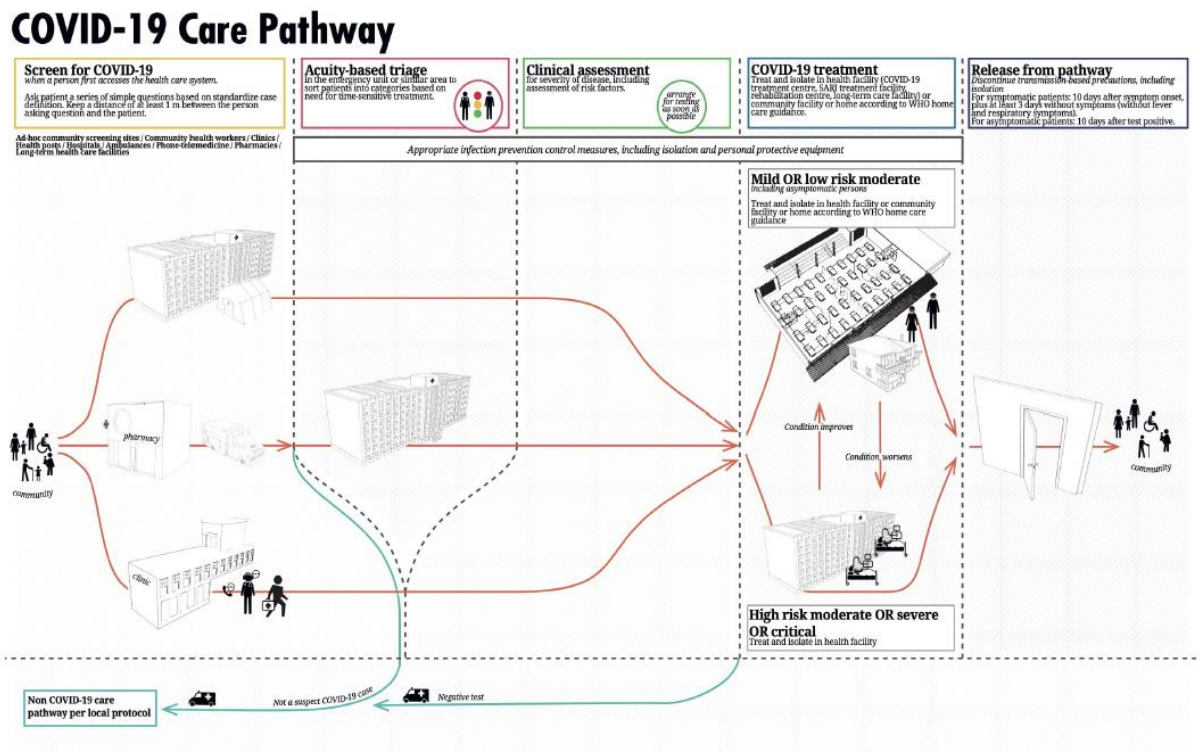
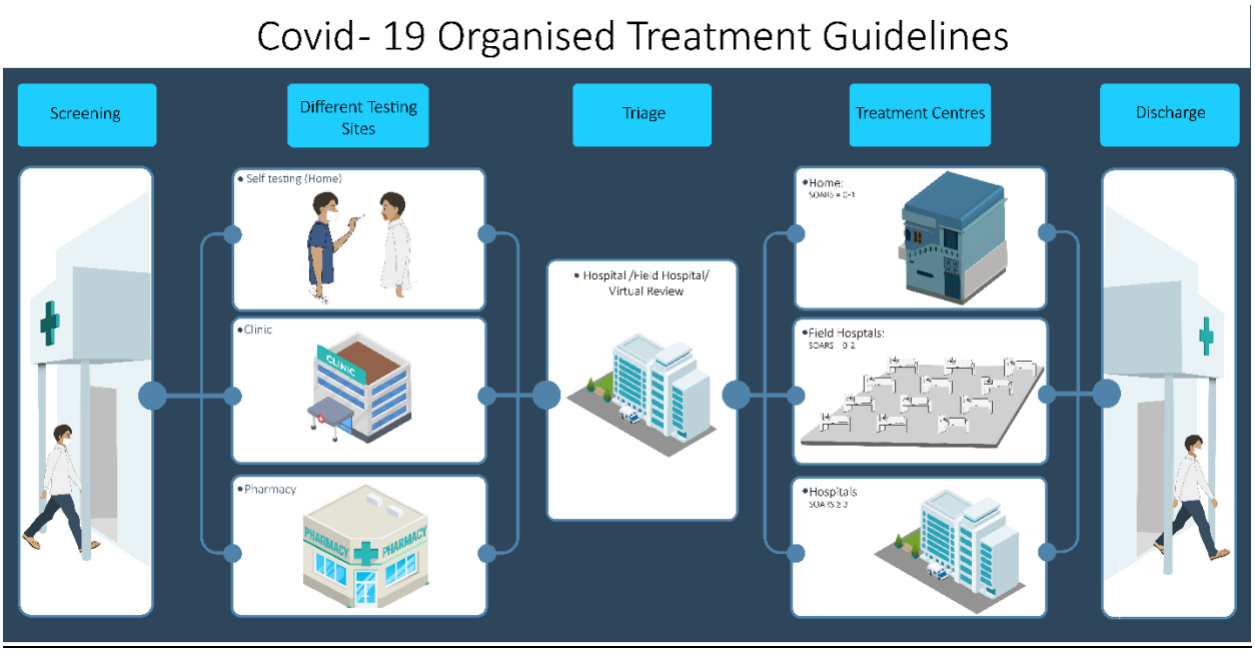


Figure 4: Recommended model for low resource countries
Screening, community or front of hospital testing, triage using WHO scale and/or triage tools.
WHO 1-2, SOARS 0-1: Home based care and if isolation difficult: field hospital or shelters.
WHO 3-4: Field Hospitals, Fang Cang Shelters
WHO 5-9: Hospitals with ICU units



Treatment

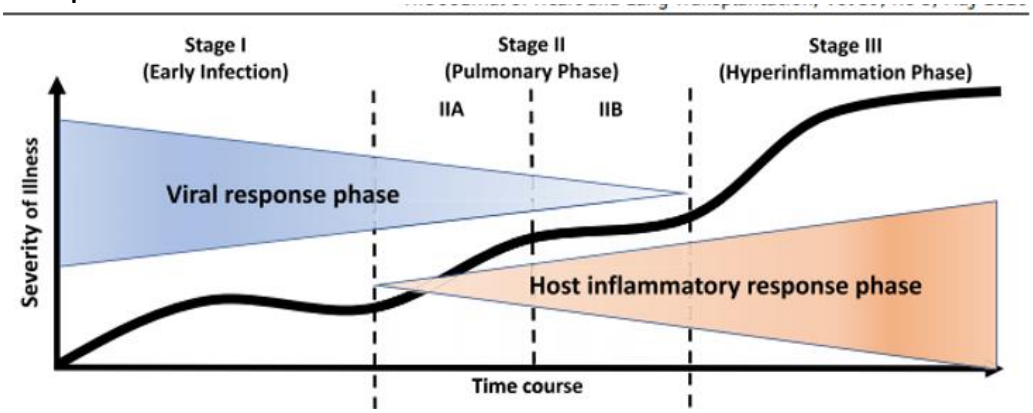
Treatments are rapidly evolving and appear to be effective when used selectively in 2 phases of illness: the active early viraemic phase (within 7 days of symptoms) and the subsequent inflammatory phase (Figure 5). It is important to assess the stage of the patient's illness and manage it appropriately as side effects accumulate with inappropriate timing of treatment.[33,34] Reduction of the viral load during the viraemic phase is effective but not in the latter phase.

Treatments that best provide this are antiviral agents such as Remdesivir but not many others (see Table 4). Neutralising antibodies against the spike protein (REGENERON) and convalescent plasma are also useful in this phase but should only be given if the patient is deteriorating and at risk of decline.[35,36]

Most mild patients recover without any treatment. However, inhaled budesonide has been assessed in a wide range of age groups with mild-moderate severity, managed at home with significant mortality reduction benefits.[37,38]

Other systemic immune suppressive therapies such as Dexamethasone, Tocilizumab should be given to those with WHO Grade 5 and above who required oxygenation and/or ventilatory support. It is most important that evidence-based regimes are strictly adhered to, unless administered as part of clinical trials.[39] This will reduce side effects particularly in high-risk populations with comorbidities such as diabetes and immune suppression. Table 4 provides a full summary of the recommendations from International regulatory and review bodies with clear delineation of harm, good and uncertainty.

Figure 5: Principles of treatment



Standardisation of care using care pathways: an example of UK algorithm of common therapies for admitted patients.

INPATIENT MANAGEMENT

Time/Date of initial treatment: ____/____/____ ____:____ Name of clinician: _____

1. INITIAL TREATMENT

If RA SpO2<92% (unless COPD/OHS/CCF)

- ➔ Give supplemental oxygen – target Sats up to 94%
- ➔ Prone if needed
- ➔ Anticoagulation as per risk of VTE: Therapeutic/Prophylactic (see Anticoagulation and Thromboprophylaxis policy). CTPA to be considered after consultant/respiratory review
- ➔ Perform PCT and **STOP** antibiotics if below 0.25 mcg/L (Refer to MicroGuide)
  1. Send sputum sample and blood cultures
  2. Choice of antibiotics based on hospital guidelines (community acquired pneumonia; hospital acquired pneumonia; sepsis)
  3. Total duration of antibiotics - 5 days
- ➔ Treat other comorbidities
- ➔ Prescribe Covid medications if indicated (see medications on page 4)

Table 4: Treatment of COVID-19

Severity	Treatment	WHO[40]	NICE[41]	NIH[42]	ERS[43]	AIIMS[44]	Severe side effects

Mild	Supportive management. Isolation. Nutrition. Hydration. Antipyretics. Monitoring oxygen saturations.						
Moderate	Inhaled budesonide						Oral candidiasis
	Ivermectin						GI disturbance, rash
Hospitalised	**Anti-Virals**						Risk of AKI
	• Remdesivir						
	• Ritonavir/Lopinavir						
	• Favirpiravir						
	• Molnupiravir						
	• Interferons						
	Corticosteroids						GI ulcer, Raised BM, Delirium
	• Dexamethasone						
	• Hydrocortisone						
	• Methylprednisolone						
	Cytokine inhibitors						Immunosuppression
	• Tocilizumab						
	• Baricitinib						
	• Fluvoxamine						
	Convalescent plasma						Poor evidence
	Soluble ACE2						Animal trials only
	Monoclonal antibodies						Immunosuppression
	• REGENERON						
	• Bamlanivimab						
	Anticoagulation						Risk of bleeding
	• Prophylactic						
	• Therapeutic						
	Vitamins						Avoid overuse
	• Vitamin D						
	• Zinc						
	Ivermectin						GI disturbance, rash
	Colchicine						GI disturbance
	Azithromycin						Prolongs QT interval
	Hydroxychloroquine						Seizures, hypoglycaemia
	Stem cells						
	UV light						Risk of sunburn
Oxygen requiring	Target Sats	94-98%	94-98%	92-96%	92-96%	92-96%	Aim 88-92% if T2RF
	Proning						Physical factors / airway
	Humidification						
Ventilatory support (NIV)	HFNO						
	CPAP						
	BiPAP						
ITU care	Early ventilation						
	Later ventilation						
	ECMO						

	Recommended (Benefit > Harm)		Unclear / Unavailable guidelines		NOT recommended (Harm > Benefit)

Vaccination

Figure 6: Latest vaccination rates across some countries

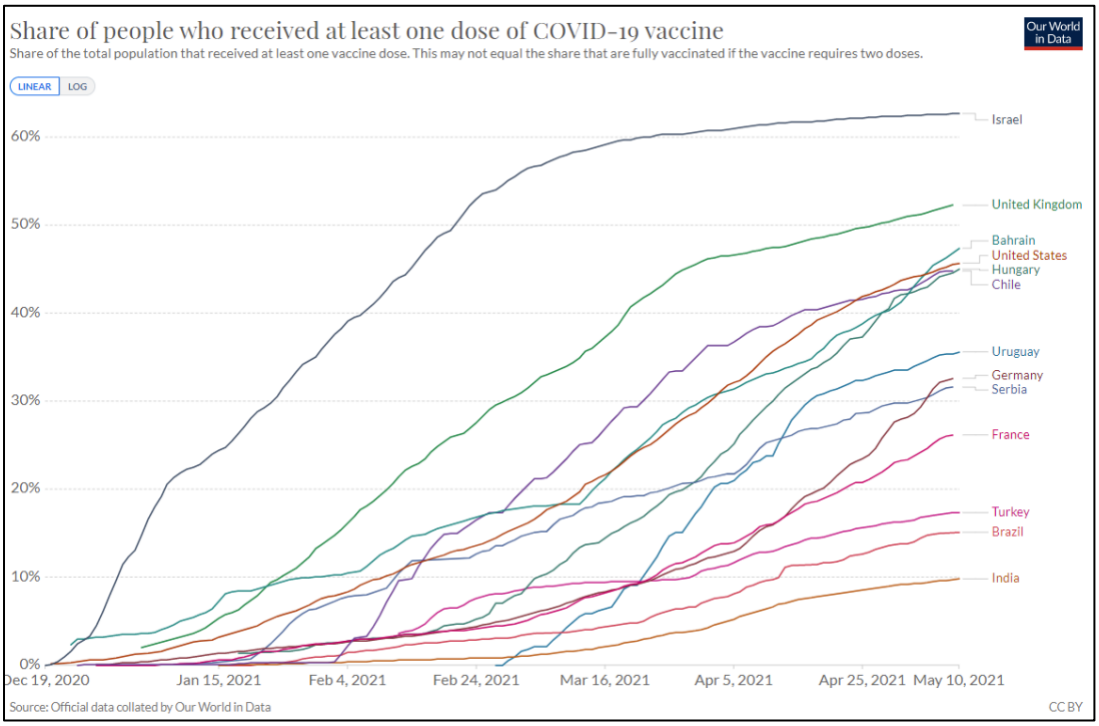


Table 5: Vaccine types and trials

Manufacturer (vaccine name)	Type of vaccine	Doses	Populations in phase III trials Study size Countries in trial	Efficacy against variants B.1.17. B.1351 P1.	Side effect noted	Efficacy post vaccination 1st dose 2nd dose
Pfizer and Biontech (Comirnaty)	mRNA	2	37706 pts; 152 sites US, Argentina, Brazil, South Africa, Germany, and Turkey. 49% female, 83% White, 9% Black, 28% Hispanic, 35% obese, 21% had at least one coexisting condition. Median age 52 years, 42% >55y[45]	85.9%[46] 75.0%[46] Unknown	Injection-site reactions and generalised 'flu-like' symptoms.[45]	92.6%[47] 94.8%[45]
Oxford and AstraZeneca (AZD1222/ CHADOx1)	Viral vector	2	11636 pts 2 countries UK and Brazil. 60.5% female 83% White 4% Black 4% Asian. 88% (18-55 years).[48]	70.4%[49] 10.4%[50] Unknown	Injection-site reactions and generalised 'flu-like' symptoms.[48] 79 cases of rare blood clots alongside low levels of platelets following administration of 20.2 million doses in the UK. EMA estimate of 5 cerebrovascular events/million people. UK recommends that unvaccinated adults (18–39y) should be offered an alternative where no delay or barrier present. The advice is based on falling case numbers changing the balance of risks and benefits, and the availability of alternatives vaccines.[51]	76.0%[52,53] 82.4%[52]
Moderna and NIH (mRNA-1273)	mRNA	2	30351 patients 99 sites in US. 51.4% female; 79.2% White 10.2% Black ; 4.6% Asian, 20.5% Hispanic ; Median age 51y; 24.8% >65y.[54]	Unknown for all variants	Injection-site reactions and generalised 'flu-like' symptoms.[54]	80.0%[55] 94.1%[54]
Novavax (NVX-CoV2373)	Protein	2	15203 pts 33 sites in UK 18-84 y 27% > 65.[56]	86.3%[56] 60.1%[57] Unknown	Analyses of the UK (phase 3) and South Africa (phase 2b) trials showed that the vaccine is well-tolerated, with low levels of severe, serious and medically attended adverse events.[56]	Unknown 89.7%[56]
Johnson & Johnson (Ad26.COV2.S)	Viral vector	1	43783 pts 8 countries US, Argentina, Brazil, Chile, Mexico, Columbia, Peru and South Africa 45% female, 59% White 19% Black 3% Asian 45% Hispanic. 34% >60 years. 41% >1 comorbidity associated with an increased risk for progression to severe COVID-19.[58]	Unknown 64.0%[59]Unknown	Injection-site reactions and generalised 'flu-like' symptoms. US Food and Drug Administration (FDA) temporarily ceased administration of vaccine due to risk of thrombosis in April 2021. 15 unusual blood clots in 8m participants all in women. The blood clots in the brain were described as thrombosis with thrombocytopenia syndrome. On the 23rd of April 2021, the FDA concluded that the known and potential benefit of the outweighs risks.[60]	66.1%[61] N/A

Conclusion

Low resource healthcare systems have a challenging time ahead with the COVID-19 pandemic mandating swift and significant re-organisation of services.

The most important interventions are

- prophylactic early vaccination and
- public health measures to combat spread. Lockdown, social distancing and other well-known public health measures have clearly reduced morbidity, mortality and provided time for services to gather resources and set up safer environments.

Countries that prioritised bio-security, acted promptly and decisively to reduce viral importation and established effective test, trace and isolated programs with high levels of adherence supported by national lockdowns have limited case numbers and lowered mortality. Once the R_0 or infection rates are high, re-organisation of healthcare resources is fundamental to successful pandemic management.

Service delivery must be divided into

(1) immediate management of the acutely unwell without overwhelming healthcare systems and
(2) national vaccination programs.
(3) The use of prognostication scores to stratify proven cases into high and low risk groups creates the opportunity for community-based care models.
(4) Lower risk patients can be safely managed at home either with clinician supervision or independently.
(5) If home isolation is difficult, which it is for many, then Covid shelters/field hospitals are a real consideration.
(6) Triage of the deteriorating patient or the sick to acute hospitals with ICU facilities, ventilatory support and early palliative support is crucial to managing resources well with overall reduced mortality.

Utility of the WHO scales and validated prognostication scores provides objectivity to assessments. In this instance, the use of prescriptive clinical pathways to standardise care will improve overall clinical outcomes and avoid wasteful use of expensive medicines and unproven therapeutics.

Lastly, vaccination drives with at least one dose in the naïve, vulnerable, and frail is clearly protective as noted by the reductions in infection in Israel and now the UK.

Early data from COVID-19 patients who have recovered note adequate booster responses with just one dose of the vaccine. Serological testing to identify suitable 'single-dose' candidates could improve vaccine coverage in the population, especially where demand is high and vaccine availability challenged.

This review aims to help provide data and models to enable experiential organised management of services in low resource economies as part of the global pandemic medical response.

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