

# Opioidi u terapiji bola

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# KLASIFIKACIJA OPIOIDA

Prirodni	Polusintetski	Sintetski
<p><i>Morfin</i> <i>Codein</i> <i>Papaverine</i></p>	<p><i>Heroin</i> <i>Hidromorfin</i> <i>Hidrokodein</i> <i>Buprenorfin</i></p>	<p><i>Butorfanol</i> <i>Tramadol</i> <i>Metadon</i> <i>Pentazocin</i> <i>Meperidin</i> <i>Fentanyl</i> <i>Sufentanil</i> <i>Alfentanil</i></p>

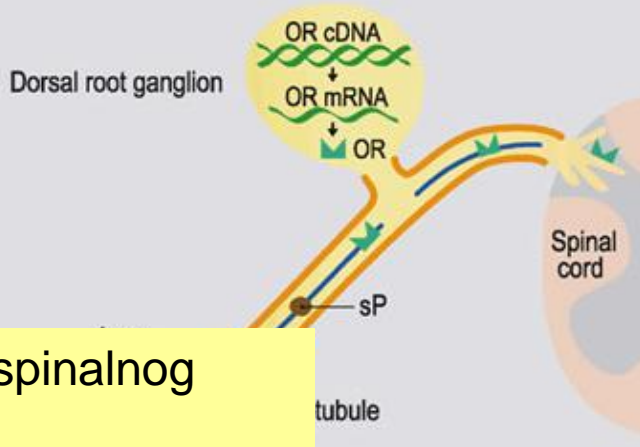
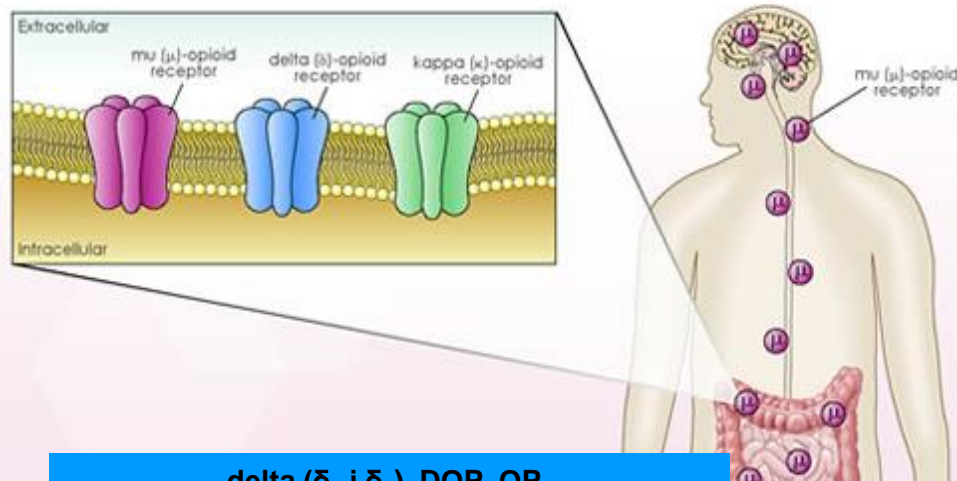


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**Receptori spregnuti sa proteinom G**  
40% homologni receptorima za somatostatin

**Receptori za endogene opioide:**  
Endorfin, dinorfin, enkefalin,  
endomorfin, nociceptin



**sinteza u spinalnog gangliji**

**aksonski transport**

**delta ( $\delta_1$  i  $\delta_2$ ), DOP, OP<sub>1</sub>**  
pons, amigdale, olfaktorni bulbus, kora, PNS  
analgezija, antidepresija, zavisnost  
**enkefalin**  
endorfin

**kapa ( $\kappa_1, \kappa_2, \kappa_3$ ), KOP, OP<sub>2</sub>**  
hipotalamus, periakvaduktna siva masa  
analgezija, sedacija, disforija, mioza  
**dinorfin**

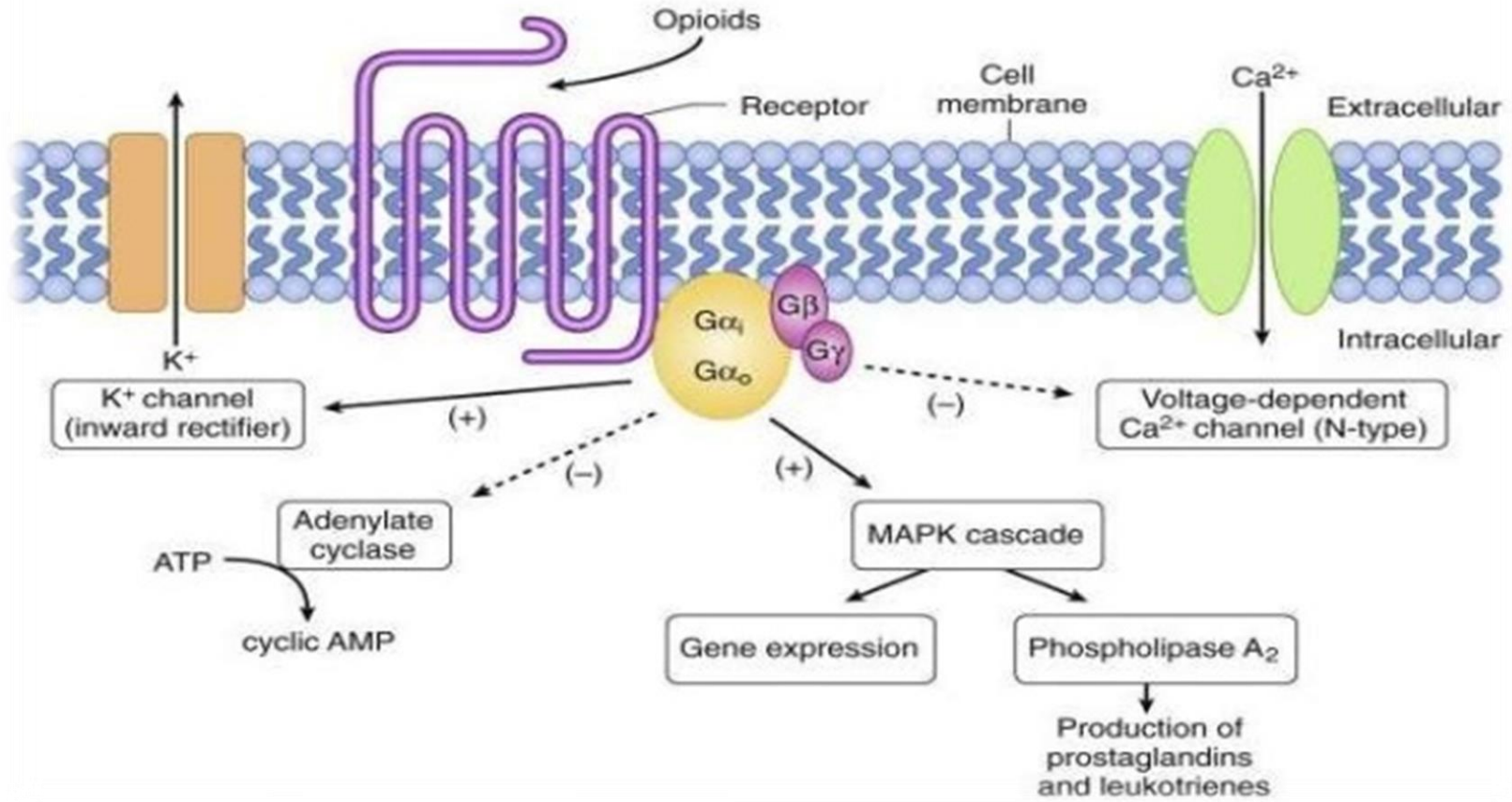
**mi ( $\mu_1, \mu_2, \mu_3$ ), MOP, OP<sub>3</sub>**  
MS, MO, kora, talamus, periakvaduktna siva masa, PNS, GIT  
 $\mu_1$  analgezija, zavisnost  
 $\mu_2$  euforija, zavisnost, mioza  
 $\mu_3$  nepoznata  
**morfin**  
 $\beta$  endorfin  
endomorfin  
enkefalin  
dinorfin

**receptori za nociceptin (ORL<sub>1</sub>), NOP, OP<sub>4</sub>**  
kora, hipotalamus, hipokampus, amigdale, MS, anksioznost, depresija, apetit...  
**Nociceptin (orphanin FQ)**

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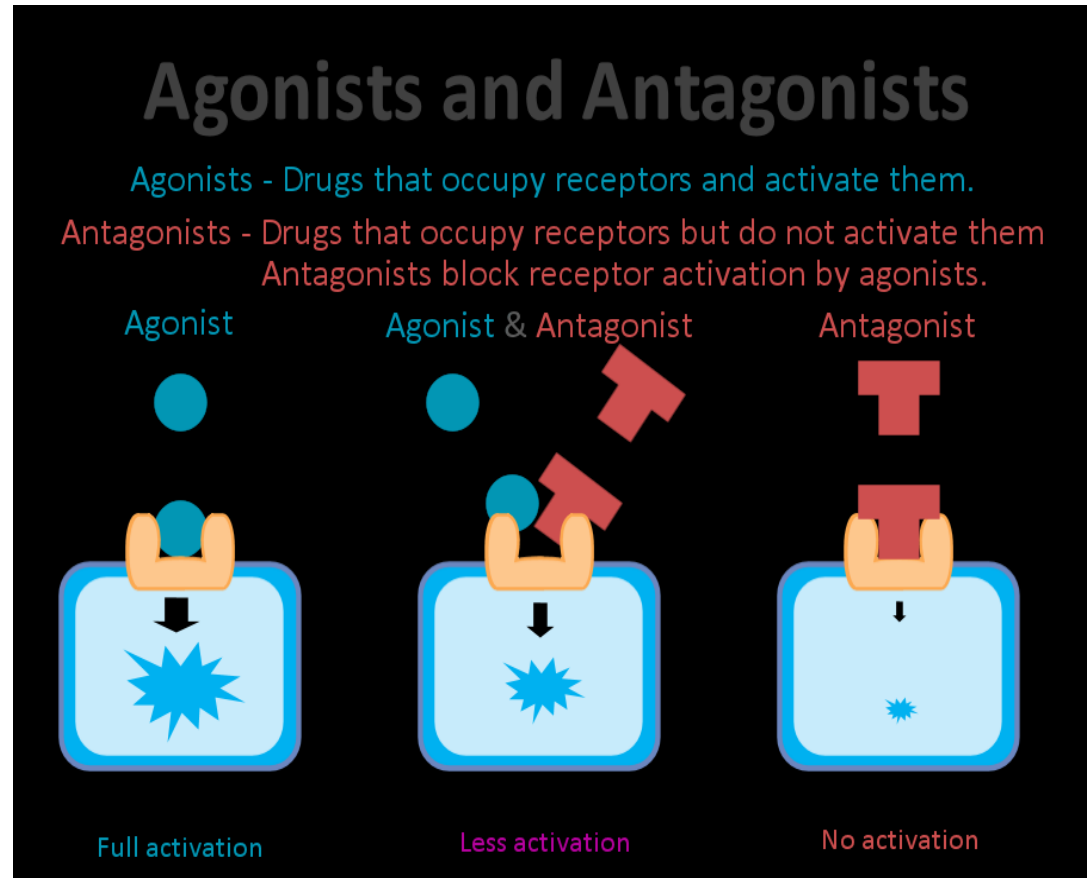


# Mechanism of action of Opioid Receptors



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- **Agonisti**
- **Antagonisti**
- **Mješovito dejstvo**



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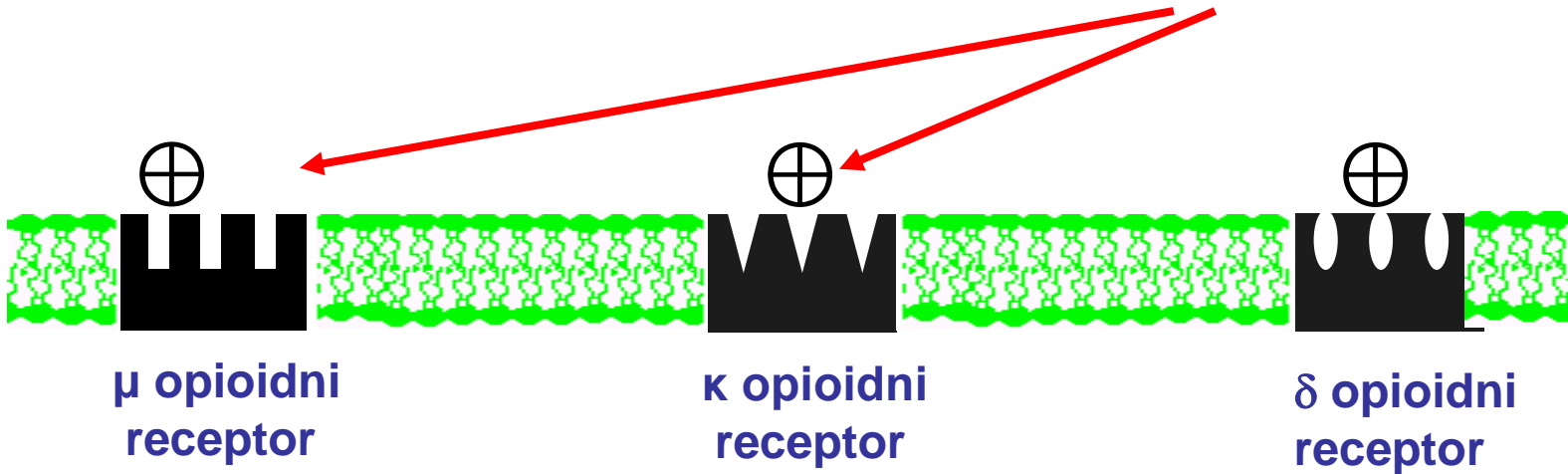


# Glavnom agonisti $\mu$ receptora, ali djeluju i na druge receptore

- Morphine
- Heroin
- Codeine
- Fentanyl

Agonist na  $\kappa$  receptore,  
sa djelimičnom antagonist. djelov.  
na  $\mu$  receptore

- Pentazocine



**$\mu$  opioidni  
receptor**

Analgezija  
Respiratorna depresija  
Euforija/sedacija  
Psihička zavisnost  
Smanjnje GI motiliteta  
Mioza

**$\kappa$  opioidni  
receptor**

Analgezija  
Sedacija  
Mioza

**$\delta$  opioidni  
receptor**

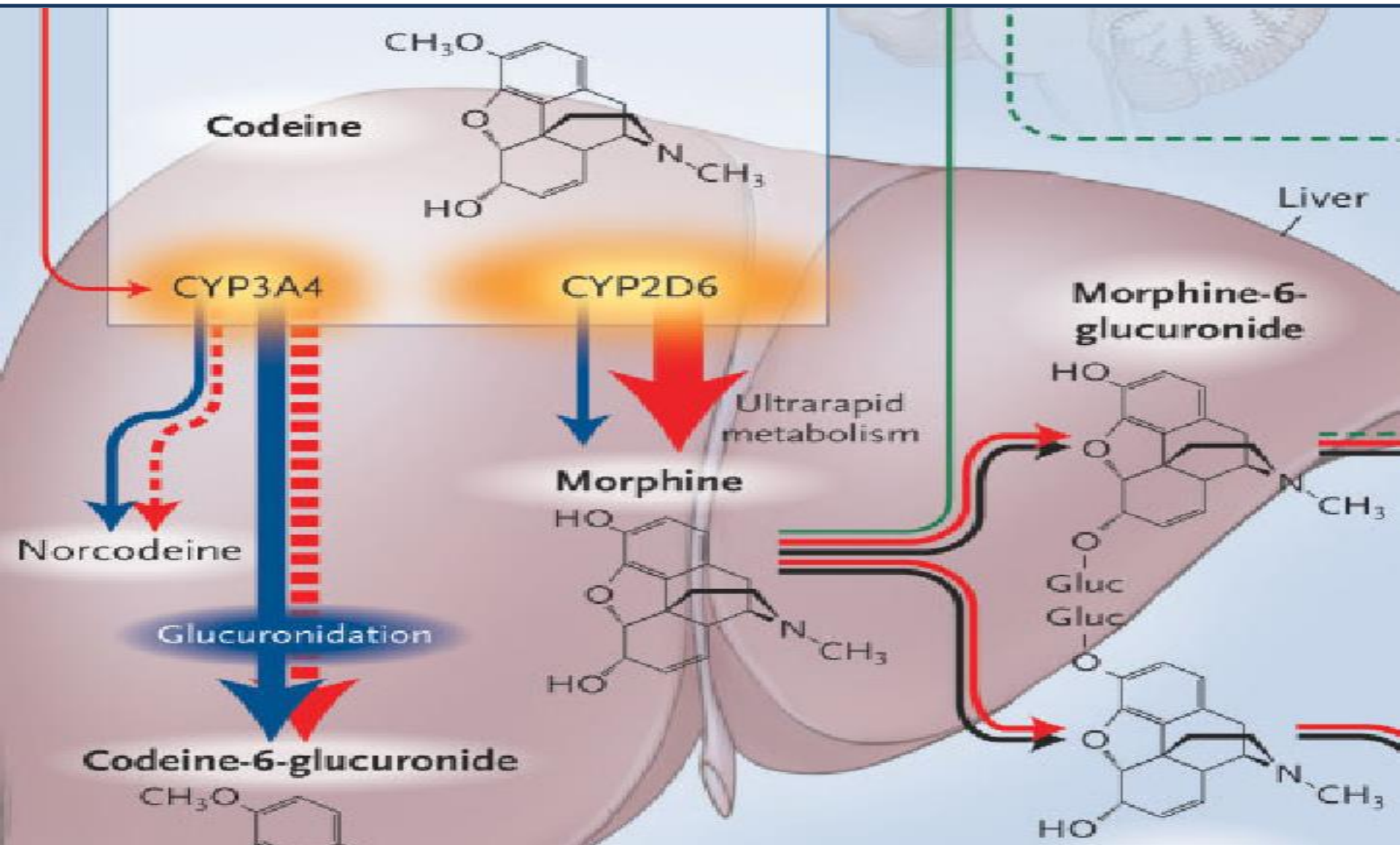
Analgezija

**Antagonist djeluje na  $\mu$ ,  $\kappa$ ,  $\delta$  receptore**

• Naloxone

• Naltrexone

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VRLO JAKI OPIOIDI	JAČINA
-Sufentani	1000
-Fentanil	100-300
-Remifentanil	200
-Alfentanil	40-50
-Buprenorfin	10-40
JAKI	
-Butorfanol	8-11
-Hidromorfon	7-10
-Metadon	1,5
-MORFIN	1
SLABI	
Kodein	0,3
Petidin	0,2
VRLO SLABI	
-Tramadol	0,05-0,09
MORFIN = 1	

Pr







-001)



**MODERATE**

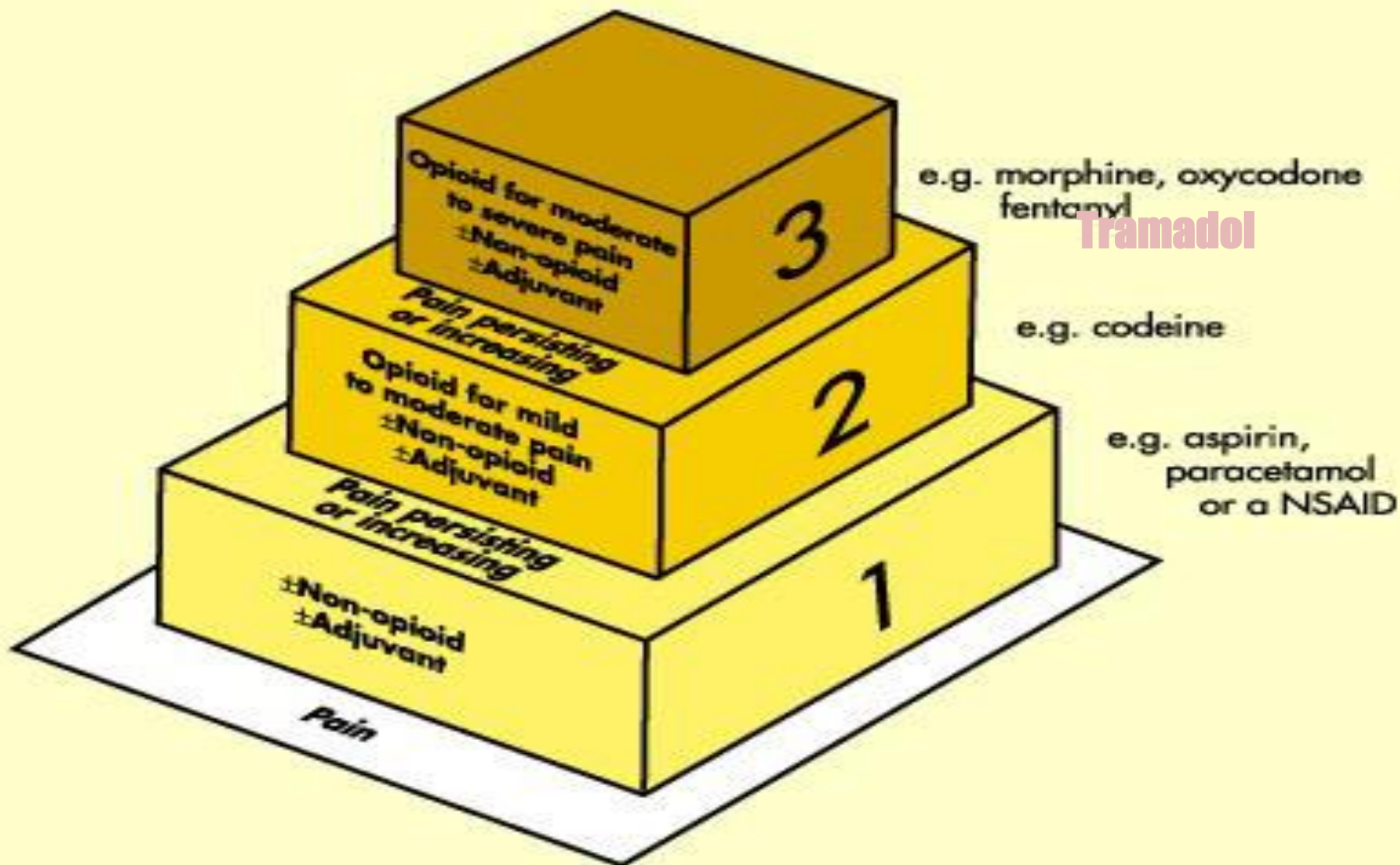
# UNIVERSAL PAIN ASSESSMENT TOOL

This pain assessment tool is intended to help patient care providers assess pain according to individual patient needs. Explain and use 0-10 Scale for patient self-assessment. Use the faces or behavioral observations to interpret expressed pain when patient cannot communicate his/her pain intensity.

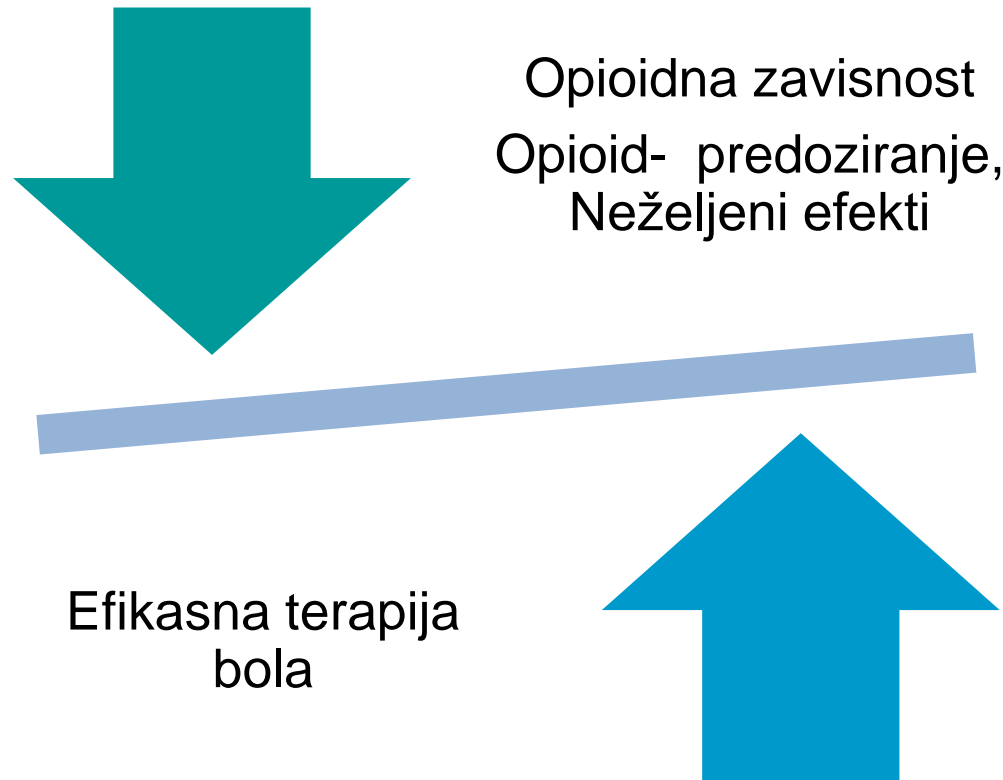
	0	1	2	3	4	5	6	7	8	9	10
<b>Verbal Descriptor Scale</b>	<b>NO PAIN</b>		<b>MILD PAIN</b>		<b>MODERATE PAIN</b>	<b>MODERATE PAIN</b>			<b>SEVERE PAIN</b>		<b>WORST PAIN POSSIBLE</b>
<b>WONG-BAKER FACIAL GRIMACE SCALE</b>											
	Alert Smiling		No humor serious flat		Furrowed brow pursed lips breath holding	Wrinkled nose raised upper lip rapid breathing			Slow blink open mouth		Eyes closed moaning crying
<b>ACTIVITY TOLERANCE SCALE</b>	<b>NO PAIN</b>		<b>CAN BE IGNORED</b>		<b>INTERFERES WITH TASKS</b>	<b>INTERFERES WITH CONCENTRATION</b>			<b>INTERFERES WITH BASIC NEEDS</b>		<b>BEDREST REQUIRED</b>
<b>SPANISH</b>	<b>NADA DE DOLOR</b>		<b>UNPOQUITO DE DOLOR</b>		<b>UN DOLOR LEVE</b>	<b>DOLOR FUERTE</b>			<b>DOLOR DEMASIADO FUERTE</b>		<b>UN DOLOR INSOPORTABLE</b>
<b>TAGALOG</b>	Walang Sakit		Konting Sakit		Katamtamang Sakit	Matinding Sakit			Pinaka-Matinding Sakit		Pinaka-Malalang Sakit
<b>CHINESE</b>	不痛		輕微		中度	嚴重			非常嚴重		最嚴重
<b>KOREAN</b>	통증 없음		약한 통증		보통 통증	심한 통증			아주 심한 통증		최악의 통증
<b>PERSIAN (FARSI)</b>	بدون درد		درد ملایم		درد معتدل	درد شدید			درد بسیار شدید		بدترین درد ممکن
<b>VIETNAMESE</b>	Không Đau		Đau Nhẹ		Đau Vừa Phải	Đau Nặng			Đau Thật Nặng		Đau Đớn Tận Cùng
<b>JAPANESE</b>	痛みがない		少し痛い		いくらか痛い	かなり痛い			ひどく痛い		ものすごく痛い

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# Rizik vs. Benefit Evaluacija



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# AKUTNI BOL

- Akutni bol je normalan, predvidiv fiziološki odgovor na štetni hemijski, termički ili mehanički stimulus vezan za traumu, hirurški zahvat ili akutnu bolest.
- Akutnu bol prate objektivni znaci
  - Ubrzanje pulsa
  - Porast krvnog pritiska
  - Ne verbalni znaci i simptomi kao što su ekspresija lica i grčenje mišića .

# PROCJENA BOLA

- Inicijalna procjena bola uključuje:
  - Lokaciju
  - Intenzitet
  - Senzorni kvalitet
  - Ublažavajuće I otežavajuće faktore
  
- Svaki novi napad bola zahtijeva novu sveobuhvatnu procjenu.

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# Ponovna procjena bola

- Minimalno svakih 8 sati
- Kod ordiniranja lijekova
  - IV unutar 15 minuta od ordiniranja
  - PO/IM/SC unutar 1 sata od ordiniranja

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# Multimodalna analgezija

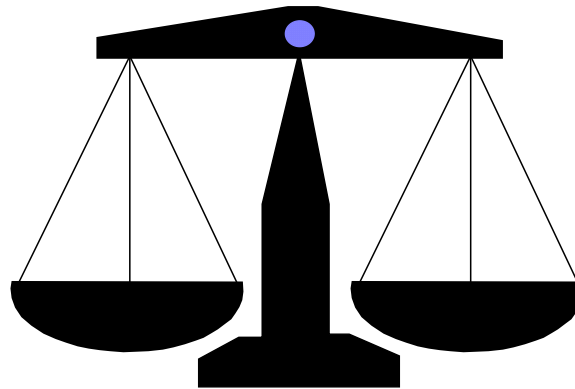
- Ovaj termin opisuje upotrebu različitih modaliteta da bi se obezbijedilo ublažavanje bola djelovanjem na različitim dijelovima prenosa bola.
  - Uključuje:
    - Farmakologiju (opioidi, NSAIDS, gabapentanoidi....)
    - Relaksacione tehnike (biofeedback, duboko disanje)
    - Regionalnu analgeziju (nervne blockove, epiduralne katetere)

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# Multimodalna analgezija

**Analgezija**



**Neželjena  
dejstva**

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# ODGOVORNO PROPISIVANJE OPIOIDA

- Procjena rizika za zloupotrebu opijata.
- Faktori rizika za zloupotrebu:
  - Muškarci između 18 i 45 godina.
  - Lična ili porodična opterećenost zloupotrebe opijata
  - Psihijatrijska oboljenja u anamnezi (depresija, anksioznost, opsesivno-kompulzivne bolesti)

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# IZBOR OPIOIDA

1. Odrediti kada započeti ili nastaviti sa opioidima
2. Izbor opioida, doze, dužine ordiniranja i prekid th.
3. Procijeniti rizik

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# Izbor opioida

1. Određivanje početka i nastavka th opijatima
  - a) Opijati nisu prva linija terapije
  - b) Uspostaviti cilj terapije
  - c) Raspraviti o rizik/ benefit

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# Izbor opioida

- a) U startu koristiti brzo djelujuće opioide
- b) Koristiti najmanju efektivnu dozu
- c) Ordinirati kratkodjelujući opijat za akutnu bol

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# SVJETSKA ZDRAVSTVENA ORGANIZACIJA (SZO)

Tri koraka u pristupu terapije bola

- **KORAK BR 1 – BLAŽI BOL (1-3/10)**
- Non - opoidi
- Dodati adjuvantnu terapiju  
(npr.) led, toplota

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# SZO PREPORUKA

- **KORAK BR. 2 (BLAG DO UMJEREN BOL) (4-7/10)**
- *Nadogradnja prvog koraka*
- *Kombinacija opioidnih analgetika (hidrokodon/acetaminofen)*
- *Obratiti pažnju na maksimizaciju adjuvantne terapije*
- Doziranje prema TT
- Obratiti pažnju na dopunske faktore ( godine starosti pacijenta, težina, druga terapija...)

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# SZO PREPORUKA

## Korak br 3 (8-10/10)

- Koristite opoide
- Dodajte dopunsku terapiju poput anksiolitika, antiemetika, mišićni relaxansi
- Početi sa opoidima kratkotrajnog dejstva
- Prebaciti se na opoide dužeg dejstva koristeći preporuke

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## ZAPAMTITI

- Intezitet bola određuje korak terapije.
- Opoidi su jedina grupa analgetika u kojoj se mora pažljivo odraditi titracija doze!!!
- Većina efekata opoida se smanjuje kroz par dana.

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# UOBIČAJEN PRVI IZBOR OPOIDA

- Kodein
- Morfijum
- Hidromorfon
- Oksikodon

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## Zajedničke karakteristike opoida

- Polu-vrijeme života lijeka 2-4 h
- Dužina trajanja analgezije iznosi 4-5 časova po određivanju adekvatne doze.
- Zadržan efekat otpuštanja iznosi između 10 i 12 časova.

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## MORFIJUM

Trenutno djelovanje: 15 do 60 min

Vrhunac efekta: 30 min do 1 h

Poluvrijeme života: 1.5 do 2 h

IV: 0.05 to 0.1 mg/kg

5 min prije procedure; max: 15 mg/doza

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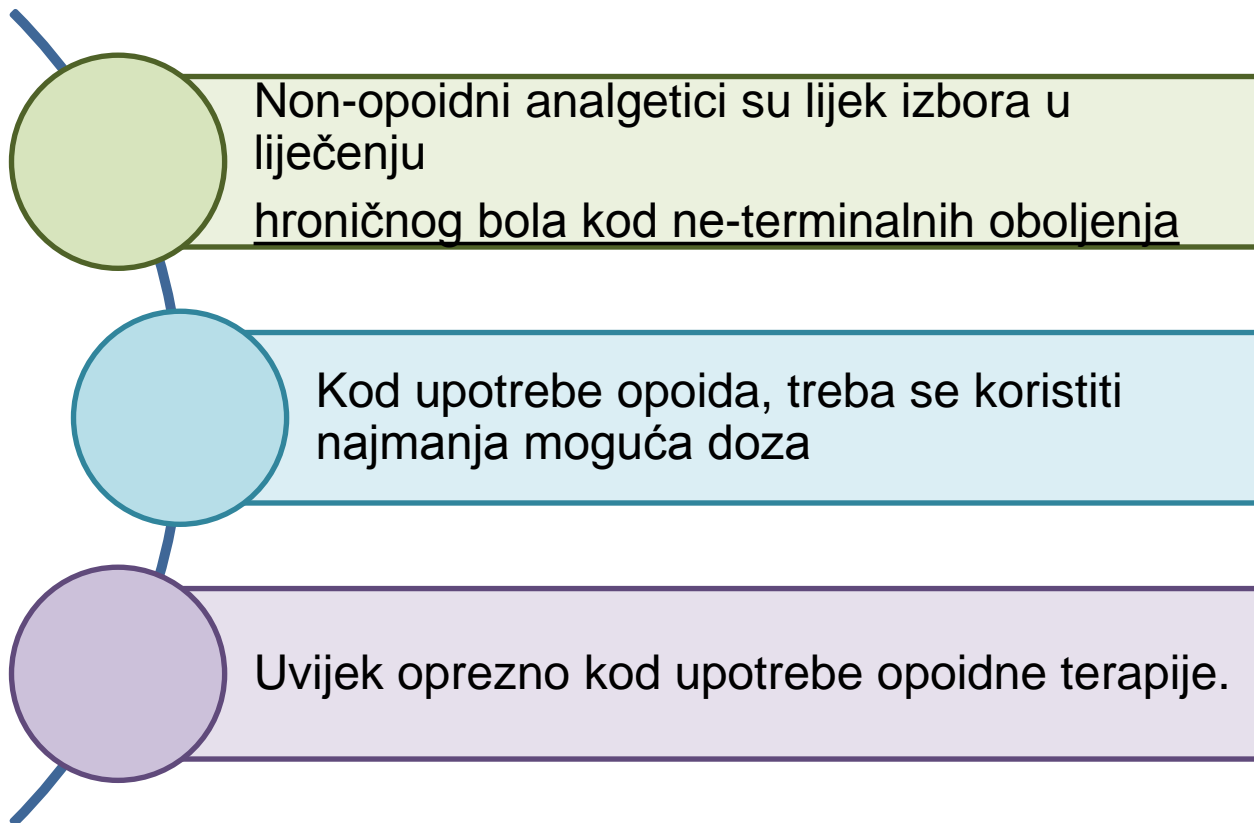
# FENTANIL

- Fentanil je potentniji 80 do 100 puta od morfijuma
- Studije pokazuju da je mnogo manja konstipacija i sedolentnost kod transdermalne upotrebe nego kod iv primjene morfijuma.

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# GUIDELINE FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN



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Dowell D, et al. CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016. *MMWR Recomm Rep* 2016;65(No. RR-1):1–49.





# Efikasnost opoida kod terapije hroničnog bola

## Kod većine studija koje su trajale $\leq 6$ nedelja

Nijedna studija nije radila procjenu bola, funkcije ili kvaliteta života sa opoidima i drugih tretmanima  $> 1$  year

## Studije koje su trajale $> 6$ nedelja su imale loše rezultate

Koji su ukazivali da dugotrajna upotreba opijata podstiče bol

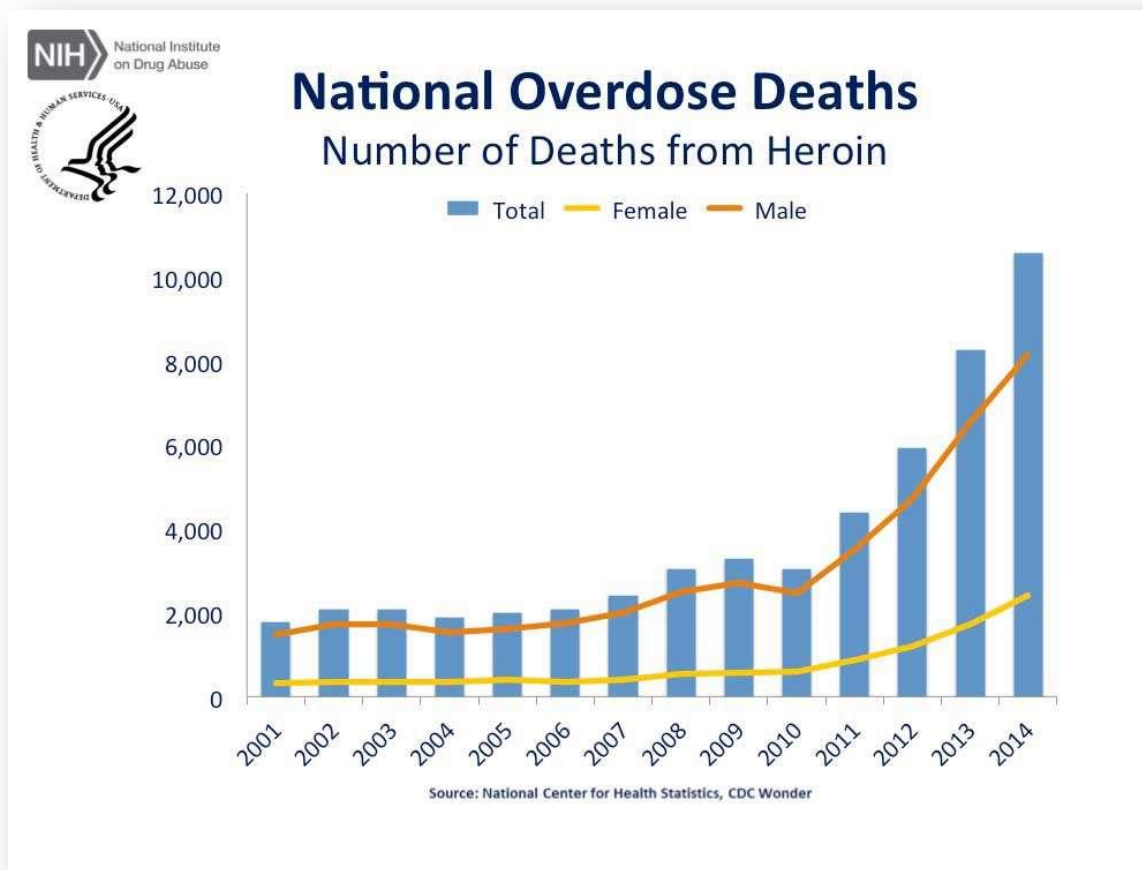
Trogodišnja prospektivna observativna studija 69,000 Post-menopauzalnih pacijentica sa rekurentnim tegobama. Pacijenti na opoidnoj terapiji su:

Manja poboljšanja u terapiji bola (ili 0.42; 95% CI 0.36 – 0.49)

Povećanje u oštećenju tjelesne funkcija /pogoršanje (ili 1.2; 95% CI 1.04 – 0.51)

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**Svaka 4 od 5 novih heroinskih ovisnika su počeli sa neadekvatnom primjenom opioidnih analgetika!**

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\*<https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>

Source: National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services.

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# HYPNOS 2019

## BANJA LUKA, 18.-21.09.2019.

