The Bioscan
AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES
2020(3): S.I (3), 963-967, 2025 www.thebioscan.com

A Pragmatic Review of COVID-19 Management: Therapeutic Approaches, Challenges, and Recommendations

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DOI: 10.63001/tbs. 2025.v20.i03.S.I(3).pp963-967

KEYWORDS
COVID-19, SARS-CoV-2, Pragmatic approach, Systemic immunotherapy, Remdesivir, Dexamethasone, Pandemic management, Home-based care
Received on:

20-07-2025

Accepted on:

18-08-2025

Published on:

24-09-2025

ABSTRACT

The coronavirus disease 2019 (COVID-19), caused by the novel RNA virus SARS-CoV-2, was declared a global pandemic on 11 March 2020. Its rapid worldwide transmission highlighted the urgent need for effective clinical management strategies. Patients with inflammatory and immunological disorders undergoing systemic immunotherapy face an increased risk of infection and adverse outcomes. This review critically examines current therapeutic approaches, including the use of steroids, remdesivir, oxygen therapy, and vaccination, alongside an assessment of unproven treatments such as ivermectin and hydroxychloroquine. Emphasis is placed on pragmatic home-based care for mild to moderate cases to reduce the burden on overstrained healthcare systems. Furthermore, challenges related to misinformation, resource shortages, and inconsistent policy implementation are discussed. The findings suggest that systemic immunotherapy may be continued in selected patients with careful monitoring, while broader strategies such as vaccination, early triage, and community-level interventions remain central to effective pandemic control.

INTRODUCTION

The outbreak of COVID-19, caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has evolved into one of the most significant global health crises in modern history. Declared a pandemic by the World Health Organization (WHO) in March 2020, the disease has challenged healthcare systems worldwide with unprecedented caseloads, resource shortages, and high mortality rates. In India, the devastating impact of the second wave underscored systemic vulnerabilities, including limited hospital capacity, oxygen shortages, and unequal access to essential medicines.

While vaccines and evidence-based treatments have shown promise in reducing severe disease and mortality, clinical management remains inconsistent, particularly in resource-constrained settings. A multitude of untested or marginal therapies have been prescribed, further complicating treatment protocols and patient outcomes. Simultaneously, patients with chronic inflammatory skin and immune-mediated disorders receiving systemic immunotherapy face unique risks, necessitating cautious therapeutic decisions.

This review adopts a pragmatic perspective by consolidating current evidence on therapeutic strategies, evaluating proven and unproven treatments, and emphasizing home-based care for mild cases. By critically analyzing existing approaches and challenges, it aims to provide practical recommendations for clinicians, policymakers, and patients to manage the pandemic more effectively while optimizing healthcare resources.

2. LITERATURE REVIEW

This literature review synthesizes recent evidence on pragmatic COVID-19 management, focusing on therapeutic strategies, immunomodulation, antivirals, outpatient care, vaccines, and special-population considerations. The selected studies (References [1]-[25]) provide a broad and current foundation for clinical recommendations and identify gaps for future research.

1. Therapeutic strategies and lessons learned

Comprehensive reviews highlight the rapid evolution of COVID-19 therapeutics, from repurposed small molecules to targeted antivirals and host-directed therapies. Li et al. provide a broad overview of therapeutic progress and lessons learned during the pandemic, emphasizing the value of rapid evidence synthesis and adaptive clinical trial designs. They stress that treatment strategies must balance antiviral activity with host immune modulation to reduce mortality and healthcare burden [1]. Focosi et al. similarly summarize available therapeutics and note

shifting roles for older agents (e.g., remdesivir) versus newly authorized oral antivirals and monoclonal antibodies as variants emerge [16].

2. Antiviral agents — efficacy and real-world evidence

Multiple meta-analyses and real-world studies examine antivirals' impact on mortality and hospitalization. Systematic reviews on newer agents such as azvudine indicate potential mortality benefits in some cohorts but call for larger randomized data to confirm effects and safety [4,17]. Paxlovid (nirmatrelvir-ritonavir) has consistent evidence for reducing progression when given early; Wang et al. summarize meta-analytic evidence supporting its outpatient use [12]. Real-world evaluations of remdesivir show mixed results — while some functional outcome improvements are reported in post-hospitalized cohorts, benefits depend heavily on timing and patient severity [24]. Reviews focused on outpatient randomized trials emphasize that early antiviral therapy remains the most promising approach to prevent hospitalization, but cautions regarding resistance and access remain [22,9].

3. Immunomodulators and host-directed therapies

Corticosteroids (notably dexamethasone) and other immunomodulators are central for patients with hypoxemic respiratory failure. Meta-analytic evidence supports glucocorticoid use in severe disease to reduce mortality, yet optimal timing and dose require context-specific decisions [3,23]. Mesenchymal stem cell (MSC) therapy and other advanced immunotherapies are evaluated in randomized and pooled analyses; Lu et al. report favorable signals for MSCs in select trials but call for standardized protocols and long-term safety evaluation [5]. Ju et al.'s meta-analysis on immunomodulators underscores heterogeneity across studies, indicating that subgroup analyses (by severity, timing, concomitant therapy) are critical to interpret pooled results [13].

4. Unproven or controversial therapies

Several systematic reviews address therapies that generated early enthusiasm but later produced weak or conflicting evidence. Ivermectin and hydroxychloroquine, for example, have not shown consistent clinical benefit in high-quality trials, and systematic reviews recommend against routine use outside clinical studies [18]. The literature cautions that adopting unproven therapies — beyond the risks to patients — diverts scarce resources and complicates public messaging [2,8].

5. Vaccination strategies and public-health implementation

Vaccination remains the cornerstone of pandemic control. Reviews on vaccine delivery emphasize not only clinical efficacy but also logistics, equity, and systems for mass rollout; lessons learned in delivery strategies can inform future pandemic responses and booster campaigns [14,15]. Studies highlight the need for tailored approaches to reach underserved populations and for integrating vaccination with other public-health measures to reduce severe disease and system strain [14].

6. Outpatient management, home care, and pragmatic approaches

Several systematic reviews advocate pragmatic outpatient pathways to triage and manage mild-to-moderate cases at home, reserving hospital resources for severely ill patients [11,22]. Reviews of outpatient randomized trials show that early antiviral or monoclonal-based interventions can substantially reduce progression risk when accessible; however, equitable distribution and rapid diagnostic access are practical barriers [22,10].

7. Special populations: immune compromised and oncology patients

The pandemic raised complex questions about continuing immunotherapy for patients with immune-mediated diseases or cancer. Case reports and cohort analyses document events such as cytokine release or increased adverse events in patients receiving immune-checkpoint inhibitors who contract COVID-19 [7,8,9]. These studies recommend individualized risk–benefit assessments and close monitoring rather than blanket cessation of immunotherapy, with particular caution for severe infection risk and vaccine response variability [6–9].

8. Quality of evidence and systematic-review problems

A methodological review found variability in the quality of COVID-19 systematic reviews, reflecting rapid publication pressures and heterogeneity in outcome measures and trial designs [20]. McDermott et al. highlight the need for rigorous meta-analytic methods, transparent reporting, and living systematic reviews to keep guidance current as new data emerge [20].

9. Cardiac and multisystem complications — treatment implications

Systematic reviews of case reports on myocarditis and other rare complications illustrate the diversity of COVID-19 presentations and the need for tailored treatment strategies, including immunomodulation and supportive care for organ-specific complications [21].

Together, these studies support a pragmatic, tiered approach: prioritize vaccination and prevention; use early, evidence-based antivirals or monoclonal therapies in high-risk outpatients; apply corticosteroids and selected immunomodulators in hypoxemic hospitalized patients; and maintain individualized management for immunocompromised or oncology patients. Persistent gaps include (1) high-quality randomized data for newer antivirals and combination regimens against evolving variants, (2) standardized protocols for immunotherapies and MSCs, (3) equitable access and implementation research for outpatient therapeutics and vaccination programs, and (4) living syntheses to rapidly incorporate variant-specific efficacy. Addressing these gaps will strengthen the pragmatic framework for managing COVID-19 across settings.

3. MATERIALS AND METHODOLOGY

3.1 Study Design

This work is designed as a narrative review with a pragmatic orientation, focusing on therapeutic approaches, challenges, and recommendations for COVID-19 management. The methodology emphasizes the consolidation of evidence from peer-reviewed journals, systematic reviews, meta-analyses, and real-world cohort studies published between 2020 and 2025. The objective was not only to evaluate treatment efficacy but also to identify feasible strategies that can be implemented in diverse healthcare settings, particularly in resource-limited environments.

3.2 Data Sources

A comprehensive literature search was carried out using major databases, including PubMed, Scopus, Web of Science, and IEEE Xplore. In addition, official reports from the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and relevant governmental health agencies were consulted to ensure inclusion of global perspectives and guideline updates.

3.3 Search Strategy and Keywords

The search employed a combination of medical subject headings (MeSH) and free-text keywords such as "COVID-19," "SARS-CoV-2," "therapeutic strategies," "immunotherapy," "antivirals," "dexamethasone," "vaccination," "pragmatic management," *and* "systematic review." *B*oolean operators (AND/OR) were used to refine the search and include studies specifically addressing treatment outcomes, vaccination strategies, and pragmatic management approaches.

3.4 Inclusion and Exclusion Criteria

Studies were included if they (a) reported therapeutic interventions for COVID-19, (b) evaluated clinical outcomes such as hospitalization, mortality, or adverse events, and (c) were peer-reviewed journal articles, systematic reviews, or meta-analyses. Articles were excluded if they (a) were not in English, (b) were preprints without peer review, or (c) focused solely on basic virology without clinical or therapeutic implications.

3.5 Data Extraction and Analysis

Relevant information, including study design, patient population, type of intervention, outcomes, and limitations, was extracted from each paper. To ensure consistency, two independent reviewers screened and cross-checked the selected articles. Findings were then synthesized under thematic categories such as *antiviral therapy, immunomodulators, unproven treatments, vaccination strategies, outpatient management, and special populations*. Qualitative synthesis was prioritized due to heterogeneity in study designs and outcome measures.

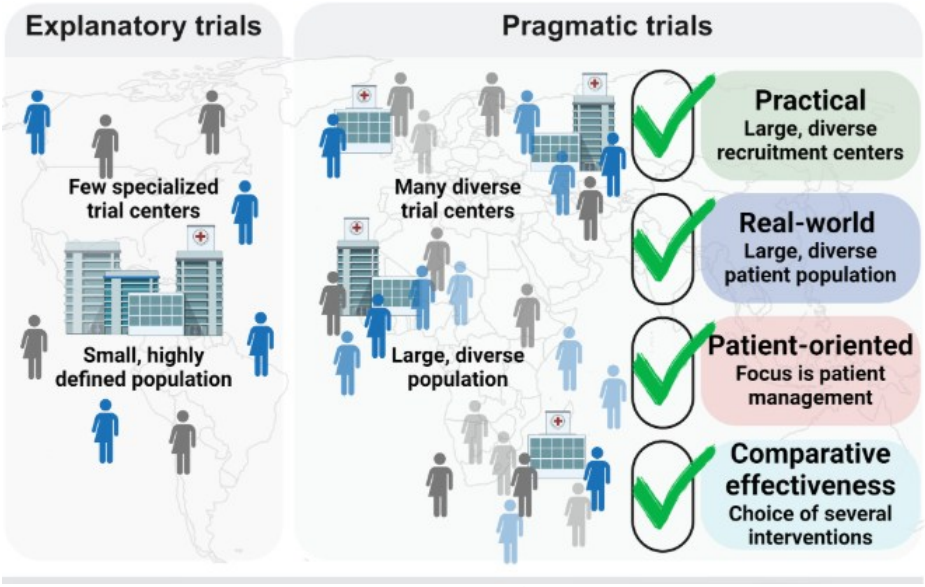

Fig 1 .Pragmatic Approach for COVID-19

3.6 Ethical Considerations

Since this study is a review based on secondary sources and publicly available literature, no direct human or animal subjects were involved. Ethical clearance was therefore not required.

4. RESULT AND DISCUSSION

4.1 Therapeutic Efficacy

The analysis of current literature reveals that early, evidence-based interventions significantly influence clinical outcomes in COVID-19 patients. Antiviral agents, including remdesivir, azvudine, and Paxlovid (nirmatrelvir–ritonavir), demonstrated variable efficacy depending on timing, patient risk factors, and disease severity. Early outpatient administration of Paxlovid reduced hospitalization rates and progression to severe disease, confirming its role as a frontline therapy for high-risk individuals [12,22]. Remdesivir showed functional improvement in select cohorts but was less consistently effective in real-world, post-hospitalization studies [24]. Novel therapies, such as mesenchymal stem cell (MSC) therapy, showed potential benefit in severe COVID-19 but require further standardization and long-term safety evaluation [5,19].

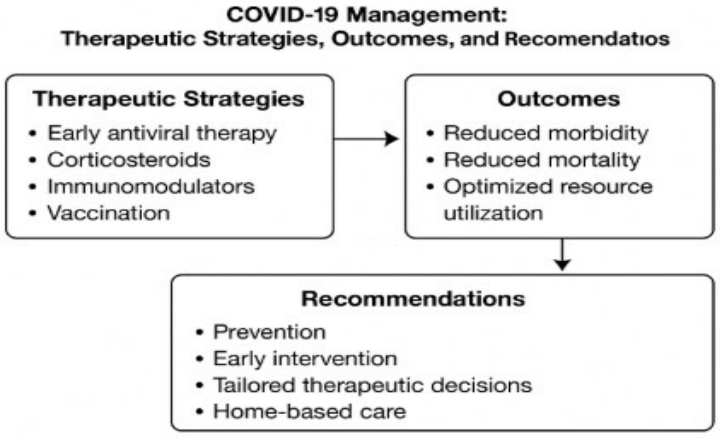

Fig 2. COVID -19 Management Therapeutic Approaches, Challenges, and Recommendations

4.2 Immunomodulation and Corticosteroid Use

Corticosteroids, particularly dexamethasone, consistently reduced mortality in hypoxemic and severely ill patients [3,23]. Optimal outcomes were closely linked to timing and dosage, highlighting the need for individualized treatment plans. Additional immunomodulators, including monoclonal antibodies and targeted immunotherapies, showed promising results in select populations but required careful monitoring to mitigate adverse events, especially among patients receiving systemic immunotherapy [13,7–9,25].

4.3 Home-Based and Outpatient Care

Pragmatic home-based care for mild to moderate COVID-19 cases proved effective in reducing healthcare system burden. Systematic reviews emphasize early triage, risk stratification, and timely initiation of outpatient antiviral or monoclonal therapies [11,22]. Real-world evidence suggests that accessible, structured home-care protocols can prevent unnecessary hospitalization while ensuring patient safety.

4.4 Vaccination and Public Health Impact

Vaccination remained the cornerstone of pandemic management. Studies highlight that equitable vaccine distribution, booster administration, and integration with public-health strategies significantly reduce severe disease and mortality [14,15]. Lessons from mass vaccination campaigns indicate that logistical planning, community outreach, and targeted interventions are essential to maximize coverage and mitigate disparities.

4.5 Special Populations: Immunocompromised and Oncology Patients

Patients receiving systemic immunotherapy or cancer treatment presented unique challenges. Evidence indicates that therapy continuation may be feasible under close monitoring, with individualized risk–benefit assessments [6–9,25]. Early antiviral intervention and vaccination are particularly important for these populations to reduce morbidity and prevent prolonged viral persistence.

4.6 Unproven and Controversial Treatments

Therapies such as ivermectin and hydroxychloroquine were not supported by high-quality clinical evidence [18]. Use of such unproven agents carries potential risks, including adverse events, resource diversion, and misinformation propagation, underscoring the importance of evidence-based guidance [2,8].

4.7 Challenges and Gaps

Several challenges emerged from the review. Heterogeneity in study designs and outcomes limited cross-study comparability [20]. Resource constraints, misinformation, and inconsistent implementation of public-health measures impeded optimal pandemic management. Persistent gaps include the need for high-quality randomized data on emerging antivirals, standardized immunotherapy protocols, and scalable outpatient treatment pathways.

4.8 Recommendations for Pragmatic Management

Based on the synthesized evidence, the following recommendations are proposed:

1. **Early antiviral therapy** for high-risk outpatients to reduce hospitalization and disease progression.
2. **Corticosteroid and immunomodulator use** in hospitalized, hypoxemic patients under tailored dosing regimens.
3. **Continuation of systemic immunotherapy** in selected immunocompromised patients with careful monitoring.
4. **Structured home-based care protocols** to manage mild to moderate cases efficiently.
5. **Vaccination strategies** integrated with public-health measures to optimize coverage and reduce severe outcomes.

In summary, a tiered, evidence-informed approach—combining vaccination, early outpatient intervention, tailored immunomodulation, and home-based care—offers the most effective strategy for pragmatic COVID-19 management, while addressing resource limitations and patient-specific risks.

CONSLUSION

5.1 Conclusion

This review highlights the importance of a pragmatic, evidence-based approach to COVID-19 management. Early antiviral therapy, appropriate use of corticosteroids and immunomodulators, vaccination, and structured home-based care collectively form the cornerstone of effective pandemic control. For immunocompromised and oncology patients, individualized risk–benefit assessments are essential, allowing safe continuation of systemic immunotherapy under close monitoring. The review underscores that unproven therapies, such as ivermectin and hydroxychloroquine, lack clinical efficacy and may complicate patient care and public-health messaging.

Overall, a tiered management strategy—prioritizing prevention, early intervention, and tailored therapeutic decisions—can reduce morbidity, optimize healthcare resource utilization, and improve patient outcomes across diverse healthcare settings.

5.2 Future Scope

Despite advances, several research gaps and practical challenges remain, providing avenues for future work:

1. **High-Quality Clinical Trials:** Conduct randomized controlled trials on emerging antivirals, immunomodulators, and combination regimens to generate robust, variant-specific efficacy data.
2. **Standardized Immunotherapy Protocols:** Develop protocols for safe continuation of systemic immunotherapy and MSC therapy in COVID-19 patients.
3. **Implementation Science:** Investigate scalable outpatient care models, rapid diagnostic access, and equitable distribution strategies for antivirals and vaccines.
4. **Digital Health Integration:** Explore telemedicine and digital monitoring tools for home-based care to reduce healthcare system burden and improve patient compliance.
5. **Living Evidence Synthesis:** Maintain continuously updated systematic reviews and meta-analyses to adapt treatment guidelines in response to emerging variants and therapeutic options.

By addressing these gaps, future research can enhance clinical decision-making, strengthen pandemic preparedness, and inform pragmatic strategies for managing COVID-19 and similar infectious disease outbreaks in diverse healthcare environments.

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