magnitude. One highly successful element of the response to Covid-19, however, was the rapid development — enabled by years of investment in basic and applied research — of highly adaptable vaccine platforms such as mRNA (among others) and the use of structural biology tools to design vaccine immunogens. The unprecedented speed with which safe and highly effective Covid-19 vaccines were developed, proven effective, and distributed resulted in millions of lives saved.[3] Over the years, many subspecialties of medicine have benefited greatly from breathtaking technological advances. The same can now be said of the field of infectious diseases, particularly with the tools we now have for responding to emerging infectious diseases, such as the rapid and high-throughput sequencing of viral genomes; the development of rapid, highly specific multiplex diagnostics; and the use of structure-based immunogen design combined with novel platforms for vaccines.[4]

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

If anyone had any doubt about the dynamic nature of infectious diseases and, by extension, the discipline of infectious diseases, our experience over the four decades since the recognition of AIDS should have completely dispelled such skepticism. Today, there is no reason to believe that the threat of emerging infections will diminish, since their underlying causes are present and most likely increasing. The emergence of new infections and the reemergence of old ones are largely the result of human interactions with and encroachment on nature. As human societies expand in a progressively interconnected world and the human–animal interface is perturbed, opportunities are created, often aided by climate changes, for unstable infectious agents to emerge, jump species, and in some cases adapt to spread among humans.[5]

An inevitable conclusion of my reflections on the evolution of the field of infectious diseases is that the pundits of years ago were incorrect and that the discipline is certainly not static; it is truly dynamic. In addition to the obvious need to continue to improve on our capabilities for dealing with established infectious diseases such as malaria and tuberculosis, among others, it is now clear that emerging infectious diseases are truly a perpetual challenge. As one of my favorite pundits, Yogi Berra, once said, "It ain't over till it's over." Clearly, we can now extend that axiom: when it comes to emerging infectious diseases, *it's never over.* As infectious-disease specialists, we must be perpetually prepared and able to respond to the perpetual challenge.

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Prescribing Opioids for Pain — The New CDC Clinical Practice Guideline

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Pain affects the lives of millions of Americans and potentially reduces their level of function, mental health, and quality of life. Yet limited access to pain treatments and lack of clarity regarding the evidence supporting pain treatments prevent many people with pain from accessing the full range of potentially helpful therapies.[1] Furthermore, there are persistent disparities in pain management according to race or ethnic group, gender, socioeconomic status, and population density, among other factors.[2] Opioids continue to be commonly used to treat pain, despite evidence that their short-term benefits are small and despite limited evidence of long-term benefits.[2,3]

In 2016, the Centers for Disease Control and Prevention (CDC) released its Guideline for Prescribing Opioids for Chronic Pain to help primary care clinicians weigh benefits and risks of opioid treatment for chronic pain.[3] The guideline's release was as-

sociated with accelerated reductions in overall and potentially high-risk prescribing of opioids[4] and with increases in prescribing of nonopioid pain medications.[5] Concurrently, new laws, regulations, and policies, in some cases purportedly derived from the 2016 guideline, went beyond — and were inconsistent with — its recommendations.[4] Such misapplication, including inflexible application of recommended dosage and duration thresholds, contributed to patient harms, including untreated and undertreated pain, rapid opioid tapers and abrupt discontinuations, acute withdrawal symptoms, and psychological distress, in some cases leading to suicidal ideation and behavior.[4] These experiences underlined the need for an updated guideline reinforcing the importance of flexible, individualized, patient-centered care. In addition, new scientific evidence supports expanded guidance and specificity regarding acute pain treatment, opioid tapering, and treatment methods for various types of pain.[2]

The 2022 CDC Clinical Practice Guideline, which is intended for clinicians prescribing opioids for adult outpatients with pain — in situations other than those of sickle cell disease, cancer-related pain, palliative care, and end-of-life care — expands guidance for acute (<1 month's duration) and subacute (1 to 3 months' duration) pain to help primary care and other clinicians (e.g., surgeons, oral health practitioners, and emergency clinicians) weigh benefits and risks of opioids and other pain treatments for outpatients or patients being discharged from hospitals, emergency departments, or other facilities.

Given new findings from systematic reviews[2] that nonopioid therapies are at least as effective as opioids for many common types of acute pain (including headaches, low back pain, neck pain, and pain related to common musculoskeletal conditions, minor surgeries, dental procedures, or kidney stones), the guideline includes a new recommendation that clinicians maximize the use of nonopioid therapies (e.g., topical or oral nonsteroidal antiinflammatory drugs [NSAIDs] or exercise) as appropriate for the patient's condition and consider opioid therapy for acute pain only if its benefits are anticipated to outweigh its risks. The guideline notes that there is an important role for opioid therapy for moderate-to-severe acute pain when NSAIDs and other therapies are contraindicated or are unlikely to be sufficiently effective (e.g., for severe traumatic injuries or major surgeries).

Like the 2016 guideline, the 2022 guideline recommends that when opioids are needed for acute pain, they should be prescribed at the lowest effective dose and for no longer than the expected duration of pain severe enough to warrant opioids. Tapering is recommended when opioid treatment is discontinued after being used continuously for more than a few days. For patients receiving opioids for 1 to 3 months (the timeframe for subacute pain), the 2022 guideline recommends that clinicians avoid continuing opioid treatment without carefully reassessing treatment goals, benefits, and risks in order to prevent unintentional initiation of long-term opioid therapy.

The updated content of the guideline outlines the benefits and risks of nonopioid pain treatments.[2] The reviews that informed the 2022 guideline reinforced the previous guideline's recommendations for judicious use of opioids for chronic pain.[2] The new guideline therefore retains the 2016 principles for prescribing opioids for chronic pain, including that clinicians should maximize use of nonopioid therapies and consider initiating opioid therapy only if the expected benefits for pain and function are anticipated to outweigh the risks and that when opioids are needed, clinicians should initiate therapy at the lowest effective dosage, carefully evaluate individual benefits and risks when considering increasing dosages, and avoid increasing the dosage above levels likely to yield diminishing returns in benefits relative to risks. These principles do not imply that nonpharmacologic and nonopioid pharmacologic therapies must all be tried unsuccessfully in every patient before opioid therapy is offered. Rather, expected benefits specific to the clinical context should be weighed against risks before therapy is initiated.

A new recommendation further outlines how clinicians can work with patients who are already receiving opioids in determining whether and how to taper these medications. New guidance informed by emerging data advises clinicians to carefully weigh benefits and risks of tapering opioids along with benefits and risks of continuing opioids and emphasizes that opioid therapy should generally not be discontinued abruptly, nor should doses be reduced rapidly. When

patients have been taking opioids for longer durations (e.g., ≥1 year), dosages that are tapered by 10% per month or slower will most likely be better tolerated than more rapid tapers. Although clinicians and patients might not always be able to agree on whether tapering is necessary, the guideline describes an approach to implementing treatment changes in a patient-centered manner, while avoiding abandoning the patient and instead drawing on clinicians' empathy and principles of shared decision making.

An independent federal advisory committee, four peer reviewers, and members of the public reviewed the draft of the updated guideline (which we wrote), and the CDC revised it in response to this feedback, which emphasized four key points: there are persistent barriers to access to pain care and evidence-based treatment; shared decision making by patients and clinicians is critical; discontinuing opioids after extended use can be very challenging and potentially harmful, especially if doses are tapered rapidly or patients do not receive effective support; and the new recommendations need to be communicated and implemented carefully. Some commenters argued that language citing specific opioid dosages and durations could too readily lead to the misapplication of thresholds as inflexible standards, whereas others felt strongly that clinicians need this specific information and that it should not be omitted.

To discourage such misapplication of thresholds, the new recommendations emphasize general principles (e.g., avoiding increasing dosages above levels likely to yield diminishing returns) rather than specific levels. In the supporting text following each recommendation, the guideline provides more specific information, including data related to dosages, to inform clinical decision making and individualized patient care. To promote more equitable access and reduce barriers to high-quality care, suggested strategies include the institution of mechanisms allowing patients whose pain unexpectedly persists to gain timely access to reevaluation. The guideline also cautions clinicians about potential bias in interpreting data from prescription drug monitoring programs and toxicology tests. Five new guiding principles have been added to inform implementation of the recommendations and support appropriate, individualized care.

The 2022 guideline aims to promote equitable access to effective, informed, individualized, and safe pain management that improves patients' function and quality of life, while clarifying and reducing the risks associated with opioid use. Ideally, new recommendations should result in greater and more equitable access to the full range of evidence-based treatments for pain, more judicious initial use of opioids, and more careful consideration and management of benefits and risks associated with continuing, tapering, or discontinuing opioids in patients who are already receiving them long term.

The CDC will monitor for these intended effects as well as for unintended effects and will work with public and private payers and share evidence that can be used to inform decisions regarding coverage for a broader range of pain therapies. Evidence to guide the best achievable pain management remains limited, and research should address critical remaining gaps, including long-term comparative effectiveness of therapies for pain. Patient–clinician communication about benefits and risks associated with opioids remains central to treatment decisions. The 2022 guideline can help inform those decisions and assist clinicians in meeting patients' unique needs.

The views expressed in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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