Current Dermatology Reports
https://doi.org/10.1007/s13671-022-00368-3

COVID-19 IN DERMATOLOGY (J. M. GELFAND, SECTION EDITOR)

Outpatient Management of COVID-19: A Primer for the Dermatologist

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Accepted: 4 August 2022

Abstract

Purpose of Review To summarize diagnostic and therapeutic management of COVID-19 in the outpatient setting for dermatologists.

Recent Findings Paxlovid (nirmatrelvir-ritonavir) is the preferred treatment in patients with mild symptoms at high risk of progression to severe SARS-CoV2 infection. Additional options include monoclonal antibodies (bebtelovimab), remdesivir, and molnupiravir.

Summary Dermatologists need to be aware of recent developments in diagnostic and therapeutic management of COVID-19 in the outpatient setting, as their patients may rely on dermatologists to provide advice, particularly in cases where treatments for dermatological disease may impact the risk of COVID-19 and/or vaccine efficacy.

Keywords COVID-19 · Outpatient management · Diagnostic testing · Therapeutic management

Introduction

Two years into the COVID-19 pandemic, diagnosis, prevention, and treatment strategies have dramatically advanced making SARS-CoV2 infection a manageable infectious disease that should result in mortality only in very rare circumstances.

Dermatologists have an important role to play in the diagnosis, prevention, and treatment of COVID-19 given that SARS-COV-2 is highly contagious, impacting all clinical populations. In addition, many patients in dermatology do not have regular contact with primary care physicians and may rely on dermatologists instead for medical advice. For example, a cohort study using a large claims database showed that in 22–31% of male patients and 17–26% of female patients had no primary care visits in the year after establishing care with their dermatologist [1]. Therefore, dermatologists may need to provide recommendations for patients presenting with preliminary symptoms suspicious for COVID infection. Of special importance, treatments used by dermatologists may impact the efficacy of COVID-19 vaccines and/or may make patients more susceptible to SARS-COV-2 infection and severe COVID-19 illness. Some large database studies have suggested that high dose prednisone, methotrexate, mycophenolate mofetil, JAK inhibitors, and in particular B cell depleting agents (e.g., rituximab) may increase susceptibility to COVID-19 and poorer outcomes [2–5]. Interestingly, TNF inhibitors appear to be associated with a decreased risk of severe COVID-19 compared to the general population, and other biologics commonly used in dermatology such as dupilumab, and biologics that target IL12/23, IL17, or IL23 seem to have a neutral impact on the risk of poor COVID-19 outcomes [5].

Clinical Suspicion and Diagnosis of COVID-19

Signs and Symptoms

The most common initial presenting symptoms for the current variant of concern at time of publication (Omicron) include runny nose (76.5%), headache (74.7%), sore throat

This article is part of the Topical Collection on *Covid-19 in Dermatology*

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Published online: 20 August 2022

(70.5%), sneezing (63%), cough (49.8%), and hoarse voice (42.6%) [6•]. Symptoms such as anosmia or ageusia were identified as specific symptoms of SARS-CoV2 infection in the beginning of the pandemic[7] but are present in less than 20% of Omicron cases [6•]. This study further showed that while sore throat and hoarse voice are consistently more prevalent during omicron wave than prior variants, symptoms such as brain fog, fever, headaches, and dizziness are significantly less prevalent in omicron cases [6•]. Studies have suggested that symptoms in the Omicron variant are less severe than initial variants of the pandemic, with lower rates of hospitalization, ICU admission, and mortality [6•, 8].

The Omicron variant has demonstrated a shorter incubation period compared to earlier variants, with symptoms occurring approximately 3 days after exposure vs. 4–5 days with earlier variants [9–11]. Infection with Omicron variants are also associated with shorter duration of symptoms, with symptoms resolving within 7 days infection vs. 9 days with infections caused by the Delta variant [6•].

Dermatologic Signs

Early descriptive studies hypothesized an association of pernio-like acral lesions with SARS-CoV2 infection [12, 13], but further analytical studies including SARS-CoV2 serology and immunohistochemical staining of SARS-CoV-2 from skin biopsies of patients who had previously been diagnosed with SARS-CoV-2-related skin eruptions did not support this association[14–16]. Other case series and case reports have also suggested that urticaria-like lesions, morbilliform rash, lupus flares, and retiform purpura in hospitalized patients may be nonspecific manifestations of SARS-CoV2 infection [17–19]. Psoriasis flares and new onset psoriasis have also been reported in the context of COVID-19 infection [20–23]. Therefore, testing for acute SARS-CoV2 infection should be considered in patients with new onset psoriasis or flares of existing psoriasis particularly if there is a high level of COVID-19 in the community.

Testing Recommendations

The Center for Disease Control and Prevention (CDC) recommends that patients should be tested if they present with symptoms concerning for COVID-19 or 5 days after close-contact exposures to a patient with COVID-19 (closer than six feet for 15 or more minutes over the course of 24 h to someone who has tested positive) [24, 25••]. Asymptomatic individuals may also be tested in certain circumstances including travel or screening programs for work or school. Nucleic acid amplification test (NAAT) is often preferred; if not possible, an antigen test may be used. Using antibody testing as the sole basis for diagnosis of acute infection is not recommended because positive antibody testing can also indicate prior vaccination or prior infection [25••].

NAAT Tests

NAAT tests remain the preferred method of testing for COVID-19. RT-PCR assays amplify specific portions of viral RNA, typically targeting regions of the SARS-CoV-2 genome encoding spike, envelope, and nucleocapsid proteins [25••]. One review showed that NAAT tests have an overall sensitivity of 89.1% and specificity of 98.9% [26]. Another review reported that for nasal specimens, sensitivity of NAAT was 86% and specificity 99%, compared to sensitivity of 85% and specificity of 99% for saliva swabs [27]. Typically NAAT tests use multiple targets to detect the virus, so even SARS-CoV2 variants with genetic variations of these targets are less likely to be impacted. However, if symptomatic COVID-19 is still suspected after a negative test result, repeat testing should be considered [25••].

Antigen Tests

Antigen tests have played an important role in expanding point-of-care COVID-19 testing, offering a quick turnaround time and ease of access. Antigen tests use synthetic antibodies to bind any SARS-CoV2 viral antigens that may be present nasal or saliva specimens, indicating active infection. Antigen tests are typically less sensitive than NAAT tests and have the highest sensitivity in the presence of symptoms, in particular within 1 week of symptom onset [28]. In a Cochrane review of 64 study reports, including 16 antigen tests, sensitivities ranged from 34 to 88% between brands, while specificity was overall high at 99.6%. In addition, sensitivity was higher in symptomatic patients (72% vs. 58% in asymptomatic), and within the first week of symptom onset (78% vs. 51% in the 2nd week of symptom onset) [28]. Due to the higher rate of false negatives, the CDC recommends that negative antigen test results in symptomatic patients suspicious for COVID-19 still require confirmation with NAAT or repeat testing after 48 h [25••].

Antibody Tests

According to the National Institutes of Health (NIH) guidelines, serologic tests are not recommended to assess immunity or as the primary test of COVID-19 [25••]. Serologic tests are not useful in the acute setting, as antibodies take weeks to develop, and may reflect prior immunization or infection. In a review of 57 studies using 25 commercial tests, IgM antibodies against spike (S), or nucleocapsid (N) proteins were detected in 23% of COVID RT-PCR + patients within 1 week after symptom onset, 58% within 2 weeks,

and 75% within 3 weeks, whereas IgG antibodies against S or N proteins were detected in 30% within 1 week, 60% within 2 weeks, and 88% within 3 weeks [29]. Another review evaluating sensitivity and specificity of antibody testing reported a sensitivity of enzyme-linked immunosorbent assays (ELISA) of 84%, lateral flow immunoassays 66%, and chemiluminescent immunoassay (CLIAs) 98% [30].

Therapeutic Management

Any patient with a COVID-19 concern, whether it be a high risk contact, or presence of symptoms, should contact their medical provider, as home testing should be done and if indicated there are now many outpatient treatment options to reduce risk of progression to severe disease. More immediate medical attention should be sought in those with severe dyspnea (including dyspnea at rest), oxygen saturation below 90%, chest pain, confusion, dizziness, or altered mental status as patients may have additional complications of COVID-19 that require hospitalization [25••]. COVID-19 can cause extrapulmonary complications including cardiac injury such as myocarditis, thromboembolic events such as pulmonary embolism, encephalopathy, and inflammatory complications such as multisystem inflammatory syndrome (MIS-C) in children [25••].

Those with mild COVID-19 with risk factors for progression to severe disease are candidates for outpatient management with the treatments described below. Risk groups for progression to severe disease include immunocompromised patients, age ≥ 65 years, age < 65 years with clinical risk factors (Table 1), [25••] unvaccinated individuals of any age, or vaccinated individuals who have not received a vaccination booster.

Nirmatrelvir-Ritonavir (Paxlovid)

Nirmatrelvir-ritonavir, or Paxlovid, is an oral antiviral comprised of a novel protease inhibitor (nirmatrelvir) and a booster (ritonavir) that was granted an emergency use authorization (EUA) in 2022 for treatment of outpatient COVID-19 in high risk adult and pediatric (≥ 12 years, ≥ 40 kg) patients. It is considered the first line treatment option for early outpatient management of

Table 1 Patient characteristics that may increase rates of severe COVID-19 infection

Level of evidence	Clinical risk factors
High risk	Asthma
	Cancer
	Cerebrovascular disease
	Chronic kidney disease
	Chronic lung disease (interstitial lung disease, pulmonary embolism, pulmonary hypertension, bronchiectasis, COPD)
	Chronic liver disease (cirrhosis, non-alcoholic fatty liver disease, alcoholic liver disease, autoimmune hepatitis)
	Cystic fibrosis
	Diabetes mellitus
	Disabilities (congenital malformations, cerebral palsy, ADHD, intellectual disability, learning disabilities, spinal cord injury, limited self-care or activities of daily living)
	Cardiac disease (heart failure, coronary artery disease, cardiomyopathy)
	HIV
	Mental health disorders (mood disorders, schizophrenia spectrum)
	Dementia
	Obesity
	Primary immunodeficiencies
	Pregnancy or recent pregnancy
	Physical inactivity
	Smoking, current, or former
	Solid organ or hematopoietic cell transplantation
	Tuberculosis
	Use of immunosuppressive medications
Suggestive high risk	Overweight
	Sickle cell disease
	Substance use disorders
	Thalassemia
Mixed evidence	Alpha 1 antitrypsin deficiency
	Bronchopulmonary dysplasia
	Hepatitis B, hepatitis C
	Hypertension

COVID-19 due to its high efficacy, wide availability, and excellent safety profile. Nirmatrelvir blocks the SARS-CoV-2-3CL protease necessary for viral replication, while ritonavir slows metabolism of nirmatrelvir to increase its efficacy. The EPIC-HR trial was a clinical trial of 2246 patients comparing nirmatrelvir-ritonavir to placebo in unvaccinated patients treated within 3–5 days of symptom onset. The incidence of hospitalizations was 0.77% in the treatment group vs. 7.0% in the placebo group, with similar rates of adverse effects. In addition, all 13 deaths in the study group occurred in the placebo group [31••].

Nirmatrelvir-ritonavir dosing is 300 mg nirmatrelvir (two 150 mg tabs) and 100 mg ritonavir taken twice daily for 5 days and must be initiated within 5 days of symptom onset. Dose adjustment for reduced kidney function is required. For patients with eGFR 30–59 mL/min, dosing is 150 mg nirmatrelvir–100 mg ritonavir twice daily for 5 days. Those with eGFR < 30 ml/min or severe hepatic impairment should not receive nirmatrelvir-ritonavir [25••]. Furthermore, although the EPIC-HR trial excluded pregnant and lactating individuals, the NIH guidelines recommend nirmatrelvir-ritonavir in pregnant patients, as pregnancy is associated with poor outcomes and the potential benefits likely outweigh risks [25••]. Adverse events in that were numerically more common in the nirmatrelvir-ritonavir group compared to placebo were dysgeusia (6% and < 1%, respectively), diarrhea (3% and 2%), hypertension (1% and < 1%), and myalgia (1% and < 1%). The proportions of subjects who discontinued treatment due to an adverse event were 2% in the nirmatrelvir-ritonavir group and 4% in the placebo group [32].

The greatest hurdle to prescribing nirmatrelvir-ritonavir is the multitude of significant drug interactions, as both nirmatrelvir and ritonavir are CYP3A4 substrates and ritonavir is an inhibitor. Some medications may require dose adjustment during nirmatrelvir-ritonavir course, and some medications may be prohibited (Table 2) [33]. For example, interactions between drugs like rivaroxaban and salmeterol are significant and severe and thus patients taking these medications should not receive nirmatrelvir-ritonavir. Additional recommendations regarding dose adjustment and drug co-administration can be found in the Management of Paxlovid Drug Interaction guidelines from the IDSA [34].

There are further reports of rebound COVID-19 symptoms after nirmatrelvir-ritonavir treatment [35]. These studies have reported rebound symptoms between 2 and 8 days after initial recovery. There were no hospitalizations or deaths in any of these reports [36–38]. The CDC does not recommend additional treatment with nirmatrelvir-ritonavir or other anti-SARS-CoV2 therapies for rebound symptoms [35] Fig. 1.

Molnupiravir

Molnupiravir is a ribonucleoside prodrug that inhibits viral replication. Its phosphorylated form is incorporated into viral RNA and misdirects the viral polymerase during replication and causes errors in the viral genome. In the MOVe-OUT study in 2022, a phase 3 trial of 1433 patients comparing molnupiravir to placebo showed a 30% reduction risk of hospitalization or death on day 29 (6.8% in treatment vs. 9.7% in placebo) [39••]. Since molnupiravir has a lower efficacy in phase 3 trials, molnupiravir is generally recommended if nirmatrelvir-ritonavir is unavailable or contraindicated [25••].

Molnupiravir is administered as a dose of 800 mg by mouth twice daily for 5 days. Molnupiravir is contraindicated in children (younger than 18 years old). The FDA emergency use authorization also does not recommend use in pregnant patients due to fetal toxicity observed in animal studies, and recommends contraception during until 4 days after treatment with molnupiravir [25••]. However, per NIH recommendations, if no other therapies are available, pregnant people at risk of progression may choose molnupiravir therapy after a documented risk and benefit discussion with the prescribing clinician, particularly if beyond 10 weeks gestation beyond embryogenesis [25••].

Monoclonal Antibodies

Bebtelovimab is a recombinant human monoclonal antibody that binds the spike protein of the SARS-CoV-2 virus. In vitro data have shown that bebtelovimab neutralizes the variant of concern at the time of publication (Omicron B.1.1.529) [40], while clinical trial studies are limited to a phase 2 trial pre-print [41]. The NIH recommends using bebtelovimab if nirmatrelvir-ritonavir and remdesivir are not options [25••].

Bebtelovimab is administered within 7 days of symptom onset as a dose of 175 mg IV in a single injection over 30 s. Patients should be observed for at least 1 h after injection [25••].

Other monoclonal antibodies such as sotrovimab, casirivimab-imdevimab, and bamlanivimab-etesevimab are not recommended by the NIH as they do not have activity against Omicron sub-variant [25••, 42, 43].

Remdesivir

Remdesivir is a viral RNA polymerase inhibitor that is available under EUA for the treatment of outpatients at high risk of severe COVID-19. Though initially remdesivir was used in treatment of hospitalized patients [44], later trials showed that early administration of a short course of remdesivir prevented progression of disease [45, 46••,

Table 2 Medications for which co-administration with nirmatrelvir-ritonavir is contraindicated or not recommended

Medication	Recommended course of action per FDA or IDSA
Rivaroxaban, salmeterol	Severe interaction – avoid using nirmatrelvir-ritonavir due to increased drug effects
Simvastatin, lovastatin	Hold 12 h prior to first dose of nirmatrelvir-ritonavir, hold during 5 days of treatment, and restart 5 days after completing nirmatrelvir-ritonavir
Atorvastatin, rosuvastatin	Consider discontinuation during treatment with nirmatrelvir-ritonavir, no need to hold prior to or after completing nirmatrelvir-ritonavir
Hormonal contraceptives containing ethinyl estradiol	Additional non-hormonal method of contraception during the 5 days of nirmatrelvir-ritonavir treatment and until one menstrual cycle after stopping nirmatrelvir-ritonavir should be recommended
HIV medications	Aside from maraviroc, HIV antiretrovirals can be co-administered with nirmatrelvir-ritonavir without dose adjustment. Follow up with the HIV care provider is recommended
Clopidogrel	Avoid nirmatrelvir-ritonavir for 6 weeks after coronary stenting
Apixaban	Dose dependent: -Apixaban 2.5 mg: Consider holding nirmatrelvir/ ritonavir -Apixaban 5 mg or 10 mg: Reduce dose by 50% until 3 days after nirmatrelvir/ritonavir
Alfuzosin, amiodarone, apalutamide, carbamazepine, clozapine, colchicine, dihydroergotamine, dronedarone, ergotamine, flecainide, lurasidone, methylergonovine, midazolam oral, pethidine, phenobarbital, phenytoin, pimozide, propafenone, propoxyphene, quinidine, ranolazine, rifampin, sildenafil (for pulmonary arterial hypertension), St. John's Wort, triazolam	Contraindicated while on nirmatrelvir-ritonavir
Apemaciclib, amlodipine, bedaquiline, bepridil, betamethasone, bosentan, budesonide, buspirone, ceritinib, ciclesonide, clarithromycin, clonazepam, cyclosporine, dabigatran, dasabuvir, dasatinib, dexamethasone, diazepam, digoxin, diltiazem, elbasvir/grazoprevir, encorafenib, erythromycin, felodipine, fentanyl, fluticasone, glecaprevir/pibrentasvir, hydrocodone/oxycodone, ibrutinib, isavuconazonium sulfate, itraconazole, ivosidenib, ketoconazole, lidocaine, methadone, methylprednisolone, midazolam parental, mometasone, neratinib, nicardipine, nifedipine, niolotinib, ombitasvir/paritaprevir/ritonavir, prednisone, quetiapine, rifabutin, rivaroxaban, salmeterol, sirolimus, sofosbuvir/velpatasvir/voxilaprevir, tacrolimus, trazodone, triamcinolone, valsartan, venetoclax, verapamil, vinblastine, vincristine, voriconazole, warfarin	Coadministration with nirmatrelvir-ritonavir should be avoided; the FDA recommends consultation with prescriber of the drug regarding holding, dose adjustment, or special monitoring
Tamsulosin	Dose-dependent: -Tamsulosin 0.4 mg: No change (monitor blood pressure) -Tamsulosin 0.8 mg: Consider holding or decrease to 0.4 mg
Bupropion, isosorbide mononitrate, paroxetine, risperidone, tramadol	No dose adjustment required

47–49]. In the PINETREE trial in 2022, 562 patients who received a 3 day course of remdesivir from an outpatient provider within 7 days of symptom onset reduced the rates of hospitalization and death by 87% (0.7% in treatment vs. 5.3% in placebo), suggesting that timely administration of the medication was effective in preventing more severe disease [46••].

Remdesivir is administered as a dose of 200 mg IV on day 1, then 100 mg IV on day 2 and 3. Infusions should be administered over 30–120 min, and patients observed for at least 1 h after infusion for potential hypersensitivity reactions [25••]. Remdesivir is not widely used due to the logistical challenges of its administration.

Other Treatments

High Titer Convalescent Plasma

Convalescent plasma is plasma obtained from donors who have recovered from COVID-19. Studies have shown mixed evidence in preventing disease progression in outpatients. Some studies show reduced hospitalization and severity of disease in outpatients [50, 51], but some studies showed no benefit [52, 53]. The NIH currently recommends against use of convalescent plasma collected prior to the Omicron variant and has insufficient evidence for or against the use of convalescent plasma after Omicron emerged [25••]. However, convalescent plasma is included in the

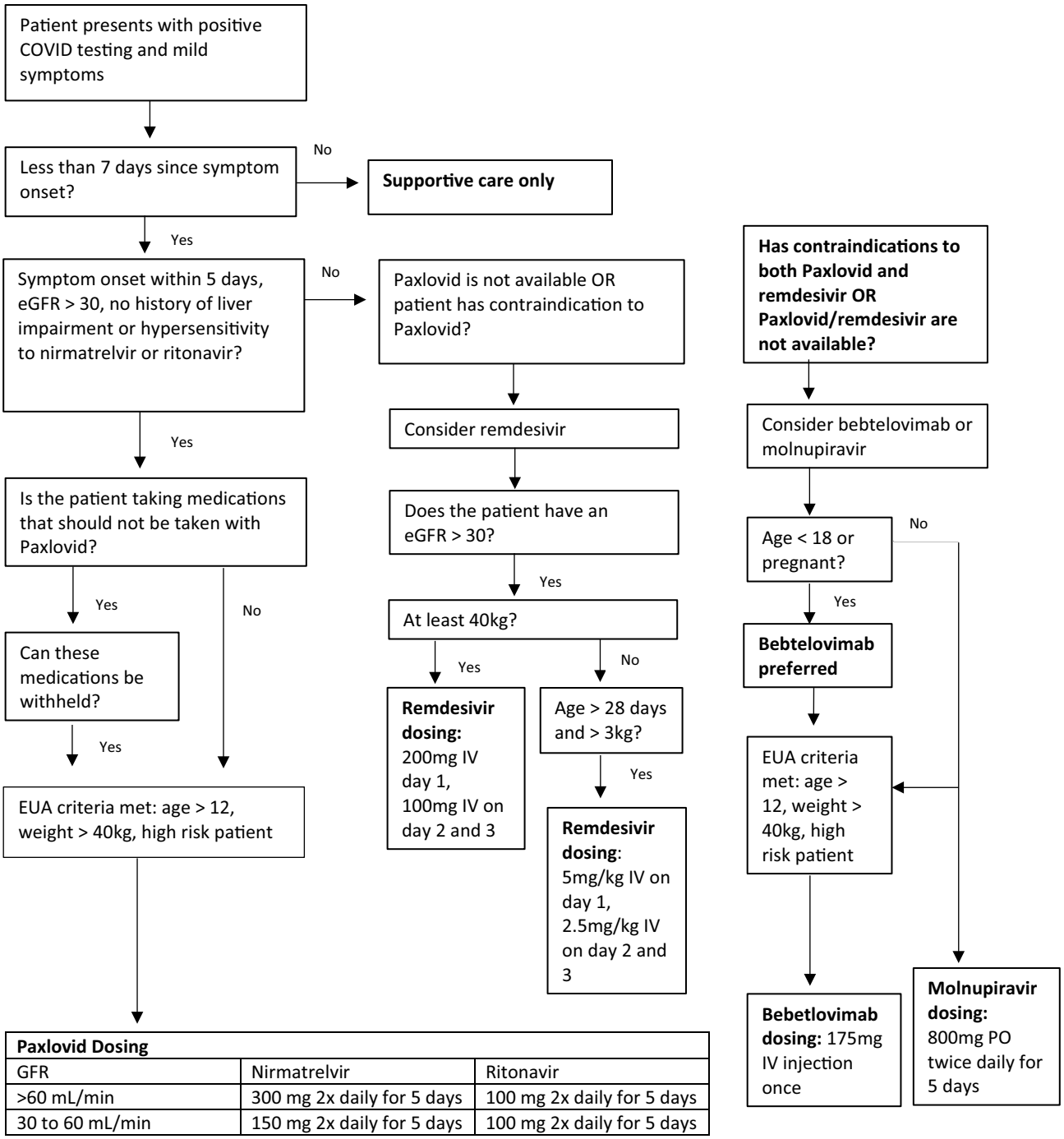

Fig. 1 Approach to outpatient therapeutic managementaccording to NIH guidelines, including nirmatrelvir-ritonavir, remdesivir,bebtelovimab, and molnupiravir dosing [25••, 54]

Infectious Diseases Society of America (IDSA)/CDC guidelines as a potential therapy in immunocompromised patients [54•].

Corticosteroids

Though systemic corticosteroids play a role in reducing inflammation in acute hospitalized patients with COVID-19 [55], they are not recommended for use in outpatients in the absence of another indication per NIH recommendations. Inhaled corticosteroids are of uncertain benefit; two trials indicated reduction in hospitalization [56, 57] while one did not show a significant reduction in hospitalization [58], and no trials indicated a mortality benefit.

Fluvoxamine

Some data has suggested that the antidepressant fluvoxamine may reduce progression to severe disease. The TOGETHER trial was a randomized trial of 1497 outpatients and showed a lower rate of a composite of hospitalization or emergency room visits due to COVID-19 progression, at 11% in the treatment group vs. 16% in the placebo group. However, the decrease in composite was primarily driven by a reduction in emergency department visits, and other outcomes such as mortality were not different in the placebo vs. treatment group [59]. The FDA has declined to issue an EUA covering fluvoxamine [60].

Medications with Evidence Against Use in COVID

In the beginning of the pandemic, there was initially discussion on certain medications hypothesized to have benefit on mortality or time to recovery from COVID-19, due to anti-inflammatory or anti-viral properties of these medications in vitro, which caused some patients to use these medications in hopes it would treat COVID-19. However, with further studies, evidence suggests that these medications offer no benefit for treating COVID-19.

Ivermectin

In the early months of the pandemic, mixed evidence on the benefit of ivermectin was published mostly in small and low-quality studies [61], some of which have now been identified as potentially fraudulent [62]. In contrast, several recent large clinical trials show that ivermectin shows no benefit in treating COVID-19 infection. In a trial of 400 patients [63], in the I-TECH trial with 490 patients [64], and the TOGETHER trial with 3515 patients [65], treatment with ivermectin did not result in decreased rates of hospitalization or severe infection. It is estimated that Medicare and private insurers in the US spent nearly $130 million for ivermectin treatment of COVID-19 over a 1 year period [66], representing a large amount of federal spending on ineffective care. The NIH recommends against use of ivermectin in patients for COVID-19 [25••].

Hydroxychloroquine

Hydroxychloroquine was shown to have no mortality benefit in hospitalized patients or outpatients, nor does it have any role in preventing COVID-19 [67–70]. In outpatients, a randomized controlled trial of 491 patients were treated with oral hydroxychloroquine or placebo within 4 days of symptom onset showed no different in symptoms over 14 days after treatment [70], and another randomized controlled trial of 293 patients treated with hydroxychloroquine vs. placebo showed no difference in risk of hospitalization, disease progression over 28 days, or time to resolution of symptoms [68]. The NIH recommends against use of hydroxychloroquine in patients for COVID [25••].

Azithromycin

In several large clinical trials including ATOMIC2 [71], ACTION [72], and PRINCIPLE [73], azithromycin showed no benefit in terms of symptom resolution at 14 days or recovery at 28 days in outpatients treated with azithromycin vs. placebo. The NIH recommends against use of azithromycin in patients for COVID [25••].

Treatment Algorithm

The IDSA, CDC, and NIH recommendations for outpatient treatment differ in terms of treatment prioritization [25••, 54•, 74]. The NIH and CDC guidelines state that use of Paxlovid (nirmatrelvir/ritonavir) or Veklury (remdesivir) is preferred, [25••, 74] although both of these medications must be used early in the disease course (within 5 or 7 days of symptom onset, respectively). Meanwhile, bebtelovimab and molnupiravir may be used in patients for whom neither nirmatrelvir-ritonavir nor remdesivir are appropriate therapies or are not available. The IDSA recommendations state that recommended options include nirmatrelvir-ritonavir, remdesivir, molnupiravir, and neutralizing monoclonal antibodies, and makes no prioritization between therapeutic choices in its algorithm. In addition, convalescent plasma is included in the

Table 3 Comparison of outpatient treatment guidelines from the NIH, CDC, and IDSA

	NIH, CDC guidelines	IDSA guidelines
Nirmatrelvir-ritonavir	Preferred therapy (Strong recommendation)	Suggested outpatient options include nirmatrelvir-ritonavir, remdesivir, molnupiravir, and monoclonal antibodies. Decision making regarding choice of agent should be made based on patient specific actors, product availability, and institutional capacity and infrastructure
Remdesivir	Preferred therapy after nirmatrelvir-ritonavir (moderate recommendation)	
Molnupiravir	Alternative therapy after nirmatrelvir-ritonavir and remdesivir (weak recommendation)	
Monoclonal antibodies (bebtelovimab)	Alternative therapy after nirmatrelvir-ritonavir and remdesivir (weak recommendation)	
Convalescent plasma	Insufficient evidence to recommend for or against use of high-titer CCP collected after Omicron	Suggest use in those with immunosuppressive disease or treatments (low level of evidence)

IDSA treatment algorithm (last updated June 21, 2022) [54•] for immunosuppressed patients, but NIH recommendations state that there is insufficient evidence to recommend for or against convalescent plasma in these patients (last updated April 8, 2022) [25••]. Table 3 compares the IDSA, NIH, and CDC guidelines [25••, 54•, 74]. In practice, however, medication administration may be limited by logistics and patient or provider preferences; for instance, remdesivir is difficult to administer via IV for 3 days in the outpatient setting. As such, ultimately treatment decisions depend on patient-specific factors and shared decision-making by the provider and patient.

Conclusions

Fortunately, there now multiple treatment options available for management of outpatient COVID-19, in particular for high risk patients, and we hope treatment options continue to expand. Given the nature of SARS-CoV-2, therapeutic management will continue to change, driven mostly by circulating variants of concern, with drugs targeting the spike protein such as monoclonals continuously changing to viral mutations, and oral antivirals being more durable, as their viral targets are much less susceptible to viral resistance. Guidelines will also continue to change, and what will remain most important is informed patients and educated healthcare providers, having knowledge of what treatment and management options are available and how to get them, in particular for our more vulnerable patients.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13671-022-00368-3.

Author contribution Conceptualization: JMG. Literature search and data analysis: SW, JMG. Writing—original draft preparation: SW. Writing—review and editing: JMG, CC. Supervision: JMG.

Declarations

Competing interests Dr. Gelfand served as a consultant for Abbvie, BMS, Boehringer Ingelheim, Celldex (DSMB), FIDE (which is sponsored by multiple pharmaceutical companies) GSK, Happify, Lilly (DMC), Leo, Janssen Biologics, Neumentum, Novartis Corp, Pfizer, UCB (DSMB), Neuroderm (DSMB), Regeneron, Trevi, and Mindera Dx., receiving honoraria; and receives research grants (to the Trustees of the University of Pennsylvania) from Amgen, Boehringer Ingelheim, and Pfizer Inc.; and received payment for continuing medical education work related to psoriasis that was supported indirectly pharmaceutical sponsors. Dr. Gelfand is a co-patent holder of resiquimod for treatment of cutaneous T cell lymphoma. Dr Gelfand is a Deputy Editor for the Journal of Investigative Dermatology receiving honoraria from the Society for Investigative Dermatology, is Chief Medical Editor for Healio Psoriatic Disease (receiving honoraria) and is a member of the Board of Directors for the International Psoriasis Council, receiving no honoraria. The other authors have no relevant financial or non-financial interests to disclose. Dr. Calabrese serves as a consultant for Sanofi, AstraZenica and Lilly, and Speakers' bureau for Sanofi.

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