



# Cancer pain during an epidemic and a pandemic

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## Purpose of review

As our global population ages, cancer has become more prevalent. Thankfully, oncologic treatments are highly effective, leading to significantly improved rates of long-term survival. However, many of these therapies are associated with persistent pain syndromes. Clinicians caring for people with cancer must understand how the influence of the current epidemic of opioid misuse and the coronavirus disease 2019 (COVID-19) pandemic have complicated cancer pain management. Creative solutions can emerge from this knowledge.

## Recent findings

Persistent pain due to cancer and its treatment can be managed through multimodal care, although efforts to mitigate the opioid misuse epidemic have created challenges in access to appropriate treatment. Isolation measures associated with the COVID-19 pandemic have limited access to nonpharmacologic therapies, such as physical therapy, and have exacerbated mental health disorders, including anxiety and depression.

## Summary

Cancer pain treatment requires more nuanced assessment and treatment decisions as patients live longer. Societal factors multiply existing challenges to cancer pain relief. Research is needed to support safe and effective therapies.

## Keywords

cancer, opioids, pain, survivors

## INTRODUCTION

Cancer remains greatly feared, as does pain associated with malignancy. For many, past experiences of bedside vigils with loved ones evoke memories of extreme pain and suffering. Advances in our understanding of pain management at the end of life have led to more effective control of pain and other distressing symptoms. For most people dying from cancer with access to skilled clinicians and appropriate pharmacotherapy, the final days can be peaceful, spent with loved ones sharing meaningful time together. Numerous clinical practice guidelines have been advanced to inform clinicians regarding optimal cancer pain care throughout the oncology experience [1–4].

Over the decades, the principles applied to end of life care were also used in the care of those surviving cancer. Although highly effective for some individuals, others developed adverse effects from long term opioid therapies, including opioid misuse [5]. Societal issues complicated this care, notably an exploding epidemic of substance misuse and related deaths. Cancer patients are not immune from these influences and in some cases, the added uncertainty and potential mood disorders related to surviving

cancer may place these individuals at greater risk. Additionally, some malignancies are associated with potentially harmful behaviors, including smoking and alcohol intake, making patients with these cancers at enhanced danger for misuse.

## PREVALENCE OF CANCER PAIN

The magnitude of these challenges is significant. Globally, there were more than 18 million new cancer cases in 2020, and this number is estimated to be more than 28 million by 2040 [6]. Based on current data, close to 40% of men and women living in the developed world will be diagnosed with cancer at some point during their lifetime. The treatment of these cancers often results in serious, and in

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## KEY POINTS

- Cancer pain remains highly prevalent and may be increasing due to painful complications of highly effective cancer therapies.
- Societal events such as the rising number of overdose deaths associated with substances and the current coronavirus disease 2019 pandemic have challenged access to effective cancer pain therapies.
- Solutions include greater adoption of telemedicine for pain assessment and treatment, patient and family education about safe opioid use and storage, along with improved access to addiction specialists.

some cases, persistent pain syndromes. More than half of people undergoing cancer treatment experience pain, while more than two-thirds of those with metastatic or advanced disease report pain. Approximately 40% of cancer survivors acknowledge pain and 38% of these patients in one systematic review reported moderate to severe pain [7,8].

## COMPETING CHALLENGES

At the same time as this increasing magnitude of cancer pain, drug overdose deaths are escalating, with more than 100 000 individuals in the United States dying during a 12-month period. Nearly 73% of these deaths involved opioids. Similar increases in overdose deaths are noted globally. It is believed the social isolation demanded by measures to mitigate the coronavirus disease 2019 (COVID-19) pandemic, along with associated mental health challenges, have contributed to these figures.

Efforts are urgently needed to balance the effects of these three competing crises – ongoing cancer pain prevalence, escalating drug overdose deaths, and consequences of efforts to control the COVID-19 pandemic. Clinicians caring for people with cancer must conduct assessments of pain and other symptoms with attention to the ever-widening array of painful syndromes that can occur as a result of cancer treatment. Current and desired functional status is evaluated, as improved activity is the primary outcome for pain therapy, rather than focusing solely on pain intensity. At the same time, the history must include an understanding of factors that might place patients at risk for substance use disorder (SUD) [9,10]. Pharmacologic decisions involving opioids are based upon the etiology of the pain and the risk associated with opioid use. Optimal treatment employs multimodal therapy

that includes pharmacologic, behavioral, physical, integrative and invasive therapies. Access to consultants with expertise in these treatments, along with addiction medicine, psychology, psychiatry and palliative care, are essential to provide optimal relief. Experience with telemedicine expanded during the COVID-19 pandemic, teaching us about the strengths and limitations of this delivery along with needs for refinement.

## OPIOID USE: BENEFITS AND CHALLENGES

Current clinical practice guidelines concur that opioids are the cornerstone of cancer pain management [1,2]. Because there are no clear data regarding the benefit of one opioid over another, selection should be personalized based upon the patient's prior experience, their underlying organ function, optimal route (oral, parenteral, transdermal, rectal and buccal/sublingual), preferred formulation (tablets, capsules, liquids) and whether immediate release and/or controlled release delivery is required.

### Reduced access, prescribing and dispensing: unintended consequences

Although highly effective, access to opioids has been greatly challenged by the unintended consequences of efforts to reduce opioid related deaths [11,12]. Reduced production of opioids has led to shortages, diminishing or delaying access to essential medications [13]. Many pharmacies carry limited supplies and some decline stocking any controlled substance [14]. Insurers require time-consuming, labor intensive prior authorizations which cause delays, narrow formulary options and increase high co-pays for patients [15]. These obstacles and increased concern about regulation and fear of legal action on prescribing opioids has affected prescribing practices. Total opioid volume (as measured by morphine milligram equivalents or MME) per capita by prescriptions filled decreased by one fifth from 2008 to the period ending in 2018 with the greatest decline of 41.5% in those prescriptions paid by commercial insurance [16]. The estimated number of opioid tablets dispensed declined from 17.8 billion in 2012 to 11.1 billion in 2018 [17].

These declines in access to opioids are being seen in oncology settings [18]. In a study of more than 4000 cancer patients living in a rural area, more than 60% never received a prescription for a Schedule II opioid [19]. When patients are given a prescription, several studies report a reduction in the MME prescribed by oncologists. One study revealed a decrease in MME from 78 to 40 mg [20] and a decline in MME of 37% from 2011 to 2017 for people with

cancer-related bone metastases [21<sup>1</sup>]. Another large study of Medicare fee-for-service decedents with poor prognosis cancers found a drop in the MME from 85.6 mg to 64.6 mg and fewer individuals receiving a long acting opioid [22<sup>2</sup>]. Associated with these findings was an increase in pain-related emergency department visits from 13.2% to 50.8% from 2007 to 2017.

### Effect on patients and loved ones

People with cancer and their loved ones feel the consequences of all of these influences. They report complex and conflicting emotions such as fear of addiction, along with stigma and guilt as a result of these access issues and negative media messaging about opioids. Many have responded to these barriers by avoiding conversations with clinicians about pain, omitting doses or reducing their overall dose of opioid [23<sup>3</sup>,24]. These behaviors can ultimately contribute to inadequate pain control.

Moreover, despite these significant declines in doses of opioids prescribed and dispensed, the numbers of people dying from opioid overdose continue to rise. These deaths are now largely due to escalation in use of illicit fentanyl and heroin. Although clinicians should not become complacent in preventing misuse of prescription opioids, or in reducing access of these agents into the community, a global, strategic response is urgently needed to halt the overdose epidemic by reducing access to illicit substances.

### CORONAVIRUS DISEASE 2019: ADDITIONAL CHALLENGES TO CANCER PAIN CONTROL

The COVID-19 pandemic has worsened the unintended consequences of measures to combat the opioid epidemic. Efforts to mitigate the COVID-19 pandemic have resulted in additional challenges in oncology, including cancer pain management. Exercise programs, physical therapy and other rehabilitation efforts crucial to cancer pain management were closed early in the pandemic. When they reopened, anxiety regarding infection by the coronavirus led to reduced participation in these vital programs, especially those immunocompromised by cancer therapies. To address uncertainty and distress ordinarily associated with a cancer diagnosis that was then exacerbated by the fear of COVID-19 infection, the majority of mental healthcare providers adjusted their practices to incorporate telehealth [25]. Although telehealth is a valuable tool, many patients lack the technology and access to broadband internet to allow these types of

encounters, including older adults and those living in underserved or rural areas [26]. Imagine a very ill patient driving to park next to their local library to access internet so they could interact with providers from their car via telehealth. These scenarios were common in the oncology setting, at times leading to delays in diagnostic techniques or cancer therapies that might better assess and treat the cancer, and in many cases, reduce pain. In fact, oncologists reported significant fears about delays in cancer screening, diagnosis and treatment as a result of the pandemic, along with an exacerbation of existing levels of burn-out [27].

Loss has compounded these challenges. Many have lost family members, their livelihood, their homes, and vital interactions with loved ones. And these losses, along with the stress of isolation and quarantine due to the pandemic have led many to develop risky behaviors. Alcohol intake has increased dramatically during this period. For those with preexisting substance use disorder, isolation and virtual access to support meetings have severely challenged efforts to maintain sobriety [28], including those people with the powerful concurrence of co-morbid SUD and cancer.

### SOLUTIONS

Despite these worrying conditions, optimism is warranted. Dedicated clinicians, working with researchers, legislators, professional organizations and patient advocacy groups, can develop creative solutions can address some of these challenges. Tools, education and access to specialists are a few of these creative solutions.

#### Telehealth

Enhanced application of telehealth can support cancer care, as well as advance cancer pain assessment and treatment [29]. Virtual physical therapy and creative strategies for exercise have been developed by many cancer wellness communities. Advances in mental health delivery, including virtual therapy sessions and support groups, along with on-line education and coaching, can enhance knowledge while building resilience [28]. Virtual sessions can also provide grief and bereavement support for those experiencing loss of a loved one through cancer, opioid overdose or COVID-19. Telehealth has also been successfully employed to support sobriety through SUD treatment [30,31].

To optimize the use of telehealth improved delivery systems are required, such as platform improvement with integration into the electronic health record (EHR). Digital infrastructure must be

advanced with greater access to tablets, computers, smartphones, online programs – for the public and professionals. Navigators, and in some settings volunteers, could assist those patients with limited digital literacy. Grants for robust internet access for rural or underserved communities are necessary. Reimbursement for telemedicine must be sufficient. Clarification from federal regulators is needed to understand any licensure, credentialing and reimbursement issues when providing care across state lines or country borders.

## Education

Although the current opioid overdose epidemic is linked with illicit drug use, ongoing access to prescription medications for people with cancer demands education on safe use, storage and disposal. Despite continuing media attention to the rising numbers of opioid-related deaths, studies of people with cancer reveal many remain unaware of safe storage practices, such as locking up the medication rather than leaving it out on the kitchen counter [32,33]. Education by healthcare professionals regarding safe storage and disposal improve safe practices [34]. Vital teaching points include not sharing the medication with others, locking up the opioid, and disposing of unused or expired medications [35]. Family and others assisting in the patient's care should be included in these educational efforts.

## Access to specialists

The oncology workforce is being challenged by insufficient numbers of oncologists, many who are nearing retirement [36]. There are similar shortages in access to addiction providers [37]. As the prevalence of both cancer and SUD increase, addiction providers are needed to address the needs of these unique populations. And they are not a heterogeneous group. Some patients have been in addiction treatment and have maintained their sobriety for many years, while others continue to actively use opioids and other substances. And some individuals refuse to consider they may have SUD despite meeting many of the criteria for this disorder. And finally, there are those patients with no past history of any SUD, but who begin to display concerning behaviors once treated with an opioid. Most professionals in the oncology field have received little training in the care of any of these types of patients.

Additionally, most current models of addiction treatment require total abstinence which may not be feasible in a person with advanced malignancy and significant, painful tumor burden. Optimally

addiction providers, including psychiatrists, psychologists, advanced practice providers and others, would be embedded in the oncology clinic to allow seamless care, much like the models of palliative care being delivered in cancer clinics [38]. These addiction specialists would initiate medication assisted therapy (MAT) such as buprenorphine and would provide consultation on management of those patients currently receiving either methadone or buprenorphine.

## CONCLUSION

Cancer pain management has been complicated by the convergence of multiple influences, particularly the explosion of deaths associated with substance use disorder along with the repercussions of the COVID-19 pandemic. All of these have challenged safe and effective relief of pain. Solutions such as telehealth, education, and improved access to specialists have the potential to mitigate the unintended consequences of these tragedies.

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## Conflicts of interest

*There are no conflicts of interest.*

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- of special interest
- of outstanding interest

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