

疼痛控制指引更新

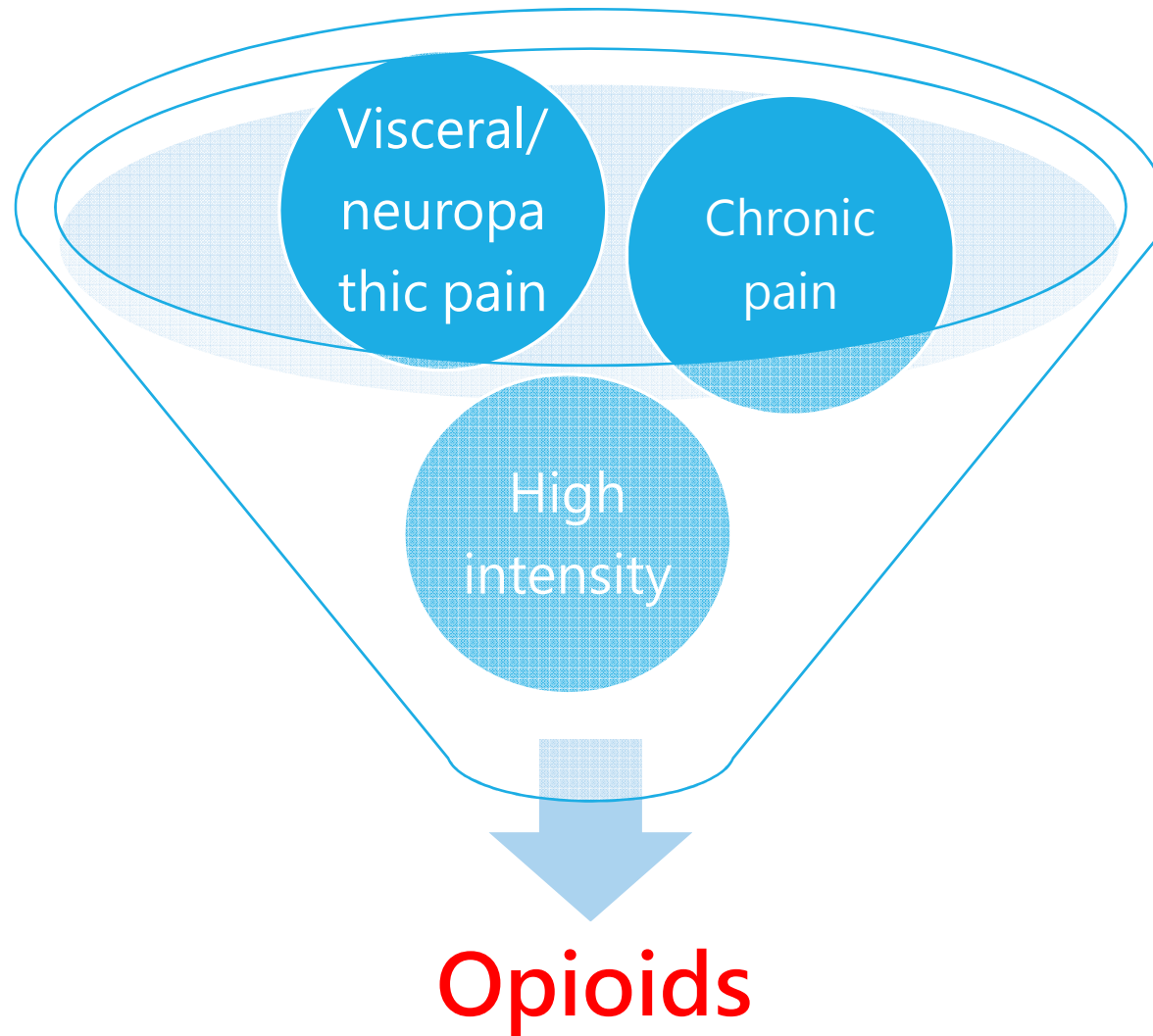
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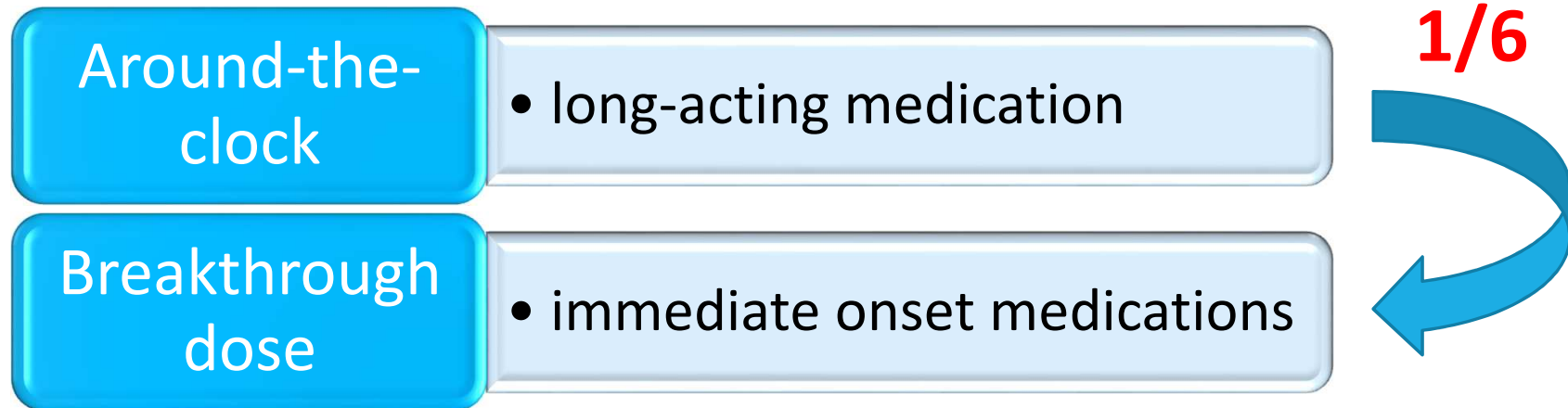


Why Opioids for Cancer Pain?



Pain Management Goal

Treatment goal:
breakthrough ≤ 3 /day, severity ≤ 3

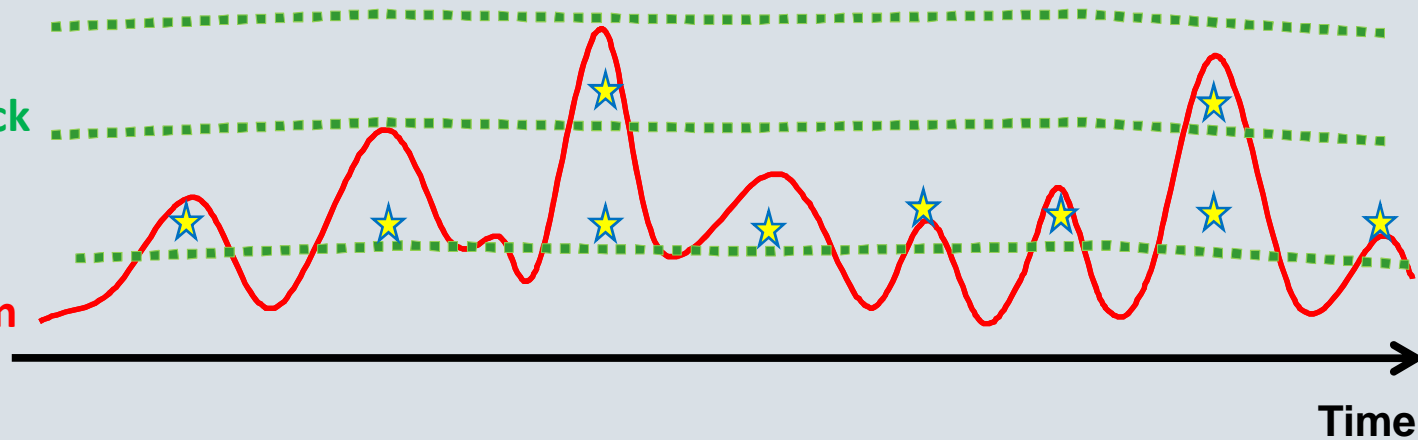


IV morphine =
3X oral morphine

Adequate Analgesia = Balance between Pain and Side Effects

Around the clock
analgesics

Pain



長效藥物劑量不足痛癢反覆疼痛
長效藥物劑量過量副作用增加
突發性疼痛次數與藥物副作用的平衡

Analgesics

Non-Opioids

- acetaminophen
- NSAIDs
- COX-2 inhibitor

- 對內臟性及神經性疼痛效果不佳
- 強度不足
- 適合當癌症疼痛處理的配角

Weak Opioids

- codeine
- tramadol

- 仍有天花板效應→無法調整劑量配合病人需求
- 無法跟strong opioids併用

Strong Opioids

- morphine
- fentanyl
- hydromorphone
- oxycodone
- buprenorphine

- 無天花板效應→可配合病人需求調升劑量
- 癌症疼痛處理最重要的藥物

癌症疼痛藥物指引更新

1. 不特別強調弱效性鴉片類藥物的使用
2. 更多的強效性鴉片類藥物(strong opioids)選擇
3. 超速效藥物(rapid onset opioids)的出現

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WHO Pain Guideline 1986

■ By mouth

■ By clock

■ By ladder

■ For individual



Why do patients with moderate-severe pain need to receive weak opioids?

WHO 1986

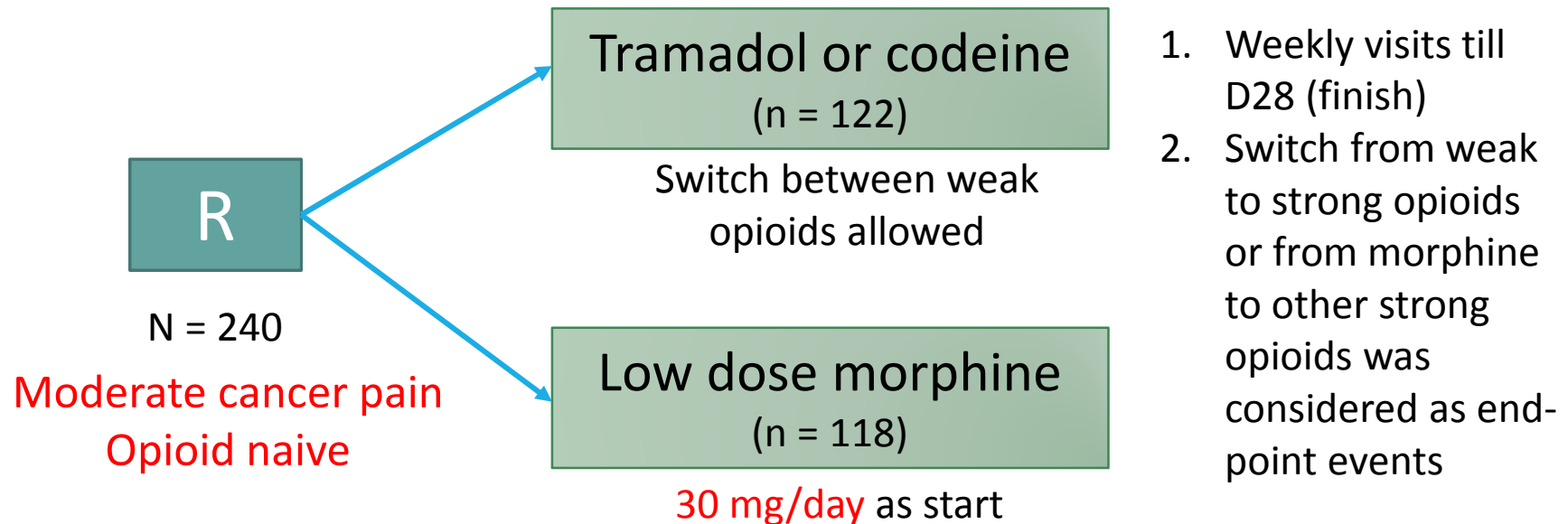
- By mouth
- By clock
- ~~■ By ladder~~
- For individual

WHO 2018

- By mouth
- By clock
- For individual
- With attention to detail

Patients should be started on an analgesic with a strength appropriate to their assessed pain severity.

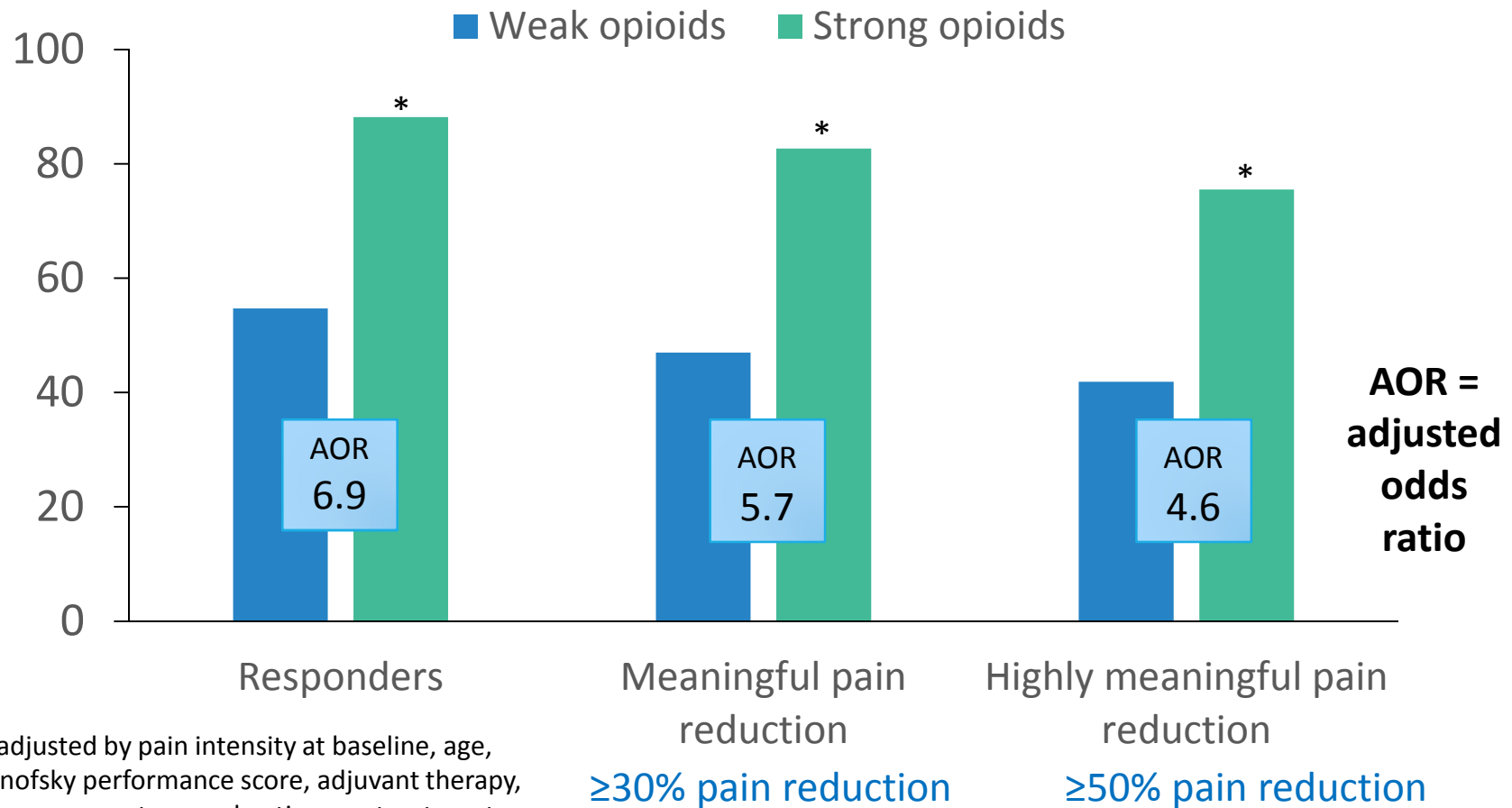
Strong vs. Weak Opioids



Primary outcome: the number of responder patients, defined as a **20%** reduction in pain intensity

Treatment Outcomes

35% pts starting with weak opioids shifted to strong opioids within 28 days



Odds ratio adjusted by pain intensity at baseline, age, gender, Karnofsky performance score, adjuvant therapy, rescue therapy, cancer type and anticancer treatment.

Side Effects

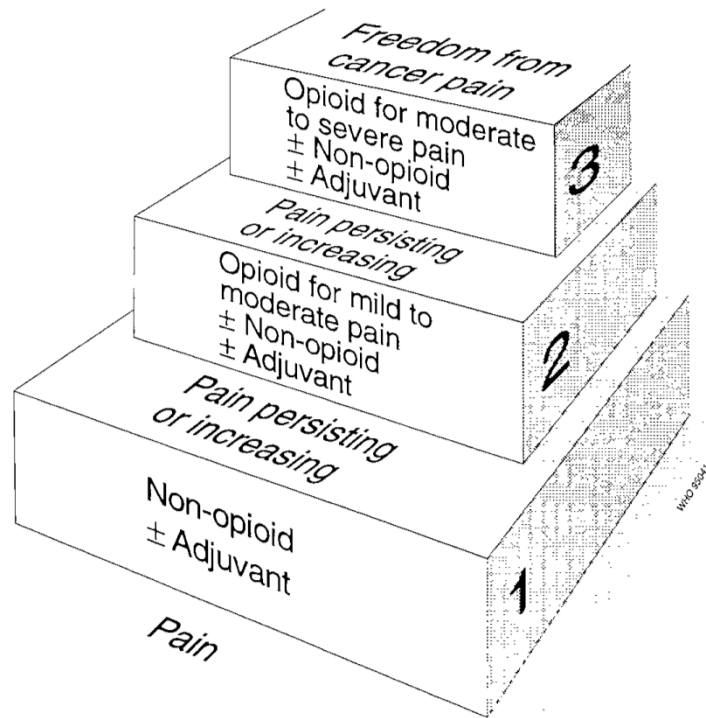
ESAS Item	Weak Opioids	Morphine	<i>P</i>
Pain	4 (1-6)	1 (0-3)	< .001
Tiredness	3 (2-6)	2 (1-3)	< .001
Nausea	1 (0-3)	1 (0-1)	.03
Depression	2 (1-4)	1 (0-2)	< .001
Anxiety	2 (0-4)	1 (0-2)	< .001
Drowsiness	3 (1-4)	1 (0-2)	< .001
Appetite	2 (1-5)	1 (0-2)	< .001
Well-being	3 (1-5)	1 (0-2)	< .001
Shortness of breath	0 (0-1)	0 (0-0)	.01
ESAS overall symptom score	19 (10-17)	10 (6-15)	< .001

NOTE. Data are presented as median (interquartile range).
Abbreviations: ESAS, Edmonton Symptom Assessment System.

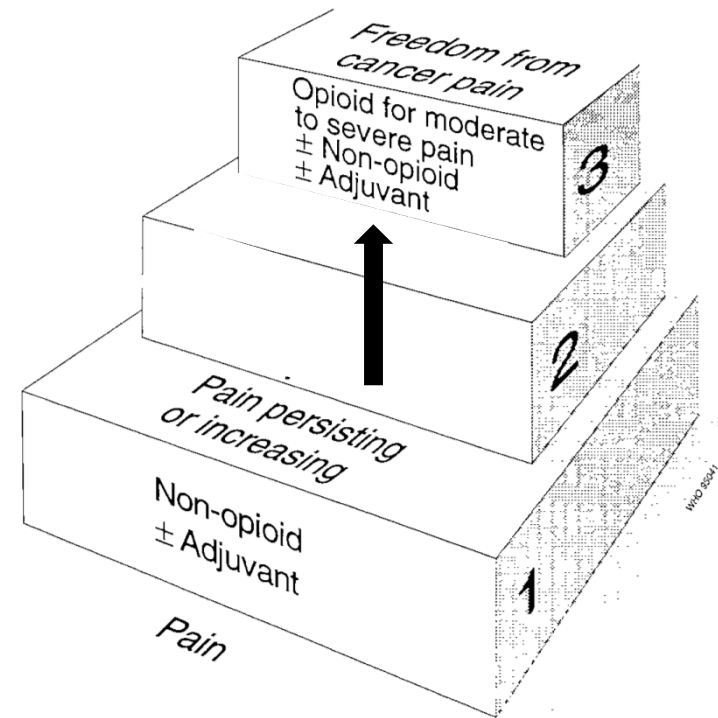
Current Long-Acting Strong Opioids in Taiwan

Content	Medication and Dosage	Morphine equivalent dose per day
Morphine	MXL 60mg qd	60mg
Oxycodone	Oxycontin 10mg q12h	30-40mg
Hydromorphone	Jurnista 8mg qd	40mg
Fentanyl patch	Durogesic 12 μ g/hr	30mg
Buprenorphine	Transtec 35 μ g/hr	60mg

3-Step Opioids to 2-Step Opioids



Patients with moderate to severe cancer pain



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Morphine

- Extended release:

1. MXL[®] (60 mg/cap) qd use
2. Morphine sulfate SR (30mg/tab) q12h use

- Immediate release:

1. Morphine sulfate (15 mg/tab)
2. Morphine sulfate oral solution (2 mg/ml)

- Injection: morphine HCl



MXL[®]

MXL默痛舒持續性藥效膠囊之專利製程，將有效成分均勻包裹在直徑0.25mm-1.8mm的多重緩釋微粒，不受PH值影響，於腸胃道穩定釋放達24小時。

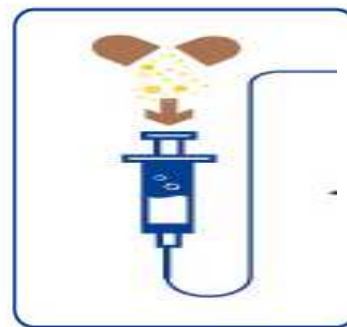


MXL® 彈性給藥方式



打開膠囊，
倒入冷飲料服用

飲料不能加溫



打開膠囊，
管灌服用

前後以脂質液體灌洗

Oxycodone

- μ - & κ - receptor agonist
- Predictable bioavailability
- Potency: 1.5-2 X morphine
- Extended release:
 - Oxycontin[®] 10mg/tab, 20mg/tab
 - q12h use
- Immediate release:
 - Oxynorm[®] 5 mg/cap



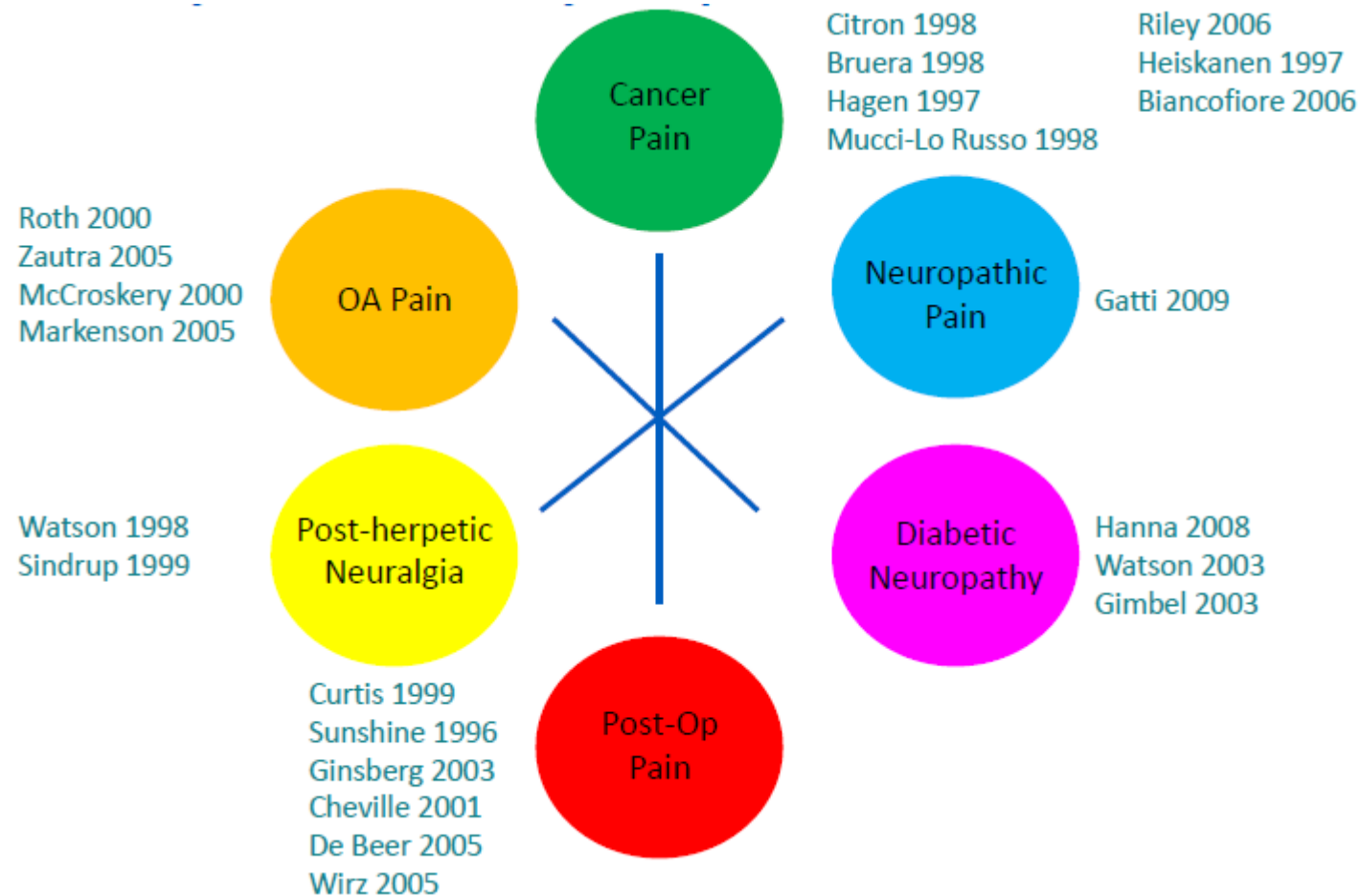
10 mg



20 mg



Broad-Spectrum Coverage of Oxycodone



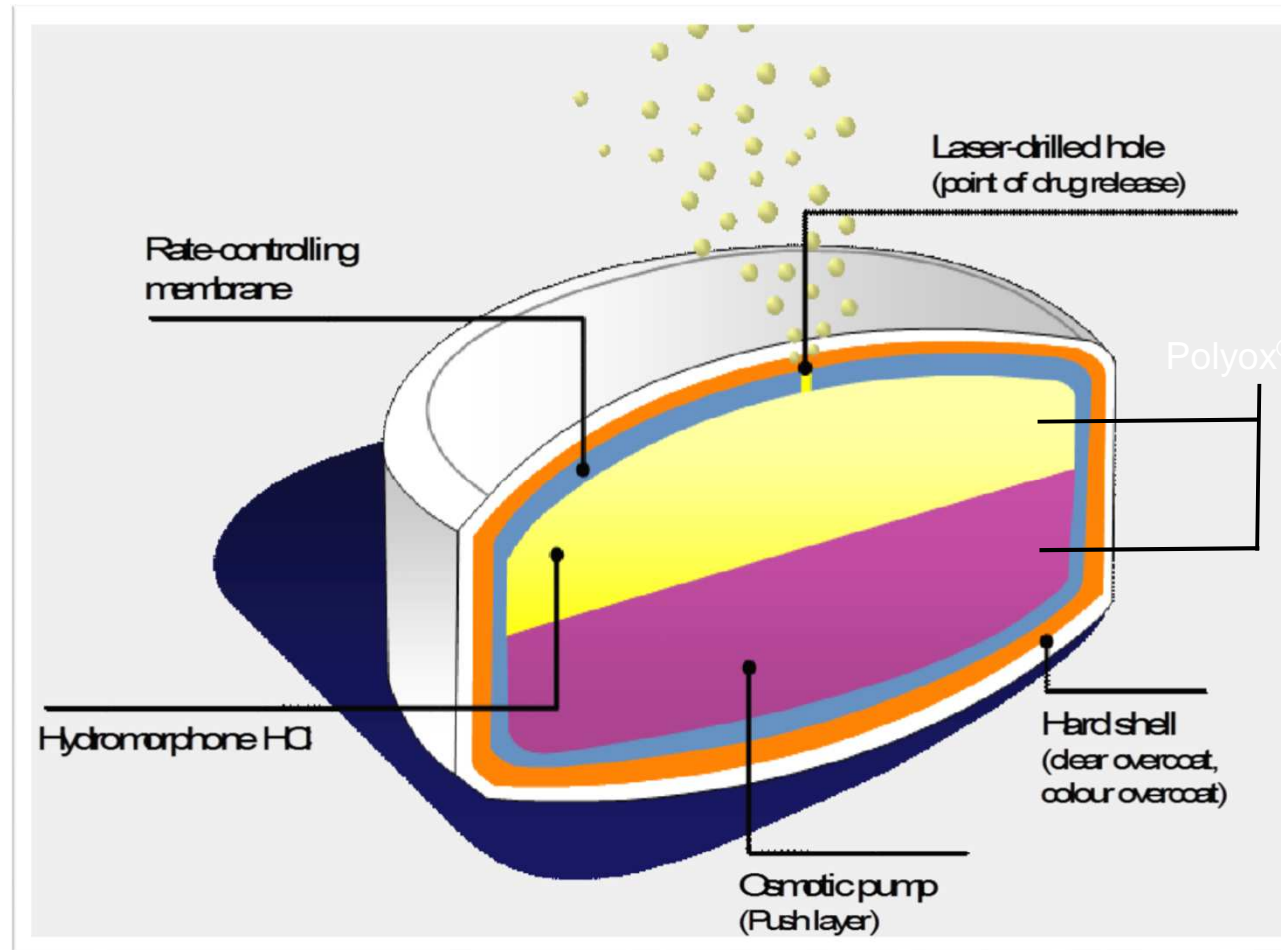
Hydromorphone

- Metabolized via glucuronidation → Little interaction with the cytochrome P450 enzymes
- Stable blood concentration
- Potency: **5X morphine**
- Extended release:
Jurnista[®] 8 mg/tab, **qd** use



Hydromorphone OROS[®]

Jurnista[®]



Fentanyl

■ Extended release: transdermal patches

1. Durogesic[®] (matrix劑型; 12, 75 $\mu\text{g/hr}$)
2. Fentanyl patch (儲藥槽型; 25, 50 $\mu\text{g/hr}$)



■ Rapid onset opioids: transmucosal

1. Painkyl[®]
2. Fentora[®]



Matrix vs. Reservoir System



	Durogesic [®] D-TRANS [®]	Fentanyl Patch
Patch structure	Flexible matrix	Reservoir system with gel
Patch size	Smaller! 12.5µg/h – 5.25 cm ² 75µg/h – 31.5 cm ²	25 µg/h – 18.7 cm ² 50 µg/h – 40.6 cm ²
Fentanyl	Dissolved in the adhesive layer	Embedded in gel of water/ethanol/hydroxyethyl cellulose
Permeation enhancer	None	Ethanol

Buprenorphine

Temgesic®

- Sublingual; short-acting
- Might interfere with effects of strong opioids

Transtec®

- Transdermal patch
- 長效劑型需按時長期使用
 - 35 µg/h ~ fentanyl 25 µg/h
 - 52.5 µg/h ~ fentanyl 37.5 µg/h
- 固定一周其中二天更換貼片

Although a partial opioid receptor agonist,
clinically act as a strong opioid

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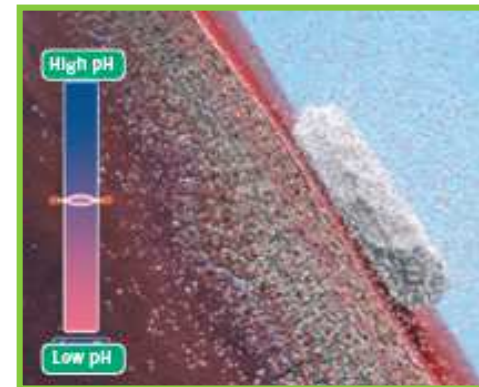
Rapid Onset Opioids

1. Transmucosal routes to speed up onset (~ 10-15 mins)
2. Not affected by GI motility or nausea
3. Only for breakthrough pain



Fentanyl buccal soluble film

Painkyl® 口頰或唇內



Fentanyl buccal tablet

Fentora® 口頰或舌下

Breakthrough Pain Is NOT.....

- Uncontrolled background pain
- Pain occurring in the absence of background pain
- Pain occurring in the absence of ATC medication
- Pain occurring during the titration of ATC medication
- Pain resulting from inadequate ATC medications (e.g. end-of-dose failure)

癌症疼痛藥物指引更新

考慮二階段用藥的概念

- Low dose strong opioids for moderate-severe cancer pain

更多的強效性鴉片類藥物(strong opioids)選擇

- Hydromorphone, Oxycodone, Buprenorphine

超速效藥物(rapid onset opioids)的出現

- Transmucosal fentanyl
- 