



Brief Tips to Defeat Breakthrough Cancer Pain

台灣癌症安寧緩和醫學會

高醫附設醫院
血液腫瘤科
卓士峯
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Cancer pain or cancer-related pain

- High prevalence
 - 59% of patients undergoing cancer treatment
 - 64% of patients with advanced disease
 - 33% of patients after curative treatment
- One of the symptoms patients fear most.

	All enrolled patients (<i>n</i> = 3289)		<i>P</i> value
	HNC patients (<i>n</i> = 708)	Patients with other cancers (<i>n</i> = 2581)	
Pain status			
Pain documented by physician (<i>n</i> , %)	586 (82.76%)	1689 (65.44%)	< 0.001
Cancer-related pain (<i>n</i> , %)	357 (50.42%)	1010 (39.13%)	< 0.001
Non-cancer-related pain (<i>n</i> , %)	83 (11.72%)	454 (17.59%)	< 0.001
Cancer treatment-related pain (<i>n</i> , %)	166 (23.45%)	235 (9.10%)	< 0.001
**Need pain treatment (<i>n</i> , %)	611 (86.29%)	1859 (72.03%)	< 0.001
**Any pain in the past 7 days (<i>n</i> , %)	429 (60.59%)	1136 (44.01%)	< 0.001
Pain management			
Currently taking any analgesics (<i>n</i> , %)	381 (53.81%)	891 (34.5%)	
*Currently taking any oral analgesics (<i>n</i> , %)	369 (52.19%)	870 (33.7%)	
Currently using non-oral analgesics (<i>n</i> , %)	77 (10.88%)	153 (5.93%)	
Currently using non-opioid analgesics (<i>n</i> , %)	210 (29.66%)	404 (15.6%)	
Currently using weak opioid analgesics (<i>n</i> , %)	181 (25.56%)	405 (15.6%)	
Currently using strong opioid analgesics (<i>n</i> , %)	132 (18.64%)	275 (10.65%)	< 0.001
***Any other non-pharmacological therapy (<i>n</i> , %)	45 (6.36%)	372 (14.41%)	< 0.001

臨床醫師有紀錄下來的疼痛



高於

病患反映還需要疼痛治療

The non-oral analgesics included transdermal analgesics. The non-pharmacological adjuvant therapy included massage, acupuncture, exercise, rehabilitation, Qigong herbal medicine, and aromatherapy

* With at least two causes of pain

** These questions were answered by patients

One patient with head and neck cancer did not answer these two questions

Optimize pain treatment outcomes in 5 dimensions (5As)

- **Analgesia**: optimize analgesia (pain relief)
- **Activities**: optimize activities of daily living (psychosocial functioning)
- **Adverse effects**: minimize adverse events
- **Aberrant drug taking**: avoid aberrant drug taking (addiction-related outcomes)
- **Affect**: relationship between pain and mood

Outline

- 認識突發性癌症疼痛
- 找到突發性癌症疼痛
- 擊敗突發性癌症疼痛



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“Breakthrough pain”:

a transitory flare of pain in the setting of chronic pain managed with opioid drugs.

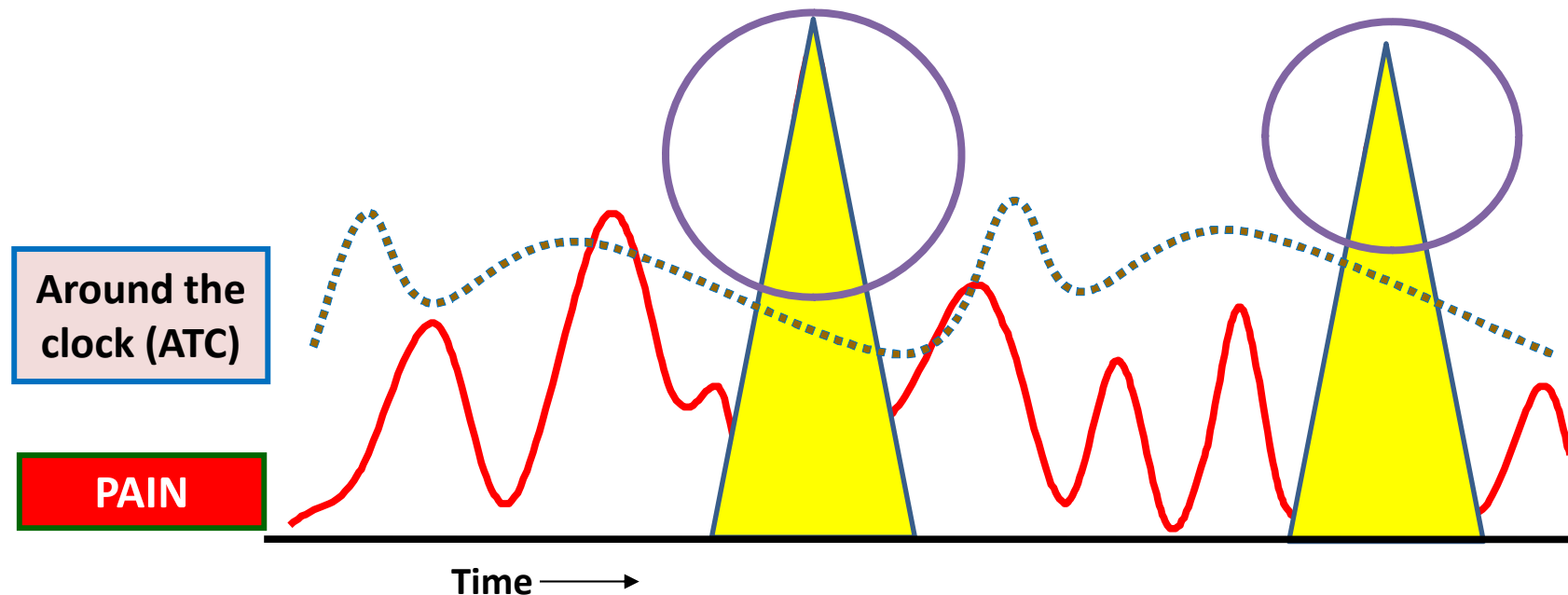
-慢性疼痛控制良好的情況下，出現的短暫劇烈性疼痛。

Portenoy RK, Hagen NA. Breakthrough pain: definition, prevalence and characteristics. *Pain*. 1990;41(3):273-281.



Breakthrough pain → (突發性疼痛)

- Fast onset 來得快 (3~5分鐘達最痛)
- Short duration 去得快 (平均30~60分鐘)
- High intensity 強度強 (平均強度為7.3分)
- Frequent in nature 頻繁發生
(建議控制在一天三次以內)



Oxycodone
(Oxycontin)



hydromorphone
(Jurnista)



Buprenorphine
(Transtec)

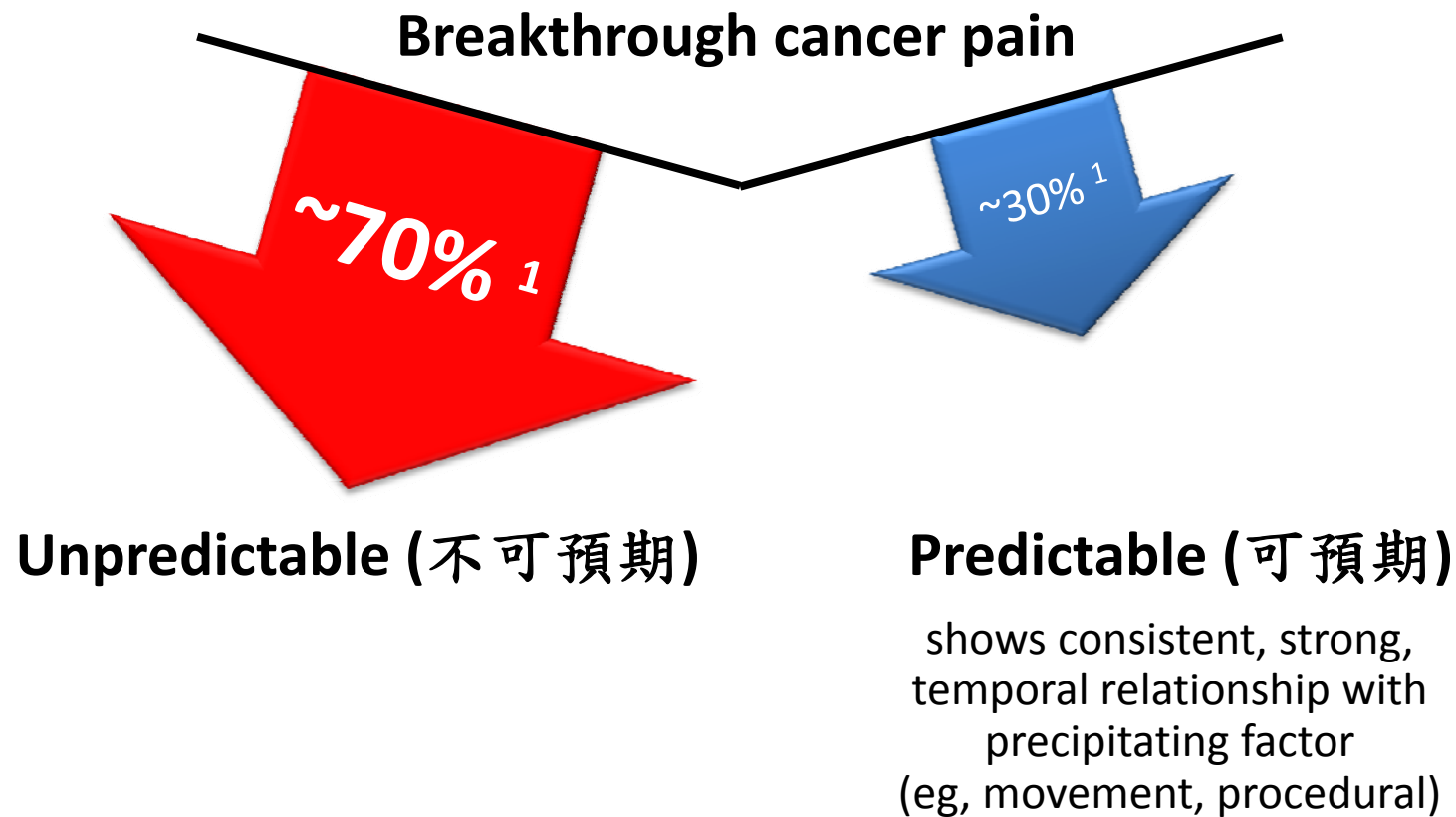


Fentanyl Patch

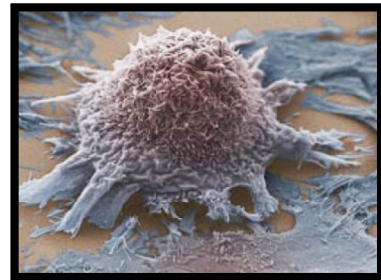


MXL, morphine cont





**Treatment delay/
Abandon treatment**



Tumor progression

&



Treatment procedures

vicious cycles



Breakthrough pain



Anorexia

Depression



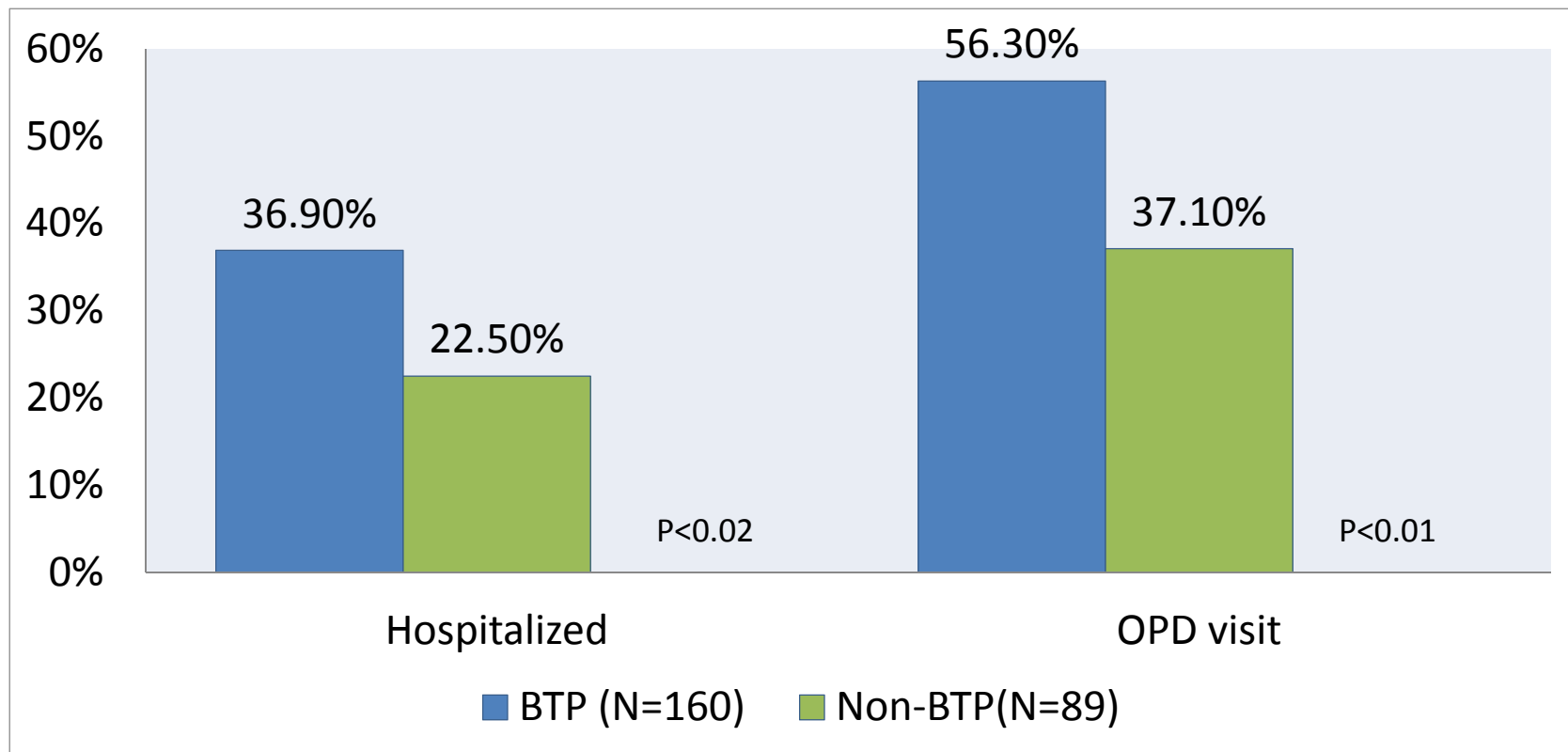
&

Cachexia



1. Nathaniel P. Katz, Kavita L. Gajria, Alicia C. Shillington, Judith J. Stephenson & Qing Harshaw (2017), Postgraduate Medicine, 129:1, 32-39
2. Clin Oncol 2011; 23: 393-398
3. American Pain Foundation. Breakthrough Cancer Pain Survey Fact Sheet. American Pain Foundation; 2012

有突發性疼痛的病人有較高的住院率及門診回訪率



疼痛控制不好，生活品質變黑白

-睡不好、吃不好、情緒不好



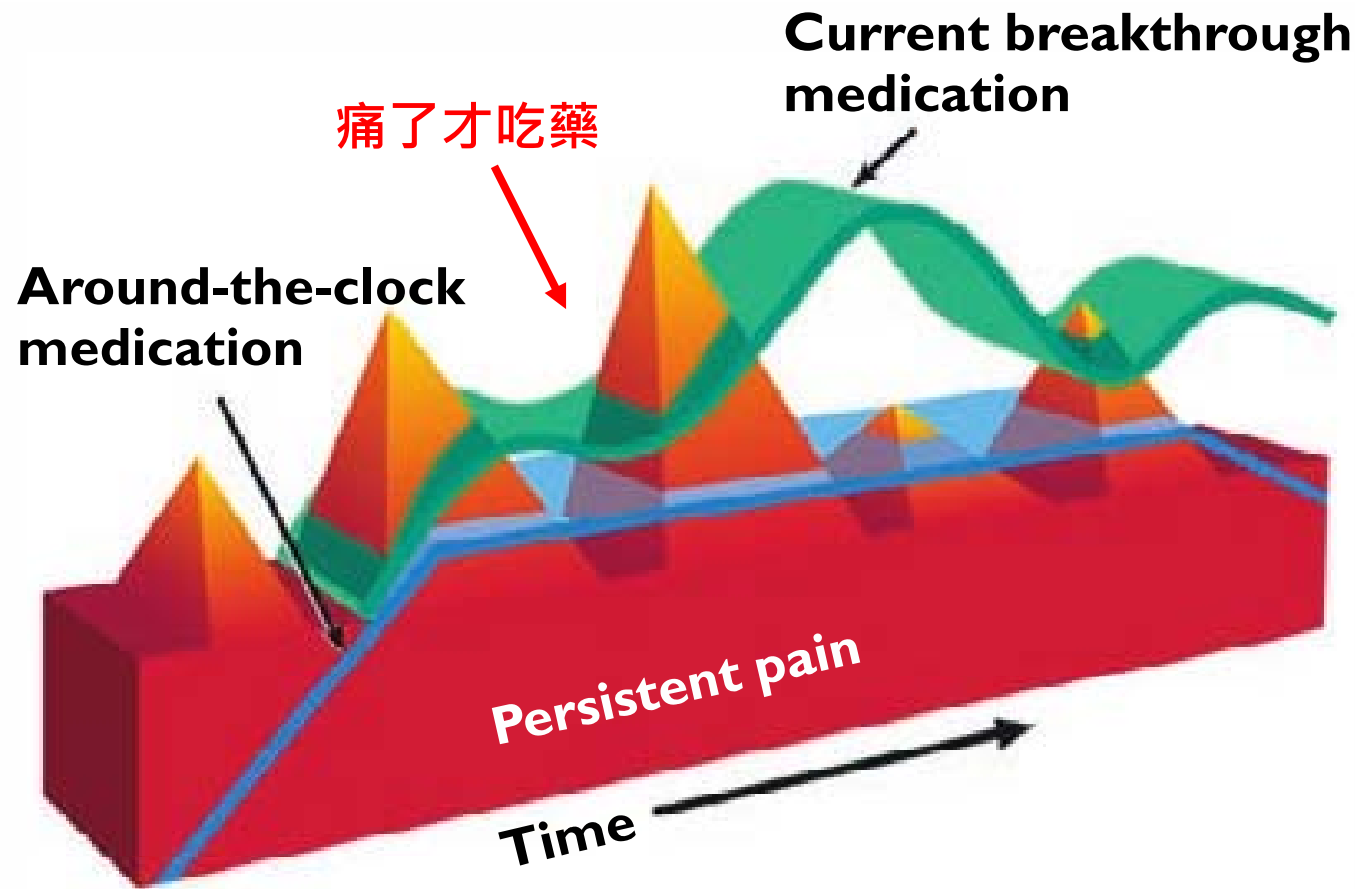
Outline

- 認識突發性癌症疼痛
- 找到突發性癌症疼痛
- 擊敗突發性癌症疼痛



不可預期突發性疼痛:

-防不勝防，生活品質殺手



病人對於突發性疼痛的回饋

- It is terrible
- It feels like being beaten with a bat that's wrapped with barbed-wire
- The doctor got mad at me when I told him the pills did not work
- My doctor was dismissive
- Breakthrough pain occurs right in the hospital and still does not get good treatment
- When I told my doctor I was still having pain on my medicine, I was labelled as “drug-seeking” and this was put in my chart

為何癌症病人沒說“痛”？

1. Patients want their oncologists to focus on their cancer, not on their pain.
2. Patients want their doctors to like them.
3. Patients want to save the medication for when the pain gets really bad.
4. Patients think more pain means more cancer.
5. Patients don't want to give in to the disease.
6. Patients think the need for strong pain meds means they're dying.
7. Patients are worried about becoming addicted.

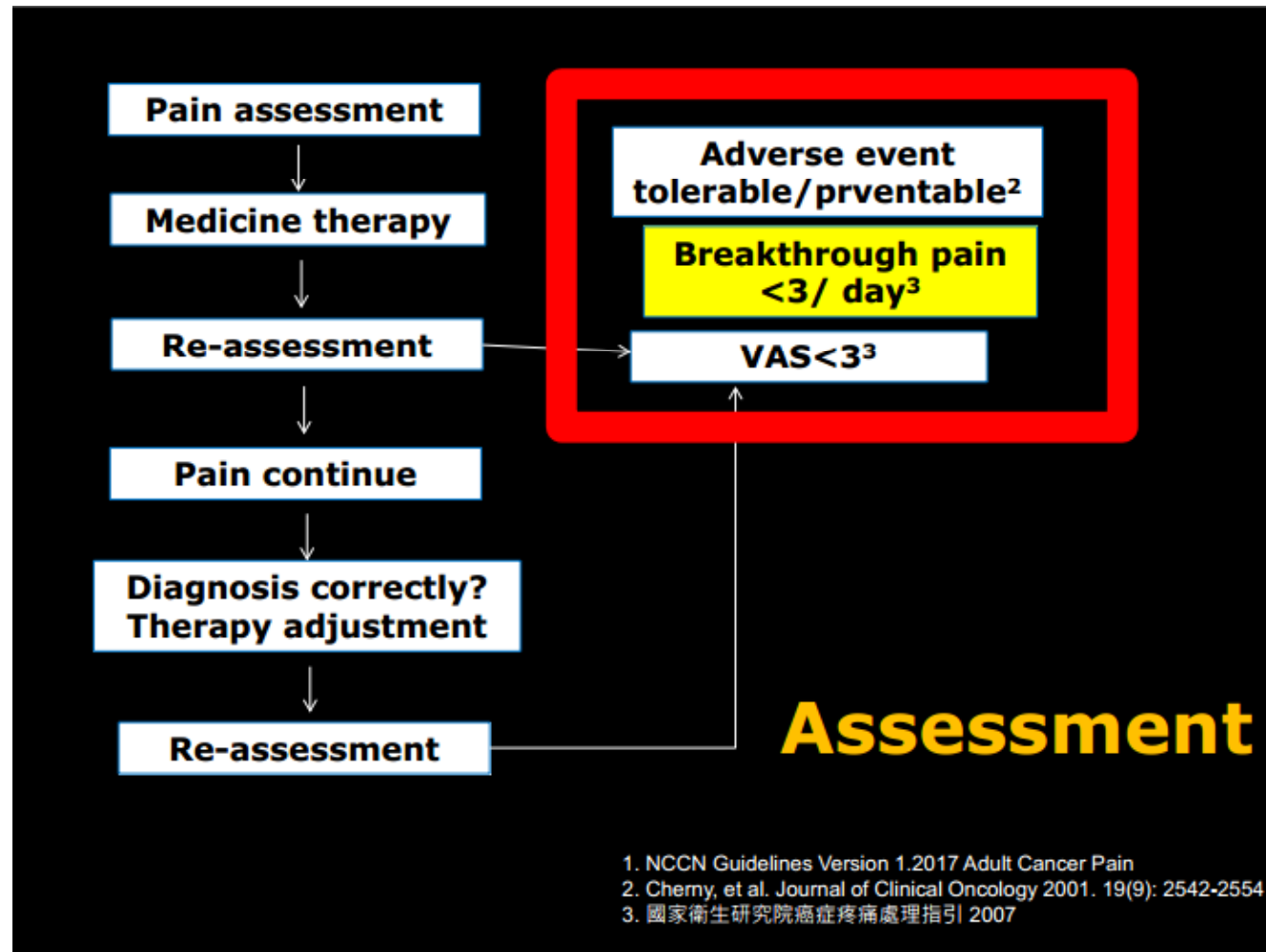
疼痛控制” 加分” 的關鍵因素

“Proactively pain assessment”
主動問

Optimal dose for pain control

Adverse event management

“再評估” 才知道藥品適不適合病人



「一看二問三觀察」： 評估住院病人突發痛控制情形

病人「吃了PRN藥品後」...

■ 一看:

看病患的PRN用藥記錄，一天用幾次PRN?

→ 若這幾天都一天用超過三次，則考慮增加ATC

■ 二問:

吃了要等很久才有效嗎? → 若等很久，考慮換onset更快的

吃了後疼痛強度下降夠多嗎? → 若效果不夠好，考慮加劑量

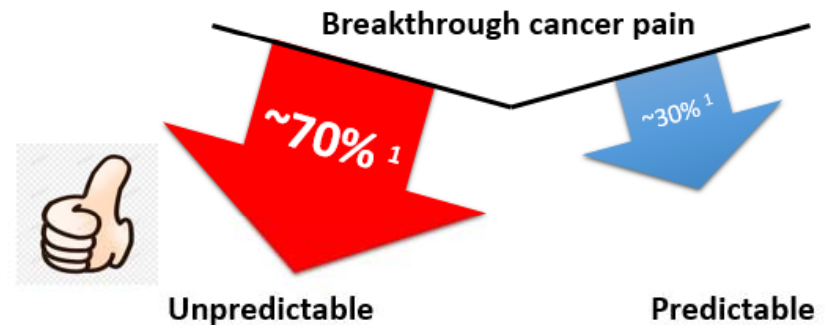
■ 三觀察:

調整用藥後，觀察病人疼痛是否改善

門診快速評估

病人反映:

- “無緣無故痛起來”
→可能遇到不可預期突發性疼痛



- “PRN藥品效果不好”
 - “吃了要等很久才不痛” → PRN速度不夠快
 - “吃了有效但還是會痛” → PRN劑量不足 → 調整PRN劑量

門診怎麼問？

過去一週曾經有疼痛
狀況嗎？

有固定做什麼才痛
嗎？

我開給你的短效藥(膠囊
/錠劑/藥水)效果好嗎？

是速度不夠快？還是痛的
程度降的不夠低？

好像有耶

無緣無故就痛

效果不太好...

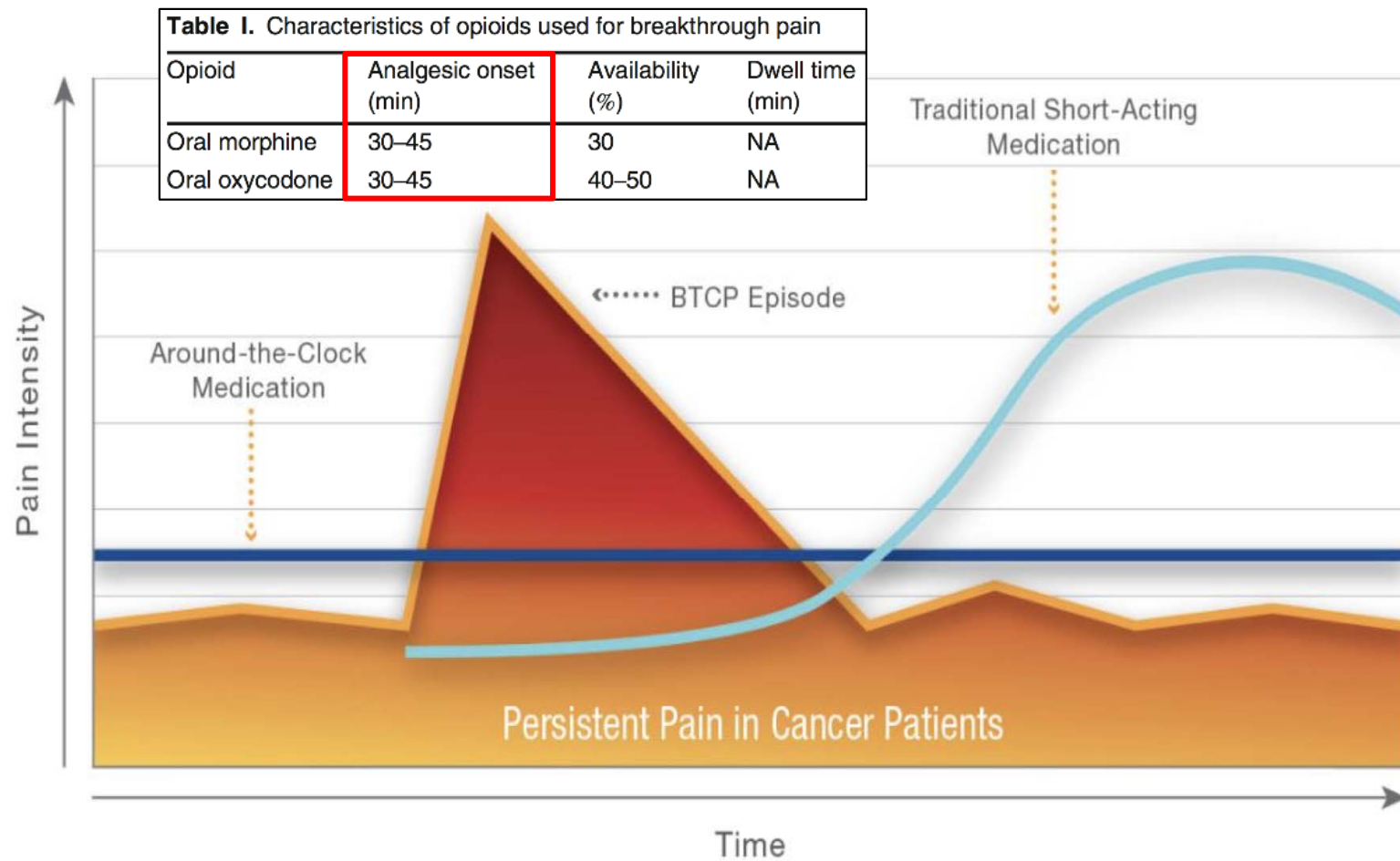
- (1) 不夠快→吃了
要等很久
- (2) 效果差→吃了
有比較好但還
是會痛

Outline

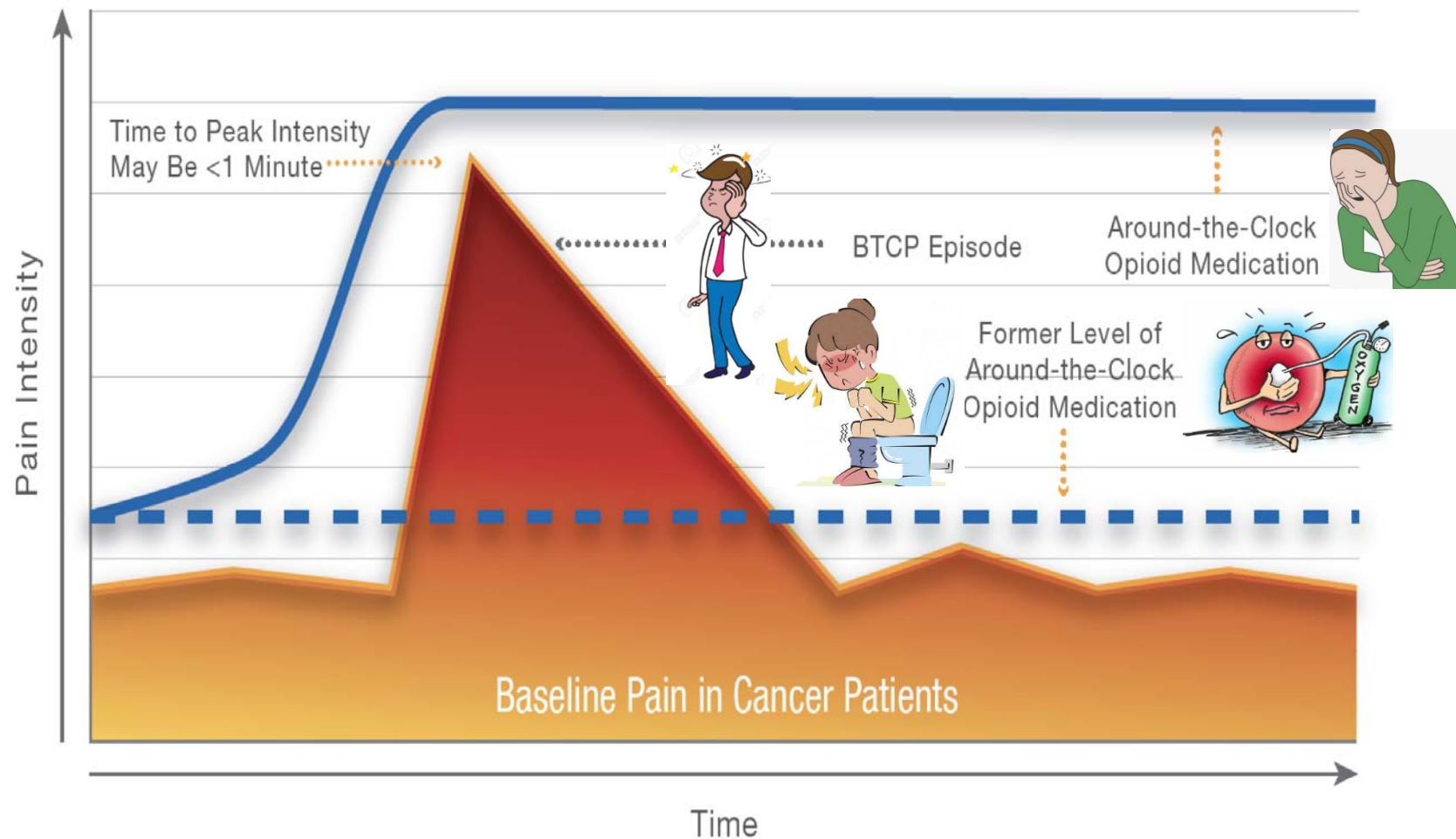
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傳統口服藥品對付突發性疼痛:緩不濟急!

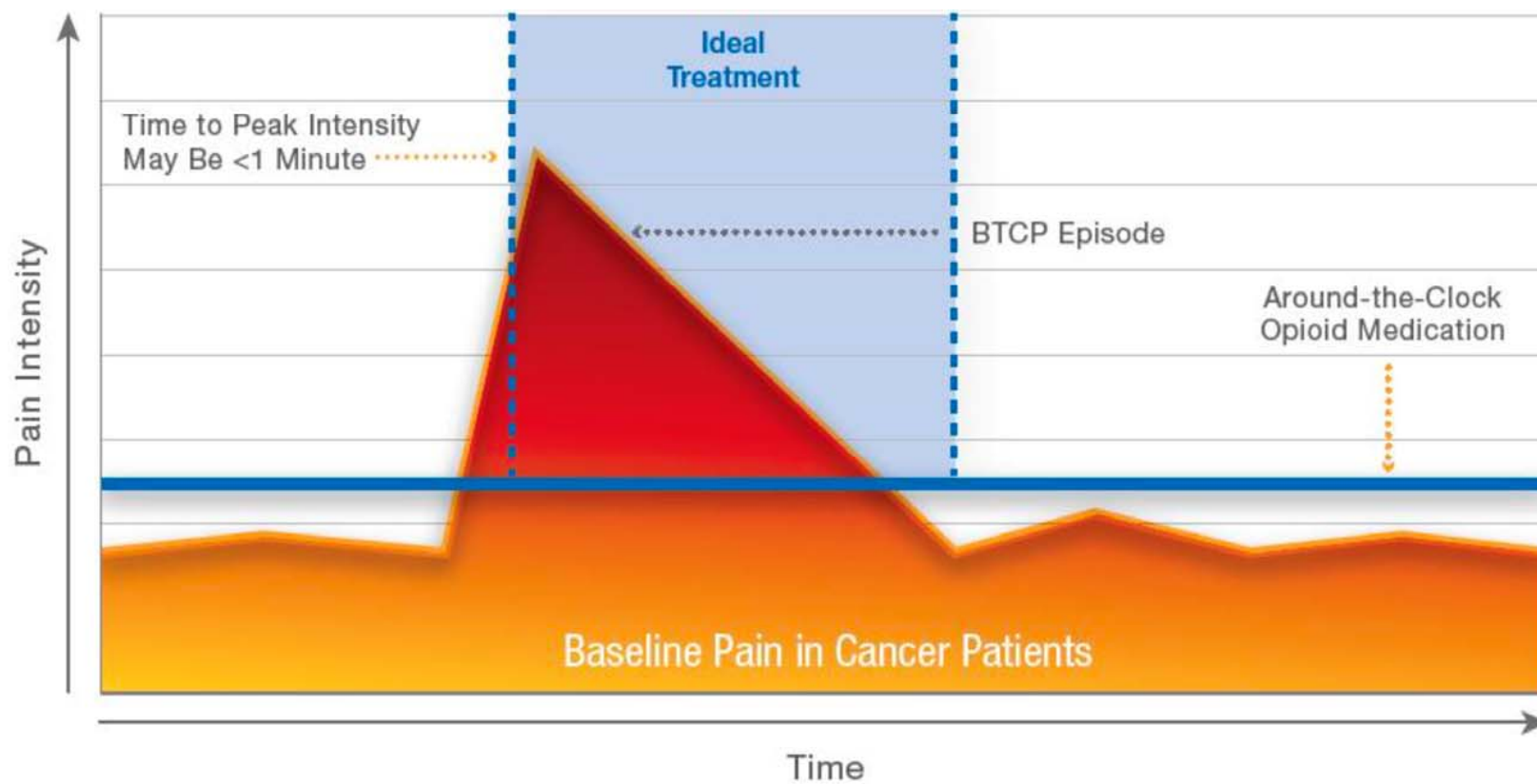


為了不讓突發痛發生，直接墊高ATC劑量...

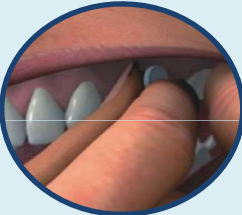
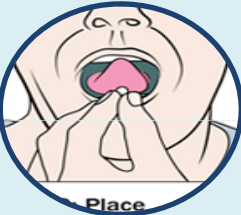


理想的突發痛治療:剛剛好就好!

Onset、Duration與突發痛相當



Rapid-onset-opioid (ROO)

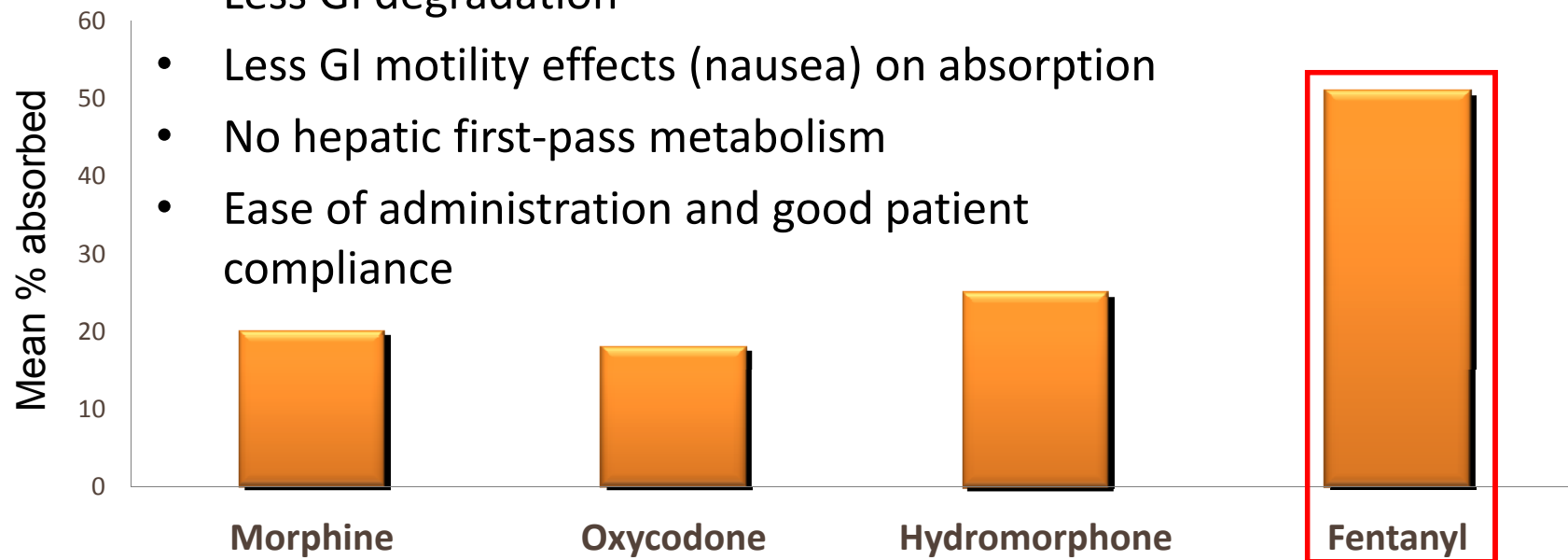
Painkyl®					
1st Generation	2st Generation	3rd Generation	Sublingual	Intranasal	Intranasal
					
1998	2006 2008	2009	2008	2009	2009
Actiq®(US)	Fentora® (US)/ Effentora®(EU)	Onsolis®(US)	Rapinyl®/ Abstral®(EU)	Instanyl® (EU)	Lazanda®(EU)
					
Oral transmucosal lozenge	Fentanyl buccal tablet	Fentanyl buccal soluble film	Sublingual Fentanyl	Intranasal Fentanyl spray	Fentanyl pectin nasal spray
OTFC	FBT	FBSF	SLF	INFS	FPNS

BTcP=breakthrough cancer pain; ROO=rapid-onset opioid; FBSF=fentanyl buccal soluble film;
FBT=fentanyl buccal tablet; FPNS=fentanyl pectin nasal spray; INFS=intranasal fentanyl spray;
OTFC=oral transmucosal fentanyl citrate; SLF=sublingual fentanyl.

1. Smith, H. S. (2013). Journal of Pain Research 6, 189-200
2. Stanley, Theodore H. "The fentanyl story." *The Journal of Pain* 15.12 (2014): 1215-1226.

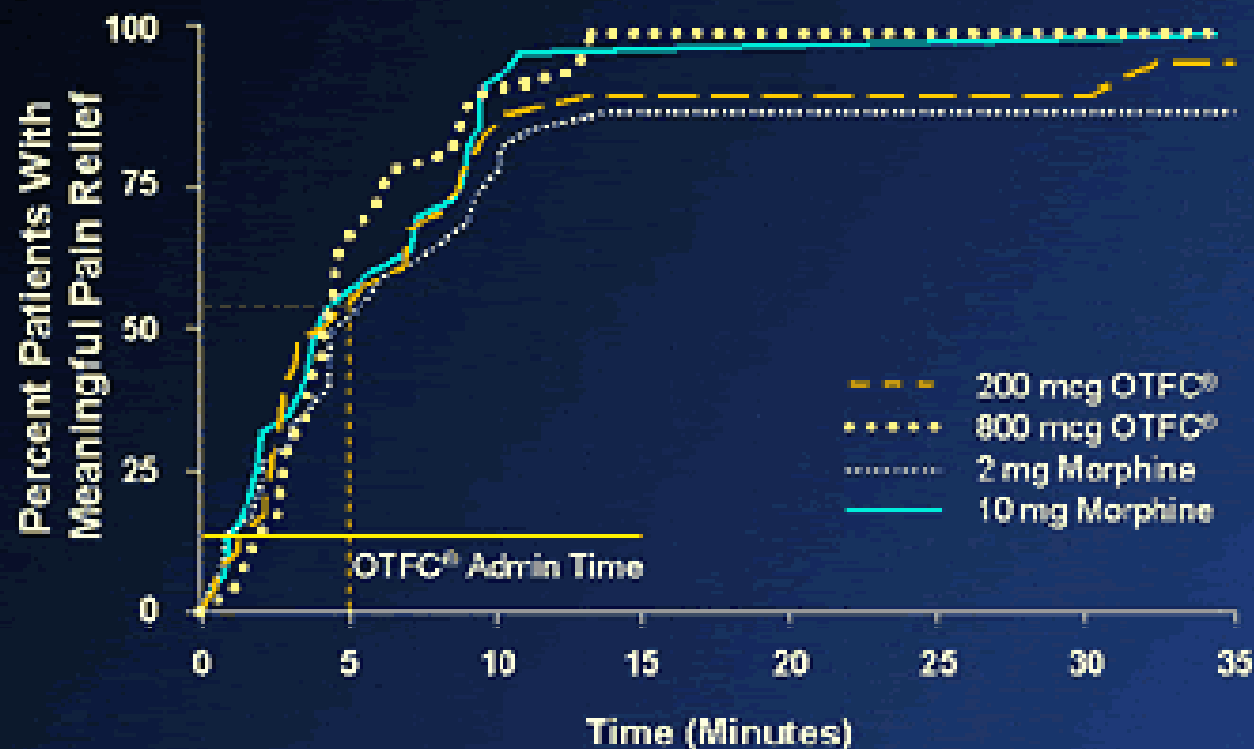
Why are all ROOs fentanyl?

- **Rapid drug delivery** to systemic circulation
- Less GI degradation
- Less GI motility effects (nausea) on absorption
- No hepatic first-pass metabolism
- Ease of administration and good patient compliance



	Hydrophilic ←————→ Lipophilic			
Potency	1	2	4	100

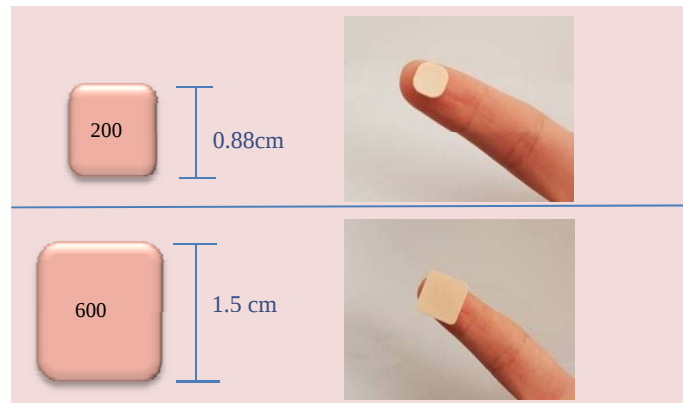
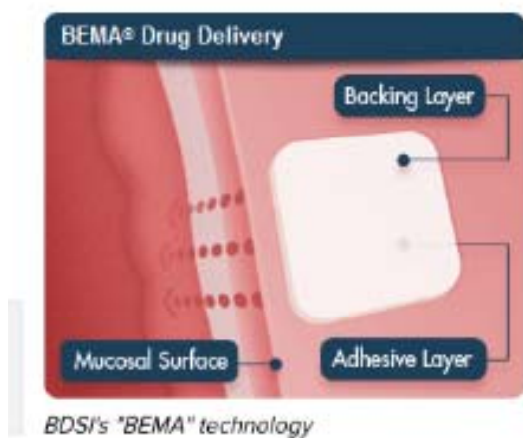
Onset of Pain Relief: OTFC® vs IV Morphine



Adapted from Sevarino FB, et al. *Anesth Analg* 1997;84:S330.

The Newest Generation of ROO in Taiwan: Painkyl® Fentanyl buccal soluble film (FBSF)

Transmucosal fentanyl	Onset of analgesia	Duration
Buccal soluble film (FBSF)	9–15 min	1-2 hrs



口頰給藥

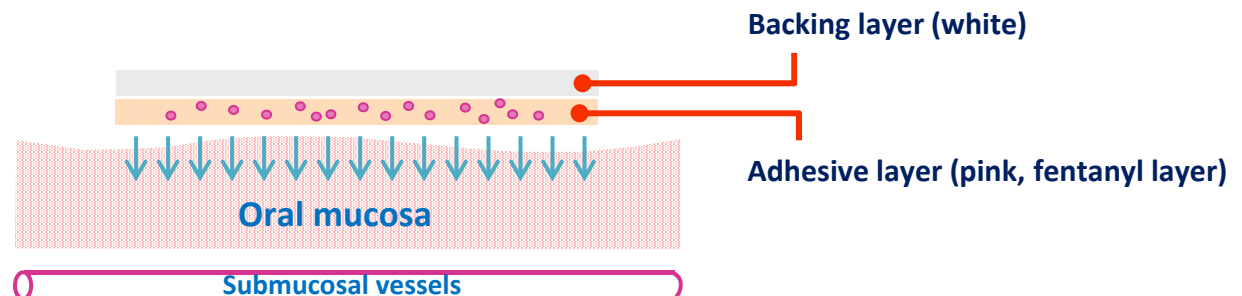
唇內給藥

BEMA technology

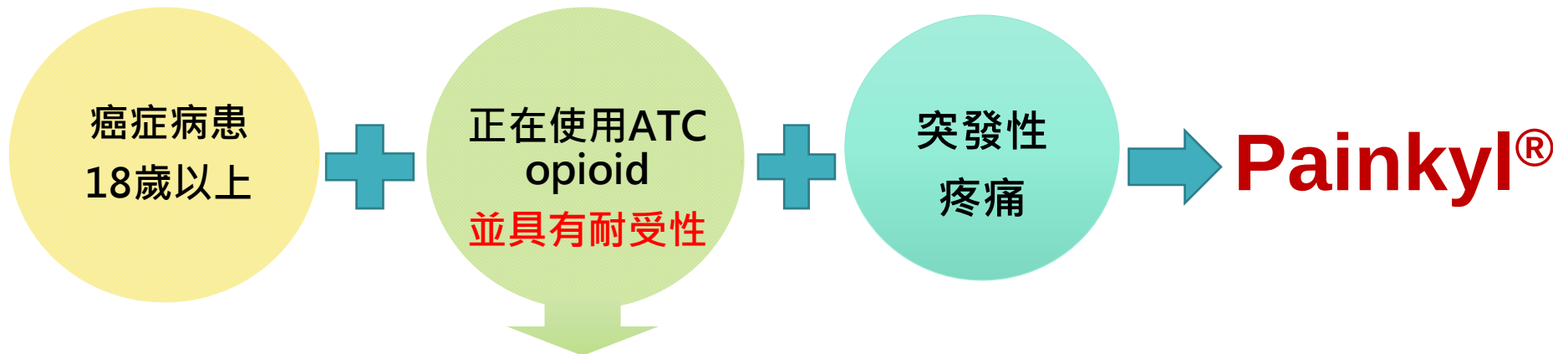
Bio Erodible Muco Adhesion

生物可溶性黏膜黏附雙層釋放技術

(德國生產，美國進口)



Indications to use Painkyl®



•Patients considered opioid tolerant:

- 60 mg oral morphine/day
- 25 mcg transdermal fentanyl/ hour
- 8 mg oral hydromorphone/day
- 30 mg oral oxycodone/day
- 25 mg oral oxymorphone/day,

or an equi-analgesic dose of another opioid **for one week or longer.**

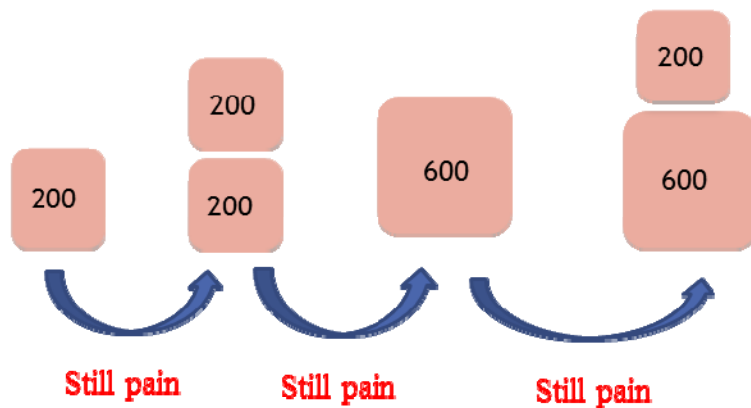
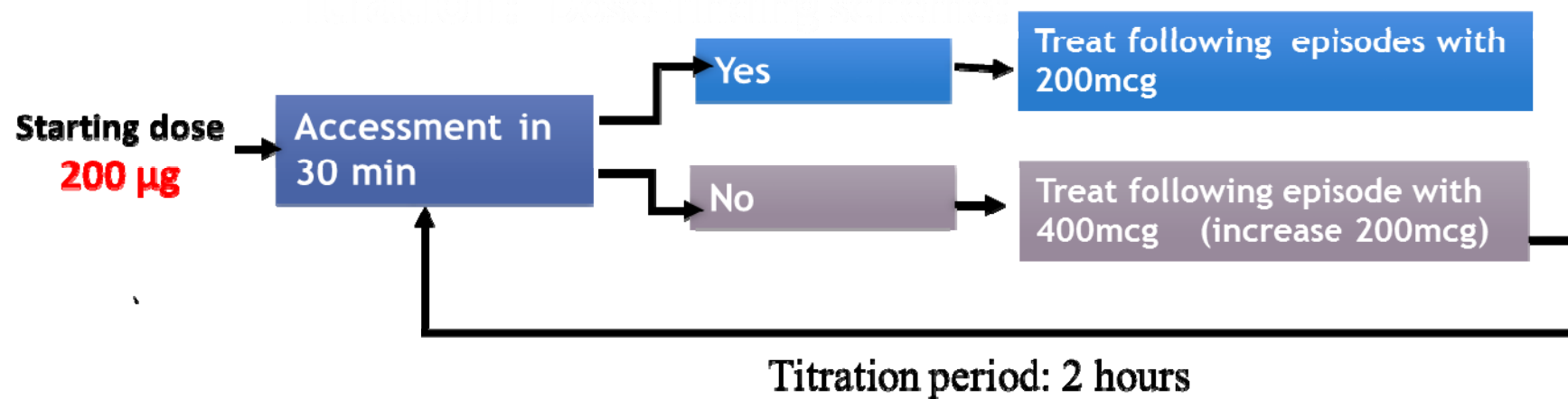
- Patients must remain on around-the-clock opioids while taking Painkyl®

Taiwan's **NHI** for Fentanyl citrate

1.1.9. Fentanyl citrate 口頰溶片或口頰錠

1. 限用於突發性疼痛(breakthrough pain)，並已接受過口服 morphine 至少 60mg/day、oxycodone 至少 30mg/day、hydromorphone 至少 8mg/day、或 fentanyl 貼片劑至少 25/mcg/hr 或其他等止痛劑量之類鴉片藥物達一星期(含)以上之 18 歲(含)以上癌症患者。
2. 不得用於急性或術後疼痛之處置。

Titration of Painkyl® to Effective Dose

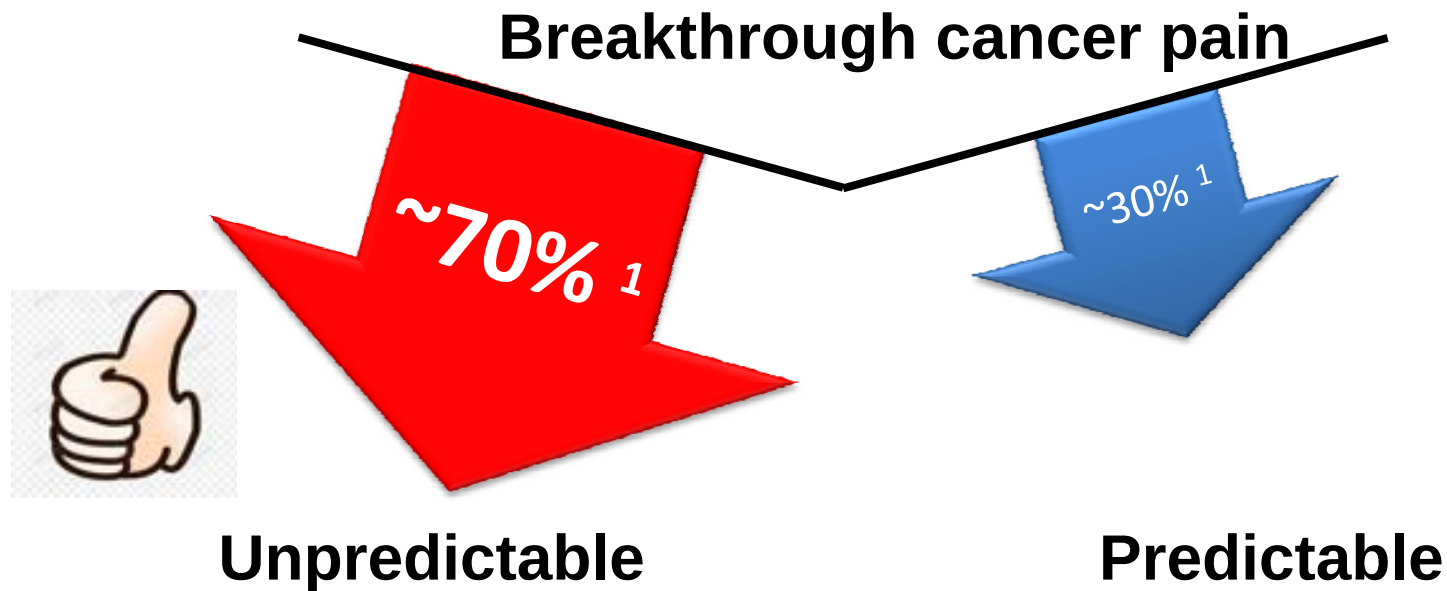


If patients experienced BTcP **more than four times** per day, considering to increase ATC dose

Case Sharing

- 57 y/o oropharyngeal cancer (T4N0M0), right neck
- Post CCRT -> Partial response
- Persistent mass lesion(+) -> Pain
- Pain control:
 - Fentanyl (25) 4 patches
 - Morphine(15) 2# Q4H
- Breakthrough pain: 1-2times, VAS:7
 - IV morphine 2 vials
 - Shift to Painkyl -> OK

The role of Rapid-Onset -Opioids



不可預期突發性疼痛 **首選**
2

可預期突發性疼痛二線 **用藥**
3

1. Mercadante S, Marchetti P, Cuomo A, et al. Cancers (Basel). 2018 Jun 1;10(6). pii: E175.
2. 2018 ESMO clinical practice guideline: Management of cancer pain in adult patients
3. 2020 NCCN guideline: Adult Cancer Pain version 1

Thank you very much!!

