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يونيورسيتي إسلام انتارابغسا ملسيا

Issues and Challenges of Opioids in Chronic Non-Cancer Pain

Seminar at Lahore University Pakistan
27th May 2021

Assoc Prof Dr Che Suraya Zin
Kulliyyah of Pharmacy IIUM

Contents of the Presentation

Opioid history

- Friedrich Wilhelm Serturner
- German pharmacist
- Isolated Morphine in 1803 and named it after the Greek god of Dreams “MORPHEUS”

Opioids

Strong analgesics

Weak opioids-codeine, tramadol, dihydrocodeine

Strong opioids-oxycodone, fentanyl, morphine

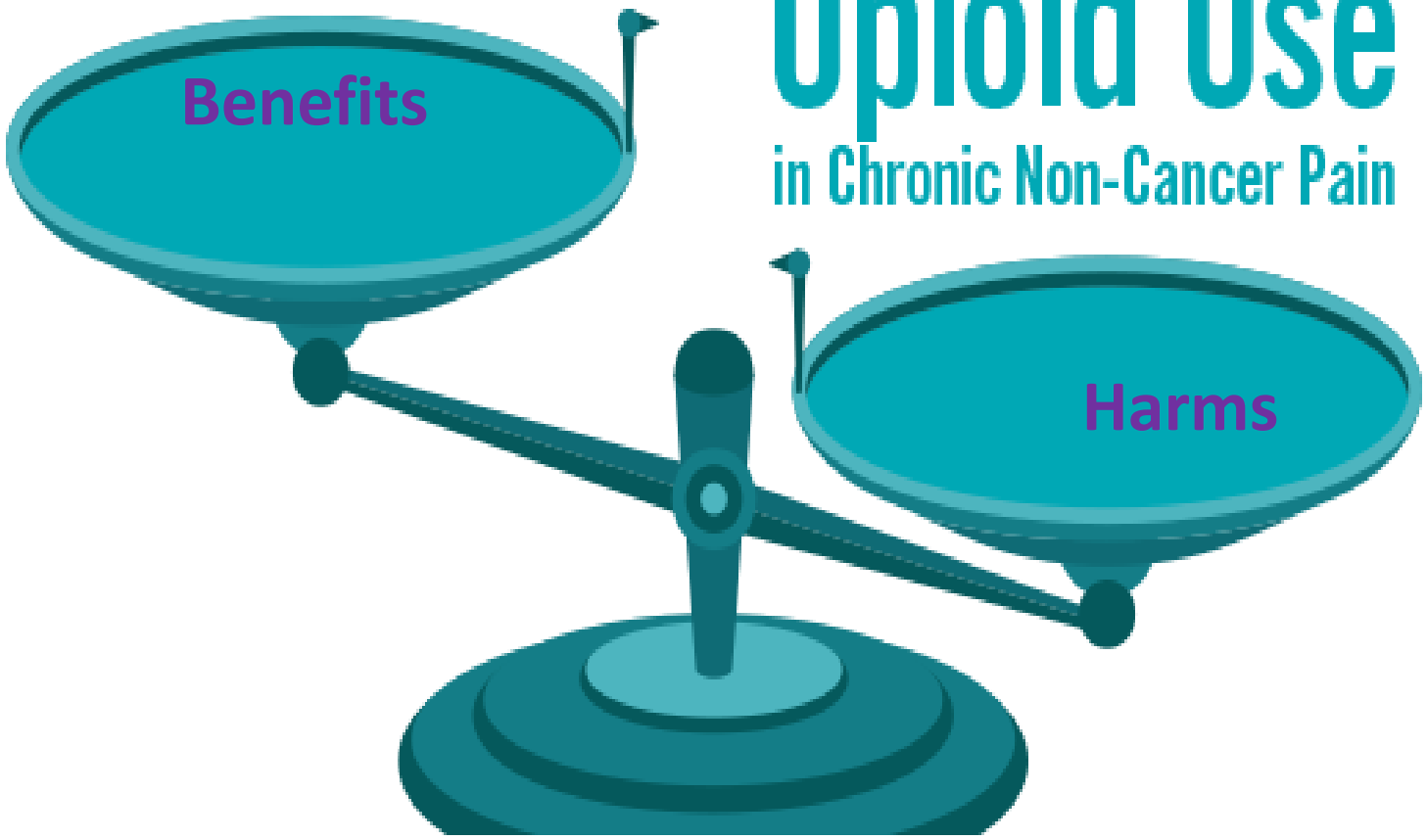
Opioid use

- Cancer pain ✓
- Acute pain ✓
- Post surgical pain ✓

Controversy

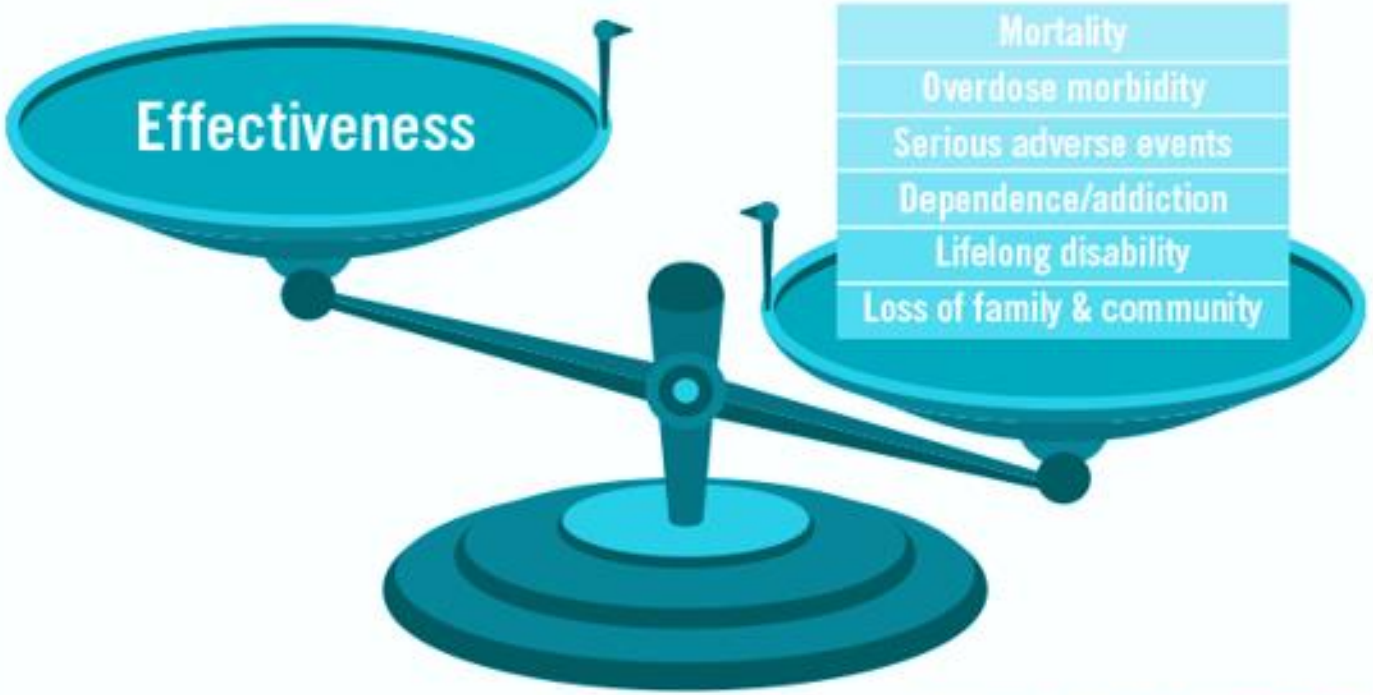
- Chronic non-cancer pain

Opioid Use
in Chronic Non-Cancer Pain



Weighing Risks and Benefits

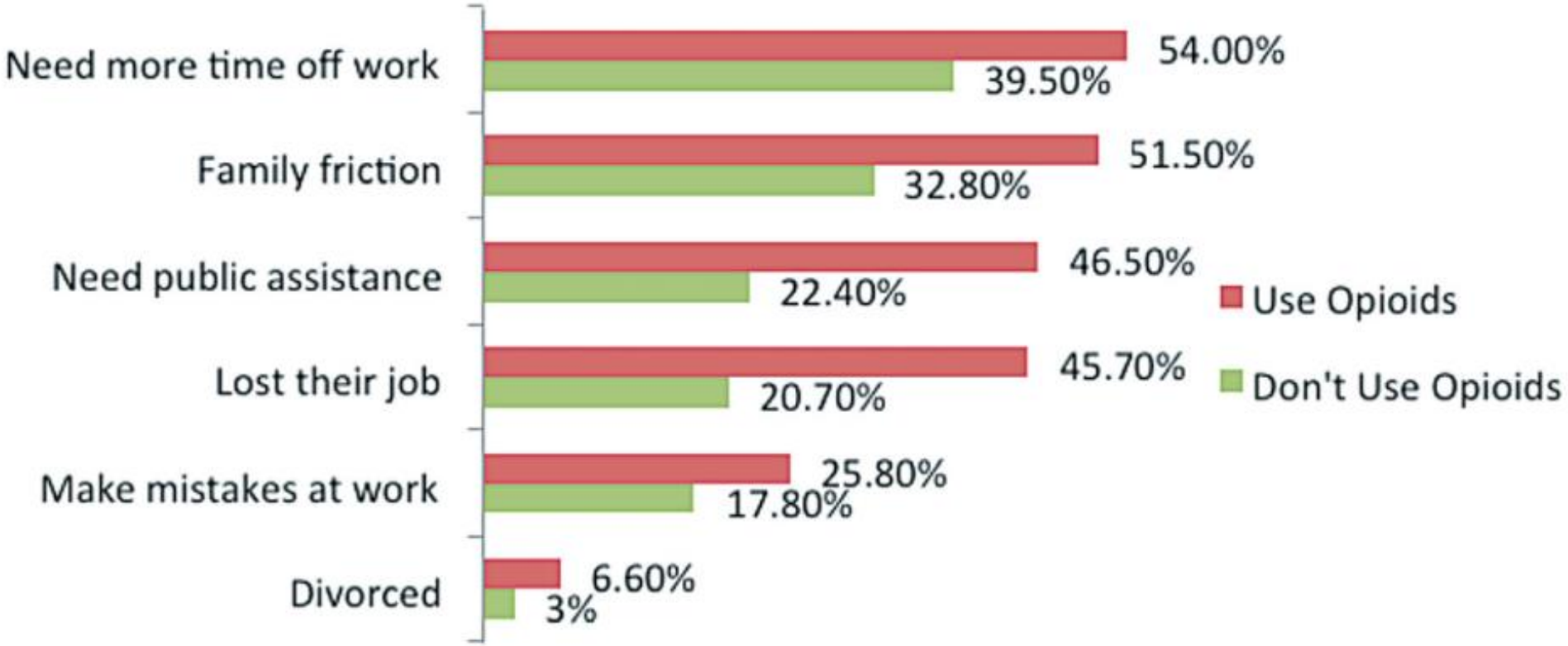
The figure below depicts the risks and benefits that should be weighed when considering the use of opioids for chronic non-cancer pain.



Source: Adapted from: Franklin GM. *Neurology* 2014;83:1277-1284.

Opioids Cause Greater Personal and Social Problems

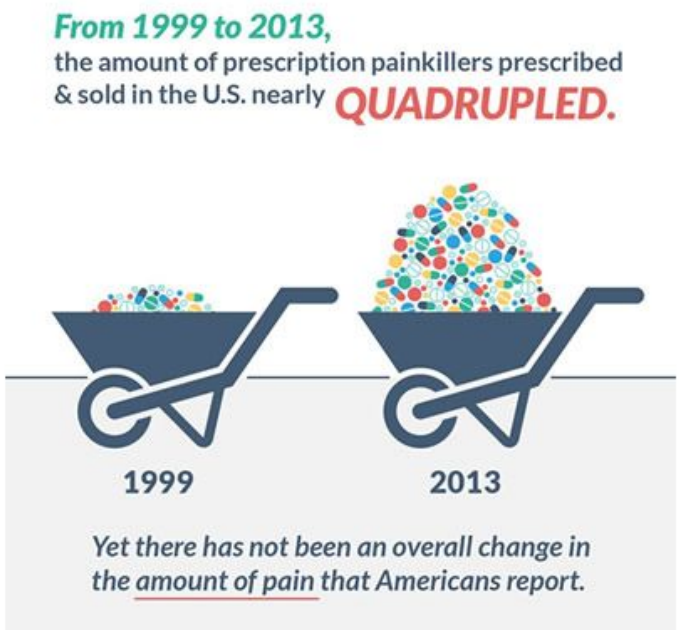
Experiences of U.S. Chronic Pain Sufferers



Despite the controversy

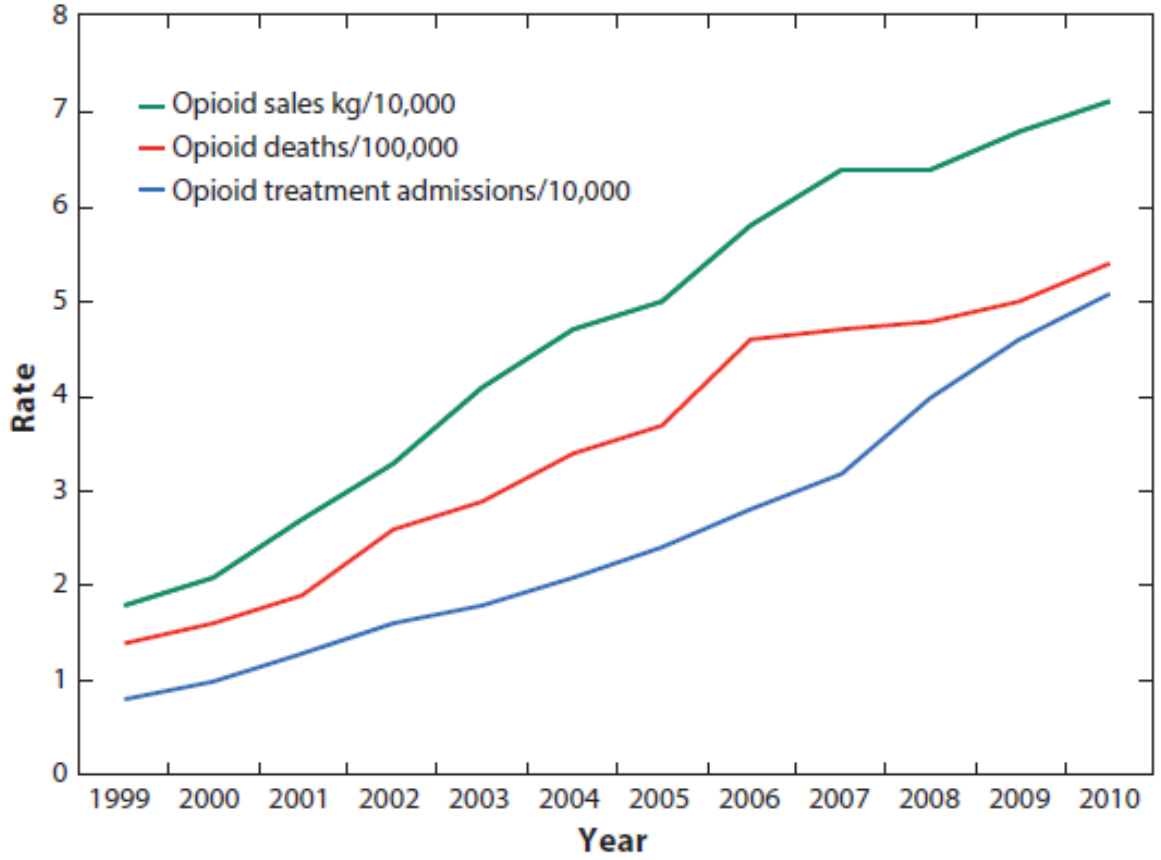
Opioid prescriptions increased tremendously

Prescription Rates



- In 2012, **health care providers wrote 259 million prescriptions** for opioids

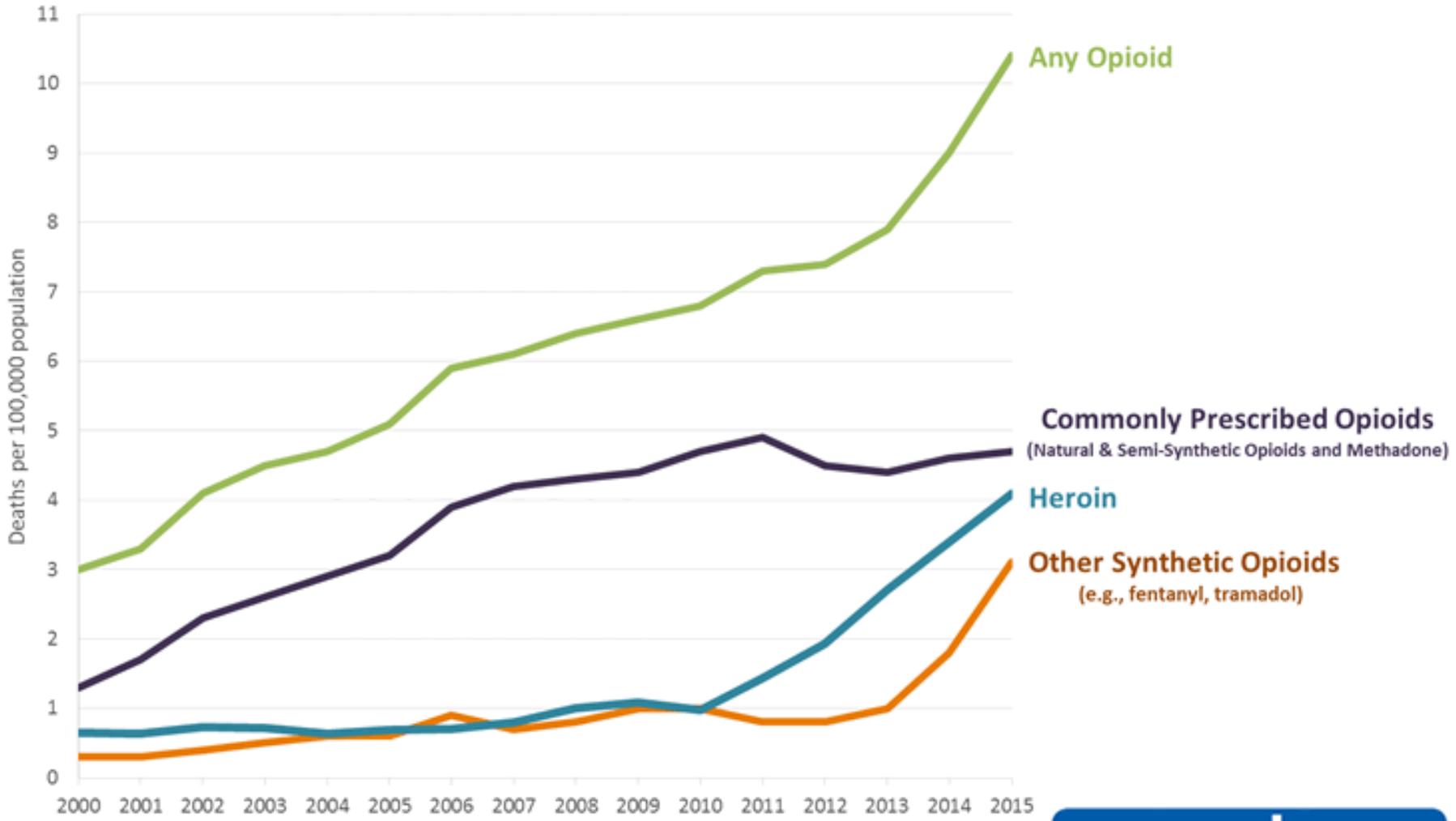
http://www.cdc.gov/drugoverdose/epidemic/providers.html
http://www.cdc.gov/drugoverdose/data/prescribing.html



- Increase in opioid sales is parallel with the increase in opioid deaths

CDC (Cent.Dis.Control Prev.). 2011. Vital signs: overdoses of prescription opioid pain relievers—United States, 1999–2008. *MMWR* 60:1487–92

Overdose Deaths Involving Opioids, United States, 2000-2015



SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2016. https://wonder.cdc.gov/.

www.cdc.gov
Your Source for Credible Health Information

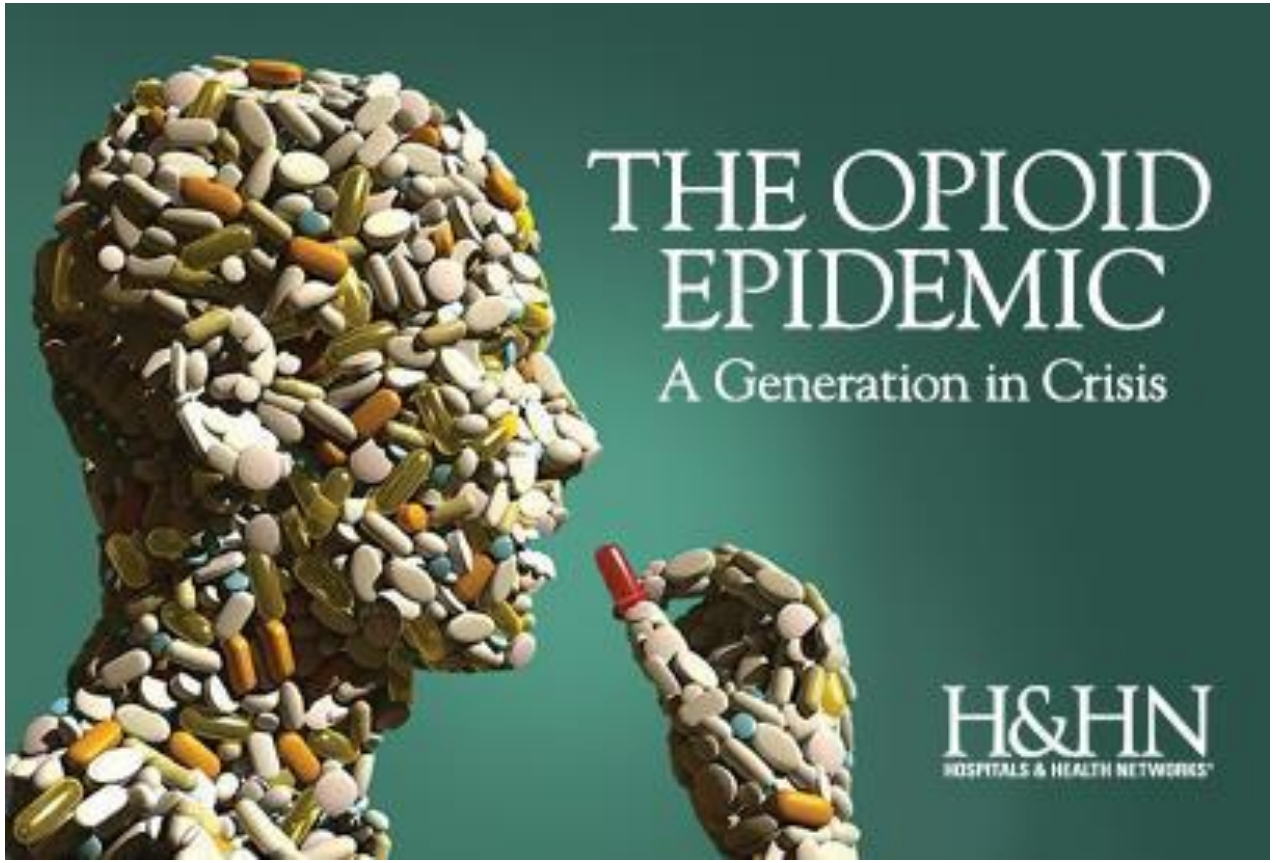
"Opioid epidemic 'getting worse instead of better,' public health officials warn"

—10.5.2017—

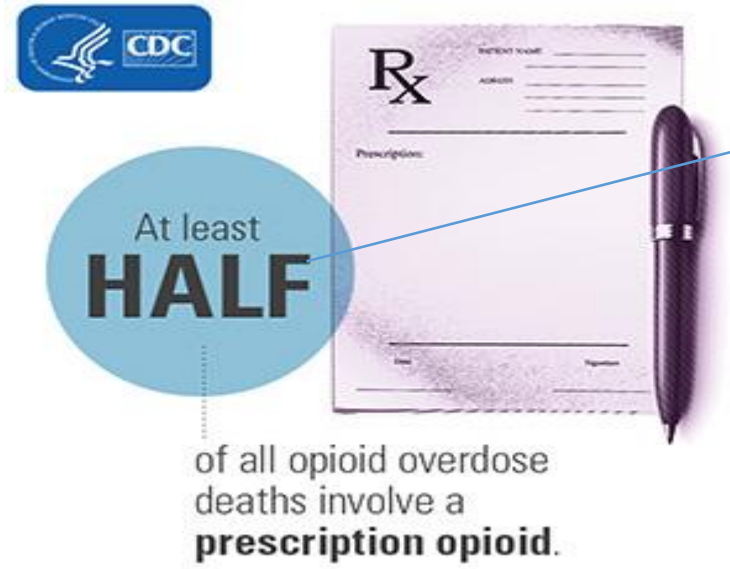
USA TODAY

Opioid epidemic

- worst drug overdose epidemic in US history



Source of opioids



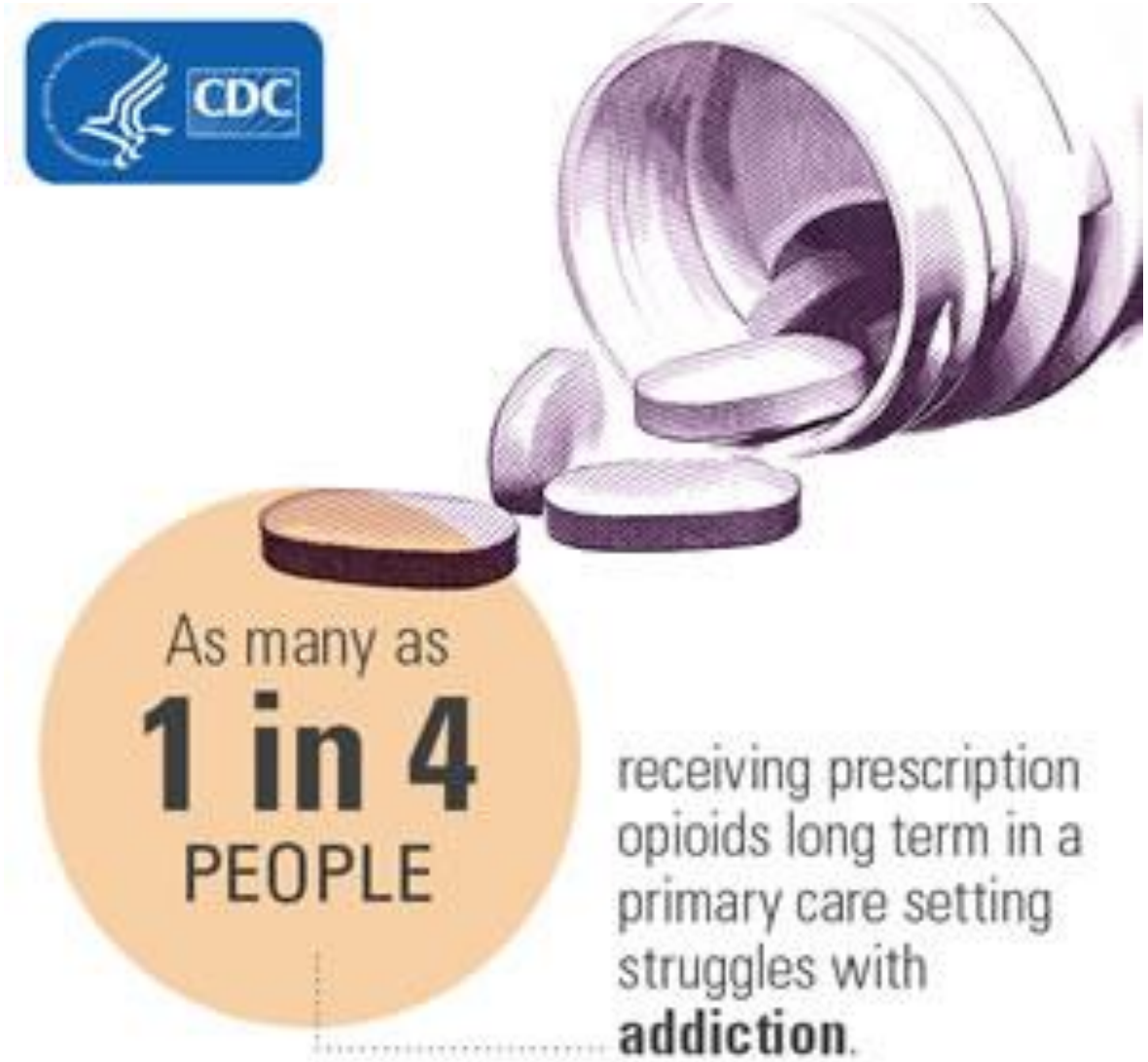
50%

Among those receiving the opioid prescriptions

60% of deaths occurred in patients receiving prescriptions based on prescribing guidelines by medical boards

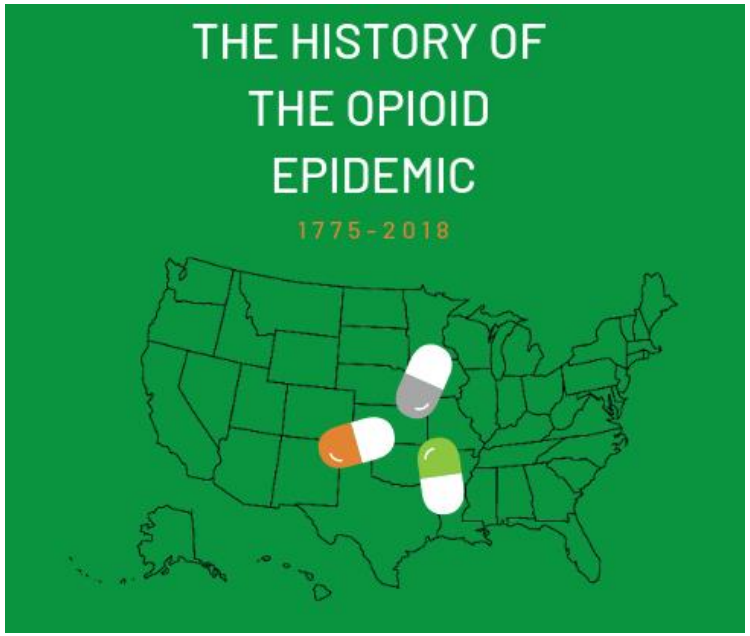
40% of deaths occurred in individuals with substance use disorders who obtained opioids through multiple prescriptions, doctor shopping, and drug diversion.

Manchikanti L, Helm S II, Fellows B, Janata JW, Pampati V, Grider JS, Boswell MV. Opioid epidemic in the United States. Pain Physician 2012; 15:ES9–38.


CDC
As many as
1 in 4
PEOPLE
receiving prescription opioids long term in a primary care setting struggles with addiction.

Drug dealers are no longer the primary source of illicit drugs. Our greatest enemy is now inappropriate prescribing patterns

Machikanti et al. opioid epidemic


THE HISTORY OF
THE OPIOID
EPIDEMIC
1775-2018


OPIOID
EPIDEMIC
Prescription
Analgesics
Addicts
Pills
Doctor
Fatal
Death
Medical
Consumption
Painkillers
Health
Dependence
Drugs
Pain
Crisis
Overdose
Problem
Pills

Opioid epidemic- how they get there..

- About 20 years ago,
- compassionate advocacy for better treatment of chronic pain
- aggressive marketing of opioid formulations
- led to a sharp increase in the prescribing of opioid analgesics for patients with chronic noncancer pain(CNCP) in most developed countries.

Opioid epidemic-how they get there

1970s-80s

NEW PAIN KILLERS
Percocet (oxycodone and acetaminophen)[1] and Vicodin (hydrocodone and acetaminophen)[2] come on the market. Both are short-acting pain relievers.

1980s: OPIOIDS DEEMED 'SAFE'
Two events indicate that opioids are safe to prescribe for chronic pain and not addictive.

One is a letter, "Addiction Rare in Patients Treated with Narcotics," published in the New England Journal of Medicine in 1980. Another is a study, "Chronic Use of Opioid Analgesics in Non-Malignant Pain: Report of 38 Cases," published in 1986 in Pain.

[1] california-drug-rehabs.com, [2] NY Magazine, [3] The New Yorker

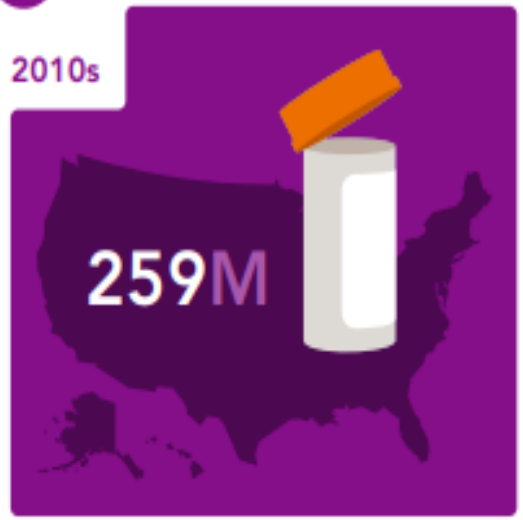
1990s-00s

1996: OXYCONTIN DEBUTS
OxyContin, a long-acting painkiller, hits the market. In an aggressive marketing campaign, the drug's manufacturer claims OxyContin is less addictive than its short-acting cousins, Percocet and Vicodin.[1]

2002: OVERDOSE DEATHS
Overdose deaths from opioid drugs, including heroin, reach over 10,000.[2]

[1] NY Times, [2] National Institute on Drug Abuse

2010s



2012: 259 MILLION
In 2012, the number of prescriptions written for opioid pain medication reaches 259 million, enough for every adult in the United States to have a bottle of pills.[1]

2015: OPIOID DEATHS NEARLY TRIPLE
Overdose deaths from prescription opioids and heroin reach 33,000,[2] almost triple the number of overdose deaths since 1999.[3]

2016: CDC GUIDELINES
The CDC releases guidelines for prescribing opioids for chronic pain. It encourages non-opioid therapies, prescribing lower doses and short-acting opioids, and monitoring progress. These guidelines do not pertain to pain related to cancer, palliative or end-of-life care.[4]

2016: OPIOID DEATHS KEEP RISING
The New York Times estimates drug overdose deaths in 2016 at over 59,000. They are the leading cause of death of Americans under 50.[5]

2016: AND 2017: PRESIDENTS ACT
In 2016 Former President Obama asks Congress for over $1 billion to fight the opioid epidemic.[6] And in 2017 President Trump signs an executive order to create the President's Commission on Combating Drug Addiction and the Opioid Crisis.[7]

[1] CDC, Dowell, [2,4] CDC, [3] National Institute on Drug Abuse, [5,6] NY Times, [7] nbcnews.com

Pain

the 5th vital sign™

American Pain Society

"The biggest misconception is that the U.S. is normal in how it handles prescription opioids."

– Dr. Keith Humphreys, Psychiatry and Behavioral Sciences, Stanford University

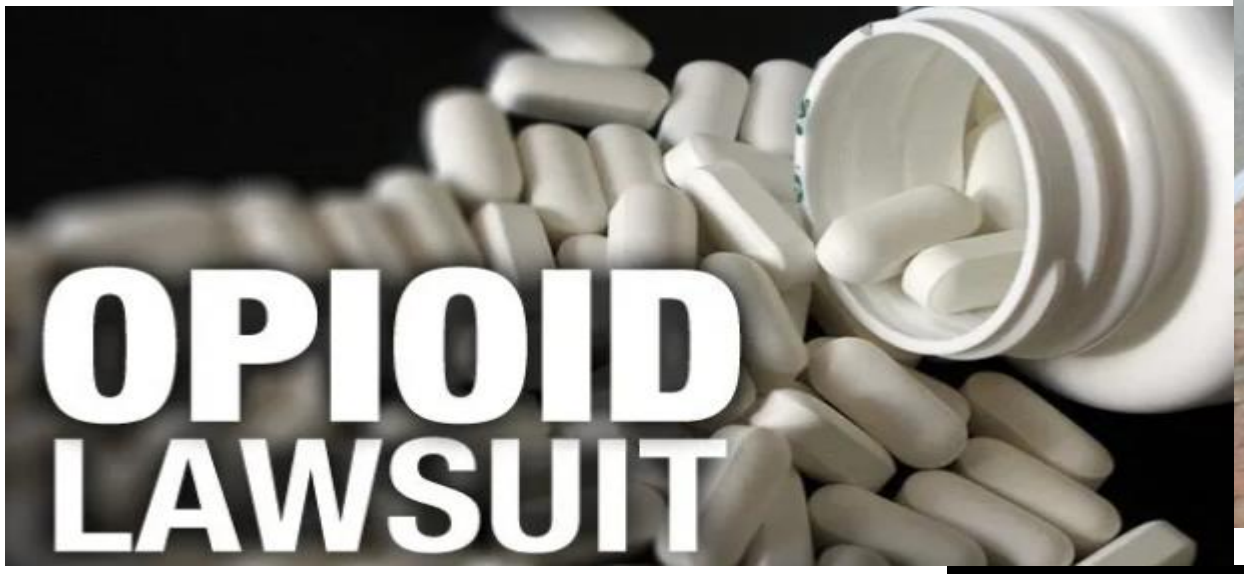
OPIOID CRISIS

- 130+ Americans die each day from opioid overdose
- Drug overdoses killed more Americans in 2016 than the Vietnam War
- Fentanyl most often responsib opioid overdoses

The Washington Post

As opioid epidemic spread, some drug company workers eyed profits: "Just like Doritos, keep eating."

Keep eating



Source: © Josh Reynolds/AP/Shutterstock

The effects of opioid addiction on communities have sparked mass protests against the companies involved in marketing them - particularly Purdue Pharma and its majority shareholders, the Sackler family

People at higher risk of opioid overdose death

- High doses of opioid
- Concurrent use/co-medications of opioids with sedating substances such as benzodiazepine, antidepressants

Opioid doses

50–99 mg/day (3.7- fold increase in overdose risk)

>100 mg/day (8.9-fold increase in overdose risk)

Compared to 1-20 mg/day

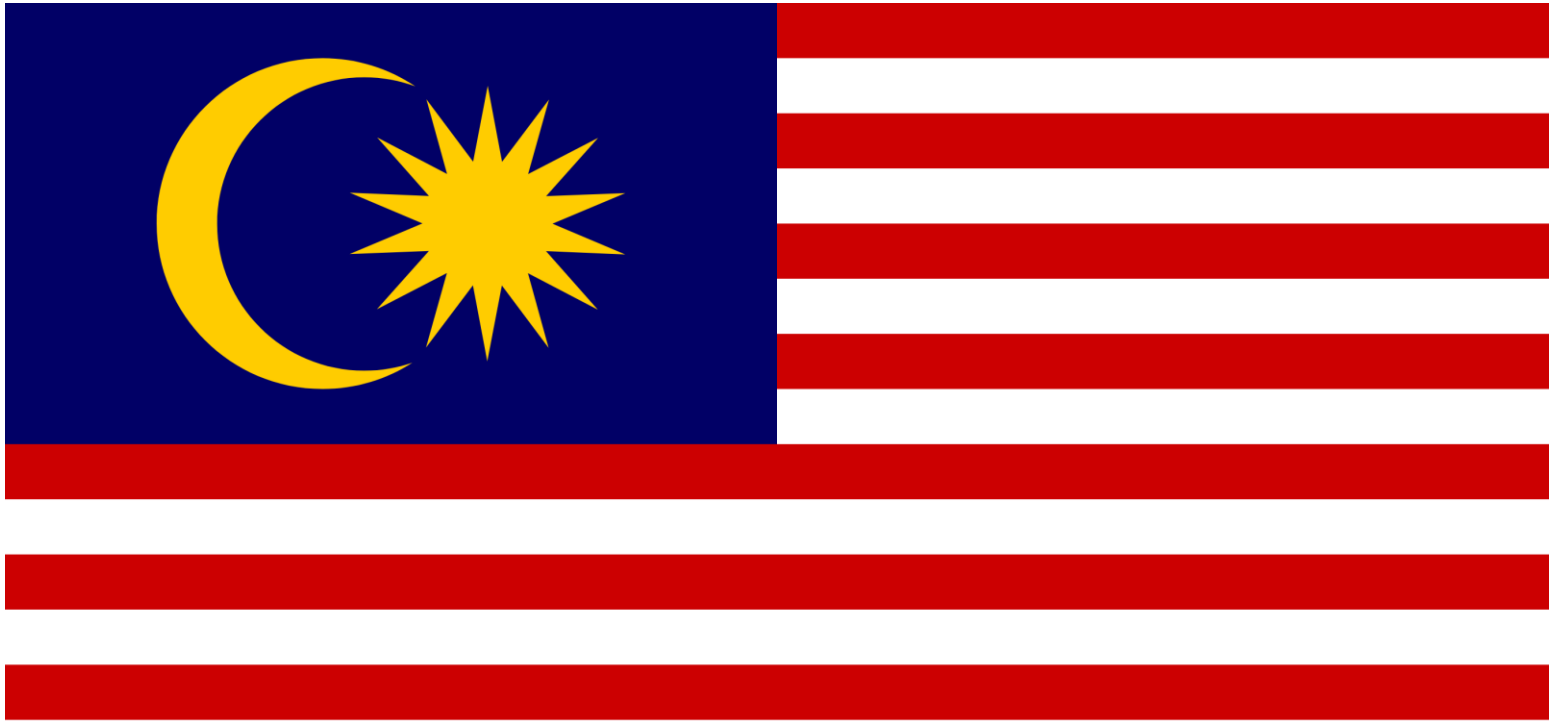
Dunn et al., 2010

Co-medications

It was also reported that the risk of overdose death was increased 15-fold in patients filling both opioid and benzodiazepine prescriptions compared with those filling neither prescription

Peirce GL et al, *Med Care*. 2012;50(6):494–500.

Experience from Malaysia?



Let’s look at our local data

1. Dose and duration of opioid use

ORIGINAL ARTICLE

Dose and Duration of Opioid Use in Patients with Cancer and Noncancer Pain at an Outpatient Hospital Setting in Malaysia

Che S. Zin, PhD*; Norny A. Rahman, PhD*; Che R. Ismail, BPharm*; Leong W. Choy, MClin Pharm†

*Kulliyyah of Pharmacy, International Islamic University Malaysia, Kuantan, Malaysia; †Jabatan Farmasi, Hospital Tengku Ampuan Afzan (HTAA), Kuantan, Malaysia

Zin et.al.,Pain Practice 2016

Patients and methods

Outpatient opioid prescriptions from 2013- 2014

Patient level opioid use

1015 opioid prescriptions for 347 patients

Opioid dose in oral morphine equivalents(OMEQ)

OMEQ

$$= Quantity\ of\ opioid\ for\ each\ prescription\ \times strength\ (mg) \times Equianalgesic\ ratio\ of\ opioid$$

Total OMEQ per patient

$$= Sum\ of\ OMEQ\ for\ each\ patient\ for\ a\ particular\ year$$

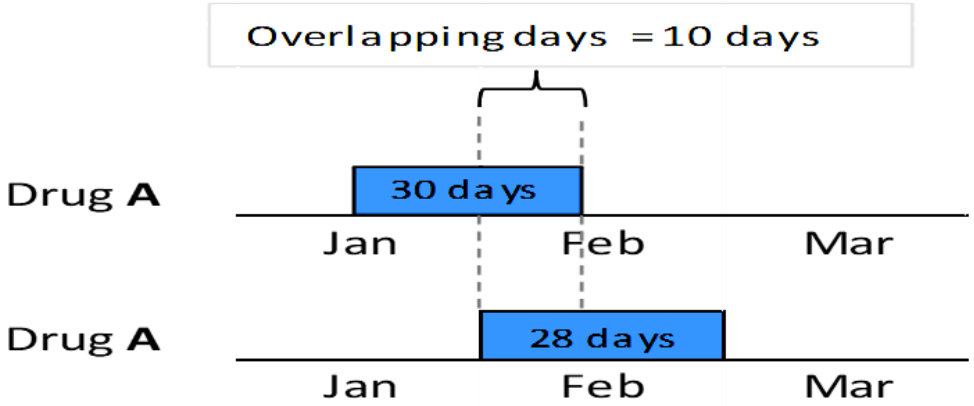
Dose per day

$$= \frac{Total\ OMEQ\ dose\ for\ each\ patient\ \ during\ \ a\ particular\ year}{Total\ days\ of\ supply\ for\ each\ patient\ \ during\ a\ partciular\ year}$$

Days of Supply

$$\textbf{Days of supply} = \frac{Quantity\ supply\ of\ each\ prescription}{Number\ of\ daily\ dose}$$

- **Total days supply per patient during a particular year** were calculated by adding the days supply of each prescription prescribed for a particular patient during the year.
- The overlapping days between the prescriptions for each patient were subtracted from the total days supply to derive the actual duration of days supply



Total days supply = 58 days - 10 days
= 48 days

STATA® release 15

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. regress pri mpg wei for leng turn displ , cl(rep)

Regression with robust standard errors                Number of obs =        69
                                                      F(  3,     4) =         .
                                                      Prob > F      =         .
                                                      R-squared     =    0.5762
Number of clusters (rep78) = 5                        Root MSE      =    1985.6

------------------------------------------------------------------------------
             |               Robust
       price |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         mpg |  -18.41822   55.51588    -0.33   0.757    -172.5947    135.7583
      weight |   4.751837   .5855439     8.12   0.001     3.126186    6.377487
     foreign |   3495.959   918.6167     3.81   0.019     945.4697    6046.447
      length |  -78.42922   19.86622    -4.11   0.015    -131.3655   -25.49292
        turn |  -128.8468   132.6541    -0.97   0.386    -497.1536    239.461
displacement |   11.1948   2.387374     4.69   0.009     4.564391    17.82522
       _cons |   8744.885   8998.512     0.97   0.386    -16238.99    33728.76
------------------------------------------------------------------------------
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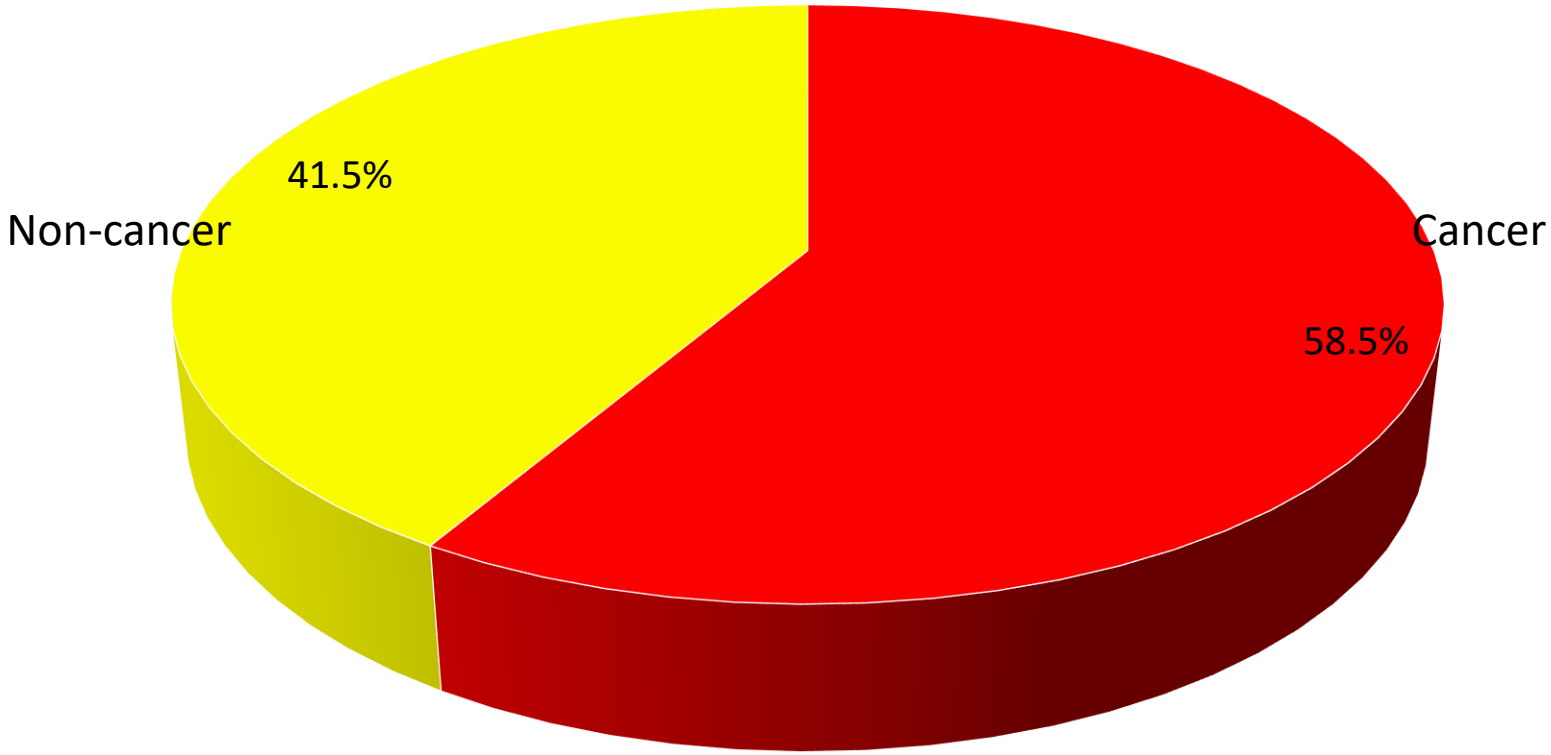
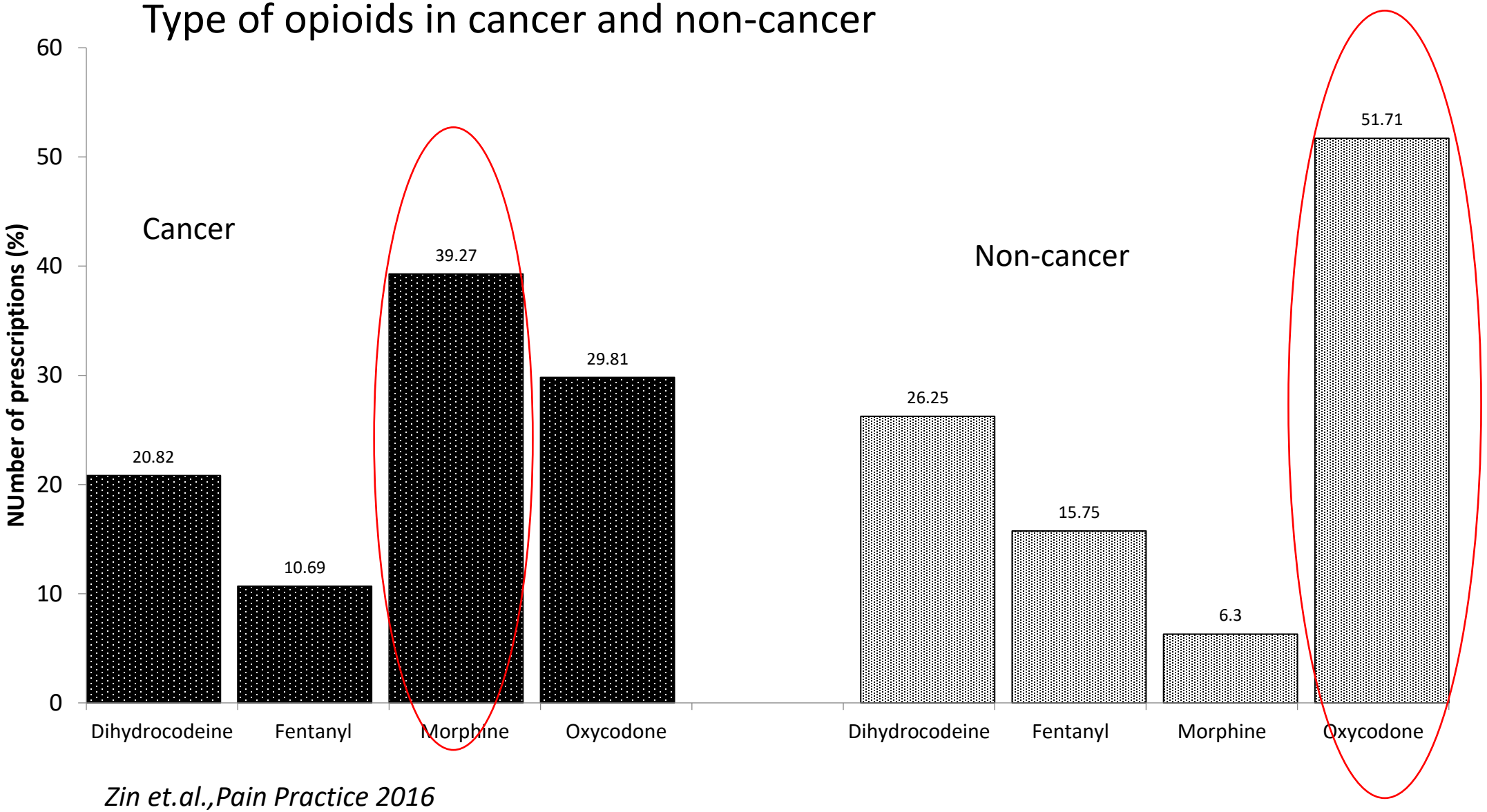
Opioid prescriptions issued for patients with cancer and non-cancer



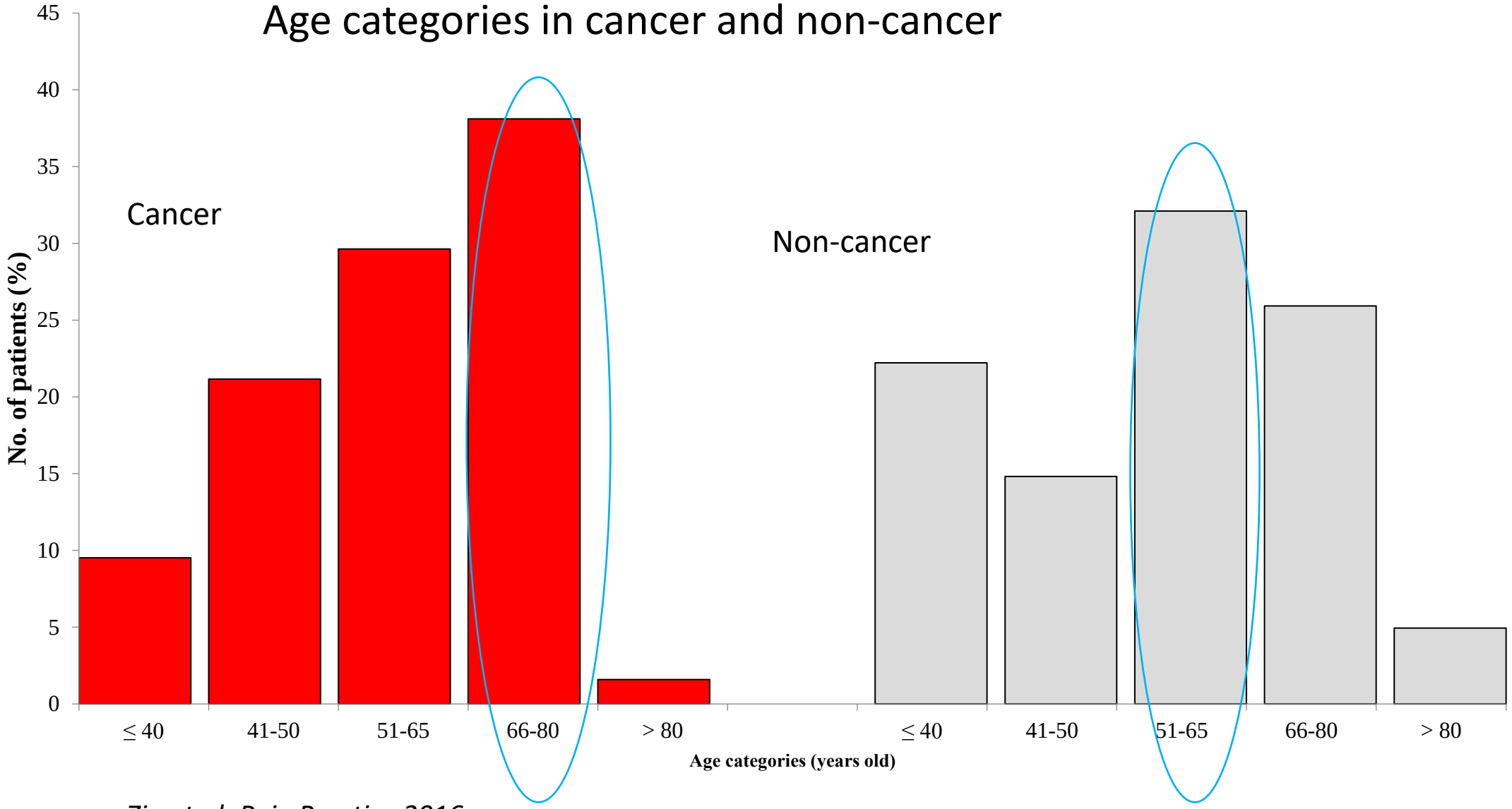
Zin et.al.,Pain Practice 2016

Type of opioids in cancer and non-cancer



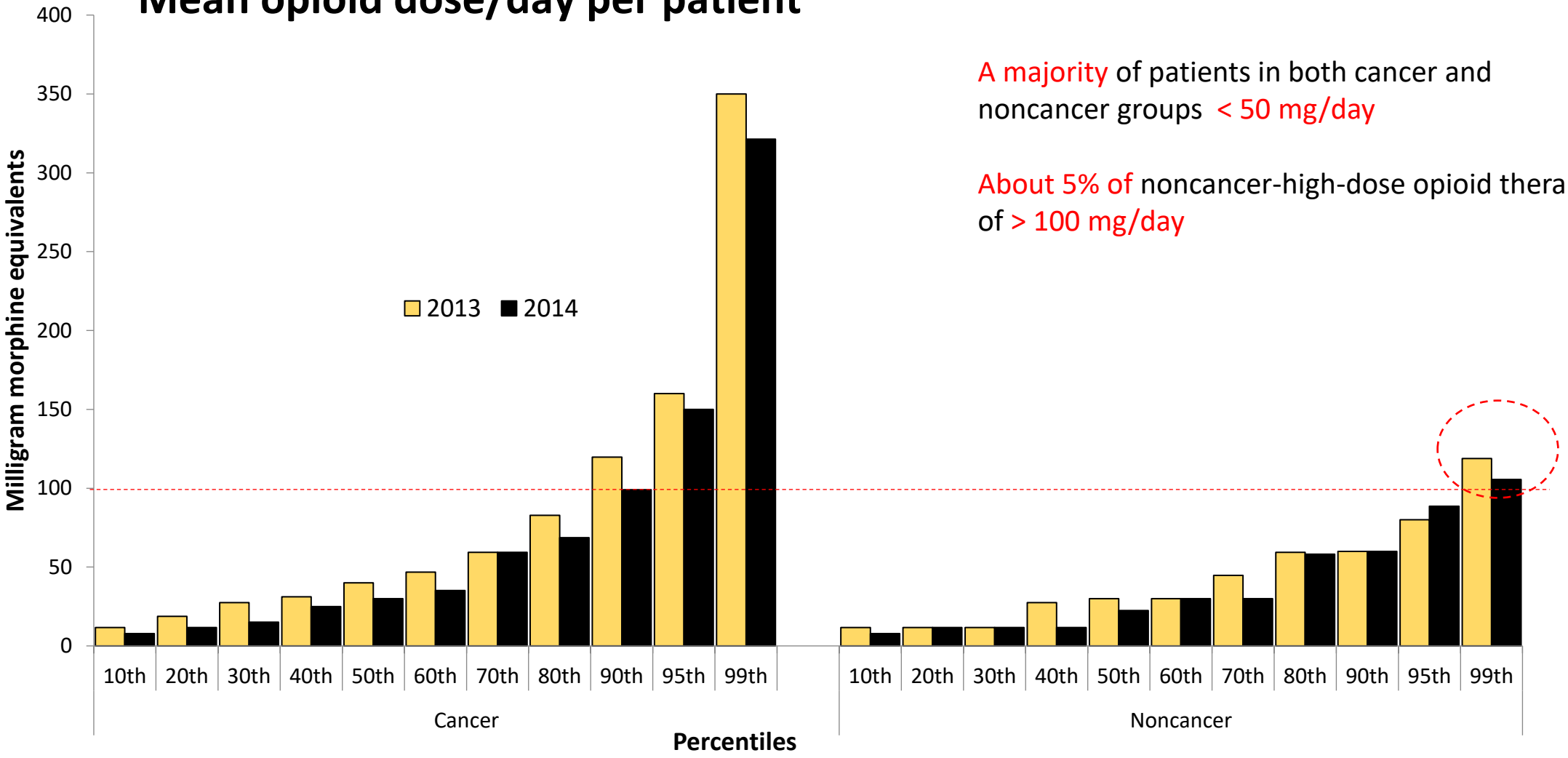
Zin et.al.,Pain Practice 2016

Age categories in cancer and non-cancer



Zin et.al.,Pain Practice 2016

Mean opioid dose/day per patient

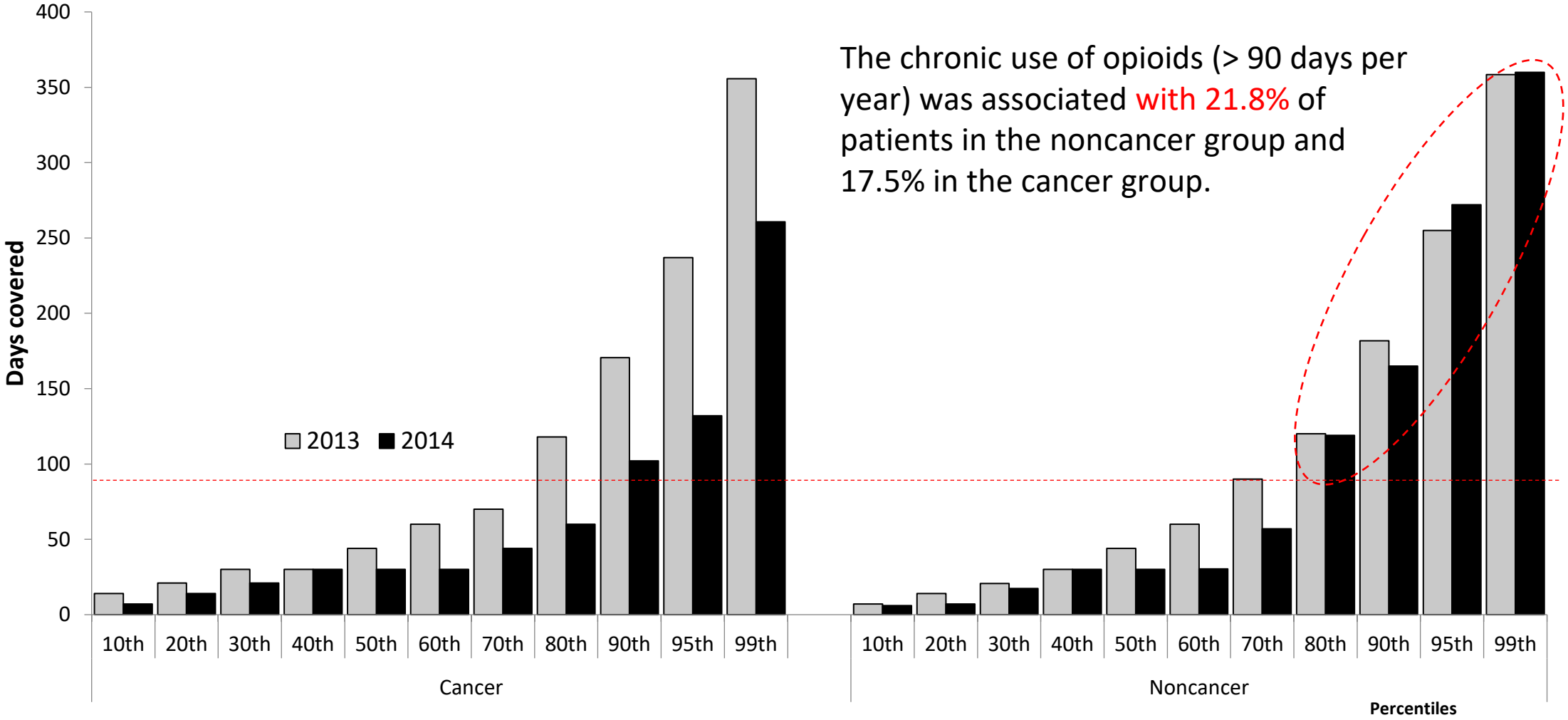


A majority of patients in both cancer and noncancer groups < 50 mg/day

About 5% of noncancer-high-dose opioid therapy of > 100 mg/day

Zin et. al., Pain Practice 2016

Mean total days covered with opioid per patients



The chronic use of opioids (> 90 days per year) was associated with 21.8% of patients in the noncancer group and 17.5% in the cancer group.

Zin et. Al., Pain Practice 2016

Main findings

- ~40% for non-cancer pain and ~60% for cancer pain
- Oxycodone was the most prescribed for non-cancer pain
- A majority of patients were prescribed < 50 mg/day
- ~5% of patients with noncancer pain –high dose opioid therapy of > 100 mg/day
- Chronic use of opioids in 21.8% (non-cancer group) and 17.5% (cancer group)

The patterns of opioid use in patients with noncancer pain were similar to those found in other studies

2. Co-medications

Journal of Pain Research

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Co-prescription of opioids with benzodiazepine and other co-medications among opioid users: differential in opioid doses

This article was published in the following Dove Press journal:
Journal of Pain Research
25 January 2017
Number of times this article has been viewed

Che Suraya Zin
Fadhilah Ismail

Kulliyyah of Pharmacy, International Islamic University Malaysia, Bandar Indera Mahkota, Kuantan, Pahang, Malaysia

Purpose: This study investigated the patterns of opioid co-prescription with benzodiazepine and other concomitant medications among opioid users. Opioid dose in each type of co-prescription was also examined.

Patients and methods: This cross-sectional study was conducted among opioid users receiving concomitant medications at an outpatient tertiary hospital setting in Malaysia. Opioid prescriptions (morphine, fentanyl, oxycodone, dihydrocodeine and tramadol) that were co-prescribed with other medications (opioid + benzodiazepines, opioid + antidepressants, opioid + anticonvulsants,

Patients and methods

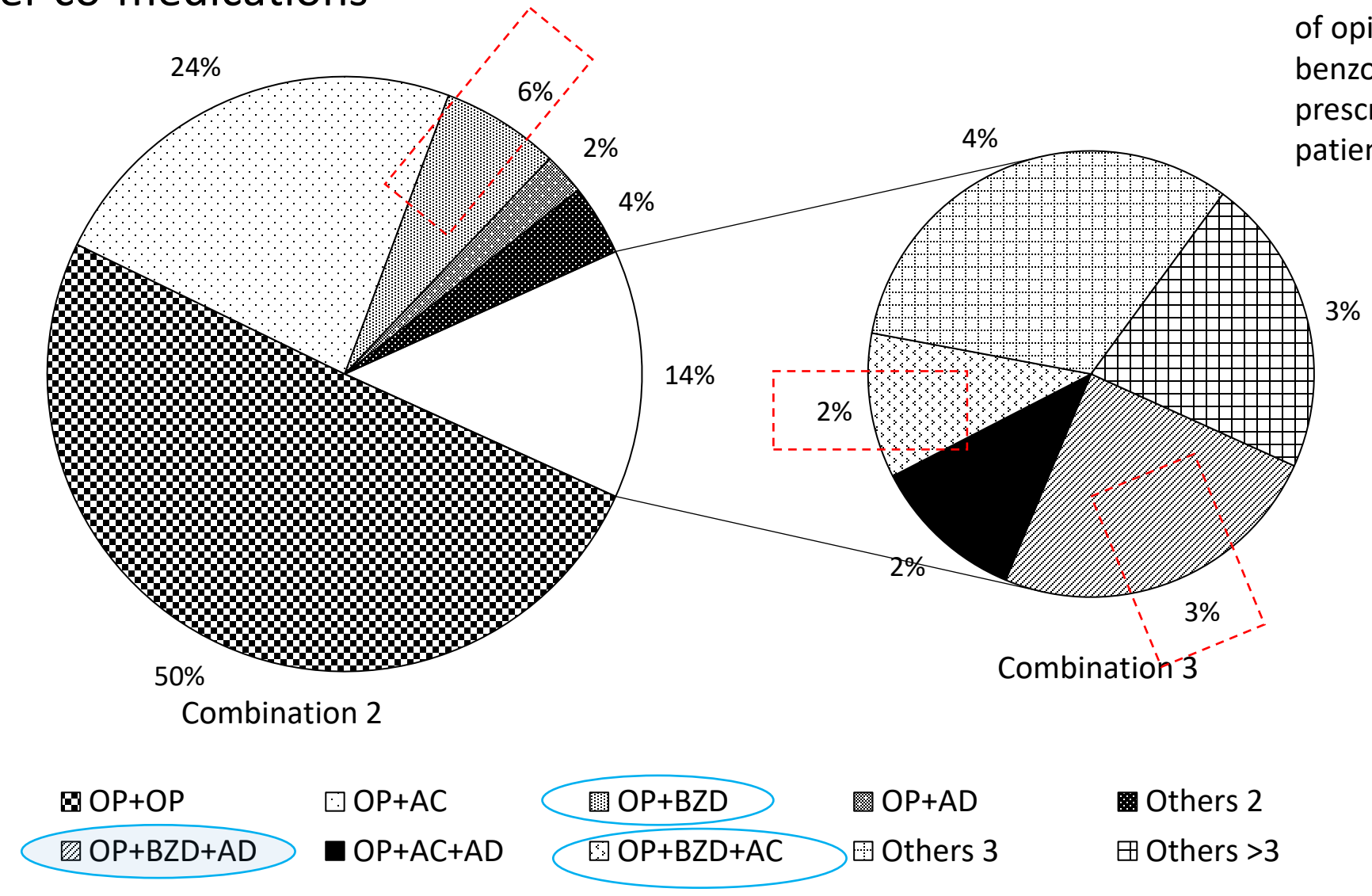
Outpatient opioid prescriptions from 2013- 2014

Patient level opioid use

1059 opioid prescriptions for 276 patients

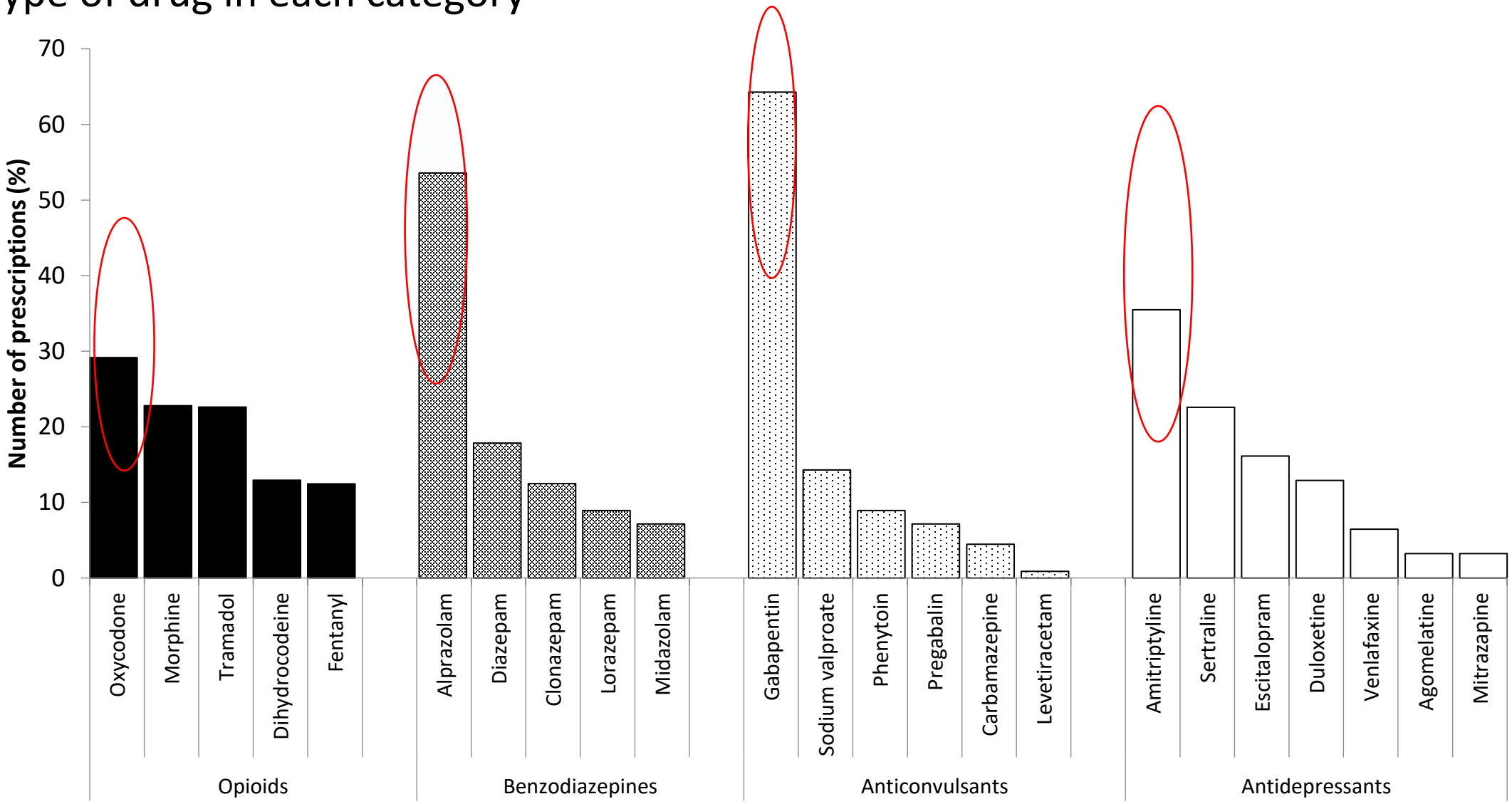
Co-prescriptions of opioid with benzodiazepines and other co-medications

The co-prescriptions of opioid with benzodiazepine were prescribed to 12.3% of patients,



Zin et.al.,Pain Practice 2016

Type of drug in each category



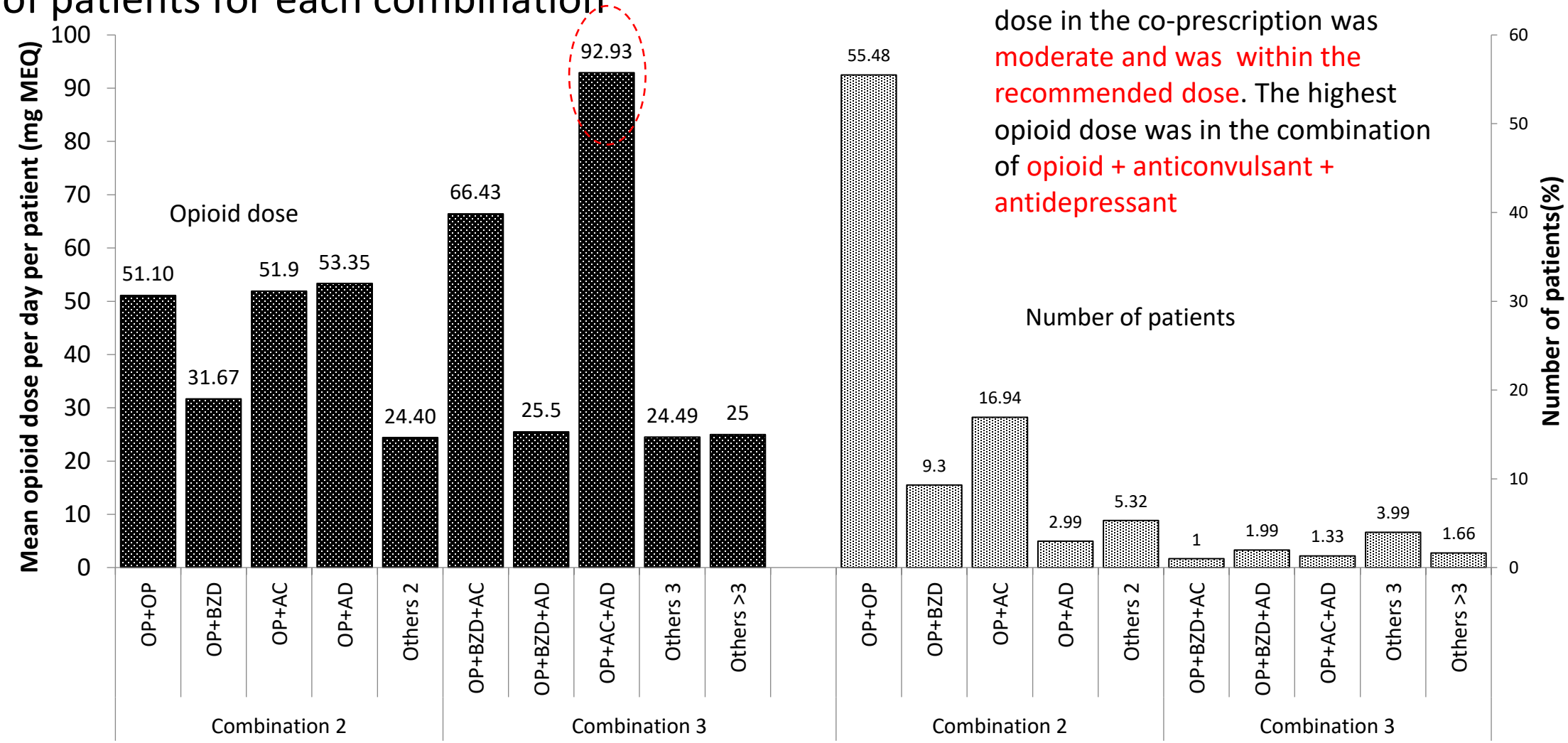
Zin et.al.,Pain Practice 2016

Table 1 Details of opioid combinations and the most common drugs used in each combination

Category	Combination	Details of combination	Most common drugs used in each combination
Combination 2	OP + OP	Opioid + opioid	Morphine + oxycodone
	OP + BZD	Opioid + benzodiazepine	Tramadol + alprazolam
	OP + AC	Opioid + anticonvulsant	Oxycodone + gabapentin
	OP + AD	Opioid + antidepressant	Oxycodone/morphine/fentanyl + amitriptyline
	Others 2	Opioid + hypnotics or opioid + antipsychotic	Tramadol + zolpidem + haloperidol
Combination 3	OP + BZD + AC	Opioid + benzodiazepine + anticonvulsant	Tramadol + alprazolam + sodium valproate
	OP + BZD + AD	Opioid + benzodiazepine + antidepressant	Tramadol + alprazolam + sertraline
	OP + AC + AD	Opioid + anticonvulsant + antidepressant	Tramadol/fentanyl + gabapentin + amitriptyline
	Others 3	Opioid + benzodiazepine + hypnotics or opioid + benzodiazepine + antipsychotics or opioid + anticonvulsant + hypnotics or opioid + antidepressant + hypnotics or opioid + anticonvulsant + antipsychotics or opioid + antipsychotics + hypnotics	Tramadol + zolpidem + olanzapine + alprazolam
	Others >3	Others >3 (more than three drugs combination)	Tramadol + alprazolam + quetiapine + sodium valproate

Abbreviations: OP, opioid; BZD, benzodiazepine; AC, anticonvulsant; AD, antidepressant.

Mean opioid dose/day per patients and number of patients for each combination



The individual opioid dose in the co-prescription was moderate and was within the recommended dose. The highest opioid dose was in the combination of opioid + anticonvulsant + antidepressant

Zin et.al.,Pain Practice 2016

Main findings

- 12.3% of patients received co-prescriptions of opioid + benzodiazepine
- Dose of opioid in this combination 31 to 66 mg/day
- Tramadol and alprazolam was the main combination of opioid and BZD
- For controlled drug (oxycodone and alprazolam) the main combination

- The overall findings on the use of co-medications in this study reflect the prevalence of comorbidities and more severe pain among opioid users, and this biopsychosocial issue of chronic pain requires comprehensive approaches involving multidisciplinary pain management team
- In view of safety concerns with certain co-prescriptions, those who were using opioids with benzodiazepines appear to represent a particularly high-risk group.

3. Patterns of initial opioid prescribing

BMJ Open

Patterns of initial opioid prescription and its association with short-term and long-term use among opioid-naïve patients in Malaysia: a retrospective cohort study

Che Suraya Zin,[1] Nor Ilyani Nazar,[1] Norny Syafinaz Abdul Rahman,[1] Wan Rohaidah Ahmad,[2] Nurul Sahida Rani,[3] Kim Swan Ng[4]

To cite: Zin CS, Nazar NI, Rahman NSA, *et al*. Patterns of initial opioid prescription and its association with short-term and long-term use among opioid-naïve patients in Malaysia: a retrospective cohort study. *BMJ Open* 2019;**9**:e027203. doi:10.1136/bmjopen-2018-027203

ABSTRACT

Objective This study examined opioid prescription initiation patterns and their association with short-term and long-term opioid use among opioid-naïve patients.

Design This study was designed as a retrospective cohort study.

Setting and participants In this study, we analysed the prescription databases of tertiary hospitals in Malaysia. This study included patients aged ≥18 years with at

Strengths and limitations of this study

- The novel use of initial prescription data to identify patient characteristics associated with short-term and long-term use of opioids is a strength.
- The findings are robust as the analysis addressed all aspects of the study and results were based on a large sample from tertiary care settings.
- The analysis did not consider opioid prescriptions

BMJ Open: first published as 10.1136/bmjopen-2018-027203 on 2 July 20

Patients and methods

- Patient level opioid use
- Age >18 years with at least with one opioid prescription
- 2011-2016
- 33752 opioid naïve patients who received 43432 opioid prescriptions
- Opioid naïve patients (had no opioid prescriptions in the 365 days prior the study) and were followed 365 days after the initial opioid prescription

Dose/day and day supply in patients who became short and long term opioid users

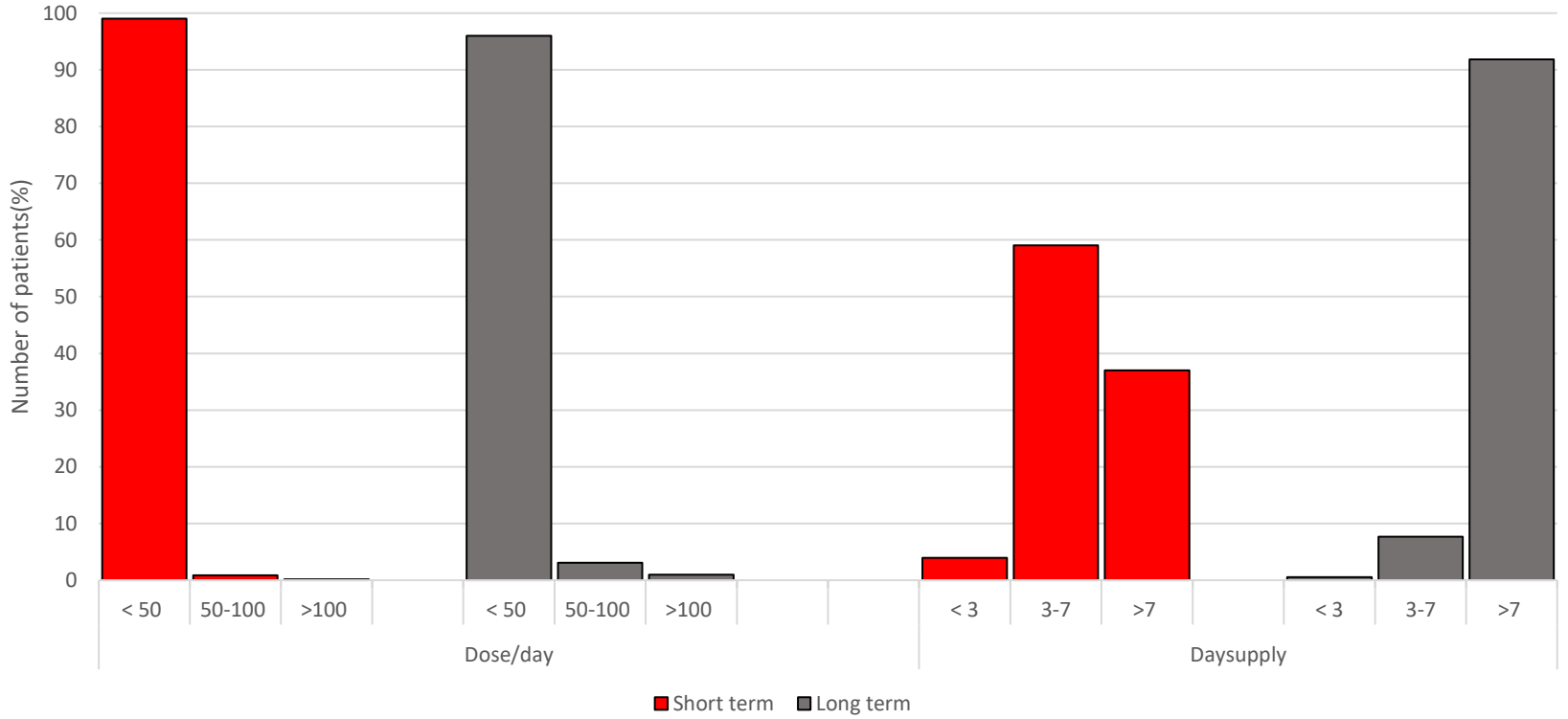


Fig 1 Dose per day and day supply per patient in patients who became short or long term users after the initiation of opioid

Formulation and department

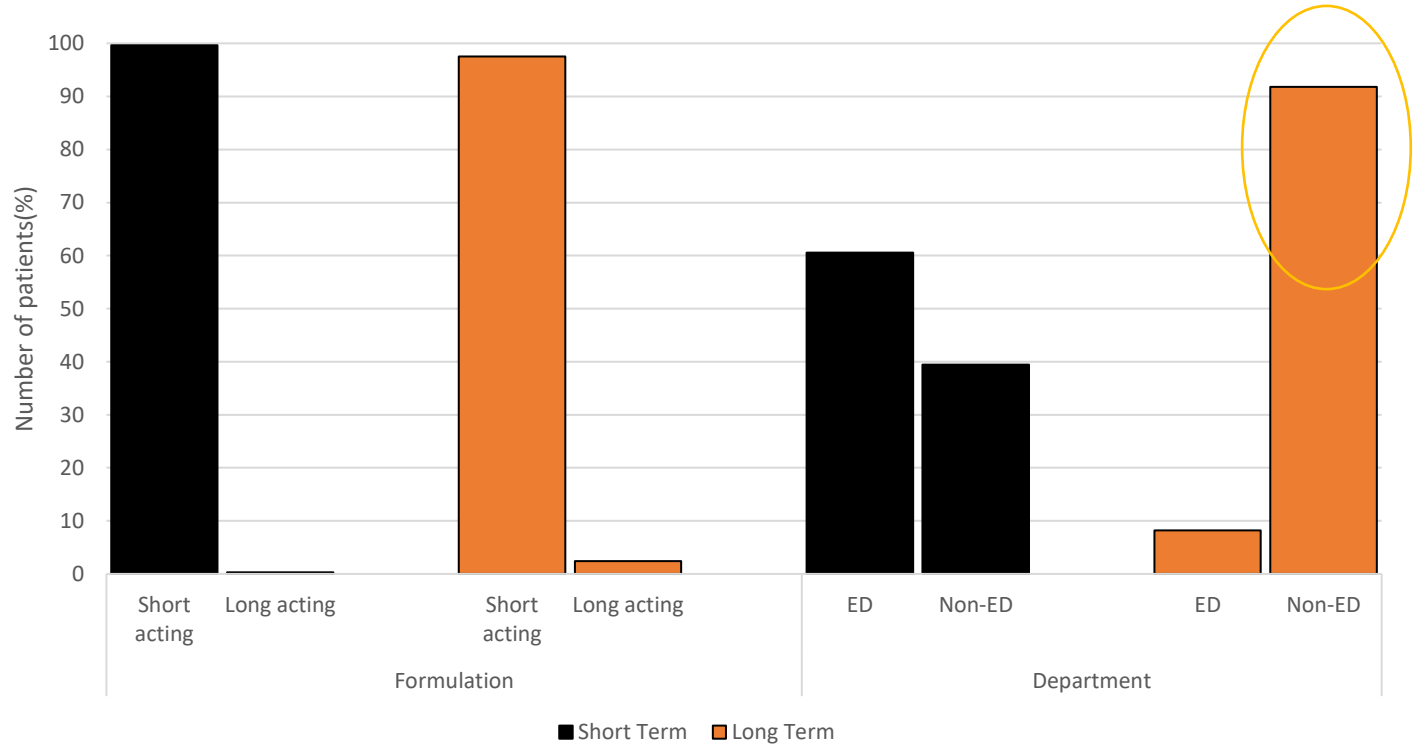


Fig 2 Department issuing the opioid and formulation of opioid during the initial prescription in patients who became short term and long term opioid users.

Main findings

- 11.6% of opioid-naïve patients became long-term opioid users in the subsequent 365 days after receiving their initial opioid prescription in a Malaysian tertiary hospital setting.

Main findings

- During the initial opioid prescription,
  - Short-term opioid users were predominantly prescribed opioids
    - For 3–7 days (59.06%)
    - by the emergency department (ED, 60.56%),
  - Long-term opioid users were primarily prescribed opioids
    - For ≥7 days (91.85%) by
    - By non-ED hospital departments (91.8%).
- Factors associated with long-term opioid use:
  - increasing opioid daily doses, prescription period ≥7 days and long-acting opioids initiated by non-EDs

- CDC recommends the use of opioid therapy for ≤3 days, and states that therapy for >7 days is seldom required
- Because treatment for acute pain often leads to long-term opioid use

Edlund MJ et al *Clin J Pain* 2014;30:557–64.
Dowell D et al .*JAMA* 2016;315:1624–45.

- Information regarding the high-risk characteristics of initial opioid prescriptions is important as acute opioid therapy can quickly progress to long-term use. This information may help clinicians to have greater control over opioid prescriptions to mitigate the chances of unintentional chronic use of opioids.

4. Opioid dose escalation

Journal of Pain Research

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ORIGINAL RESEARCH

Sex differences in high opioid dose escalation among Malaysian patients with long term opioid therapy

This article was published in the following Dove Press journal:
Journal of Pain Research

Che Suraya Zin[1]
Nor Elina Alias[1]
Nor Hidayah Taufek[1]
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Purpose: This study evaluated the risk of opioid dose escalation as it relates to sex differences among patients receiving opioids for long-term therapy.

Patients and methods: This retrospective cohort study was conducted in tertiary hospital settings in Malaysia using electronic prescription records. Opioid naïve patients, aged ≥18 years, who were undergoing long-term opioid therapy of ≥90 days, with at least one opioid prescription (buprenorphine, morphine, oxycodone, fentanyl, dihydrocodeine or tramadol) between 1st January 2011 and 31st December 2016, were included in the study. They were followed until (i) the end of the study period, (ii) death from any cause or (iii)

://www.dovepress.com/ by 210.48.221.4 on 24-Apr-2019
sonal use only.

Patients and methods

- Retrospective cohort study
- Opioid naïve patients, aged ≥18 years, who were undergoing long-term opioid therapy of ≥90 days, with at least one opioid prescription
- 1st January 2011 and 31st December 2016
- They were followed until (i) the end of the study period, (ii) death from any cause or (iii) discontinuation of therapy from their first opioid prescription without any intervals of ≥120 days between successive prescriptions.
- A total of 4688 patients (58.8% women, 41.3% men) on long-term opioid therapy were identified.

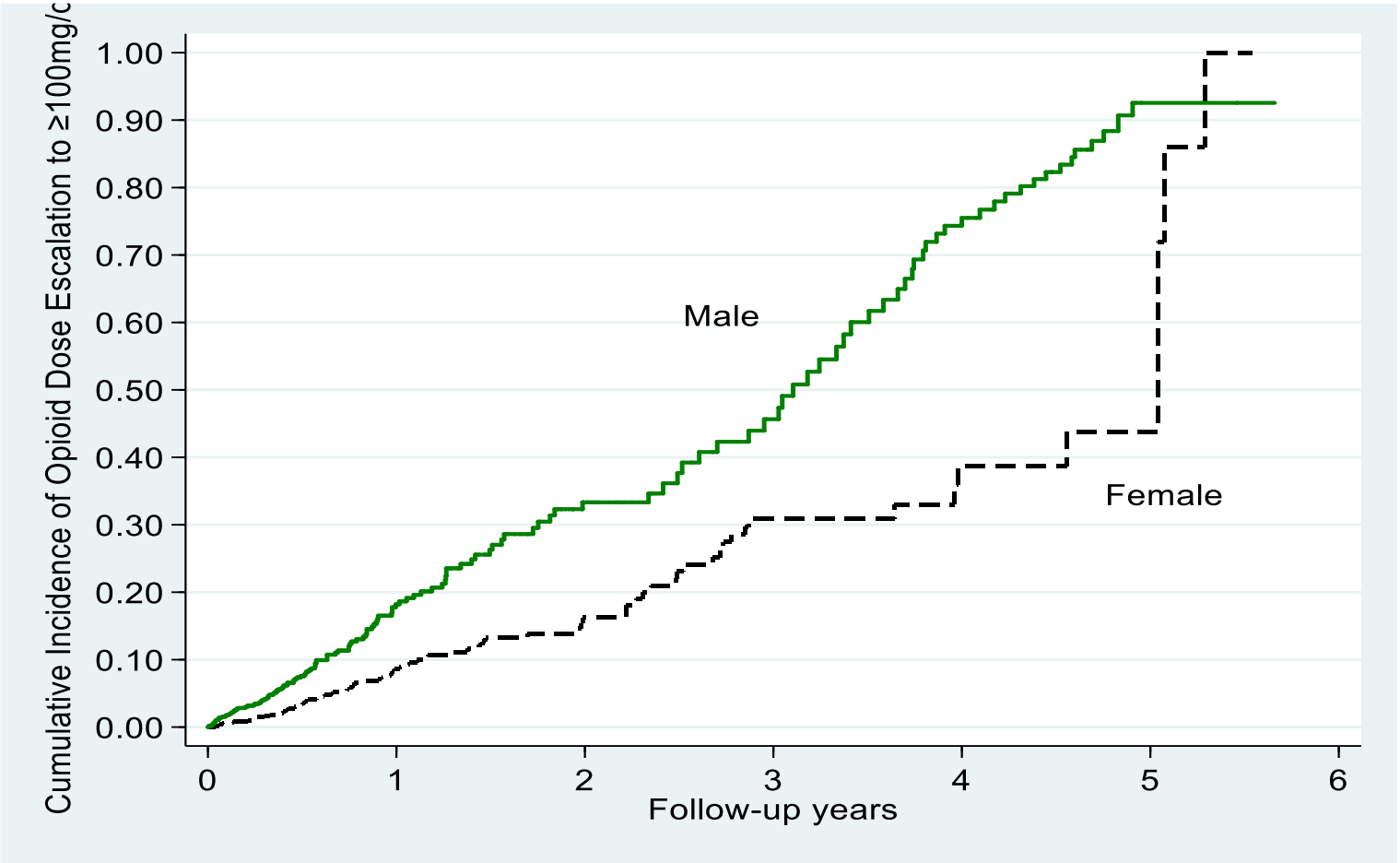

Figure 1. Kaplan-Meier curves of high opioid dose escalation to an average daily dose exceeding 100 mg of morphine (or equivalent) among men and women

Main findings

- Among long term opioid users, 248 (5.29%) were escalated to high opioid doses of ≥100 mg/day and 69 (1.47%) were escalated to ≥200 mg/day.
- female patients were prescribed long-term opioid therapy more frequently than men
- The risk of high-dose opioid escalation was more likely to occur in men than in women

Among the patients with long-term opioid therapy, men are at higher risk of high dose escalation of opioid compared to women. Opioid related morbidity and mortality can be prevented by understanding the different risk associated with prescription opioid use by sex differences. Further research is needed to identify other risks of opioid related harms and its related outcomes in order to stratify the risk. Such an endeavour can be an effort towards minimising the unwanted consequences of opioid therapy

5. Overall analgesic use

Journal of Pain Research

Dovepress
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Open Access Full Text Article

ORIGINAL RESEARCH

Trends and patterns of analgesic prescribing in Malaysian public hospitals from 2010 to 2016: tramadol predominately used

This article was published in the following Dove Press journal:
Journal of Pain Research

Che Suraya Zin[1]
Nor Ilyani Nazar[1]
Norny Syafinaz Rahman[1]
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Wan Rohaidah Ahmad[2]
Nurul Sahida Rani[3]
Mary Suma Cardosa[4]
Kim Swan Ng[4]
Felicia Loh Ye[5]

Purpose: To examine the trends of analgesic prescribing at public tertiary hospital outpatient settings and explore the patterns of their utilization in nonsteroidal anti-inflammatory drugs (NSAIDs), tramadol, and opioid patients.

Patients and methods: This cross-sectional study was conducted from 2010 to 2016 using the prescription databases of two tertiary hospitals in Malaysia. Prescriptions for nine NSAIDs (ketoprofen, diclofenac, celecoxib, etoricoxib, ibuprofen, indomethacin, meloxicam, mefenamic acid, and naproxen), tramadol, and five other opioids (morphine, fentanyl, oxycodone, dihydrocodeine, and buprenorphine) were included in this study. Annual number of patients and prescriptions were measured in repeat cross-sectional estimates. Descriptive statistics and linear

Patients and methods

- Cross-sectional study was conducted from 2010 to 2016 using the prescription databases of two tertiary hospitals in Malaysia.
- Prescriptions for nine NSAIDs (ketoprofen, diclofenac, celecoxib, etoricoxib, ibuprofen, indomethacin, meloxicam, mefenamic acid, and naproxen), tramadol, and five other opioids (morphine, fentanyl, oxycodone, dihy- drocodeine, and buprenorphine) were included in this study.
- 192,747 analgesic prescriptions of the nine NSAIDs, tramadol, and five other opioids were given for 97,227 patients

Number of prescriptions over 7 years

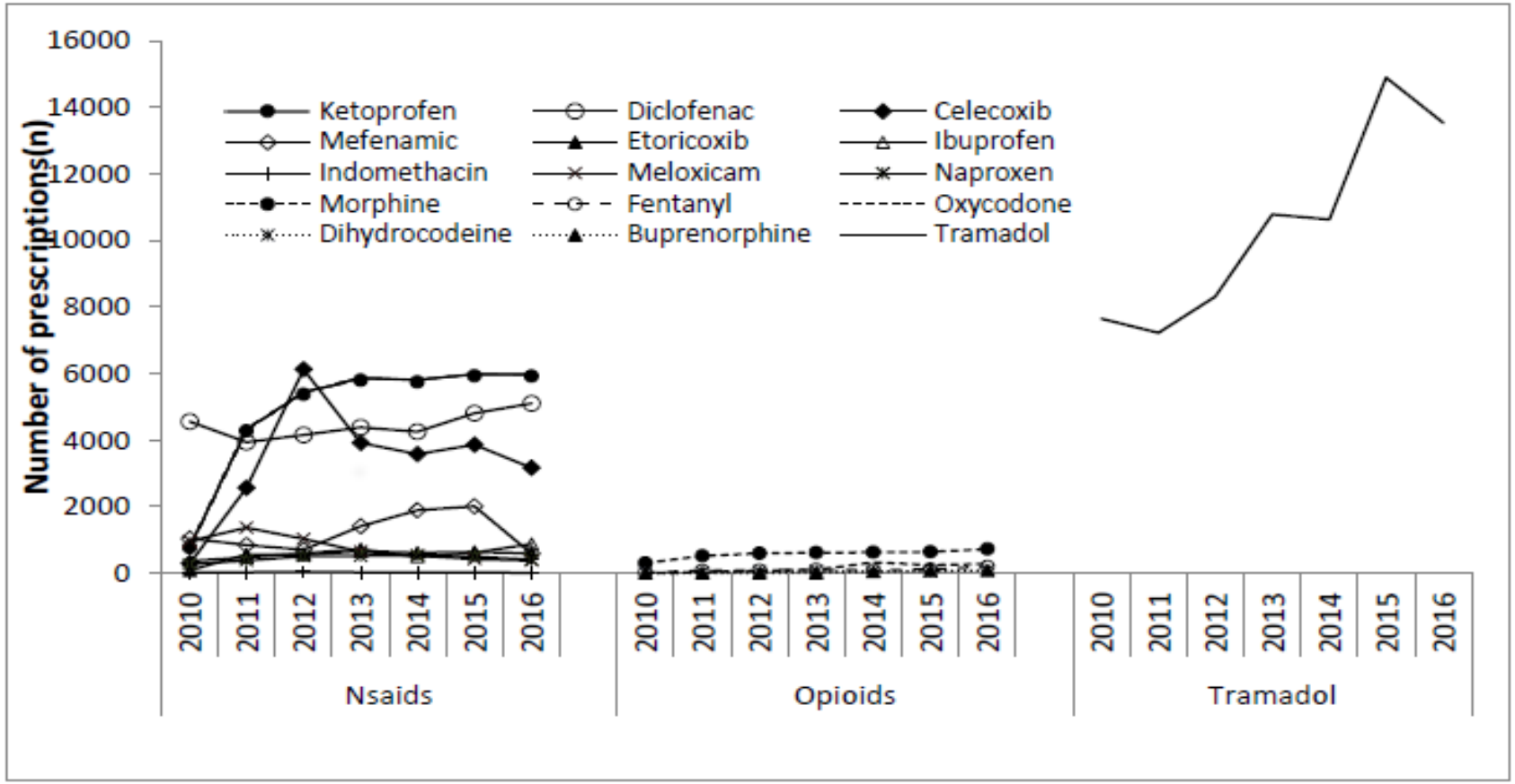

Figure 1 Number of prescriptions for Nsaids, Opioids and Tramadol from 2010 to 2016

Number of patients

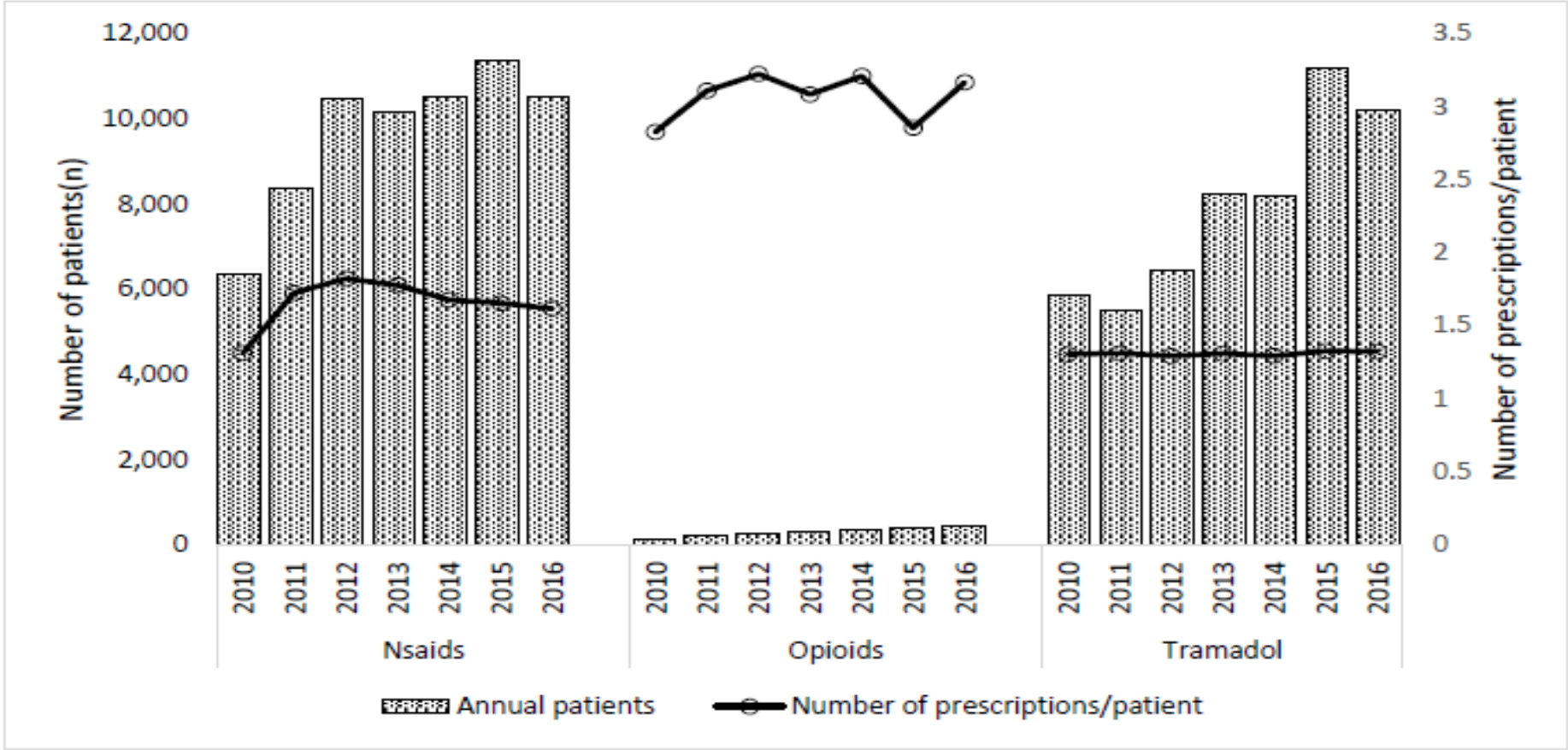

Figure 2 Number of annual patients and number of prescriptions per patient for Nsaids, Opioids and Tramadol from 2010 to 2016

Issuing departments

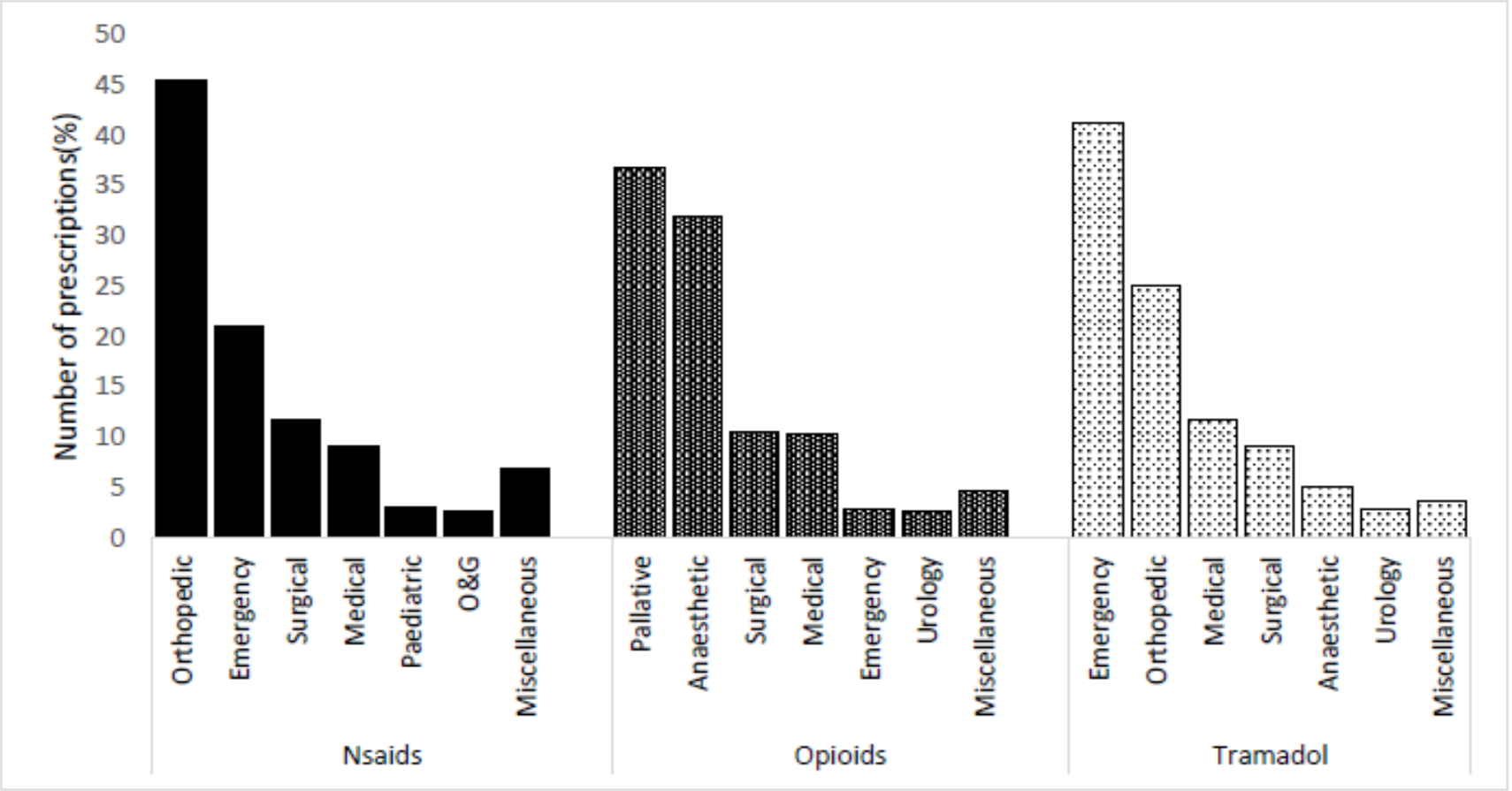

Figure 3 Prescribing of Nsaids, Opioids and Tramadol by issuing departments

Main finding

- Tramadol has been the most frequently prescribed analgesic at outpatient hospital settings in Malaysia.
- The prescriptions for NSAIDs were primarily for ketoprofen, diclofenac, and celecoxib, whereas the opioids predominantly prescribed were morphine and oxycodone.
- The overall utilization of analgesics in Malaysia has increased steadily, with opioid utilization increasing at a greater rate

Tramadol in other countries

thebmj

BMJ 2019;365:l2095 doi: 10.1136/bmj.l2095 (Published 14 May 2019)

EDITORIALS

Check for updates

Tramadol is not "opioid-lite"

Prescribe with care and review treatment regularly

Cathy Stannard *consultant in complex pain/Pain Transformation Programme clinical lead*

NHS Gloucestershire CCG, Gloucester Business Park, Brockworth GL3 4FE, UK

For newspapers, broadcasters, and even researchers, the US

accounts for additional analgesic effects but also extra adverse

drugs, gave tramadol a clear run without competition. From the early days of tramadol prescribing, tramadol related deaths rose steadily, and in consequence the drug was reclassified as a schedule 3 controlled drug in the UK in 2014.[6 7]

So how should we position tramadol in the repertoire of pain management? For long term pain, little evidence exists for the effectiveness of any opioid, including tramadol, beyond the duration of a clinical trial.[8] Opioids probably help fewer than

OPEN ACCESS

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Chronic use of tramadol after acute pain episode: cohort study

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ABSTRACT

OBJECTIVE

To determine the risk of prolonged opioid use in patients receiving tramadol compared with other short acting opioids.

DESIGN

Observational study of administrative claims data.

SETTING

United States commercial and Medicare Advantage insurance claims (OptumLabs Data Warehouse) January 1, 2009 through June 30, 2018.

PARTICIPANTS

Opioid-naive patients undergoing elective surgery

increase in the adjusted risk of persistent opioid use (1.25 to 1.69; 0.5 percentage points; P<0.001), and 41% increase in the adjusted risk of a CONSORT chronic opioid use episode (1.08 to 1.75; 0.2 percentage points; P=0.013).

CONCLUSIONS

People receiving tramadol alone after surgery had similar to somewhat higher risks of prolonged opioid use compared with those receiving other short acting opioids. Federal governing bodies should consider reclassifying tramadol, and providers should use as much caution when prescribing tramadol in the setting of acute pain as for other short acting opioids.

Thiels and colleagues' principal conclusion, a call to avoid underestimating tramadol in relation to other opioid products, should be heeded. Prescribing of any opioid should be in

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ORIGINAL REPORT

WILEY

Tramadol use in Norway: A register-based population study

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[2] National Institute of Public Health, University

Abstract

Purpose: Increasing use of tramadol for chronic non-cancer pain is concerning since tramadol users may be at risk of developing recurrent opioid use with increasing

The main finding was that although only 5.8% of opioid naïve tramadol users became recurrent users, these patients doubled the annual opioid dose during the 4-year follow-up, one-fifth proceeded to strong opioids, more than one-third had a consistent recurrent use, one-quarter was co-medicated with BZDs, one-third was co-medicated with Z-hypnotics, and one-tenth was co-medicated with both drugs. Thus, in a significant minority (about 1/20) of patients using tramadol, their first opioid prescription may be the first step towards a long-term opioid use that in many patients is combined with using other drugs with addiction potential. In the two non-palliative care patient's groups, who had

The main finding was that although only 5.8% of opioid naïve tramadol users became recurrent users, these patients doubled the annual opioid dose during the 4-year follow-up, one-fifth proceeded to strong opioids, more than one-third had a consistent recurrent use, one-quarter was co-medicated with BZDs, one-third was co-medicated with Z-hypnotics, and one-tenth was co-medicated with both drugs. Thus, in a sig-

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DOI: 10.1002/pds.4320

WILEY

ORIGINAL REPORT

A 15-year overview of increasing tramadol utilisation and associated mortality and the impact of tramadol classification in the United Kingdom

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[2] Division of Pharmacy and Optometry, School of Health Sciences, Faculty of Biology, Medicine and Health, University of

Abstract

Purpose: This study aimed to develop hypotheses to explain the increasing tramadol utilisation, evaluate the impact of tramadol classification, and explore the trend between tramadol utilisation and related deaths in the United Kingdom.

CDC guidelines on opioid use

HHS Public Access

Author manuscript

JAMA. Author manuscript; available in PMC 2019 February 26.

Published in final edited form as:

JAMA. 2016 April 19; 315(15): 1624–1645. doi:10.1001/jama.2016.1464.

CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016

Deborah Dowell, MD, MPH, **Tamara M. Haegerich, PhD**, and **Roger Chou, MD**

Corresponding Author: Deborah Dowell, MD, MPH, Division of Unintentional Injury Prevention, National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, 4770 Buford Hwy NE, Atlanta, GA 30341, (ddowell@cdc.gov).

Author Contributions: Drs Dowell and Chou had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Dowell, Haegerich.

Acquisition, analysis, or interpretation of data: Dowell, Haegerich, Chou.

Drafting of the manuscript: Dowell, Haegerich, Chou.

Critical revision of the manuscript for important intellectual content: Dowell, Haegerich, Chou

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate. (Recommendation category: A; evidence type: 3)

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids. (Recommendation category: A; evidence type: 4)

Clinicians should not initiate opioid treatment with ER/LA opioids and should not prescribe ER/LA opioids for intermittent use. In general, avoiding the use of immediate-release opioids in combination with ER/LA opioids is preferable.

5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when considering increasing dosage to 50 morphine milligram equivalents (MME) or more per day, and should avoid increasing dosage to 90 MME or more per day or carefully justify a decision to titrate dosage to 90 MME or more per day. (Recommendation category: A; evidence type: 3)

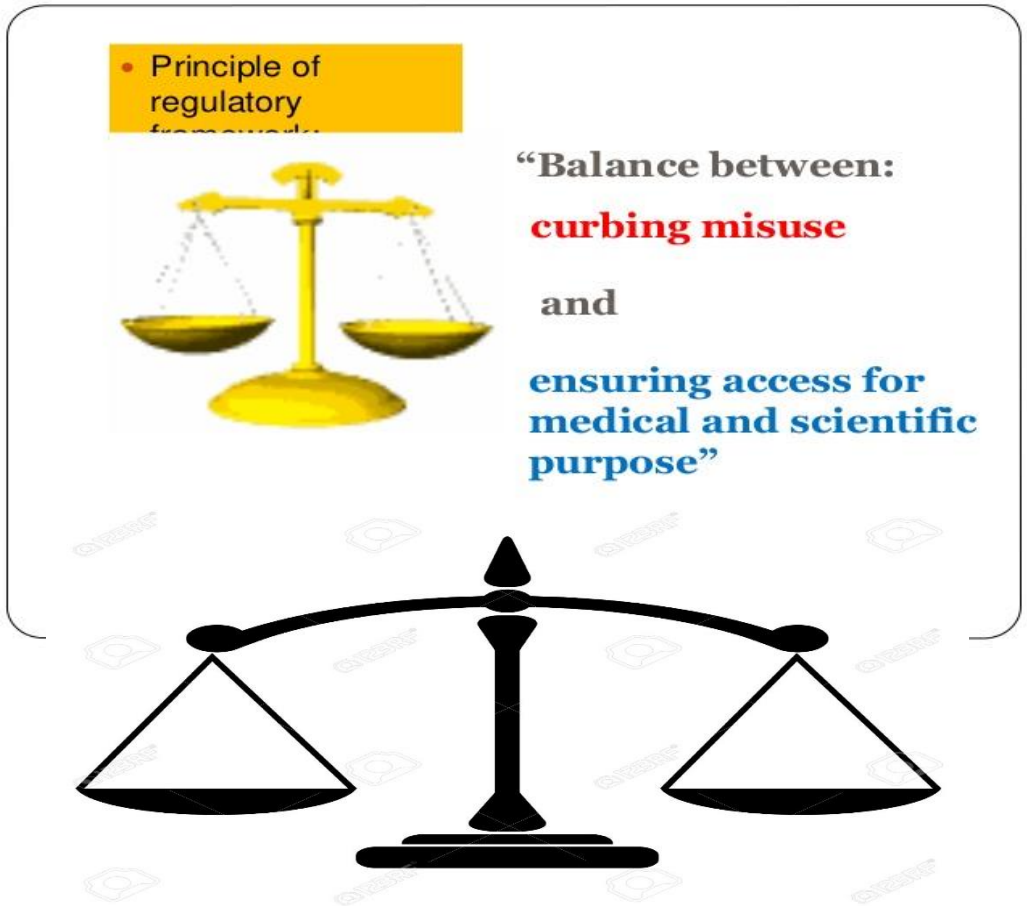
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than 7 days will rarely be needed. (Recommendation category: A; evidence type: 4)

11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible. (Recommendation category: A; evidence type: 3)

benzodiazepines concurrently whenever possible. In addition, given that other central nervous system depressants (eg, muscle relaxants, hypnotics) can potentiate central nervous system depression associated with opioids, clinicians should consider whether benefits outweigh risks of concurrent use of these drugs. Clinicians should check the PDMP for concurrent controlled medications prescribed by other clinicians and should consider involving pharmacists and pain specialists as part of the management team when opioids are co-prescribed with other central nervous system depressants. When patients require tapering

Conclusion

- Should be protected from similar negative outcomes.
- Education on opioids
- Rational use of opioids



Thank you

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