

# Opioid use disorders in patients with cancer pain

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# Emerging issues with a prolonged use of opioids

Gaps in the knowledge about the complex interactions between many facets of opioid actions

- Common adverse effects
- Endocrine system
- Immunologic system
- Hyperalgesia
- Cognitive disturbances
- **Dependence - tolerance - addiction**

# Opioid-induced aberrant behavior (OIAB)

Long-term opioid use for chronic pain is associated with **aberrant medication-taking behaviors with the prevalence varying from 5% up to 35%**. Juurlink DN et al., *J Med Toxicol* 2012

In 2008, Fishbain and colleagues performed a structured evidence-based review of 67 studies of opioid use for noncancer pain meeting pre-specified quality metrics. Aberrant drug-related behaviors were detected in **11.5%**.

In 2007, Martell and colleagues published a systematic review of the use of opioid for chronic back pain, and the few (mostly cross-sectional) studies that reported the prevalence of aberrant medication-taking behaviors, estimates ranged from **5 to 24%**.

In 2011, Boscarino *et al.* reported that **35% of longer term opioid users** (defined as those who received four or more prescriptions in the last 12 months) among randomly selected more than 2,000 patients being treated at one of the 9 primary care clinics or 3 specialty care clinics in Pennsylvania, **met DSM-5 criteria for a current or previous opioid use disorder. Similar results were obtained when using the DSM-4 criteria.**

Lack of terminology consensus. Terms like “addiction”, “misuse”, “abuse” or “dependence” are often used as synonyms. In part because criteria over opioid use disorder has changed from DSM-IV to DSM-V, text used as reference in psychiatry.

DSM-IV used the terms “dependence” and “abuse” distinctly whereas DSM-V includes both under “opioid-related disorders”.

# Spectrum of Opioid-induced Aberrant Behavior (OIAB)

## Long-term opioid use for chronic pain is associated with OIAB

### Spectrum of OIAB

#### Patient with Cancer Pain

### Opioid-Induced Aberrant Behavior

Physical dependence

Pseudo-addiction

Chemical coping

Addiction

### Physical Dependence

A state of adaptation manifested by a drug class specific **withdrawal syndrome that can be produced by abrupt cessation**, rapid dose reduction, decreasing blood level of the drug, and/or **administration of an antagonist**

### Chemical coping

Using prescribed opioids **to control non-nociceptive symptoms**. One of the major challenges in the management of cancer pain

### Pseudoaddiction

Patient exhibits distress and engages in **medication seeking because pain treatment is inadequate**. It is best addressed by improving pain control, with or without opioids

### Addiction

Aberrant use of a substance characterized by;  
**1) loss of Control, Craving**  
**2) Compulsive use and preoccupation**  
**3) Continued use despite harm**

**It is reported that up to 35% of longer term opioid users met DSM-5 criteria for a current or previous opioid use disorder.<sup>5</sup>**

1. ASCO Daily News. How to Use Opioid Therapy in Patients at Risk for Aberrant Opioid Use. Available from: <https://am.asco.org/how-use-opioid-therapy-patients-risk-aberrant-opioid-use> Accessed on Sep 10<sup>th</sup>, 2017. 2. Centers for Disease Control and Prevention. CDC Guideline for Prescribing Opioids for Chronic Pain. 2016. 3. Kwon JH et al., Chemical coping versus pseudoaddiction in patients with cancer pain. *Palliat Support Care* 2014;12(5):413-417. 4. Kaye AD et al., Prescription opioid abuse in chronic pain: an updated review of opioid abuse predictors and strategies to curb opioid abuse: part 1. *Pain Physician* 2017;20(2S):S93-S109. 5. Juurlink DN et al., Dependence and addiction during chronic opioid therapy. *J Med Toxicol* 2012;8(4):393-399.

# Chemical Coping in Cancer Patients

Kwon JH et al., Frequency, Predictors, and Medical Record Documentation of Chemical Coping Among Advanced Cancer Patients. *Oncologist*

- About 18% of patients who visited supportive care center were chemical copers (prospective study of 423 patients)

## Risks of chemical coping are higher in

- CAGE positive: screening tool
- Younger age
- High symptom score with ESAS
- Relatively good performance status

Variable	OR	95% CI	P value
CAGE	2.887	1.531-5.444	0.0010
Age (per year)	0.971	0.950-0.994	0.0123
ECOG PS (per point)	0.681	0.503-0.922	0.0130
ESAS pain, initial (per point)	1.197	1.065-1.346	0.0026
ESAS WB, initial (per point)	1.280	1.122-1.462	0.0002

45 yrs old, female, GYN cancer  
20 pieces of 200 mcg FBT/day

I had a prescription of FBT for BTP

I started to use FBT more frequently because of lack of pain control.... (**pseudoaddiction...**)

When I take the drug, I feel better, I'm less depressed and this help me to have less anxiety during the day, and pain disappears too (**chemical coping**).

Now I use the drug for these purposes, not for pain.....

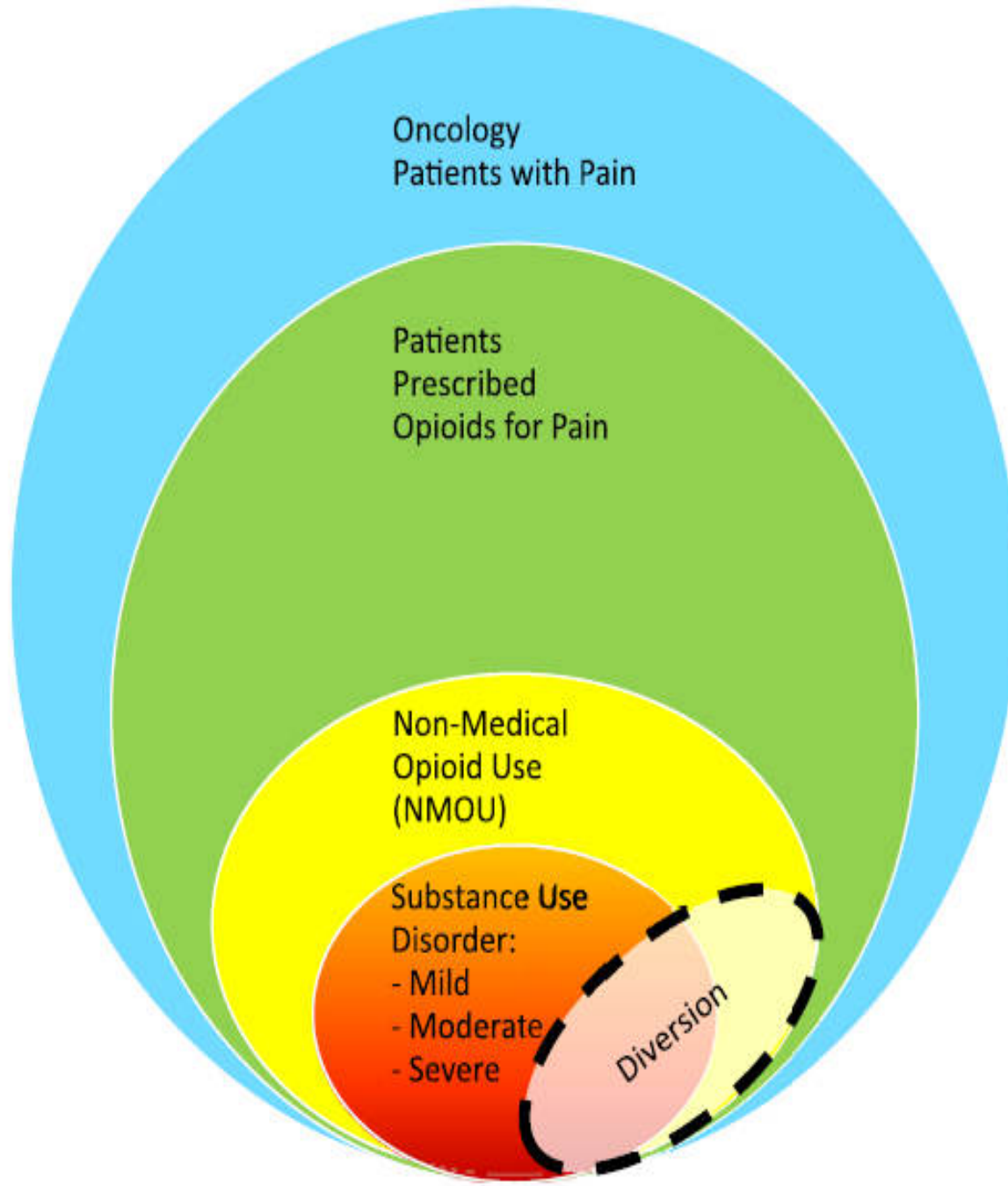


Figure 1. Spectrum of opioid use in oncology.





## Prevalence of and Risk Factors for Prescription Opioid Misuse, Abuse, Diversion and Doctor Shopping in Japan: A Survey Study

Toshifumi Takasusuki · Shinji Hayashi · Yuichi Koretaka · Shigeki Yamaguchi

opioid misuse 45.5%:

24.6% for abuse;

15.0% for diversion

10.6% for doctor shopping.

Aberrant prescription opioid-taking behaviors were higher in participants with chronic **post-cancer treatment pain** (misuse, 64.2%; abuse, 52.2%) or chronic **cancer pain** (misuse, 57.4%; abuse, 26.2%) than in those with chronic noncancer pain (misuse, 37.8%; abuse, 17.0%).

Younger age, male sex, smoking, habitual drinking, diagnosis of psychiatric disease, use of opioids other than tramadol, and use of opioids for chronic post-cancer treatment pain and chronic cancer pain were identified as risk factors for aberrant prescription opioid-taking behaviors.

Even in Japan, which has not experienced the surge in opioid consumption documented in other countries, aberrant prescription opioid-taking behaviors were observed. When prescribing opioid analgesics, universal precautions should always be taken for both cancer and non-cancer patients

Systematic Review and Meta-Analysis of the Prevalence of Chronic Pain Among Patients With Opioid Use Disorder and Receiving Opioid Substitution Therapy. Delorme et al. J Pain 2023

**Prevalence of chronic pain (CP) in patients treated with Opioid Substitution Treatment** (OST - buprenorphine or methadone) for Opioid Used Disorder (OUD),  
The prevalence was **45.3%** These patients deserve specific attention from health professionals and health authorities.  
Thus, the real challenge in OST patients is the implementation of a multidisciplinary approach to manage CP.

The urgent challenge in OST patients is to pay systematic attention to chronic pain diagnosis, along with the implementation of a multidisciplinary patient-focused approach for an appropriate management of CP.

Review  
**Prevalence of Opioid Use Disorder among Patients with Cancer-Related Pain: A Systematic Review**

Céline Preux<sup>1</sup>, Marion Bertin<sup>1</sup>, Andréa Tarot<sup>1</sup>, Nicolas Authier<sup>2,3,4</sup>, Nathalie Pinol<sup>5</sup>, David Brugnon<sup>1</sup>, Bruno Pereira<sup>6</sup> and Virginie Guastella<sup>1,2,\*</sup>

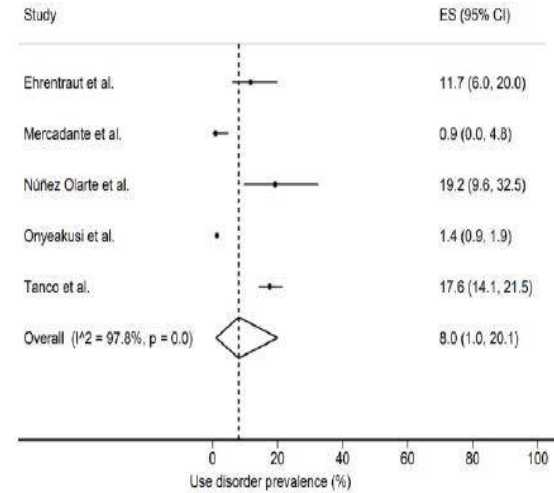
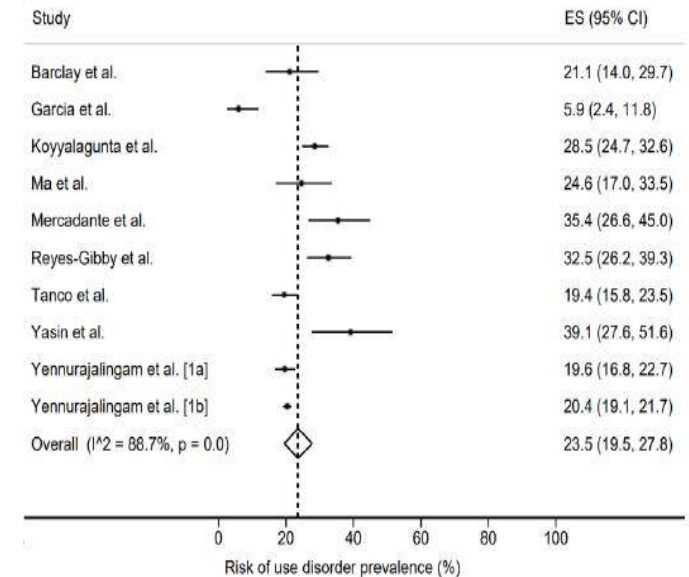


Figure 2. Use disorder prevalence [18–22].



15 studies about use disorders and risk of use disorders.

The prevalence of opioid use disorder was **8%** (1–20%) and of the risk of use disorder was **23.5%** (19.5–27.8%)


# Predicting the Risk for Aberrant Opioid Use Behavior in Patients Receiving Outpatient Supportive Care Consultation at a Comprehensive Cancer Center.

Yennurajalingam S, et al. *Cancer*. 2018

Among the 729 of 751 (97%) evaluable consults, 143 (**19.6%**) were SOAPP-positive, and 73 (**10.5%**) were CAGE-AID-positive.

Multivariate analysis revealed that the odds ratio of a **positive SOAPP** score was 2.3 for patients who had positive **CAGE-AID scores** ( $P < .0001$ ), 2.08 for **men** ( $P = .0013$ ), 1.10 per point for **ESAS pain** ( $P = .014$ ), 1.13 per point for **ESAS anxiety** ( $P = .0015$ ), and 1.09 per point for ESAS **financial distress** ( $P = .012$ ). A CAGE-AID cutoff score of 1 in 4 had 43.3% sensitivity and 90.93% specificity for screening patients with a high risk of ADB.

# Aberrant opioid use behaviour in advanced cancer

Sebastiano Mercadante <sup>1</sup>, Claudio Adile,<sup>1</sup> Walter Tirelli,<sup>2</sup>  
Patrizia Ferrera,<sup>1</sup> Italo Penco,<sup>2</sup> Alessandra Casuccio<sup>3</sup>




113 patients with advanced cancer were examined.  
About **35%** of patients were SOAPP positive.  
There was correlation between SOAPP, CAGE-AID and  
ORT. SOAPP was independently associated with a lower  
Karnofsky level, pain intensity, poor well-being

**At follow-up, no patient (0%) displayed aberrant  
behaviours, despite having a moderate-high risk.**

**The risk in our population was negligible!**

# Opioids in advanced cancer: use, storage and disposal in the home

Sebastiano Mercadante ,<sup>1</sup> Lucia Adamoli,<sup>2</sup> Giuseppe Bellavia,<sup>2</sup> Luisa Castellana,<sup>2</sup> Tommaso Favara,<sup>2</sup> Lavinia Insalaco,<sup>2</sup> Marco Mauceri,<sup>2</sup> Carla Scibilia,<sup>2</sup> Mario Lo Mauro,<sup>2</sup> Alessio Lo Cascio,<sup>3</sup> Alessandra Casuccio<sup>4,5</sup>

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ In studies in US many patients use opioids unsafely, store them in unsecure locations, and do not dispose of unused opioids, leading to increased availability of these drugs for non-medical use of opioids. However, the opioid crisis did not affected many European countries, like Italy.

## WHAT THIS STUDY ADDS

⇒ While a large number of advanced cancer patients followed at home do not store, use, and dispose of opioids safely, non-medical use was not detected

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Data of this study suggest that patient education programs should be incorporated to decrease the availability of opioids at home for abuse, diversion, and accidental poisoning







**Table 1** Questions regarding opioid use, storage and disposal at home

Do you need assistance taking the pills?	58
Do you have any painkillers you don't use at home?	51
You get rid of the pain relievers you no longer use:	
Giving them to your doctor or pharmacy	30
Throwing them down the bathroom drain	0
Throwing them in the garbage	5
Generally does not throw away the drugs	25
Do not throw away the analgesic drugs because they can be used in the future	40
You keep your painkillers:	
Where everyone can see them	73
Hidden, but not locked	26
Locked	1
Do you know the methods of disposing of the drugs? (yes/no)	65
Do your friends and family know that you are taking painkillers?	91
Do you count painkillers to see how many there are?	36
Do you think you will sometimes find fewer painkillers than expected?	10
Did you ever run out of painkillers too soon?	13
Did you share your pain relief pills with anyone else?	4
Have you missed any pain reliever pills in the past?	26
Do you agree that the abuse of analgesic drugs is a problem in our society?	64
Do you agree that analgesic pills can cause too much sleepiness, confusion and disturbances on respiration, convulsion and death if taken by others who have not had a prescription?	90
Are you aware that one dose of your pain reliever could be fatal for another?	88

A large number of patients with advanced cancer followed at home do not store, use and dispose of opioids safely. Patient education programmes should be incorporated to decrease the availability of opioids at home to avoid abuse, diversion and accidental poisoning.

# REVIEWS

## Balancing opioid analgesia with the risk of nonmedical opioid use in patients with cancer

*Joseph Arthur and Eduardo Bruera\**

**Abstract** | The current opioid crisis has brought renewed attention and scrutiny to opioid prescriptions. When patients receiving opioid therapy for pain engage in nonmedical opioid use (NMOU) or diversion, untoward consequences can occur. New evidence suggests that patients with cancer might be at a higher risk of NMOU than was previously thought, but clinical evidence still supports the use of opioid analgesics as the gold standard to treat cancer-related pain, creating a dilemma in patient management. Clinicians are encouraged to adopt a universal precautions approach to patients with cancer receiving opioids, which includes screening all patients; discussing the risks, benefits, adverse effects and alternatives of opioid therapy; and providing education on safe use, storage and disposal. Use of urine drug tests, prescription drug monitoring programmes and close observation of behaviours related to opioid use help to ensure treatment adherence, detect NMOU and support therapeutic decision-making. These measures can optimize the risk-benefit ratio while supporting safe opioid use. In this Review, we examine the role of opioids in cancer pain, the risk of substance use disorder and methods to achieve the right balance between the two in order to ensure safe opioid use.



# Aggressive treatment of chronic pain with prescription opioids **must be balanced** with the need to minimize the risks of OIAB, based on risk assessment and ongoing monitoring

(Passik SD, Issues in long-term opioid therapy: unmet needs, risks, and solutions. *Mayo Clin Proc* 2009;84(7):593-601. 2. Brady KT et al., Prescription opioid misuse, abuse, and treatment in the United States: an update. *Am J Psychiatry* 2016;173(1):18-26. 3. Kaye AD et al., Prescription opioid abuse in chronic pain: an updated review of opioid abuse predictors and strategies to curb opioid abuse (part 2). *Pain Physician* 2017;20(2S):S111-E133.

## Factors associated with increased risk of OIAB

- Younger age (18–25 years old)
- Male gender
- Psychiatric disorders (e.g. depression, bipolar disorder)
- Exposure to violence or sexual assault
- A history of substance use disorders (in particular illegal drug use)

## OIAB Risk Assessment Tools

- ORT (Opioid Risk Tool)
- SOAPP-R (Screener & Opioid Assessment for Patient with Pain-Revised)
- SISAP (Screening Instrument for Substance Abuse Potential)

## Opioid-induced Aberrant Behavior Management Strategy<sup>3</sup>

Proactive Pain Therapy

Administration of opioids for patient's pain control

**Risk assessment** of patient's OIAB

**Continuous Monitoring** of patient's pain control status and OIAB

**Develop and implement management strategies** of patient's OIAB

Proactive Pain Therapy

**Patients who have risk factors should NOT necessarily be excluded from opioid pharmacotherapy** if such treatment has been determined to be the best course of action

# Approach to non medical opioid use in pts with cancer pain

**Table 1.** Approach to nonmedical opioid use in patients with cancer pain based on universal precautions

Step	Description
1	Differential diagnosis: identify tumor and treatment-related causes of pain; identify patient factors influencing pain perception and expression; identify complex pain syndromes, e.g., neuropathic pain, concurrent chronic noncancer pain.
2	History of risk factors for nonmedical opioid use: tobacco or benzodiazepine use, depression, generalized anxiety disorder, history of substance abuse, personality disorder, posttraumatic stress disorder somatization, sexual abuse, reporting more severe pain and functional impairment, age < 65 years, high MEDD.
3	Screening instrument at first visit to identify patients at high risk (e.g., CAGE-AID, SOAPP, ORT).
4	Informed consent including patient education about substance use disorder, tolerance, and opioid adverse effects; a treatment plan that de-emphasizes opioids as sole treatment for pain.
5	Opioid agreement (written or verbal) that includes outline of patient obligations (e.g., receive opioid prescriptions from single provider, no early refills, random UDS).
6	Pre- and post-assessment of pain level and function; routine assessment of five As: analgesia, activities of daily living, adverse effects, aberrant behavior, and affect.
7	Psychological support, brief motivational interviews, increased vigilance and structure for those at high risk for opioid misuse (e.g., pill counts, shorter intervals between visits); oncologists should consider an integrated comanaged model with palliative care or interdisciplinary chronic pain team for complex patients.
8	Periodically review differential diagnosis; contribution of tumor- and patient-related factors to pain may change (e.g., patients with no evidence of disease should receive stable scheduled dose or tapered opioids, whereas patients with progressive advanced cancer may require additional breakthrough-dose opioids or opioid dose escalation).
9	Documentation of all prescriptions, office visits, agreements, and instructions.
10	Ethical concerns: discharging patients with advanced cancer and NMOU; comanagement should be considered for SUD, exercise caution regarding a diagnosis of diversion.

# Patients with cancer pain with opioid misuse

- ✓ They still need opioid therapy because of impending pain
- ✓ Most of them show chemical coping
- ✓ They need a therapeutic strategy

The Centers for Disease Control and Prevention (CDC) 2016's Guideline for Prescribing Opioids for Chronic Pain (Dowell et al., 2016) states in its 12th recommendation:

“Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder”.

The rationale is that tapering or discontinuing opioid medications could result in enhanced pain and craving with consequent use of illicit drugs and potential harms to the patient

Methadone is a synthetic  $\mu$ -opioid agonist with a long half-life approved as analgesic and treatment of opioid use disorder. It is also an NMDA-receptor antagonist, meaning that it is useful for chronic neuropathic pain.

Complex non-linear pharmacokinetics, its potential serious adverse effects including cardiac events (QT prolongation, *torsade de pointes*, arrhythmias...), risk of overdose and minor events like sedation, constipation, nausea or dizziness, must be strictly monitored.

Additionally, methadone's analgesic effects last 4-6h requiring multiple daily doses ([Heinzerling, 2019](#)).

Buprenorphine is a  $\mu$ -opioid partial agonist also approved as analgesic and treatment for opioid use disorder. It is usually combined with naloxone to deter intravenous use. It is also a  $\kappa$ -opioid receptor antagonist and may be able to reduce hyperalgesia.

Due to orphanin-receptor at higher doses it has ceiling effects and, therefore, a better safety profile compared to complete agonists like methadone ([Heinzerling, 2019](#)).





# The misuse is due to inappropriate care and poor monitoring

In 23 years (over 9000 admissions at Acute palliative care unit, La Maddalena, Palermo), only **five** patients had an aberrant use of fentanyl products at admission, and this was due after an initial prescription, then patients were themself-caring....

2 FBT

1 OTFC

1 SLF

1 FPNS

# Cancer pain management and maintenance therapy



A 65-year-old male progressively developed neck pain and dysphagia. A diagnosis of epiglottis cancer was made in October 2021. He underwent a partial exeresis of a supraglottic mass, followed by carboplatin-taxol, cetuximab, then changed to carboplatin and cetuximab.

In June 2022 nivolumab was prescribed but due to the progression of disease he was then prescribed paclitaxel, and put on the waiting list for local radiotherapy.

Due to increasing levels of pain and clinical deterioration, he was referred to a home care program. The attending home palliative care physician referred him to an acute supportive palliative care unit (ASPCU) for a difficult pain syndrome, unmanageable at home.



On admission, physical examination finding showed a large supra-clavicular neck mass with tendency to ulceration and a mixed somatic-neuropathic pain



Syndrome of severe intensity (8/10 with frequent peaks of 10/10). Imaging studies showed a progression of disease, involving muscles and vessels of the neck.

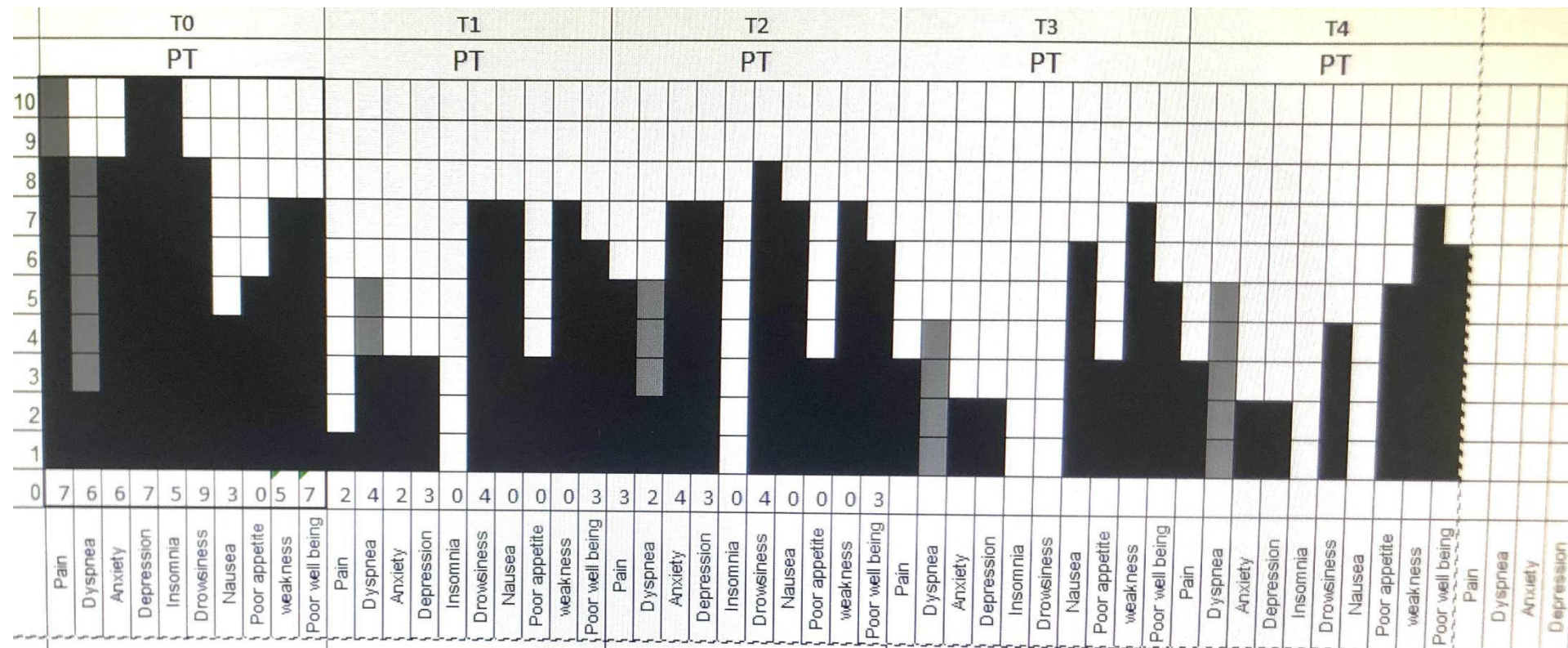
The **CAGE** (cut, annoyed, guilty, eye opener) test for drugs was positive (4/4). The Karnofsky status was 50 and the Memorial Delirium Assessment scale (MDAS) was 5. He also manifested high levels of anxiety, depression, and poor sleep.

Former addict on MTT for 30 years. The last methadone dose prescribed was 100 mg daily, although he was also taking an extra dose of 50 mg from his weekly prescribed reserve (**total 150 mg/day**).

A decision was made to split the patient's total home methadone dose into 60 mg three times a day (**180 mg/day**) with intravenous morphine 50 mg as needed for breakthrough pain.

The day after optimal pain relief with significant reduction in other symptoms.

He was discharged home on the 4th day. In follow-up phone contacts with the home care physician, the patient reported very good pain control, with no use of breakthrough medications, and no relevant problems, unless an abscess of the neck mass, requiring antibiotic therapy and frequent medications.



The management of cancer pain in patients on MMT may be challenging and complex.


An awareness of the particular pharmacological changes induced by **chronic methadone exposure**, and the common requirement for multiple **adjuvant agents**, may help to improve analgesic control

Knowledge of the **psychological factors** behind perceived drug-seeking behavior can improve communication and trust

**Social and existential** issues influencing pain perception and behavior should be considered. It is common for there to be resonance between the generations in families, and family members may share substance-misusing behavior; a factor, which may influence bereavement care. Nonpharmacological interventions can improve symptoms such as anxiety and psychological distress as components of total pain and can avoid overuse of pharmacological interventions.

Methadone may currently be underused as an analgesic agent, and its use should be considered in this group of patients in whom achieving analgesia is difficult.

It has been shown to be a cost-effective option and to have a proven role in the management of cancer pain.

47 yrs,  Advanced breast cancer  
Divorced, legal controversies for child custody with  
previous husband, and son had from a previous  
partner, economically dependent on her sister who  
care for her.  
History of depression never treated. Actually  
autoprescription of BZDs  
Labelled as addicted, using ROOS even in absence  
of pain  
  
Followed a palliative care team in Ragusa with  
phone consultation

At admission she was receiving transdermal fentanyl 50 mcg/day and FBT 600 mcg 6-8 times a day with unclear indications (described as total pain)

She was switched to methadone 15 mg/day, then increased up to 30 mg/day. Methadone dose was changed frequently (zig-zag), due to adverse effects, including dizziness, poor sleep, restlessness.

Finally she was successfully switched to transdermal buprenorphine 35 mcg/h, then increased up to 52.5 mcg/h, olanzapin 5 mg nocte, naldemedine 200 mg

Counseling

Discharge on day 14 with well controlled pain, normal sleep, no aberrant behavior.

Two months after by WA we received «many thanks, anything is ok»

# Non pharmacological strategies

- ✓ Coping
- ✓ Reassurance
- ✓ Explanation
- ✓ Communication
- ✓ Psychological support



## Step Description

- 1 **Differential diagnosis**: identify tumor and treatment-related causes of pain; identify patient factors influencing pain perception and expression; identify complex pain syndromes, e.g., neuropathic pain, concurrent chronic noncancer pain.
- 2 History of **risk factors for nonmedical opioid use**: tobacco or BDZ use, depression, anxiety disorder, history of substance abuse, personality disorder, posttraumatic stress disorder somatization, sexual abuse, reporting severe pain and functional impairment, age < 65 years, high MEDD.
- 3 **Screening instrument** at first visit to identify patients at high risk (e.g., CAGE-AID, SOAPP, ORT).
- 4 **Informed consent** including patient education about substance use disorder, tolerance, and opioid adverse effects; a treatment plan that de-emphasizes opioids as sole treatment for pain.

5 **Opioid agreement** (written or verbal) that includes outline of patient obligations (e.g., receive opioid prescriptions from single provider, no early refills, random urine test).

6. **Pre- and post-assessment of pain** level and function; routine assessment of analgesia, activities of daily living, adverse effects, aberrant behavior, and affect.

7. **Psychological support**, brief motivational interviews, increased vigilance and structure for those at high risk for opioid misuse (e.g., pill counts, shorter intervals between visits); oncologists should consider an integrated co-managed model with palliative care or interdisciplinary chronic pain team for complex patients.

8. Periodically review differential diagnosis; **contribution of tumor- and patient-related factors to pain may change** (e.g., pts with no evidence of disease should receive stable scheduled dose or tapered opioids, whereas patients with progressive advanced cancer may require additional breakthrough-dose opioids or opioid dose escalation).

9. **Documentation** of all prescriptions, office visits, agreements, and instructions.

10. **Ethical concerns:** discharging patients with advanced cancer and non medical opioid use; co-management should be considered for substance use disorder, exercise caution regarding a diagnosis of diversion.

# Opioid switching to methadone

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## Opioid switching in cancer pain: From the beginning to nowadays<sup>☆</sup>



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### ABSTRACT

Opioid switching is the process of changing from one opioid to another to obtain a satisfactory clinical balance between analgesia and adverse effects. This pharmacological technique has been introduced about 20 years ago to enhance the opioid response in advanced cancer patients with chronic pain. More information is now available. This review will examine many different aspects of opioid switching, including the history and evolution through the last decades, some clinical aspects based on the most recent experience, controversies on the indications, conversion ratios and modalities of switching in some specific circumstances, and evidence based recommendations.

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Calculate opioid consumption (prescribed and not, approximately)

Switch to methadone (ratio 1:5 – 1:10), according to the clinical condition (balancing analgesia and adverse effects)

Add olanzapine or other sedative drugs

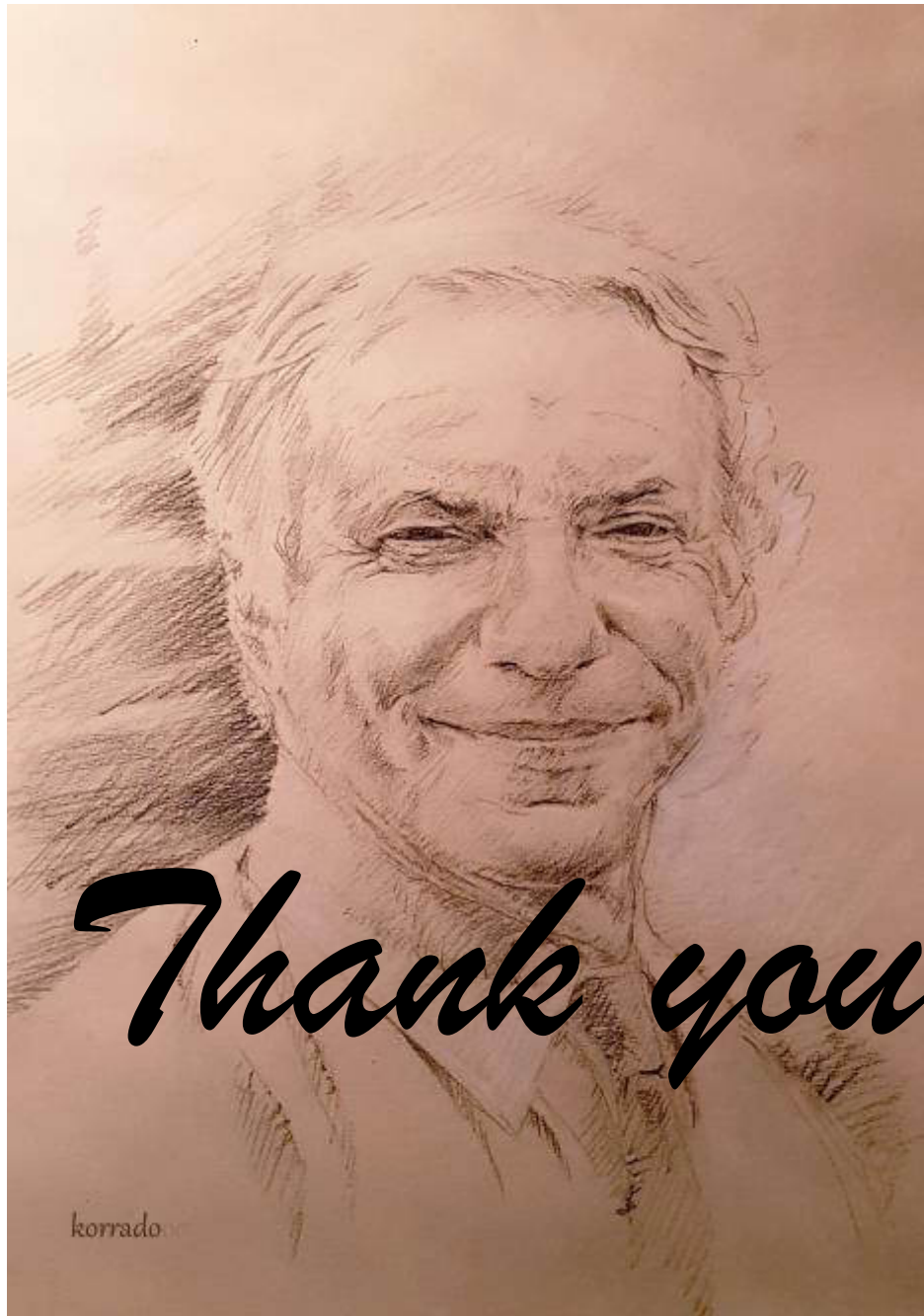
Avoid opioids as needed

Daily review of methadone doses with attempts to dose tapering (alternately buprenorphine)

Stable doses with adequate analgesia

- ✓ Maintain non pharmacological strategies continuously
- ✓ Availability: maintain frequent contacts
- ✓ Balancing analgesia and adverse effects
- ✓ Monitoring for aberrant behavior risks





**It's only palliative care, but I like it..**

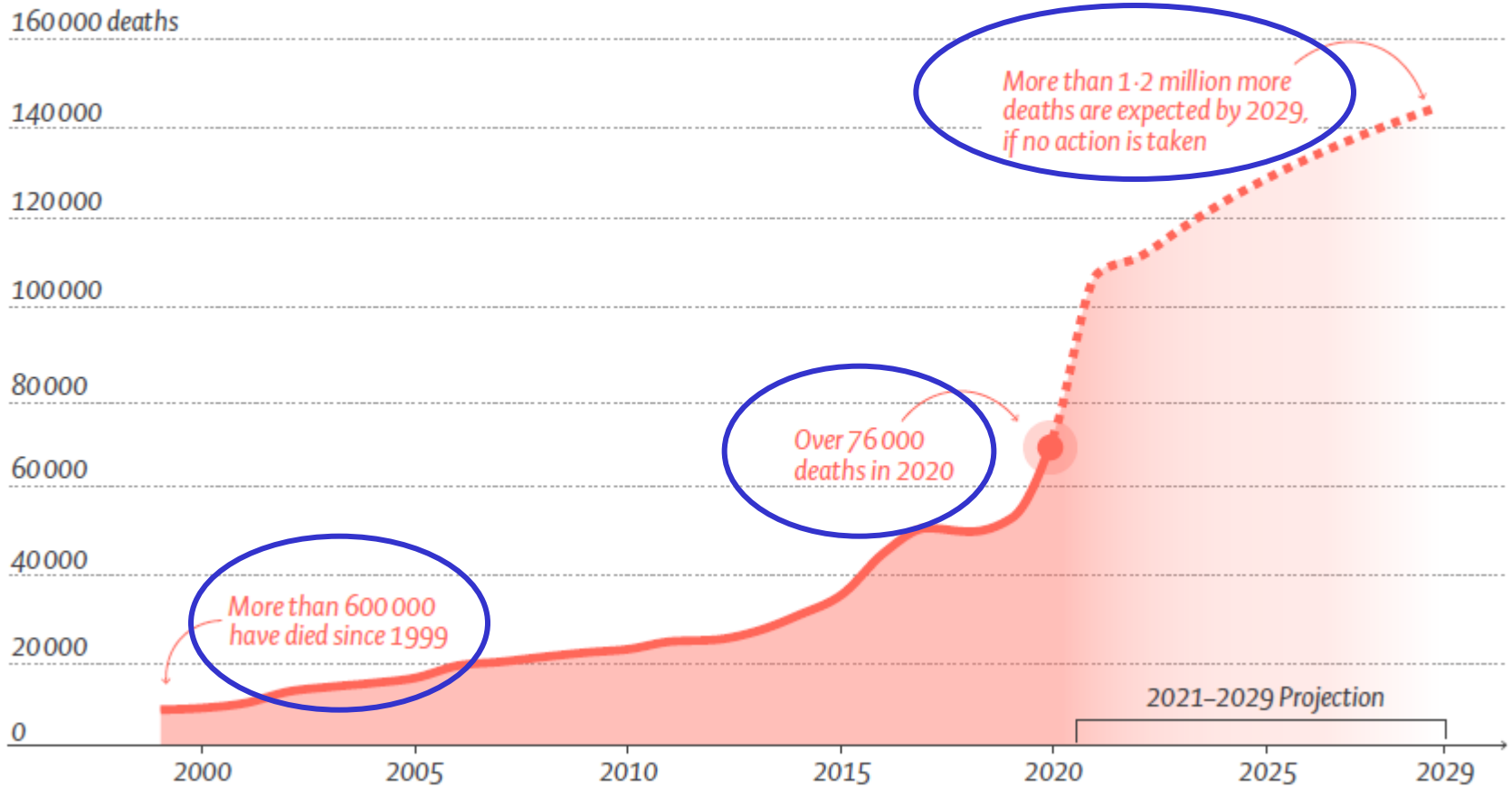


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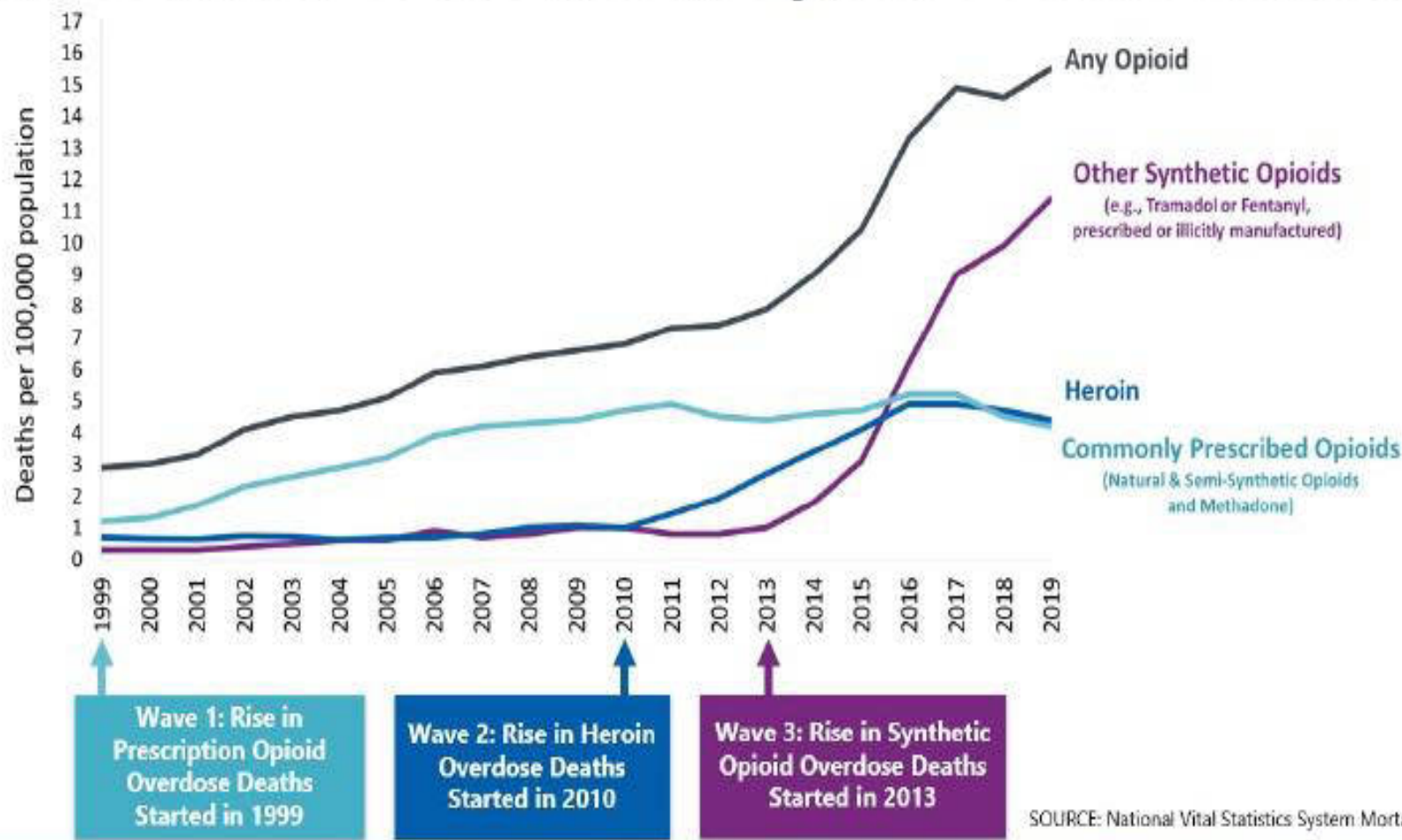




# Deaths from opioid overdose in North America



# Three Waves of the Rise in Opioid Overdose Deaths



# Potential strategies to combat the opioid crisis

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## ABSTRACT

**Introduction:** In the last few decades, the consumption of opioid analgesics in many countries, particularly the US, has dramatically increased. This rise has been paralleled by a proportional number of opioid-related deaths.

**Areas covered:** The development of opioid guidelines was a response to this health crisis with the intention of reducing the risk of harm related to opioid prescribing. These guidelines have received varying responses ranging from support to criticism. Pain physicians may often provide multidimensional management as the paradigm for responsible opioid treatment. Interventions should focus on preventing new cases of opioid addiction, identifying early cases of opioid addiction, and ensuring access to effective addiction treatment.

**Expert opinion:** Many activities have been suggested to face the opioid epidemic. Reducing supply is one of the most relevant aspects. Clinicians should find a fine balance that meets the patient's need for pain relief while minimizing the chance for abuse.

## ARTICLE HISTORY

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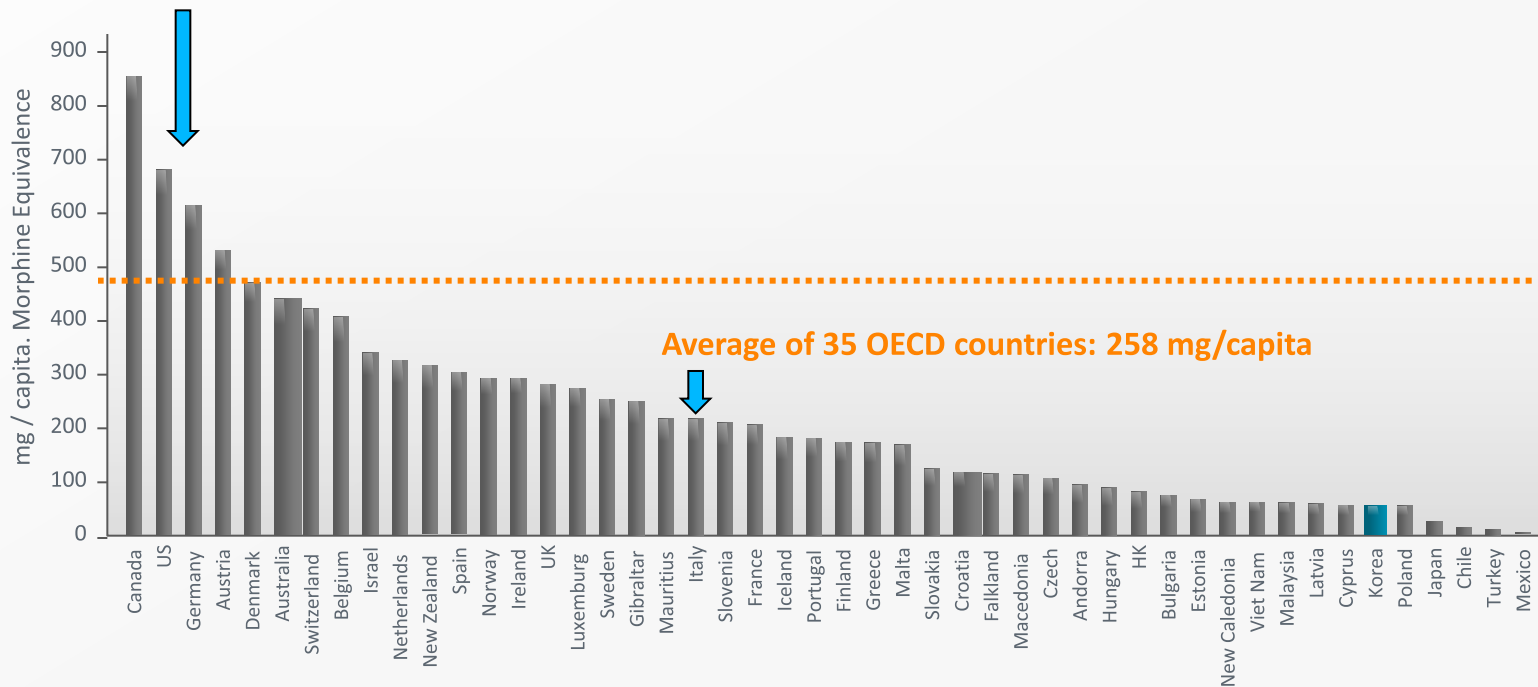
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## KEYWORDS

Non-cancer pain; opioid epidemic; misuse; overdose

## Global opioid consumption 2015

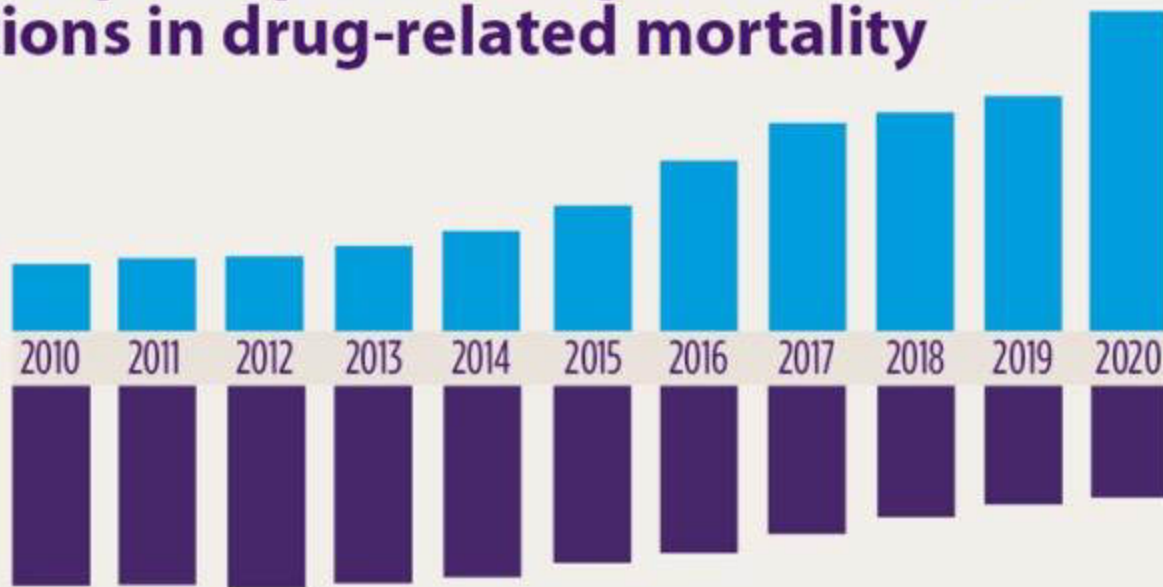
International Narcotics Control Board (INCB); World Health Organization population data  
By: Pain & Policy Studies Group (PPSG), University of Wisconsin/WHO Collaborating  
Center, 2017. Available from <https://ppsg-chart.medicine.wisc.edu/> Accessed on Sep  
10<sup>th</sup>, 2017



## Reductions in opioid prescribing have not led to reductions in drug-related mortality

Overdose deaths:  
94,134\*

Opioid prescriptions:  
143,390,951<sup>1</sup>  
(44.4% decrease since 2011)



\*Provisional data for the 12-month period Jan. 2020–Jan. 2021  
<https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>



## LETTER TO THE EDITOR

### Too much for some and too little for others

The abuse of opioid drugs in the USA represents a real emergency which led to an increased pressure on the health care system. However, opioid monitoring should be balanced with the needs of patients with cancer pain. With the increasing concerns about opioid misuse, patients may feel conflicted about using prescribed opioids to manage cancer pain due to concurrent perceptions of their risks and benefits.<sup>1-3</sup> Europe as a whole is not facing an opioid crisis and there are marked differences between European countries in trends of opioid prescribing and of proxies for opioid-related harms.<sup>4</sup> In a study performed in Italy, despite a similar percentage of patients showing a high risk of aberrant behaviors, no patient displayed clinical aberrant behaviors after 1-month follow-up.<sup>5</sup> In a Mediterranean country like Italy, with the lowest opioid consumption in Europe, this news from the United States may have catastrophic consequences. In fact, despite the lack of alarming data, on the basis of overseas opioid crisis, illegal drug trafficking, and some pressure from politicians, the National Regulatory Agency [Agenzia Italiana del farmaco (AIFA)] has suggested labeling opioid packets with a red flag: 'opioids produce addiction'. We expect that such a decision will result in further underprescription of opioids and this may amplify cultural barriers existing in Southern Europe, where we have to face exactly the opposite problem to that observed in North America. AIFA should seek advice from expert clinicians working every day in the field.

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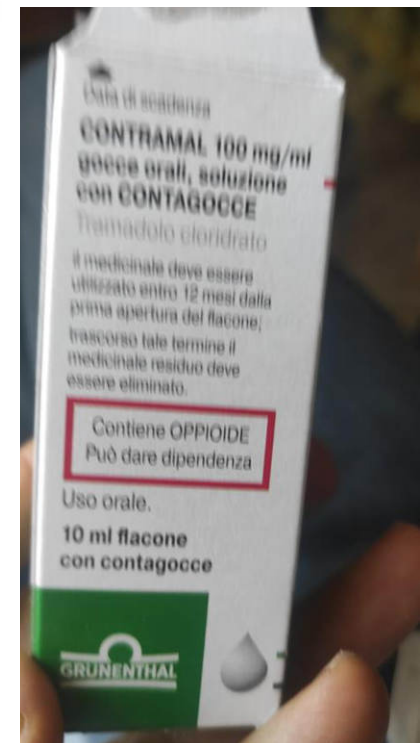
None declared.

### DISCLOSURES

The author has declared no conflicts of interest.

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Continued use of opioids increases tolerance, cause hyperalgesia, strengthen addiction and provokes a potentially harmful use.

- Improving analgesia limiting hyperalgesic states.
- Maintenance of this equilibrium represents a big challenge.



# Physician-induced aberrant behavior

- Forty-four years, cardiosurgeon, meniscectomy on spinal anesthesia
- Arachnoiditis treated with corticosteroids for two months
- Ubiquitarious osteoporosis, involvement of most vertebrae
- Cementoplasty on 4 segments of 12 vertebral fractures

At admission.

- Pectyn nasal spray 400 mcg,  
20 pieces/day !!!! (about 1/h)
- Bisphosphonates

Intravenous fentanyl tapered down



Methadone 240 mg/day, tapered down to 90 mg/day



Buprenorphine 210 mcg/h

Two months after on TD buprenorphine 140 mcg/h and water physiotherapy



Good mobility, drives car...



Next consultation for further cementoplasty and orthopedic surgery



