VIEWPOINT

What's Wrong With Advance Care Planning?

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Advance care planning (ACP) has emerged during the last 30 years as a potential response to the problem of low-value end-of-life care. The assumption that ACP will result in goal-concordant end-of-life care led to widespread public initiatives promoting its use, physician reimbursement for ACP discussions, and use as a quality measure by the Centers for Medicare & Medicaid Services, commercial payers, and others. However, the scientific data do not support this assumption. ACP does not improve end-of-life care, nor does its documentation serve as a reliable and valid quality indicator of an end-of-life discussion.

What Is ACP?

The purpose of ACP is to ensure goal-concordant care near the end of life for patients who lack decisional capacity. It is a process to support adults in understanding and sharing their values, goals, and preferences regarding future potential medical care decisions; choosing and preparing a trusted person(s) to make medical decisions; and documenting these wishes so that they can be acted on when future medical decisions need to be made. Most approaches to ACP encourage all adults to participate in the process regardless of their health status. Advance care planning is distinct from "in-the-moment" decision making, in which seriously ill patients and their families engage with their clinicians in goals of care and treatment discussions at present and regarding their current situation.

> Despite the intrinsic logic of [advance care planning], the evidence suggests it does not have the desired effect. Many clinicians may be disappointed that promoting conversations with patients well in advance of needed medical decisions has not improved subsequent care as hoped.

If ACP led to higher-quality care at the end of life, it would make sense to continue efforts to promote it and integrate it into value-based care. However, a substantial body of high-quality evidence now exists demonstrating that ACP fails to improve end-of-life care. A 2018 review of 80 systematic reviews (including 1600 original articles)[1] found no evidence that ACP was associated with influencing medical decision making at the end of life, enhancing the likelihood of goal-concordant care, or improving patients' or families' perceptions of the quality of care received. A 2020 scoping review[2] that included 62 recent high-quality articles also demonstrated no link between ACP and occurrence of goal-concordant care or patient quality of life. Additionally, these reviews found no association of ACP with subsequent health care use, including emergency department visits, hospitalizations, and critical care. Subsequently, 5 large multisite randomized clinical trials that enrolled patients with cancer (1117 patients at 23 hospital cancer centers),[3] nursing home residents (12 479 residents from 360 nursing homes),[4] older adults in primary care (759 patients from 8 primary care practices),[5] adults with serious illness (515 patients from 20 outpatient clinics),[6] and patients with heart failure (282 patients from 2 heart failure centers)[7] could not identify meaningful differences in health care use, patient quality of life, or goal-concordant care between those randomly assigned to receive either ACP or usual care.

Why Does ACP Not Achieve Its Desired Outcomes?

The inability of ACP to achieve its desired outcomes represents the gap between hypothetical scenarios and the decision-making process in clinical practice settings. The success of ACP depends on 8 steps: (1) patients can articulate their values and goals and identify which treatments would align with those goals in hypothetical future scenarios; (2) clinicians can elicit these values and preferences; (3) preferences are documented; (4) directives or surrogates are available to guide clinical decisions when patients' preferences have not changed and they lose enough decisional capacity for their ACP views to become operative; (5) surrogates will invoke substituted judgment (make the decision the patient would make if they were able) and base their treatment decisions on the patient's prior stated preferences; (6) clinicians will read prior documents and integrate patient preferences into conversations with surrogates; (7) previously expressed wishes will be honored; and (8) health care systems will commit resources and care delivery to support goal-concordant care.

Scenarios and situations in clinical practice settings rarely reflect these conditions. Treatment choices near the end of life are not simple, consistent, logical, linear, or predictable but are complex, uncertain, emotionally laden, and fluid. Patients' preferences are rarely static and are influenced by age, physical and cognitive function, culture, family preferences, clinician advice, financial resources, and perceived caregiver burden (eg, need to provide personal care, time off from work, emotional strain, out-of-pocket or noncovered medical costs), which change over time. Surrogates find it difficult to extrapolate treatment decisions in the present from hypothetical discussions with patients that occurred in the past, piece together what the patient would have

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wanted, disentangle their own preferences and emotions, or challenge physicians who recommend different treatments. When a decision must be made, prior directives are often absent, poorly documented, or either so prescriptive or so vague that they cannot promote informed goal-concordant care. Moreover, treatment choices do not occur in a vacuum but are driven by financial pressures, societal capacity to support patient and family needs, and institutional/regional cultures and practice patterns.

Should Efforts to Address the Problems of ACP Continue?

Some suggest that these data do not diminish the potential positive effects of ACP. Advocates maintain that although ACP is necessary for good end-of-life care, it is not sufficient. Why not promote and incentivize conversations with patients regarding their future values, goals, and treatment choices?

The problem with accepting these arguments and continuing along the current path is the potential for unintended consequences. Encouraging the belief that ACP is essential to good end-of-life care meaningfully detracts from other initiatives. For example, health care institutions are incentivized to devote resources that promote and measure ACP and thus direct them away from equally and perhaps more important areas of clinical care. Research demonstrates that patients leave clinically based ACP sessions with serious misconceptions about life-sustaining treatments and that advance directives are often misinterpreted by physicians, families, and surrogates.[8] In addition, the presence of an advance directive can inhibit current discussions about goals of care; this occurred in overwhelmed hospitals during the COVID-19 pandemic when treatment decisions were made according to written documents rather than discussions with patients or their surrogate.

If ACP is not essential to high-value end-of-life care, then what is? One approach is to encourage appointment of a trusted surrogate decision maker (health care proxy) in advance and to focus research and clinical efforts on improving current shared decision making between proxies and clinicians. Psychometrically valid patient-reported outcomes, including the presence and severity of symptoms and health-related quality of life, can be measured in real time; others, such as experiences of "feeling heard and understood by their clinician" and "receiving desired help for pain," are being field tested. Surveys of surrogates after the death of the patients they have represented are now a standard quality measure within the Veterans Health Administration, have shown good linkages with health care processes, and are a more direct measure of patient and family end-of-life experience than the occurrence of an ACP discussion.[9]

The history of ACP is the story of science working. There was logic to the belief that ACP would lead to better care for seriously ill patients. During the last 25 years, studies have evaluated ACP with various methods and across large groups of patients. Despite the intrinsic logic of ACP, the evidence suggests it does not have the desired effect. Many clinicians may be disappointed that promoting conversations with patients well in advance of needed medical decisions has not improved subsequent care as hoped. New research focused on training clinicians and preparing patients and families to engage in high-quality discussions when actual (not hypothetical) medical decisions must be made is needed to achieve the outcomes that ACP has not. The clinical and research communities should learn from the evidence that does not support prior hypotheses and proceed with different approaches to improve care for seriously ill patients.

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Durable Power of Attorney for Health Care

A durable power of attorney for health care is a legal document that helps people plan for medical emergencies and decline in mental functioning.

A durable power of attorney for health care names a person (often referred to as an "agent") to make medical decisions on your behalf if you are no longer able to make health care decisions for yourself. This document is also known as a **health care proxy** or **health care power of attorney**.

What Decisions Will My Health Care Agent Make for Me?

Your agent may make decisions about starting or stopping treatments (including invasive therapies like mechanical ventilation); undergoing tests, surgery, and other treatments; and enrolling in hospice. If you have another document such as a living will, your agent will use that document to guide decisions made on your behalf.

How Do I Choose a Health Care Agent?

When choosing an agent, you should select an adult whom you trust and who is comfortable taking on this responsibility. You may also select second and third agents (called "successor agents") who serve as backup if your first agent is unavailable. It is critical to discuss your values and overall goals for medical care with your agent(s). Topics you should cover include

- What is most important to you in your life?
- Do you prioritize living as long as possible or avoiding prolonged disability?
- How important to you is avoiding pain?
- Do you have spiritual, religious, or cultural beliefs that should be considered?
- Would you rather die at home or be in the hospital in the final days or weeks of life?
- Do you have existing advance directives (such as a living will) outlining your preferences for life-sustaining care, such as receiving cardiopulmonary resuscitation (CPR), mechanical ventilation, or artificial hydration and nutrition (tube feeding)?

Who Should Have a Durable Power of Attorney for Health Care?

Every adult should complete a durable power of attorney for health care, including younger and healthy individuals, because they may lose decision-making capability due to an injury or unexpected illness.

What If Someone Does Not Have a Durable Power of Attorney for Health Care?

Clinicians caring for patients who are not capable of making decisions and have no health care agent must follow their state law about the selection of individual decision makers (often referred to as "surrogates"). The default surrogate typically is a patient's guardian or spouse. If there is no guardian or spouse, the priority order of surrogate decision makers often includes adult child, parent, sibling, and other more distantly related relatives and friends, although the order varies among states.

Why Is It Better to Have a Health Care Agent Than a State-Appointed Surrogate?

A surrogate designated by state law may not be the individual whom you would have chosen to make medical decisions for you. Additionally, a default surrogate may not be aware of your wishes or may not want to take responsibility for making these medical decisions.

How Do I Access and Complete a Durable Power of Attorney for Health Care Form?

Each US state has its own durable power of attorney for health care form, which can be downloaded for free from the internet or obtained at a physician's office. This form must be signed by you and be witnessed by another designated individual. Some states require use of a notary; however, no US states require a lawyer for completion of this form.

What Should I Do With My Durable Power of Attorney for Health Care Form?

Save the original form and give a copy to your health care agent(s) as well as your primary care physician. You can also bring a copy with you if you are admitted to a hospital.

FOR MORE INFORMATION

National Institute on Aging
www.nia.nih.gov/health/advance-care-planning-health-care-directives

To find this and other JAMA Patient Pages, go to the For Patients collection at *jamanetworkpatientpages.com*.

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Perspective

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Uncomfortable Truths — What Covid-19 Has Revealed about Chronic-Disease Care in America

Marshall H. Chin, M.D., M.P.H.

"Jump off the cliff and figure it out on the way down. People think that improvisation is moving forward," comedian Keegan-Michael Key has said about improvisational comedy. "What improvisation really is, it's walking backward. . . . It's backing up that gives you discovery. . . . You back up, you can create a larger worldview."

The Covid-19 pandemic forced the medical field to jump off the cliff and figure it out. It caused rare disruptive innovation by removing previously impenetrable organizational and political roadblocks. Covid-19 also made us walk backward and see the larger worldview, in the process revealing uncomfortable truths about the U.S. health care system — including our approach to managing chronic diseases. Policy discussions surrounding telehealth coverage and scope of practice for nonphysician health professionals have narrowly focused on fee-for-service reimbursement and haven't addressed the fundamental problem with chronic-disease care: the system doesn't support optimal patient health and experience, especially for marginalized populations.

Over the past 2 years, the health care system changed — at least transiently — when it shifted to caring for patients with Covid-19 and preventing virus transmission.[1] Routine in-person visits for chronic diseases plummeted, and telehealth visits skyrocketed. Payers permitted, and increased reimbursement for, telehealth visits. States expanded scopes of practice for nonphysician practitioners, although pushback is now occurring. Lucrative elective procedures, such as joint replacement, were postponed.

At the same time, hospitalizations for chronic conditions unrelated to Covid-19 and for emergencies such as appendicitis decreased. Mortality from dementia, cardiovascular disease, and diabetes increased; it's unclear whether these trends reflected true increases or undercoding of Covid-related deaths. Rates of low-density lipoprotein cholesterol screening and glycated hemoglobin testing fell, as did new prescriptions for statins and metformin. Marginalized populations had disproportionately high morbidity from Covid-19, and survival rates were lower in underresourced hospitals in low-income neighborhoods than in well-resourced facilities. Addressing social determinants of health proved to be particularly important for good outcomes.

Bill Parcells, a coach famous for turning around bad football teams, once said, "You are what your record says you are." When it comes to managing chronic diseases such as hypertension and diabetes, the U.S. health care system's performance is inadequate. Our outcomes reflect what the system rewards.

In football, quarterbacks and wide receivers get the glory for scoring touchdowns, but the battle is won in the trenches by the meat-and-potatoes linemen. Smart football teams invest in their lines. In health care, the glory and financial rewards go to surgeries and other procedures, devices, and medications and to the providers, health care delivery organizations, and companies responsible for these interventions. But the poorly reimbursed trench battles of chronic-disease management, which involve monitoring, coaching on self-management and behavior change, and mitigation of social needs, are critical for the vast majority of time that patients spend outside the clinic in their homes, communities, and workplaces.[2] The U.S. health care system undervalues human relationships, connections, and longitudinal primary care, so it's unsurprising that it falls short in this area. Technology and human capital will need to be integrated if we are going to deliver high-quality, patient-centered care.[3]

Covid-19 has taught us important lessons that apply to chronic-disease care. First, our health care system excels at perpetuating its basic structure and supporting the powerful stakeholders who profit from this structure. We should, therefore, design chronic-disease systems to better support the health and experience of patients and the well-being of health professionals trying to meet patient needs (see box). Payment for telehealth should support and provide incentives for integrated, holistic in-person and virtual care, and it should be administered using value-based models, rather than fee-for-service structures.[4] We could create teams that assess, treat, and monitor patients, relying on the principles of effective, longitudinal primary care.[2] We should also coach patients in self-management and behavior change and partner with communities to address social and structural factors impeding good health. Determining the ideal ratio of in-person visits to virtual visits, use of remote-device monitoring, and mix of health professionals will be important.[3]

States and health care organizations could expand nonphysician practitioners' scopes of practice to increase access to chronic-disease management services, mental health services, and substance use disorder treatment for rural and other underserved populations. Allowing all professionals to practice at the top of their license would improve teams' efficiency. Despite predictions of doom, health care didn't fall apart when scopes of practice expanded during the pandemic.

In 2021, the National Academies of Sciences, Engineering, and Medicine published two reports — *Implementing High-Quality Primary Care* and *The Future of Nursing 2020-2030* (I was the Review Coordinator for the former and a member of the committee for the latter) — which recommend that teams partner with patients and communities to meet medical and social needs and that health care delivery organizations enhance employee well-being to prevent burnout. Flexible solutions could be tailored to people's needs. Systems should work for both technology-savvy patients and technology neophytes and should address the digital divide. Patients and community representatives must have seats at the table when systems are being redesigned; relationships and trust are critical for chronic care.

Second, current reimbursement systems don't adequately support the improvement of population health. We will need to level the playing field for chronic-disease care. When it comes to approval and reimbursement, new technologies and pharmaceuticals are often held to lower standards than holistic chronic-disease care processes, such as addressing social needs. For example, the Food and Drug Administration recently approved aducanumab (Aduhelm) for treating Alzheimer's disease, despite its advisory committee's recommendation against approval because of insufficient evidence of effectiveness and side effects including brain edema and microhemorrhages. The medication's annual list price of $56,000 would pay a full-time home health aide for a year.

Third, our chronic-disease systems are inequitable. Health care delivery organizations, payers, and policymakers should intentionally advance health equity and address structural racism. The health care system will continue to put people experiencing poverty and other marginalized populations at the back of the line unless we intentionally value and address their health.[5] For example, the Covid-19 vaccine-allocation guidelines from the Centers for Disease Control and Prevention (CDC)

Key Components of Chronic-Disease Care and Strategies That Have Been Reinforced by Lessons from the Covid-19 Pandemic.*

Support for health of diverse patients and communities
Ensure that patients are central and are the system's compass.
- Set goals centered on best achievable health and patient experience.
- Empower patients and families to collaborate with the care team.
- Partner with patients and communities in creating and implementing new care systems.
- Ensure that systems synergistically support patient and employee well-being.

Prevention of chronic disease, promotion of health, and care for patients with chronic disease using primary care teams, with access to specialty services as needed
Provide team-based care spanning home, community, outpatient, and inpatient settings.
- Individualize type and intensity of services and culturally tailor them to patients' needs.
- Shift more care from outpatient and inpatient settings to home and community settings.
- Provide convenient access to diagnostic and therapeutic services.
- Provide convenient access to 24-hour care.
- Allow team members to practice at the top of their licenses.
- Employ a diverse workforce that reflects the community.
- Employ community health workers.

Build strong partnerships with patients to address holistic issues and practical management.
- Provide coaching and assistance with self-management and behavior change.
- Engage in close monitoring and follow-up.
- Address patients' mental health needs.
- Address patients' social needs.

Fulfillment of system-level health and social needs
Address systemic issues that drive inequities.
- Work to dismantle structural racism within and outside the health care system.
- Collaborate with community partners to address social and structural factors affecting patients' health, including by generating and sharing real-time data.
- Develop trustworthiness.

Be guided by a road map for advancing health equity.
- Stratify clinical performance measures and patient-experience metrics by factors such as patient race and ethnic group and socioeconomic status.
- Perform root-cause analysis of health disparities.
- Design care interventions to address root causes.
- Create a culture of equity that enables implementation of reforms.
- Align payment to support advancing health equity.

Integration of human touch, relationships, and the convenience of technology
Provide an appropriate mix of in-person visits, video or telehealth visits, and remote monitoring.
- Use video or telehealth to improve access, convenience, timeliness, monitoring, and cost-effectiveness.
- Use video or telehealth to improve access to emergency care and specialty services in rural and medically underserved areas.

Design electronic health records to serve patients and clinicians.
- Integrate social needs screening.
- Integrate referrals to community-based organizations for social, self-care, caregiving, and disease self-management services, with follow-up feedback information loops as appropriate.

Flexible payment mechanisms that support advancement of population health and health equity
Provide flexible, up-front funding for chronic-disease care infrastructure, possibly involving capitation, per-member per-month payments, or bundled payments.
Tie retrospective payment to process and outcome measures that support patient-centered care and health equity.
- Implement evidence-based clinical performance measures, patient-experience measures, and population and community health measures that reward strong performance for all patients.
- Reward the reduction of disparities among groups.
- Reward strong performance and improvements in performance measures for less advantaged groups.

Align public and private payers' performance metrics to drive transformation and reduce providers' administrative burdens.
Level the playing field for reimbursing components of chronic-disease care.
Provide adequate resources to safety-net clinics and hospitals.

* Recommendations are adapted in part from the National Academies of Sciences, Engineering, and Medicine reports *Implementing High-Quality Primary Care: Rebuilding the Foundation of Health Care* and *The Future of Nursing 2020–2030: Charting a Path to Achieve Health Equity,* the Robert Wood Johnson Foundation's Advancing Health Equity: Leading Care, Payment, and Systems Transformation program's Roadmap to Advance Health Equity,[2,5] and Nundy.[3]

attempted to support equity indirectly by including frontline essential workers as a high-priority population in phase 2, but the agency rejected the National Academy of Medicine's recommendation to prioritize regions identified in the CDC's Social Vulnerability Index within each

vaccination phase. The CARES Act Provider Relief Fund initially didn't favor clinicians and organizations caring for populations with the greatest need; instead, it provided a windfall for wealthy health care organizations.

As poet Audre Lorde wrote, "The master's tools will never dismantle the master's house." Health care organizations are struggling to address structural biases and racism internally and in the broader health care system. Relying on the same processes will produce the same results. Demonstration projects have taught us much about effective chronic-disease care programs,[2] and scholars have developed a road map that identifies root causes of inequities and integrates a culture of equity with the design and implementation of care transformations and payment reforms to address these causes.[2,5] A critical challenge involves redesigning payment systems to intentionally support and provide incentives for care transformations that improve patient health and patient experience and advance health equity, including by reducing disparities and addressing social determinants of health.[2,5] Clinicians, health care delivery organizations, and payers will also need coaching to translate lessons from successful processes and programs to their specific contexts.[2,5]

An audio interview with Dr. Chin is available at NEJM.org

The Covid-19 pandemic has forced us to step back, and the wider scenery has revealed uncomfortable truths about our chronic-disease systems. Too often, these systems are based on tradition, self-interest, and revenue generation — not on patients' needs and health. We must recognize the health inequities caused by racism and self-interest and advocate for equitable chronic-disease systems that integrate human touch and relationships with lifestyle management, medications, and health technology and that address social needs and structural determinants of health.[2] We can design and implement effective chronic-disease systems if we lock on to the North Star goals of patient health, health equity, and justice.[3,5] The health care system encourages and rewards what is valued — which should be supporting the health of all people with chronic disease.

Disclosure forms provided by the author are available at NEJM.org.

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The 2021 Reauthorization of CAPTA — Letting Public Health Lead

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The Child Abuse Prevention and Treatment Act (CAPTA), the foundational child-protection legislation in the United States, has been revised more than 20 times since its original passage in 1974. For nearly 30 years, CAPTA didn't cover infants who had been exposed to drugs or alcohol in utero, until revisions in the early 2000s and 2010s required states to notify Child Protective Services (CPS) and develop "plans of safe care" for infants who were "born affected" by illegal substances or were diagnosed with fetal alcohol spectrum disorder or drug withdrawal. These policies, which were outlined in a few short paragraphs and initially not accompanied by additional funding, were largely ignored until the opioid crisis garnered public and congressional attention, which resulted in the 2016 Comprehensive Addiction and Recovery Act (CARA). CARA clarified that plans of safe care should focus on the needs of both caregivers and infants, and it further expanded CAPTA to cover infants affected by legal drugs, such as prescription opioids.[1]

January 3, 2022

COVID-19

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SPECIAL ALERT

Medication safety issues with newly authorized Paxlovid

On December 22, 2021, the US Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for **PAXLOVID**, consisting of oral tablets of nirmatrelvir that are co-packaged with oral tablets of ritonavir (an FDA-approved antiretroviral agent).

Indications

Emergency use of Paxlovid is indicated for the treatment of mild-to-moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death. Paxlovid is not authorized for the treatment of hospitalized patients, or for use as pre- or post-exposure prophylaxis for prevention of COVID-19. Paxlovid is not indicated for use longer than 5 consecutive days.

Dosing

Nirmatrelvir is available in 150 mg tablets, while ritonavir is a 100 mg tablet. For patients with normal renal function or mild renal impairment, the recommended dose is 300 mg of nirmatrelvir (two tablets) and 100 mg of ritonavir (one tablet), taken together, twice daily, in the morning and evening, for 5 days.

Dose Reduction

A dose reduction is necessary for patients with moderate renal impairment, defined as having an estimated glomerular filtration rate (eGFR) below 60 mL/minute, but more than or equal to 30 mL/minute. If patients have moderate renal impairment, they must only receive 150 mg of nirmatrelvir (one tablet) along with 100 mg of ritonavir, taken together, twice daily, in the morning and evening. Patients with severe renal impairment, with an eGFR below 30 mL/minute, should not receive the drug, as the appropriate dosage for patients with severe renal impairment has not been determined.

Important Note for Dispensing Pharmacists

Paxlovid is only available in a carton holding five blister cards, each containing the daily morning and evening doses (two nirmatrelvir tablets and one ritonavir tablet for each dose) for patients with normal renal function or mild renal impairment. For patients with moderate renal impairment, the EUA directs pharmacists to remove one of the nirmatrelvir tablets for both the morning and evening doses from each blister card before dispensing Paxlovid to facilitate proper dosing (**Figure 1**). After

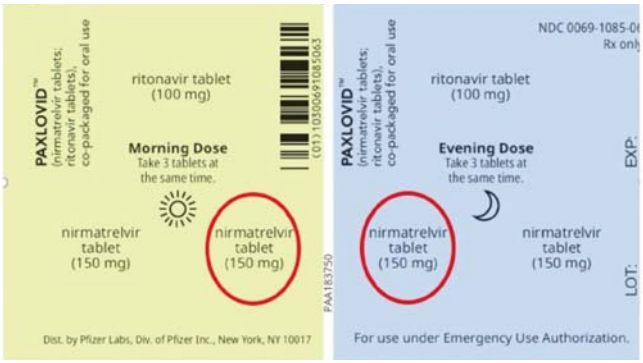

Figure 1. The red ovals in the image are where the nirmatrelvir tablets should be removed prior to dispensing Paxlovid to patients with moderate renal impairment; then, a pre-printed sticker (**Figure 2**, page 2) with dosing instructions, should be placed over the empty blisters.

removing one nirmatrelvir tablet from the morning dose and one from the evening dose on each blister card, the empty blisters on all five cards should be covered with manufacturer-supplied stickers (**Figure 2**, page 2). Pharmacies needing additional stickers should contact: C19therapies@amerisourcebergen.com. It is essential for pharmacists to take these steps, as outlined in the EUA dispensing information for patients with moderate renal impairment (www.ismp.org/ext/826).

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SPECIAL ALERT

Safety issues with Paxlovid

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Safety Concerns and Recommendations

Challenges with prescribing the dose. The prescriber may not be aware that the dose should be reduced for moderate renal impairment or that the drug should not be prescribed for patients with severe renal impairment. Thus, electronic prescribing systems should alert the prescriber to renal dosing requirements. Also, choosing the correct dose for patients with moderate renal impairment may require prescribers to manually enter the reduced dose in a text field. It is critical for prescriptions to specify the numeric dose of each active ingredient in Paxlovid as follows:

- 150 mg of nirmatrelvir with 100 mg of ritonavir for patients with moderate renal impairment
- 300 mg of nirmatrelvir with 100 mg of ritonavir for patients with normal renal function or mild renal impairment

Failure to remove tablets and cover empty blisters. One significant safety concern is that pharmacy staff may fail to remove one of the nirmatrelvir tablets from each dose of the blister card for all five days of therapy, and/or may miss applying the stickers to make patients aware that the packaging has been altered to remove unneeded tablets. Both of these steps are a requirement under the EUA, and pharmacies handling Paxlovid must ensure their pharmacists and pharmacy technicians address this issue and have a process in place to meet this requirement.

Figure 2. A pre-printed sticker with dosing instructions (provided by the manufacturer) is placed over the empty blisters where the nirmatrelvir tablets were removed for patients with moderate renal impairment.

Failure to take the tablets together. Patients will be self-administering Paxlovid at home. Thus, it is extremely important for pharmacists to counsel patients to take both the nirmatrelvir and ritonavir tablets together in the morning and evening. For patients with moderate renal impairment, pharmacists should also explain that the packaging has been altered to provide the proper dose.

Drug Interactions

Paxlovid (nirmatrelvir co-packaged with ritonavir) is an inhibitor of CYP3A, the most abundant clinically significant group of cytochrome P-450 isoenzymes, which may increase plasma concentrations of drugs that are primarily metabolized by CYP3A. At the same time, nirmatrelvir and ritonavir are CYP3A substrates; therefore, drugs that induce CYP3A may decrease nirmatrelvir and ritonavir plasma concentrations and reduce the therapeutic effect of Paxlovid. For complete information and a list of serious drug interactions and expected effects, please refer to the Paxlovid *Fact Sheet for Healthcare Providers* (www.ismp.org/ext/827).

Mandated Reporting

Providers must report all serious adverse events or medication errors potentially related to Paxlovid to the FDA MedWatch reporting program (www.ismp.org/ext/609), which is mandatory for medications available under an EUA. Please also fax a copy of the MedWatch form to Pfizer (866-635-8337). ISMP also asks providers to report errors to the ***ISMP National Medication Errors Reporting Program*** (ISMP MERP, www.ismp.org/MERP).