CMEO Snack

Early Diagnosis and Timely Treatment in SARS-CoV-2 Infections

Supported by an educational grant from Gilead Sciences, Inc.

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CMEO Snack

LEARNING OBJECTIVE 1

Apply evidence-based strategies for early diagnosis and timely initiation of appropriate SARS-CoV-2 therapies to optimize patient outcomes

Patient Case: KP

- KP is a 52-yr old female with relapsing-remitting multiple sclerosis undergoing maintenance treatment for 7 years on ocrelizumab (B-cell–depleting therapy)

Initial Presentation (Day 0)

- Reports fever, malaise, and mild cough starting 5 days ago; initially thought viral bronchitis by PCP
- She last received a SARS-CoV-2 booster **2 years ago**
- Now presents to ED with pleuritic chest pain and dyspnea

Vitals in ED

- Temp: 38.3°C *(100.9°F)*
- HR: 110 bpm
- BP: 136/82 mmHg
- RR: 30 breaths/min
- SpO2 93% on RA

Diagnostics

- CTA – Bilateral segmental pulmonary emboli (PE)
- SARS-CoV-2 (+)

Management

- Initiated therapeutic rivaroxaban
- Admitted for monitoring and further management

BP = blood pressure; CTA = computed tomography angiography; ED = emergency department; HR = heart rate; PCP = primary care provider; RA = room air; RR = respiratory rate; SpO2 = peripheral arterial oxygen saturation

Patient Case: KP

Hospital Course (Day 2)

- **Respiratory status:** Worsening cough with mild hypoxemia
- **Laboratory trends:** Rising CRP with lymphopenia

Vitals

- Temp: 38.2°C *(100.8°F)*
- HR: 108 bpm
- BP: 134/84 mmHg
- RR: 28 breaths/min
- SpO2 **90% on 2L nasal cannula**

Management

- Continues rivaroxaban for PE
- Ongoing monitoring for drug–drug interactions, bleeding risk, and VTE progression

Infectious Diseases consult has been requested.
What would be your next course of action?

CRP = C-reactive protein; PE = pulmonary embolism; VTE = venous thromboembolism

Gaps Delaying Effective Treatment

Why do patients miss the window for effective treatment?

Clinician Gaps

- Difficulty in rapidly identifying high-risk patients
- Keeping up-to-date with evolving therapeutic guidelines

Patient Gaps

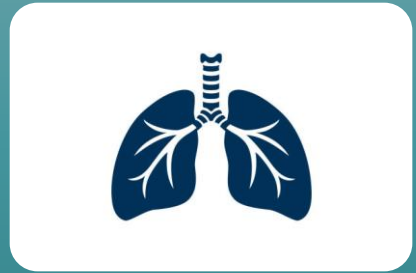
- Lack of awareness of personal risk factors (e.g., comorbidities)
- Delay in seeking care for "mild" symptoms

Access Gaps

- Disparities in access to testing, healthcare facilities, and therapeutics
- Geographic and logistical barriers

Ponce SA, et al. *BMC Public Health*. 2023;23(1):1-14. Alshahrani MS, et al. *Int J Environ Res Public Health*. 2022;19(16):9818. Wong CKH, et al. *Nat Commun*. 2023;14(1):8377.

Recognizing Early Signs of SARS-CoV-2



Respiratory Symptoms

- Cough (dry)
- SOB or difficulty breathing
- Sore throat
- Congestion/runny nose
- Chest pain

Gastrointestinal Symptoms

- Nausea
- Vomiting
- Diarrhea
- Abdominal pain
- Loss of appetite

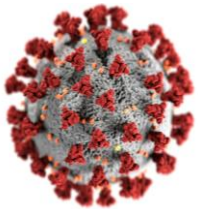
Systemic Symptoms

- Fever/chills
- Fatigue
- Muscle/body aches
- Headache
- New loss of taste or smell

SOB = shortness of breath

Centers for Disease Control and Prevention (CDC). 2024. https://www.cdc.gov/covid/signs-symptoms/index.html.

Phases of SARS-CoV-2 Infection

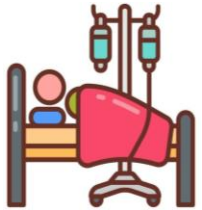


- High viral load, especially in upper respiratory tract
- May be asymptomatic
- Mild symptoms: fever, cough, fatigue, body aches

Viral Replication Phase (5-7 days from symptom onset)

- Lower respiratory tract involvement
- Pneumonia on imaging (e.g., ground-glass opacities)
- Dyspnea; falling SpO2 (hypoxemia)

Pulmonary Phase (5-12 days from symptom onset)



- "Cytokine storm": ↑ IL-6, IL-1β, TNF-α; ↑ CRP, D-dimer
- ARDS, septic shock, multi-organ dysfunction possible
- Viral load may be decreasing, but pulmonary involvement may persist

Systemic Inflammatory Phase (2-3 weeks from symptom onset)

ARDS = acute respiratory distress syndrome

Cascella M, et al. *Features, Evaluation, and Treatment of Coronavirus (COVID-19)*. 2023. https://www.ncbi.nlm.nih.gov/books/NBK554776/.
Aguilar RB, et al. *Front Med*. 2020;7:555301

SARS-CoV-2 Diagnostic Assessment Tools

Molecular Tests (NAAT – RT-PCR)

- **Performance Characteristics**
  - Detection Principle: Amplifies viral RNA for detection; provides viral load information
  - **~98%** Sensitivity, **97%** Specificity
- **Clinical Advantages**
  - RT-PCR remains the **gold standard**
  - Can detect infection **1-2 days** before symptom onset
  - Advanced assays can differentiate variants
- **Limitations**
  - Longer turnaround time: hours-days
  - Higher cost
  - Require specialized infrastructure

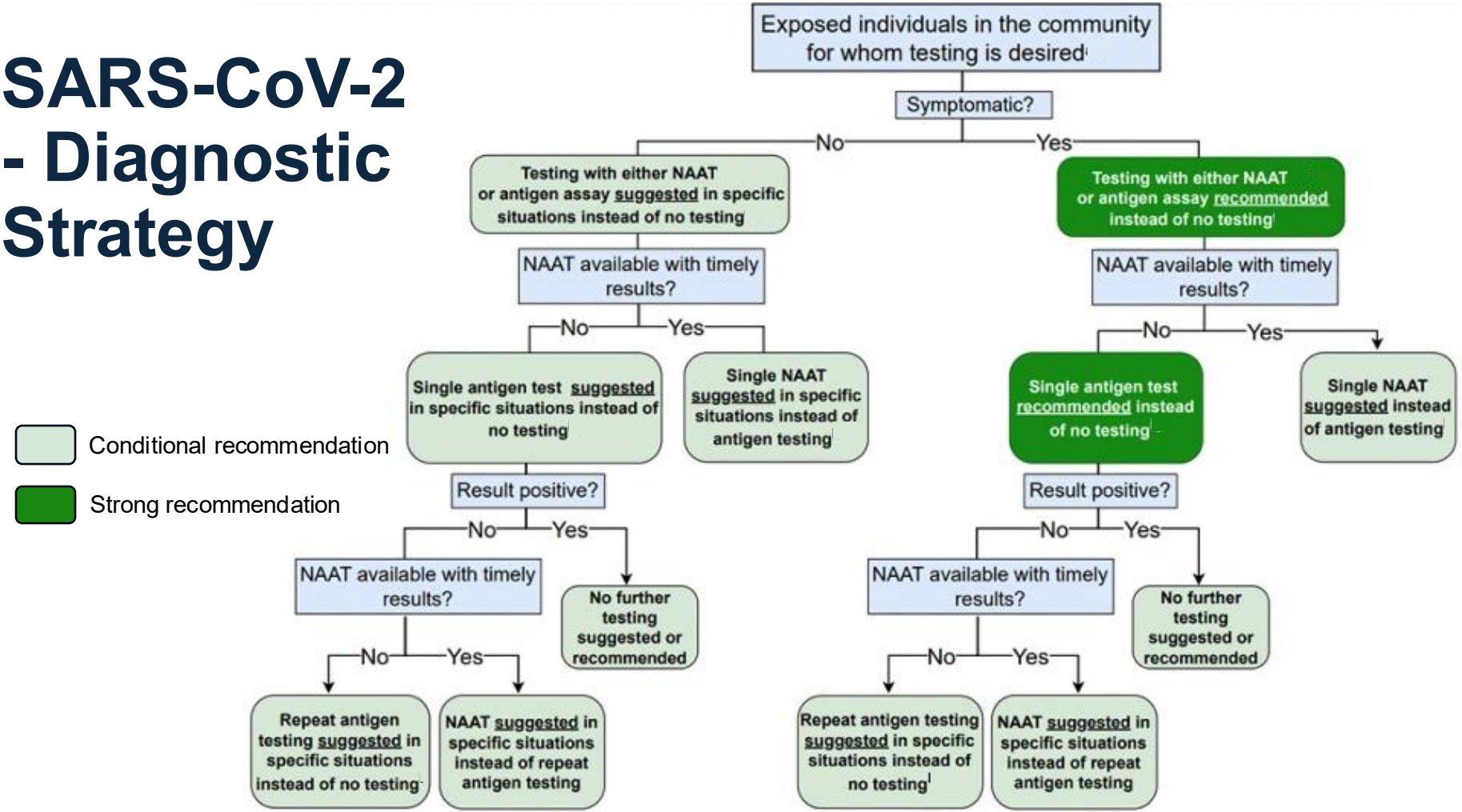
Rapid Antigen Test

- **Performance Characteristics**
  - Detection Principle: Identifies viral proteins (S or N)
  - **70-90%** Sensitivity, **94-98%** Specificity
- **Clinical Advantages**
  - Quick turn arond time: **15-minutes**
  - Point-of-care capability
  - Cost-effective
  - High-throughput screening
- **Limitations**
  - Variant performance issues
  - Timing dependent during peak viral shedding

N = nucleocapsid; NAAT = nucleic acid amplification test; RT-PCR = reverse transcription polymerase chain reaction; S = spike

Aboagye FT, et al. *Research Ideas and Outcomes.* 2025:11(6):338. Goux H, et al. *mBio.* 2024:15:e02737-24.

SARS-CoV-2 - Diagnostic Strategy



Hayden MK, et al. *C Infectious Diseases*. 2024;78(7):385-415.

Severity Thresholds: Foundational Comparison

Risk factors for severe disease progression: age > 65 years, obesity, diabetes, neoplasm, chronic heart failure, chronic liver disease, chronic lung disease, chronic kidney disease, cerebrovascular disease, immunodeficiencies, and immunosuppression

Mild-moderate

1. SpO2 **≥ 94%** in ambient air
2. Upper respiratory tract symptoms predominate
3. No signs of pneumonia on examination/imaging

Severe (not critical)

1. SpO2 **< 94%** in ambient air
2. RR **> 30** breaths/min; lung infiltrates **> 50%**
3. Low-flow supplemental oxygen via nasal cannula or mask

Critical (non-invasive Support)

1. SpO2 **< 90%** in ambient air
2. Respiratory distress and signs of end-organ damage
3. High-flow nasal cannula (HFNC) or non-invasive ventilation (NIV)

Critical (invasive support)

1. Severe respiratory failure with multi-organ dysfunction
2. ARDS; possible vasopressor requirement
3. Invasive mechanical ventilation ± ECMO

ECMO = extracorporeal membrane oxygenation

Centers for Disease Control and Prevention (CDC). 2024. https://www.cdc.gov/covid/hcp/clinical-care/management-and-treatment.html.
Infectious Diseases Society of America (IDSA). 2025. www.idsociety.org. https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/.

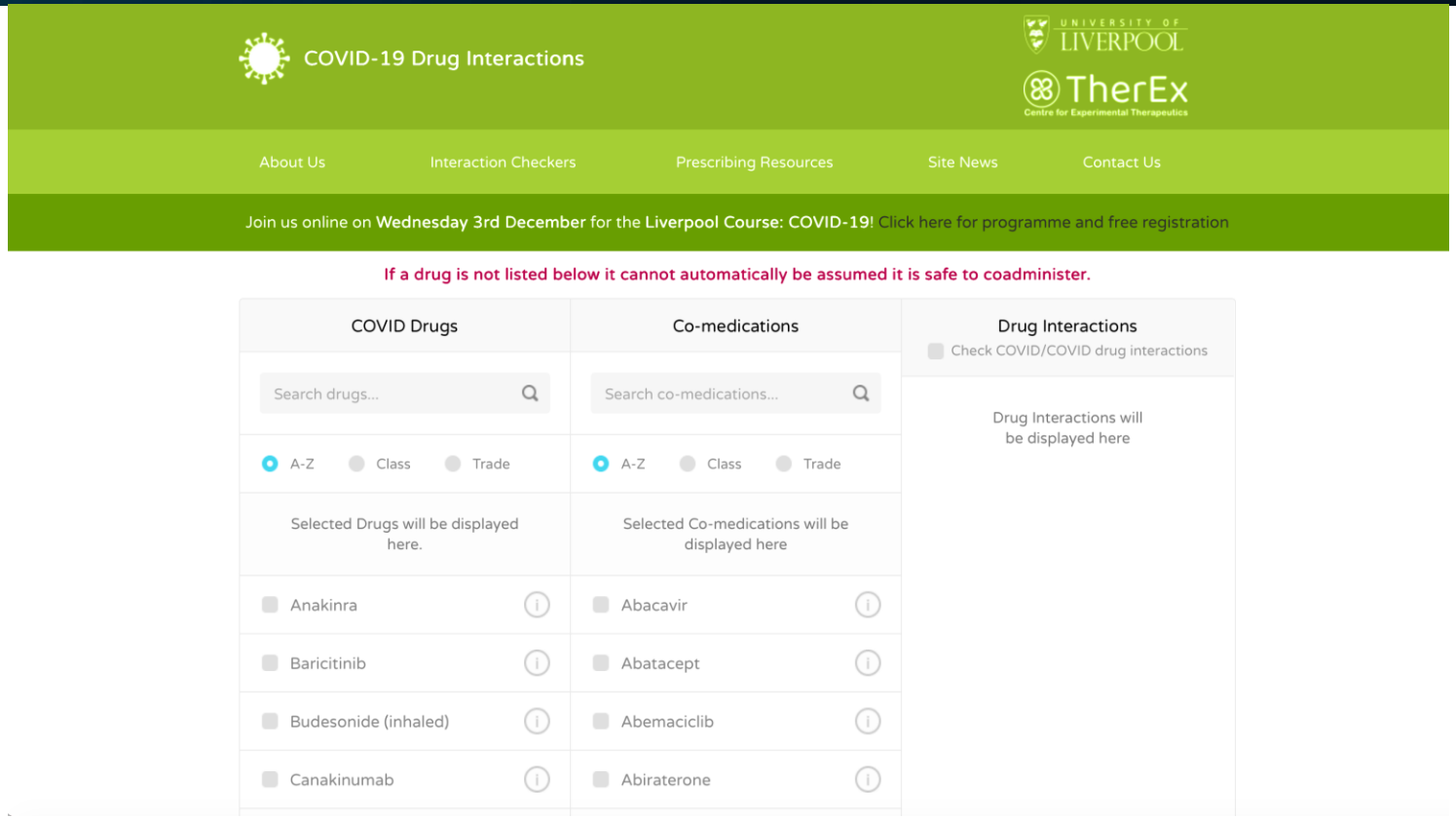
Therapeutic Window – Viral Replication Phase

Treatment Category	Optimal Window	Clinical Setting	Key Indication	Dosing Duration
Nirmatrelvir/Ritonavir	Within **5-7** days from symptom onset	Outpatient pts with high-risk of progression	High-risk pts with mild-moderate disease	300/100mg BID x 5 days
Remdesivir	Within **5-7** days from symptom onset	Outpatient pts with high risk of progression; hospitalized pts with moderate disease	Moderate disease on low-flow oxygen	200mg day 1 then 100mg daily x 4 days
Molnupiravir	Within **5** days from symptom onset	Outpatient pts with high risk of progression, ***when neither above is available***	High-risk pts with mild-moderate disease	800mg q12h X 5 days

BID = twice daily

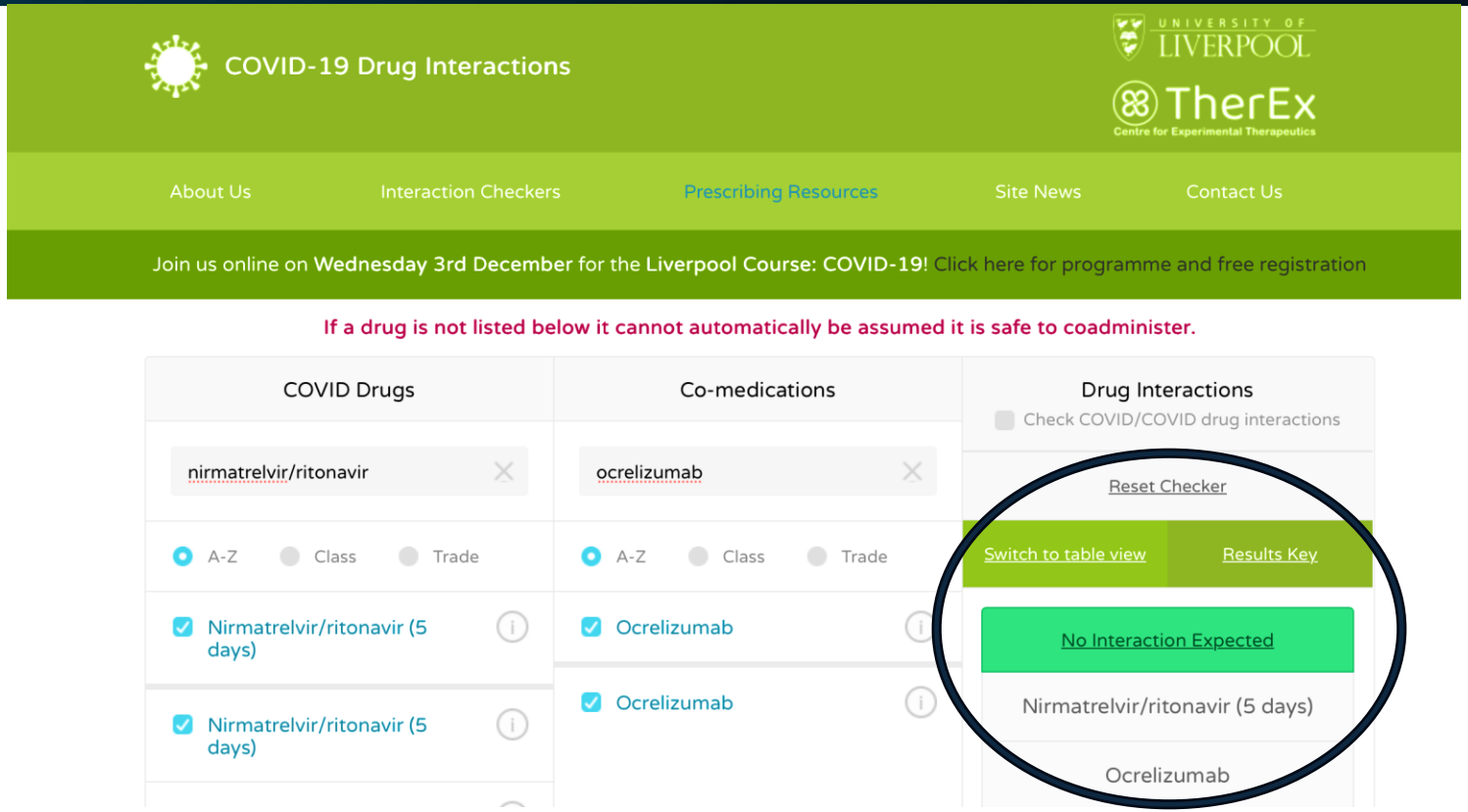
Infectious Diseases Society of America (IDSA). 2025. https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/.
Grant JM, et al. *J Assoc Med Microbiol Infect Dis Can.* 2024;8(4):245-252.

SARS-CoV-2 Drug-Drug Interactions



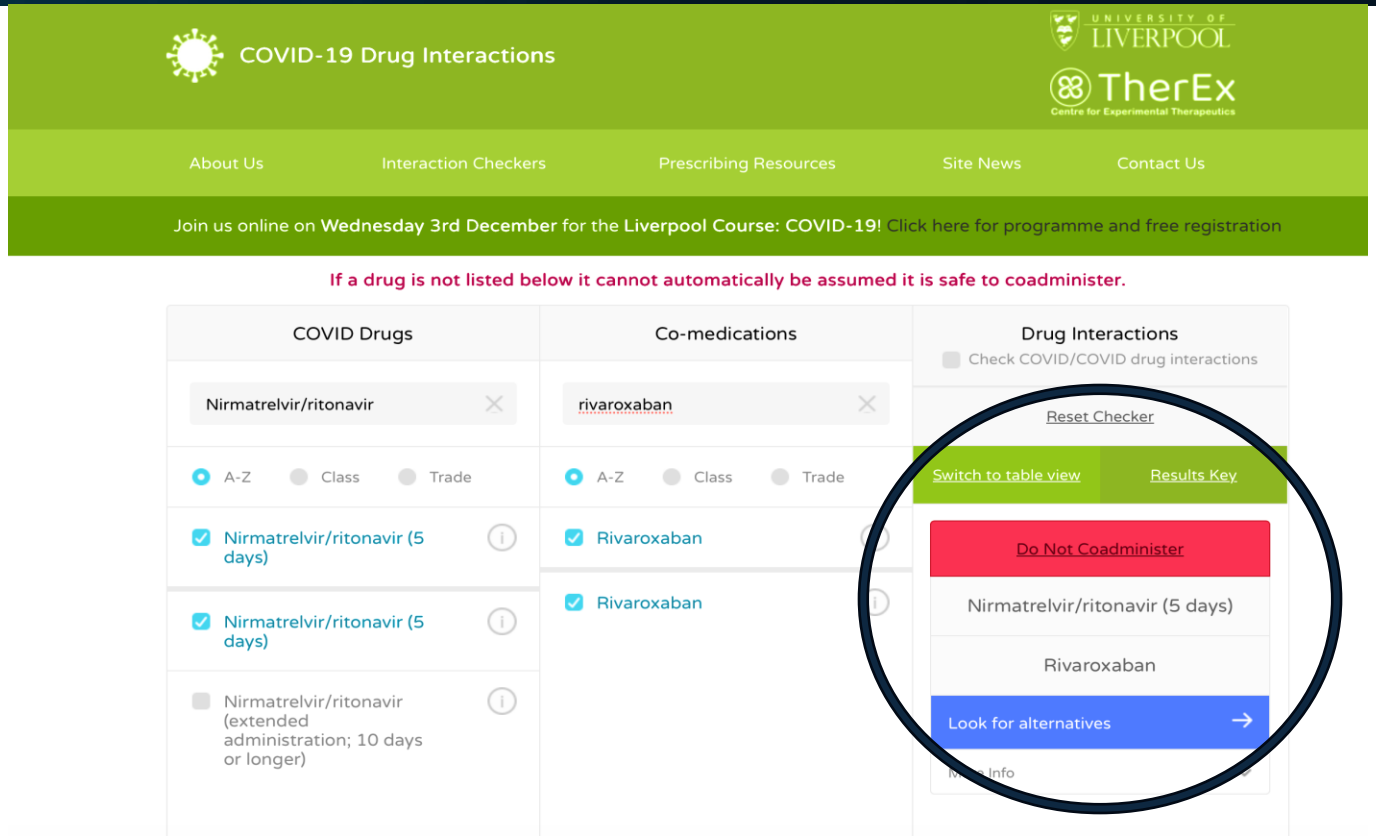
University of Liverpool. 2023. https://www.covid19-druginteractions.org/checker.

SARS-CoV-2 Drug-Drug Interactions



University of Liverpool. 2023. https://www.covid19-druginteractions.org/checker.

SARS-CoV-2 Drug-Drug Interactions



University of Liverpool. 2023. https://www.covid19-druginteractions.org/checker.

Therapeutic Window – Inflammatory Phase

Treatment Category	Optimal Window	Clinical Setting	Key Indication	Dosing Duration
Dexamethasone	When requiring oxygen support	Hospitalized patients requiring oxygen	COVID-19 pneumonia requiring oxygen	6mg daily x 10 days or until discharge
Baricitinib	Severe disease with rapid progression	Hospitalized severe/critical care	Rapid progression and high inflammatory markers	4mg daily up to 14 days
Tocilizumab	Critical disease with high inflammation	ICU/critical care	Critical disease and cytokine storm	8mg/kg single dose (max 800mg)
Low Molecular Weight Heparin (LMWH)	Within **24 hrs** of hospital admission	Hospitalized severe/critical care	Heightened risk of VTE and microvascular thrombosis	• Enoxaparin 40 mg QD • Dalteparin 32 mg (5000 IU) QD, • Tinzaparin 45 mg (4500 IU) QD

ICU = intensive care unit; QD = once daily

Infectious Diseases Society of America Guidelines (IDSA). 2025. https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/.
Grant JM, et al. *J Assoc Med Microbiol Infect Dis Can.* 2024;8(4):245-252; Schulman S, et al. *J Thromb Haemost.* 2022;20(10):2214–2225

Downstream Risk-based Stratification

Scoring Tool	Purpose	Key Components	Advantages	Limitations
4C Mortality Score (ISARIC)	In-hospital mortality prediction	Age, sex, comorbidities, RR, SpO2, consciousness level, urea, CRP	Simple calculation; good risk discrimination	Developed pre-vaccination era; includes palliative patients
CCEDRRN COVID-19 Mortality Score	ED and in-hospital mortality prediction for non-palliative patients	Age, sex, type of residence, arrival mode, CP, moderate/severe liver disease, RR upon arrival, level of O_2 provision in ED	Excellent risk discrimination; no lab tests required; bedside availability	Developed mostly in unvaccinated patients; pre-variants of concern era; geographically limited
COVID-19 SEIMC Score	30-day mortality prediction in hospitalized patients	Age, SaO2 (oxygen saturation), NLR, eGFR, dyspnea, sex	Simple calculation; clear risk stratification	Limited external validation studies
ROX Index	HFNC failure and respiratory support outcome prediction	(SpO2/FiO2)/RR	Simple calculation; real-time monitoring; non-invasive	Limited to HFNC/NIV patients; only for respiratory outcomes
NEWS2 (Modified for COVID-19)	Early warning system for clinical deterioration	RR, SpO2, oxygen use, temperature, systolic BP, HR, level of consciousness	Dynamic monitoring; early warning capability; good risk discrimination	Requires frequent monitoring; not COVID-specific

CP = chest pain; eGFR = estimated glomerular filtration rate; FiO2 = fraction of inspired oxygen; ; ISARIC = International Severe Acute Respiratory and emerging Infection Consortium; NEWS = national early warning score; NLR = neutrophil-lymphocyte ratio; ROX = respiratory rate-oxygenation; SaO2 = arterial oxygen saturation; SEIMC = Spanish Society of Infectious Diseases and Clinical Microbiology

Knight SR, et al. *BMJ*. 2020;370:m3339; Hohl CM, et al. *CMAJ Open*. 2022;10(1):E90-E99; Berenguer J, et al. *Thorax*. 2021; thoraxjnl-2020-216001.

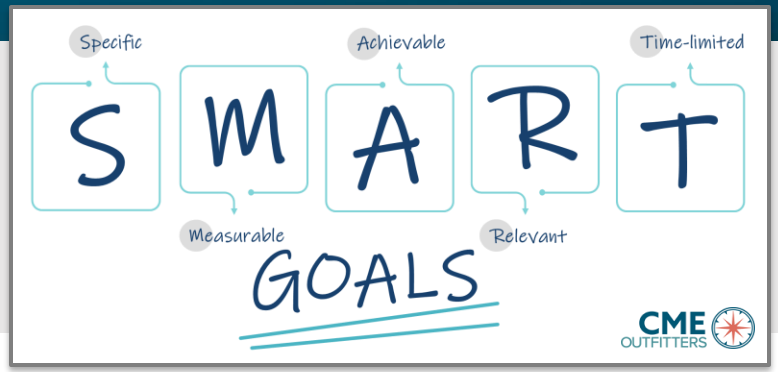
Key Takeaways for Inpatient Care

Early, algorithm-driven testing yields results quickly enough to preserve the therapeutic window for timely treatment decisions

Severity and high-risk stratification represent the pivotal first steps that direct patients onto the appropriate management pathway

Corticosteroids remain foundational therapy, with early antivirals and selected immunomodulators determined by eligibility and context

Aligning care with national/local guidance, combined with ongoing reassessment, supports optimized outcomes



Put information into action!

Takeaways from this program can be implemented into your practice to improve patient care.

- Implement a rapid diagnostic pathway so that suspected SARS-CoV-2 inpatients receive testing and a documented result to enable early treatment decisions.
- Ensure timely initiation of guideline-concordant therapy for eligible patients within the recommended window.

To Receive Credit

To receive CME/CE credit for this activity, participants must complete the post-test and evaluation online.

Participants will be able to download and print their certificate immediately upon completion.

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Other programs in this series include:

Part 1:

Guideline-Based Therapeutics for Hospitalized Patients with SARS-CoV-2 Infection

Part 3:

Risk Stratification in Hospitalized SARS-CoV-2 Patients

Part 4:

Regional SARS-CoV-2 Variants and their Impact on Inpatient Treatment

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