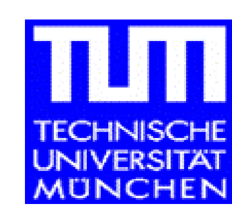
European clinical practice recommendations on opioids for chronic noncancer pain

Winfried Häuser

Technical University München
Department of Psychosomatic Medicine and Psychotherapy

Klinikum Saarbrücken
Internal Medicine I
- Gastroenterology, Hepatology, Endocrinology, Infectious Diseases, Oncology and Psychosomatic Medicine

Interdisciplinary center of Pain Medicine and Mental Health Saarbrücken



Disclosure

In relation to this presentation, I declare the following, real or perceived conflicts of interest:

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Consultant / advisory board	None

Agenda

- Is there an opioid crisis in Europe ?

A Flood of Opioids, a Rising Tide of Deaths

Susan Okie, M.D.

- Increase of opioid prescriptions
- Increase of abuse of prescribed opioids
- Increase of emergency visits (overdosage)
- Increase of deaths

- A comment on the US opioid crisis from a German point of view
- European Pain Federation (EFIC) clinical practice recommendations to ensure adequate pain relief whilst reducing addiction risk

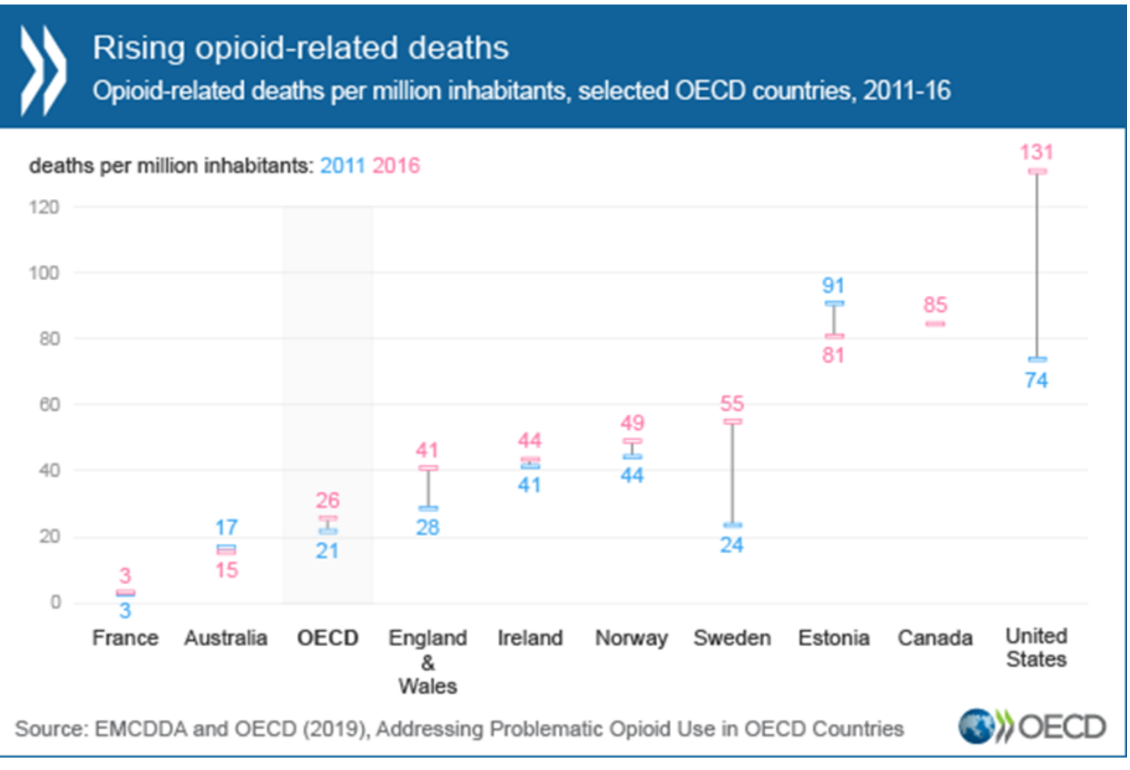
Is there an opioid crisis in Europe, too ?

Health

Opioid crisis spreads beyond Canada and U.S. to Europe, OECD says

Opioid overprescribing called one of the most important root causes of crisis in U.S.

Thomson Reuters · Posted: May 16, 2019 4:23 PM ET | Last Updated: May 16



FOCUS SERIES: FOCUS ON THE OPIOID CRISIS

Is Europe Facing an Emerging Opioid Crisis Comparable to the U.S.?

van Amsterdam, Jan PhD; Pierce, Mimi MD; van den Brink, Wim MD, PhD

Author Information

Therapeutic Drug Monitoring: February 2021 - Volume 43 - Issue 1 - p 42-51
doi: 10.1097/FTD.0000000000000789

“ The current overview, comparing opioid use and its negative consequences in Germany, France, the U.K., and the Netherlands, using the same indicators as in the U.S., demonstrates that there is no evidence of a current or emerging opioid crisis in these European countries. Scotland, however, is an alarming exception, with high rates of opioid-related harms. Considering that the use of prescription opioids has been declining rather than increasing in Europe, an opioid crisis is not anticipated there yet. Authorities should, however, remain vigilant.

Eur J Pain. 2021 May;25(5):1072-1080. doi: 10.1002/ejp.1728. Epub 2021 Feb 2.

Is Europe facing an opioid epidemic: What does European monitoring data tell us?

Thomas Seyler [1], Isabelle Giraudon [1], André Noor [1], Jane Mounteney [1], Paul Griffiths [1]

„A summary of the available evidence would suggest that while opioid-related deaths in Europe represent a large preventable health burden with differences across EU countries, Europe as a whole is not facing an opioid crisis of the size and nature seen in the US.

Is Europe facing an opioid crisis?

- A task force of the European Pain Federation (EFIC) conducted a survey with its national chapter representatives on trends of opioid prescriptions and of drug-related emergency departments and substance use disorder treatment admissions and of deaths as proxies of opioid-related harms over the last 20 years in May 2020.

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ORIGINAL ARTICLE

EJP

Is Europe also facing an opioid crisis?—A survey of European Pain Federation chapters

Winfried Häuser[1] | Eric Buchser[2] | David P. Finn[3] | Geerd Dom[4] | Egil Fors[5] | Tarja Heiskanen[6] | Lene Jarlbaek[7] | Roger D. Knaggs[8,9] | Eva Kosek[10] | Nevenka Krcevski-Škvarč[11] | Kaire Pakkonen[12] | Serge Perrot[13] | Anne-Priscille Trouvin[13] | Bart Morlion[14]

Results

- In most European countries opioid prescriptions increased from 2004 to 2016. The levels of opioid consumption and their increase differed between countries. Some Eastern European countries still have a low opioid consumption.
- Opioids are mainly prescribed for acute pain and chronic non-cancer pain in some Western and Northern European countries.
- There was a parallel increase in opioid prescriptions and some proxies of opioid-related harms in France, Finland and the Netherlands, but not in Germany, Spain and Norway. In United Kingdom, opioid overdose deaths, but not opioid prescriptions increased between 2016 and 2018.
- **There are no robust data available on whether prescribed opioids for pain patients contributed to opioid-related harms.**

Conclusions

- There are marked differences between European countries in trends of opioid prescribing and of proxies for opioid-related harms. Europe as a whole is not facing an opioid crisis. Discussions on the potential harms of opioids should not obstruct their prescription for cancer pain and palliative care.

- „ The accepted wisdom about the US overdose crisis singles out prescribing as the causative vector. **Although drug supply is a key factor,** we posit that the crisis is fundamentally fueled by economic and social upheaval, its etiology closely linked **to the role of opioids as a refuge from physical and psychological trauma, concentrated disadvantage, isolation, and hopelessness. Overreliance on opioid medications is emblematic of a health care system that incentivizes quick, simplistic answers to complex physical and mental health needs.** In an analogous way, **simplistic measures to cut access to opioids offer illusory solutions to this multidimensional societal challenge.**
  - Dasgupta. Am J Public Health 2018; 108:182-186.

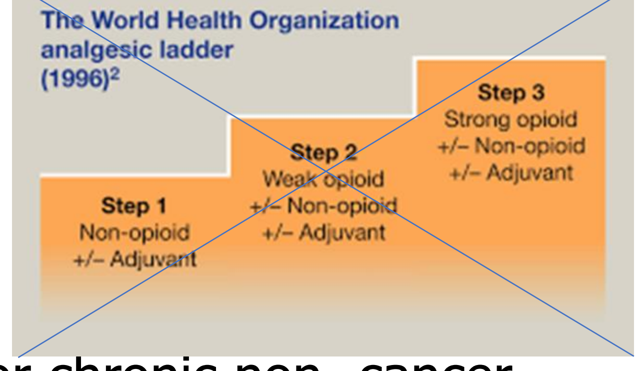
Some differences between Germany and North America

- Canada, Germany and USA belong to the countries with the highest consumption of prescribed opioids per person
  - At least one opioid prescription/year
    - USA 2015: 37.8%
    - Germany 2015: 4.5%
  - High dosage opioid therapy
    - Canada 2014: 41 % of recipients of long-acting opioids exceeded of 200 mg morphine or equivalent /d
    - Germany 2014: 10% of patients with long-term opioid therapy > 120 morphine or equivalent/d
- Estimates of opioid-addicted persons in the general population in 2018
  - Germany: 0.2 %
  - USA: 2.0%
- Drug deaths 2021
  - Germany: 0.002 % (1862 /82 Million)
  - USA: 0.3 % (107 622/ 330 Million)

Some differences between German and US Health Care System

- Physical and psychological therapies are covered by German statutory health insurance companies for patients with chronic pain and addiction care for patients with substance use disorders.
- Different attitudes of patients and physicians towards pharmaceutical pain management

Differences between German and North American guidelines on opioids



- Germany guidelines on opioids
  - First version in 2009, updated 2015 and 2021
    - Predominance of non-pharmacological therapies
    - Limited evidence for long-term effectiveness of opioids for chronic non- cancer pain
    - Potential indications and contraindications for opioids
    - No opioids for chronic pain conditions with predominantly nociplastic pain mechanisms
- North American guidelines for opioids
  - Canada 2011, update 2016
  - CDC guideline in 2016, update 2022
    - „Chronic pain"

- The clinical practice recommendations were developed by eight scientific societies and one patient self-help organization under the coordination of EFIC based on a systematic search of literature, a multistep consensus process, public comments and external reviews of international experts.

POSITION PAPER

European clinical practice recommendations on opioids for chronic noncancer pain – Part 2: Special situations*

Nevenka Krčevski Škvarč[1] | Bart Morlion[2] | Kevin E. Vowles[3] | Kirsty Bannister[4] | Eric Buchsner[5] | Roberto Casale[6] | Jean-François Chenot[7] | Gillian Chumbley[8] | Asbjørn Mohr Drewes[9] | Geert Dom[10] | Liisa Jutila[11] | Tony O'Brien[12] | Esther Pogatzki-Zahn[13] | Martin Rakusa[14] | Carmen Suarez–Serrano[15] | Thomas Tölle[16] | Winfried Häuser[17,18]

Eur J Pain. 2021;25:969–985.

POSITION PAPER

European* clinical practice recommendations on opioids for chronic noncancer pain – Part 1: Role of opioids in the management of chronic noncancer pain

Winfried Häuser[1,2] | Bart Morlion[3] | Kevin E. Vowles[4] | Kirsty Bannister[5] | Eric Buchser[6] | Roberto Casale[7] | Jean-François Chenot[8] | Gillian Chumbley[9] | Asbjørn Mohr Drewes[10] | Geert Dom[11] | Liisa Jutila[12] | Tony O'Brien[13] | Esther Pogatzki-Zahn[14] | Martin Rakusa[15] | Carmen Suarez–Serrano[16] | Thomas Tölle[17] | Nevenka Krčevski Škvarč[18]

Eur J Pain. 2021;25:949–968.

Optimization of non-opioid treatment

- *Before considering opioid treatment, we first suggest optimizing non-pharmacological treatments (e.g. exercise, physiotherapy, psychological therapies) and considering non-opioid analgesics*.
  - Weak recommendation, strong consensus

When to consider opioids

- *We suggest considering a trial of opioids if established non-pharmacological treatments and established non-opioid analgesics are:*
    - *Not effective and/or*
    - *Not tolerated and/or*
    - *Contraindicated*
    - *Not available*

Weak recommendation, strong consensus

Statement	Grading	Consensus
We suggest considering opioids for chronic secondary pain syndromes Low back pain with predominant nociceptive/ neuropathic mechanisms, Osteoarthritis pain, Diabetic polyneuropathy, Postherpetic neuralgia	Weak EBR	Consensus+
Opioids can be considered for other chronic secondary pain syndromes.	GCP	Consensus+
Opioids should not be considered for primary pain syndromes (nociplastic pain mechanisms). Primary headache, functional somatic disorders (e.g. fibromyalgia), chronic primary visceral pain, primary musculoskeletal pain, pain as a major manifestation of a mental disorder	GCP	Consensus/ Strong

Statement	Grading	Consensus
Measures prior to opioid initiation:		
- General case history and clinical status	GCP	Strong
- Screen for mental disorders	GCP	Strong
- If mental disorder indicated, access specialist assessment	GCP	Strong
- Set individual and realistic therapeutic goals	GCP	Strong
- Provide patient with documented information on opioid use including traffic/workplace issues	GCP	Strong
- Titration and driving safety : national guidelines should be discussed and documented	GCP	Strong

Statement	Grading	Consensus
Treatment with opioids:		
- Can consider only one prescribing physician at a time (or same team or nominee is primary prescriber is on leave).	GCP	Strong
- Should consider starting at a low dose (e.g., <50 mg MME/d)	GCP	Consensus/Strong
- Increase dose in a stepwise manner to reach therapeutic goals	GCP	Strong
- Exceed 90 mg MME/d in exceptional cases only	Weak EBR	Consensus/Strong
- In cases of inadequate pain relief or adverse events, a switch to an alternative opioid should be considered	GCP	Consensus/Strong
- Longer than 3 continuous months of opioid prescription should only be considered in treatment responders	GCP	Consensus/Strong

Statement	Grading	Consensus
Monitoring and documentation: - Regularly review (every 1-3 months) maintenance of therapeutic goals, indications for adverse events, evidence of opioid use disorder or misuse - Consider urine drug screening when there is suspected misuse or illicit drug use.	GCP GCP	Strong Strong
Discontinuation: - If individual therapeutic goals are not met during the titration phase or after opioid rotation, or if intolerable side-effects occur, consider stepwise discontinuation - Consider discontinuation of long-term opioids if: therapeutic goals are no longer achieved, intolerable adverse events occur, other treatments achieve therapeutic goals, urine drug tests are refused, or opioids are used in an abusive manner	GCP GCP	Strong Strong

Statement	Grading	Consensus
Medication reduction: After 6 months with a good response, consider dose reduction to assess indication for continued treatment and response to non-pharmacological treatments being used in parallel.	GCP	Strong

Problematic use of prescribed opioids

- There is a transition of patient behavior between intended use, unintended use (misuse), harmful use (abuse) and dependent (‘addicted’) use of opioids prescribed for medical reasons.
  - Good clinical practice statement. Strong Consensus

Diagnosis

- The DSM-4/5 and ICD10/11 criteria have not been designed for patients prescribed with opioids for chronic pain
  - APA explicitly states that these criteria are not appropriate for individuals taking opioids when patients are under adequate medical supervision.
  - Tolerance and withdrawal symptom criteria, which are often used as key indicators for substance use disorder in psychiatry and other medical settings, have been removed from the ICD 11 version for patients medically treated with opioids by a licensed clinician.
- Additional clinical criteria to DSM-5 opioid use disorder criteria and/or the ICD 11 opioid dependence criteria can be considered for use to evaluate for opioid use disorder.
  - Good clinical practice statement. Strong Consensus

Non-specific signals for misuse, abuse and dependence

TABLE 1 Non-specific signals for misuse, abuse and dependence (Häuser et al., 2020)

Non-specific signals for misuse

- Ingestion despite low to no efficacy
- Changing pain localization, multilocular spread (generalisation) of pain, transformation to primary pain under ongoing therapy
- Opioid-induced hyperalgesia (tendency to spread pain, increase in pain sensitivity and opioid resistance)

Non-specific signals of abuse/dependence:

- High at rest pain and discrepancy between pain indication and behaviour
- Demanding a specific opioid, especially short-acting and/or fast acting opioids
- Opioid use mainly for symptom relief other than pain (distress, anxiety, fear, depression, sleep disturbance)
- Unconcerted increases in dosage
- Urging an increase in dose without improving symptoms/function or despite an increase in side effects
- Repeated unreliability (unpunctuality, non-appearance) or lack of compliance
- Concealed use of substances with addictive potential (discrepancies in drug monitoring)
- Urging the prescription of more psychotropic substances
- Change of the agreed intake intervals, independent adjustment as required
- Defence against changes in therapy
- Changes in character under therapy (e.g. impulse control disorders) and other new psychiatric symptoms
- Misuse of other substances for psychotropic purposes
- Increase of irritability, depression, anxiety, nightmares under therapy

Signals of psychological dependence:

- Persistent resistance to changes in medication despite
- Ineffectiveness and/or symptoms of a medically undesirable psychotropic effect (euphoria, sedation, anxiety relief)
- Psychotropic (mostly dose-dependent) side effects (fatigue, listlessness, concentration disorders)
- Injection of oral/transdermal administration forms
- Intravenous and oral application of transdermal systems
- Forged prescriptions
- Steal/Borrow Opioids
- Implausible hoarding of prescribed opioids
- Concealed/denied reference by other doctors
- Illicit use of other psychotropic substances including other opioids
- Frequent loss of prescriptions
- Requiring a parenteral route of administration
- Trade of opioids with third parties
- Loss of control (e.g. repeated episodes of dosage increases or increasingly needs-based intake despite clear agreement/warning, clear immediate negative consequences of taking medication in the private and social environment)
- Compulsory use

Treatment options for opioid use disorder

- These treatment options for prescribed opioid use disorder are recommended in the view of the local resources and national legislation:
  - Opioid tapering [outpatient, inpatient (e.g., pain or psychiatric department)]
  - Continuation of therapy with a stable opioid dose to sustain pain relief or minimize withdrawal symptoms.
  - Buprenorphine or methadone/polamidon therapy with psychological therapies –if available-with regular urine drug testing (or other specimen) to exclude the use of other opioid and or other psychoactive substances

Prevention of non-medical use of prescribed opioids

- Acute pain therapy by opioids after surgical and interventional procedures should be considered to be tailored and discontinued as soon as clinically indicated.
    - Good clinical practice statement. Strong Consensus

Prevention of non-medical use of prescribed opioids

- We suggest these measures to identify and prevent abuse and misuse of prescribed opioids:
  - Risk-screening tools
  - Controlled-substance agreements
  - Compliance monitoring.
    - Weak recommendation. Strong Consensus

Lessons learned from the North American opioid crisis

- The North American opioid crisis should not impede the use of opioids for
  - Cancer pain and palliative care
  - Chronic non-cancer pain in some carefully selected and supervised patients
    - According to the European clinical practice recommendations on opioids for chronic noncancer pain of EFIC
    - European Pain Federation calls for continuous medical education on the correct use of opioids in multiprofessional and multi-modal therapeutic approaches.

The way forward – The Stanford - Lancets Commissions recommendations

- Domain 2: Opioids' dual nature as both a benefit and a risk to health
  - Recognition of the risks and benefits of opioids in the drug-approval process
  - Promote opioid stewardship in medicine
- Domain 3: Build integrated, well supported, and enduring systems for the care of substance use disorders
- Domain 4: Maximise the benefit and minimise the adverse effects of the criminal justice system's involvement with people addicted to opioids
- Domain 5: Create healthy environments that yield longterm declines in incidence of addiction
- Domain 7: Prevent opioid crises beyond the USA and Canada
  - Prevent pharmaceutical companies in the USA from exporting fraudulent and corrupting opioid promotion practices
  - Distribute free, generic morphine for analgesia to hospitals and hospices in low-income nations

Humphreys. Lancet 2022; 399:555-604

Thank you for your interest

whaeuser@klinikum-saarbruecken.de