

癌症疼痛藥物治療簡介



江佳駿
CHIACHUN CHIANG M.D.

WHO GUIDELINES FOR THE MANAGEMENT OF CANCER PAIN

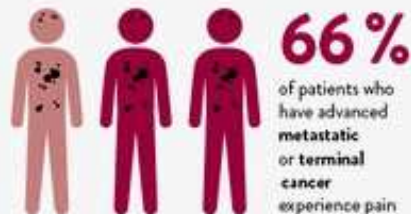
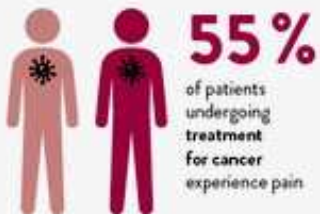


18.1 **CASES**
MILLION of cancer/year

9.6 **DEATHS**
MILLION from cancer/year

1/6 **DEATHS**
is due to cancer

PAIN is an unpleasant sensory and emotional experience associated with actual or potential damage of tissues. Individuals experience and express pain differently.



PAIN RELIEF improves the quality of life of patients with cancer.

The goal of pain management is to relieve pain to a level that allows for an **acceptable quality of life**.

Patients with cancer may require pain relief at **all stages of their disease** and not only at the end of life.

Better results in terms of pain and symptom management can be achieved when:

- palliative care is introduced **early** in the course of illness;
- an approach **tailored to each individual** is adopted together with disease-modifying therapies.



ACCESS TO PAIN RELIEF AND PALLIATIVE CARE IS A HUMAN RIGHT AND AN ESSENTIAL PART OF UNIVERSAL HEALTH COVERAGE.



治
療
指
引

癌症疼痛之 藥物治療指引

Guidelines for
the Pharmacological
Management of
Cancer Pain
in Taiwan

第七版

7th
Edition



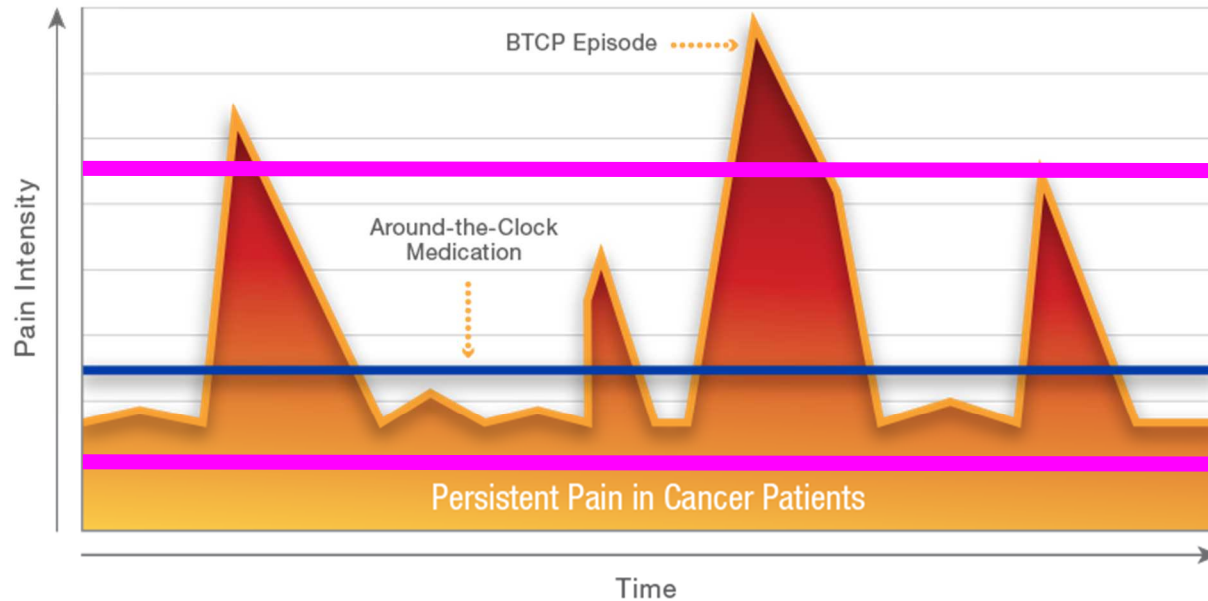
台灣疼痛醫學會



台灣癌症安寧緩和醫學會

Chronic Cancer Pain (慢性癌症疼痛)

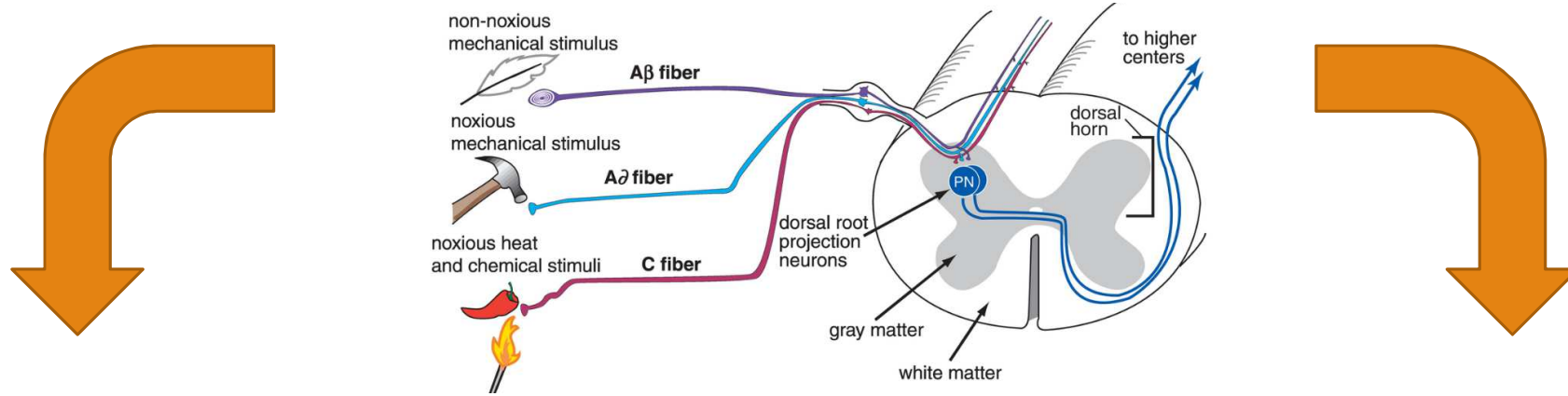
Illustration of Persistent Pain and Breakthrough Cancer Pain¹



- Causes, onset, type, site, absence/presence of radiating pain, duration, intensity, relief and temporal patterns of the pain, number of BTcPs
- Presence of trigger factors and signs and symptoms associated with the pain
- Presence of relieving factors
- Use of analgesics and their efficacy and tolerability
- Description of the pain quality:
 - Aching, throbbing, pressure: often associated with somatic pain in skin, muscle and bone
 - Aching, cramping, gnawing, sharp: often associated with visceral pain in organs or viscera
 - Shooting, sharp, stabbing, tingling, ringing: often associated with NP caused by nerve damage

非專家處方

傷害性疼痛 Norciceptive Pain



Somatic

- Nociceptors are involved
- Often well localized
- Usually described as throbbing or aching
- Can be superficial or deep

Visceral

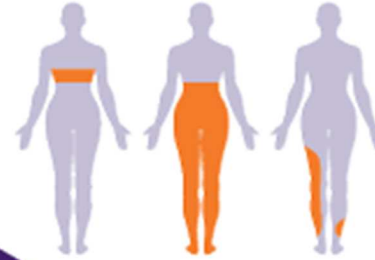
- Involves hollow organ and smooth muscle nociceptors that are sensitive to stretching, hypoxia and inflammation
- Pain is usually referred, poorly localized, vague and diffuse
- May be associated with autonomic symptoms (e.g., pallor, sweating, nausea, BP and HR change)

神經病變痛 Neuropathic Pain

Post-herpetic neuralgia
8% of herpes zoster patients



Spinal cord injury
67% of patients with spinal cord injuries



Painful diabetic neuropathy
26% of patients with type 2 diabetes



Multiple sclerosis
28% of patients with multiple sclerosis



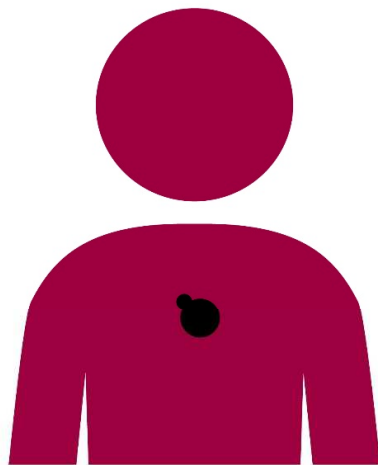
Low back nerve root pathology
10-17% of patients with low back pain



Stroke
8% of patients with stroke



Neuropathic pain
Pain caused by a lesion or disease of the somatosensory nervous system

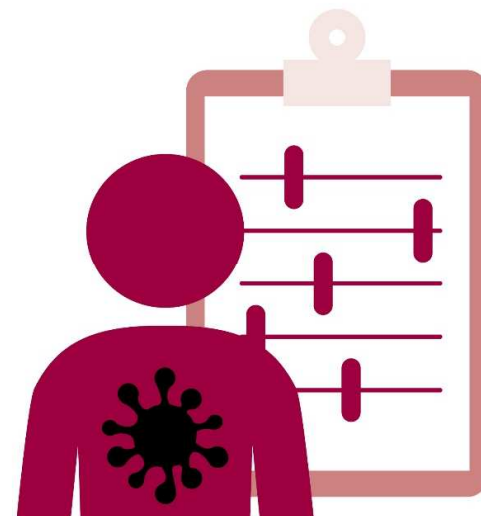


Palliative care is introduced **early** in the course of illness

止痛藥不會越吃越重
可以改善睡眠增加體力

同時開始
抗癌治療

An approach **tailored to each individual** is adopted together with disease-modifying therapies



Pain relief improves the quality of life of patients with cancer



World Health
Organization

#Cancer #PalliativeCare

Where Do Strong Opioids Come From?

OPIUM = dried latex from opium poppy

天然の尚好嗎？



Opium poppy



NATURAL

SEMI-SYNTHETIC

FULLY SYNTHETIC

Morphine

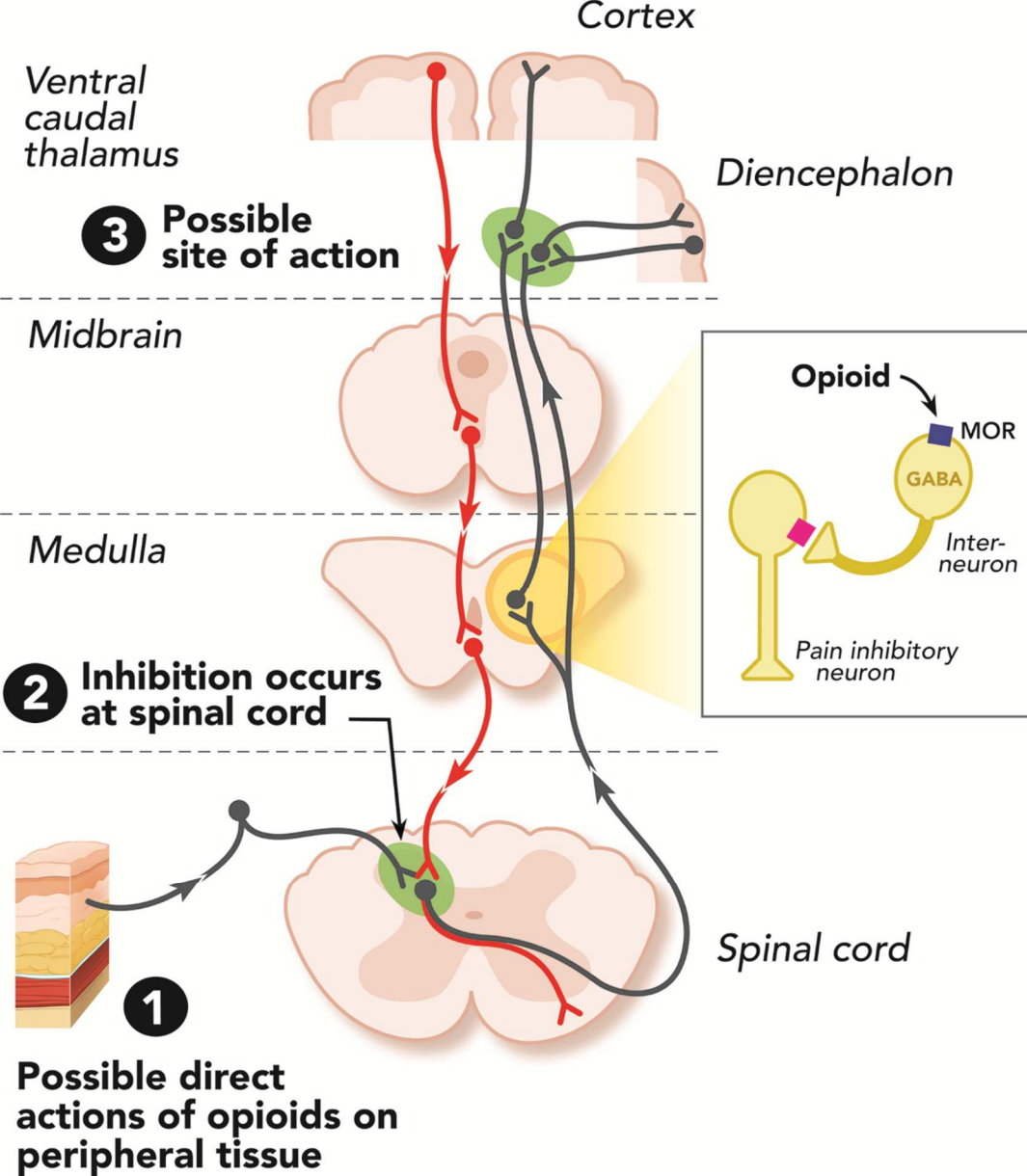
Codeine

Thebaine

↓
Hydromorphone

↓
Oxycodone
Naloxone
Buprenorphine
Others

Fentanyl Pethidine Methadone



μ receptors

鎮痛、呼吸抑制、欣快感、縮瞳、
身體依賴、鎮靜、抑制胃腸蠕動

κ receptors

鎮痛、鎮靜、縮瞳、煩躁不安

δ receptors

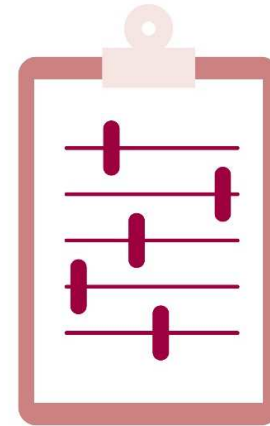
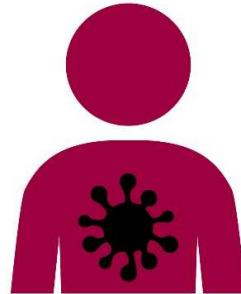
鎮痛、呼吸抑制、抑制胃腸蠕動

Given on a regular basis **by the clock** rather than on demand

Oral administration is preferred



The dose should be determined on an **individual basis**


















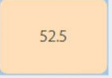
Pain relief improves the quality of life of patients with cancer



World Health
Organization

#Cancer #PalliativeCare

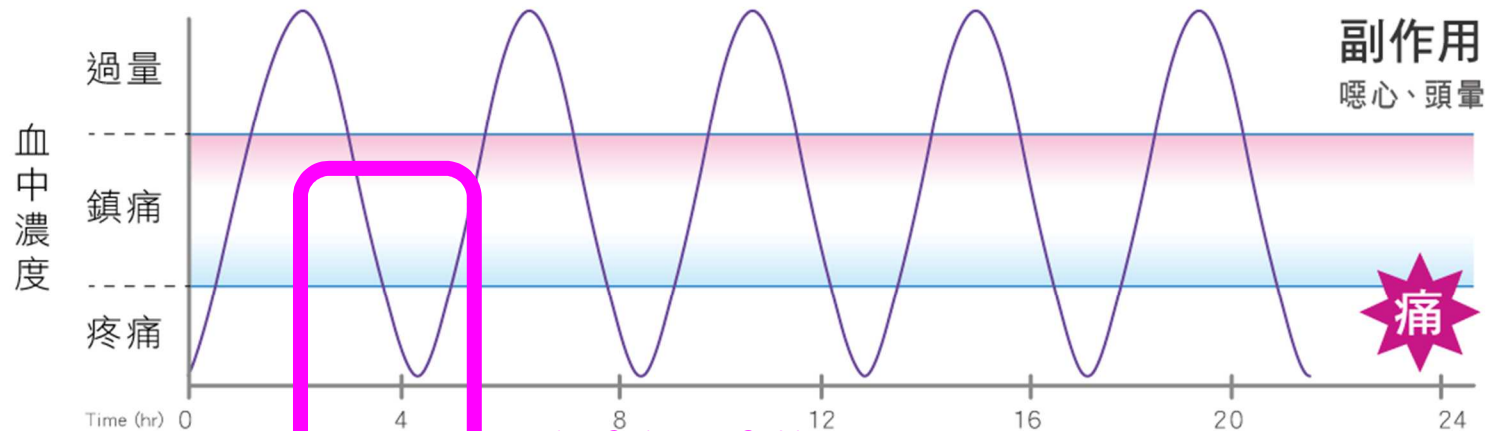
台灣現有主要長短效類鴉片藥物

	Morphine	Oxycodone	Fentanyl	Hydromorphone	Buprenorphine
速效藥物 Breakthrough Pain	 <p>Morphine Sulfate 15mg</p>  <p>Morphine Injection</p>	 <p>OxyNorm® 5mg</p>	 <p>Fentanyl Buccal Films</p>		 <p>Temgesic SL 0.2mg</p>
長效藥物 Background Pain	 <p>Morphine SR 30 mg</p>  <p>MST® 60 mg</p>  <p>MXL® 60 mg</p>	 <p>OxyContin® 10mg</p>  <p>OxyContin® 20mg</p>	 <p>12.5 µg/h</p>  <p>25 µg/h</p>  <p>50 µg/h</p>	 <p>Hydromorphone OROS 8 mg</p>	 <p>35</p> <p>Transtec 35µg/h</p>  <p>52.5</p> <p>Transtec 52.5µg/h</p>

1. 服藥頻繁

2. 高低起伏的血中濃度

劑量過高有副作用，劑量過低止痛效果不佳



✓ 提供良好疼痛控制

✓ 減少服藥頻率

✓ 穩定血中濃度

較少副作用與疼痛控制不佳發生率

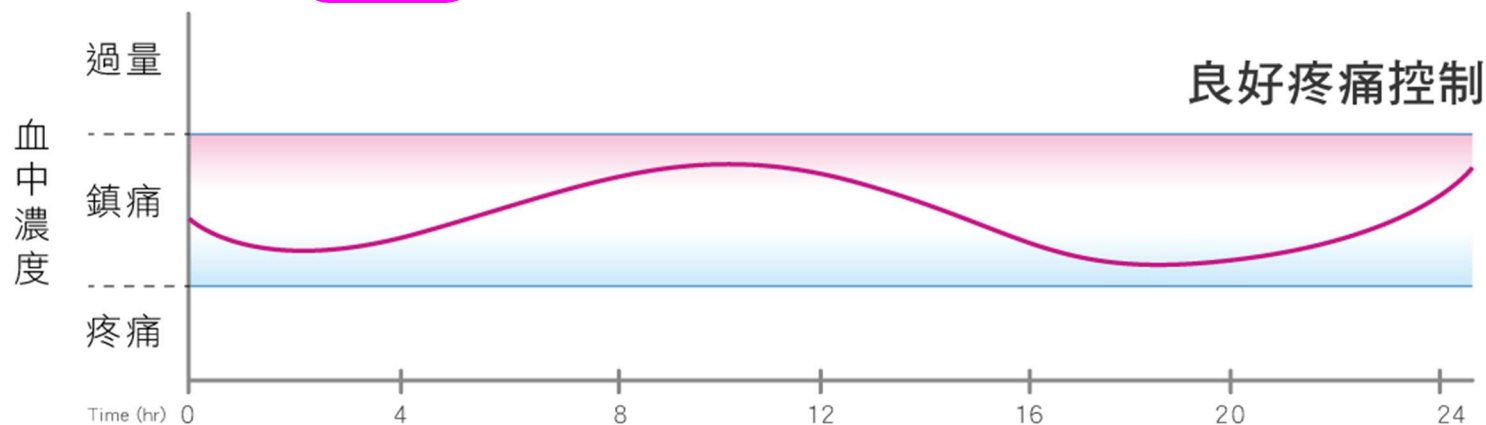
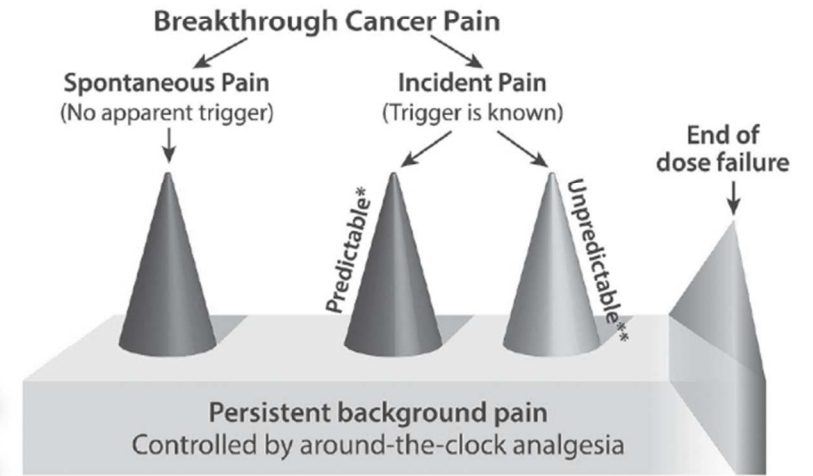
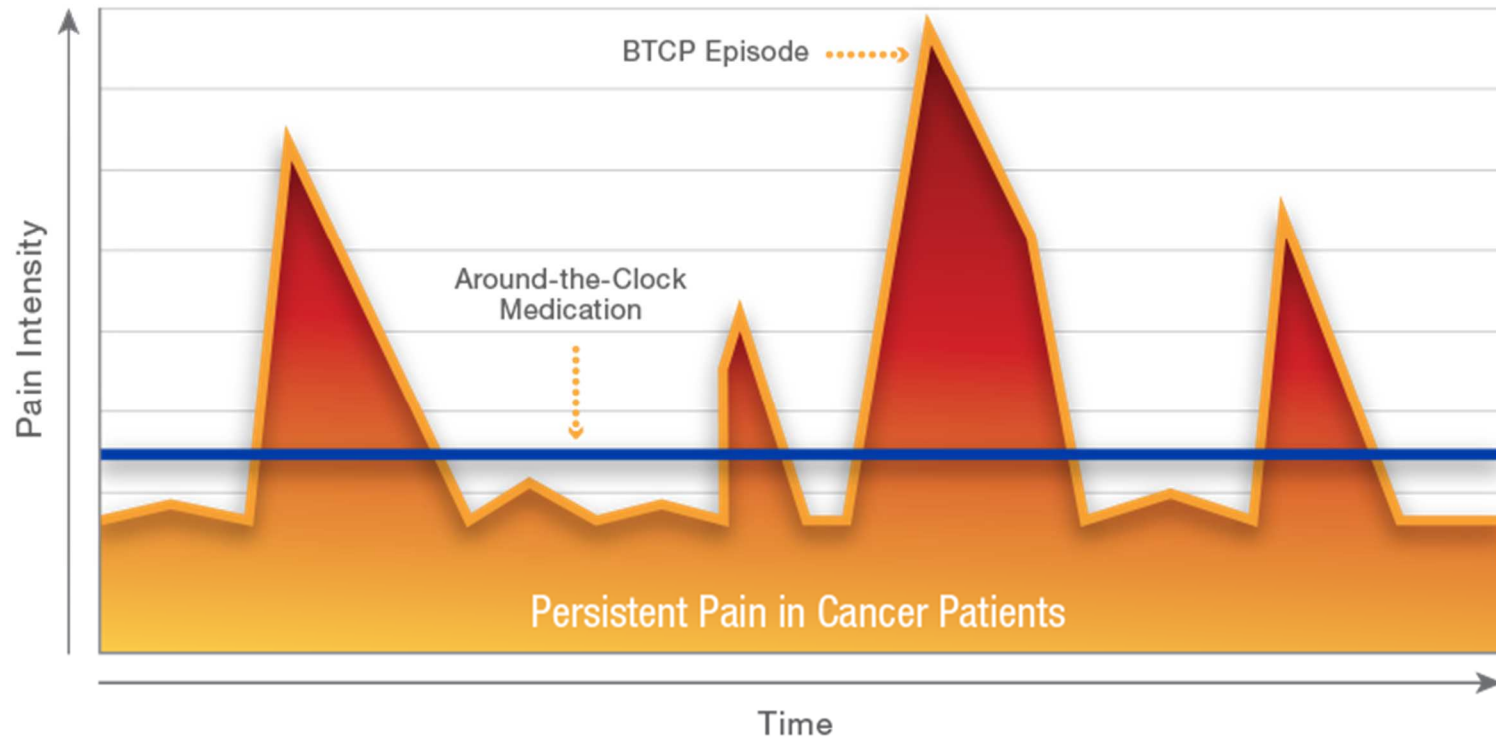
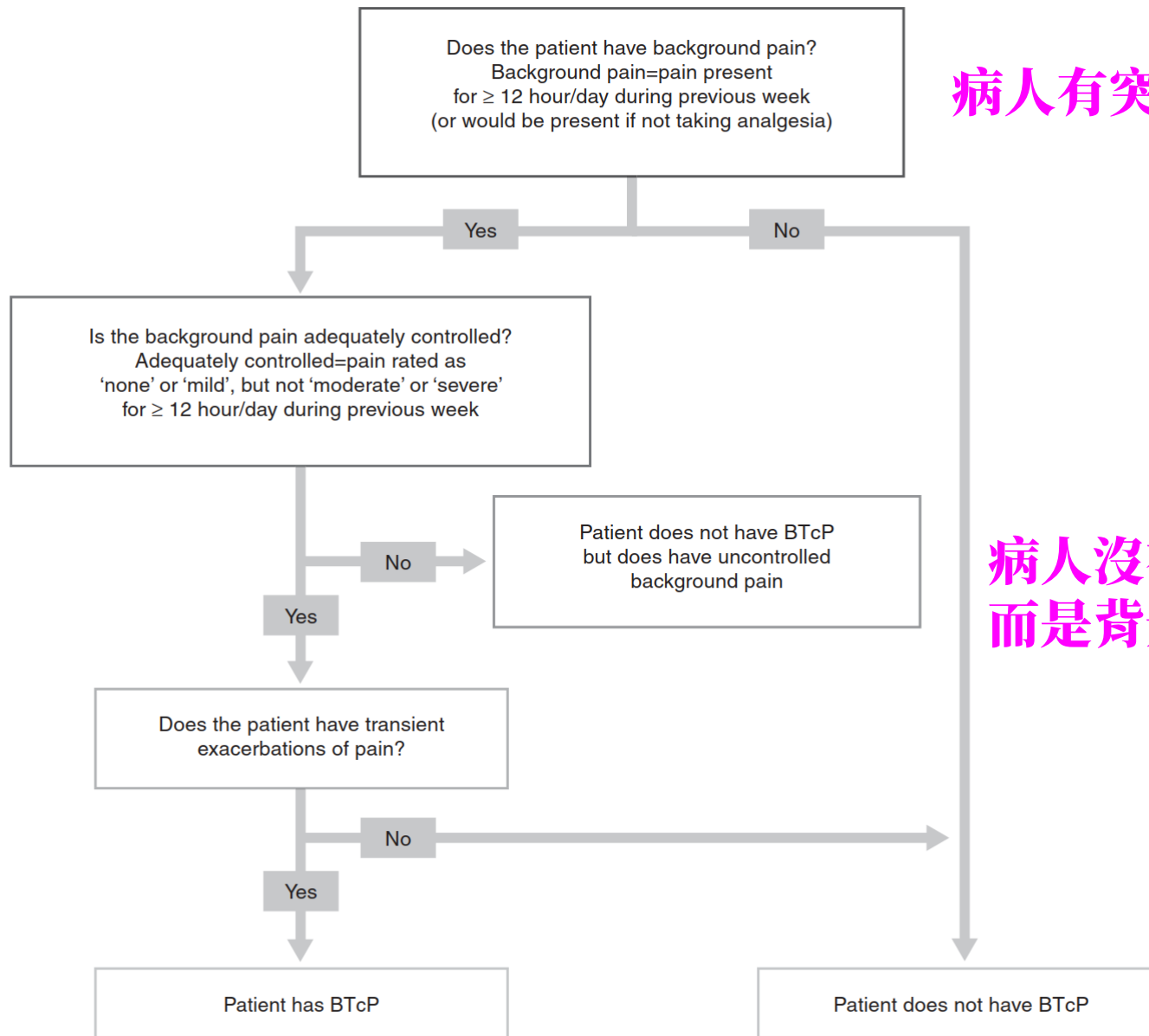


Illustration of Persistent Pain and Breakthrough Cancer Pain¹



背景疼痛控制
是否得宜?

病人的疼痛是
否符合突發性
疼痛?

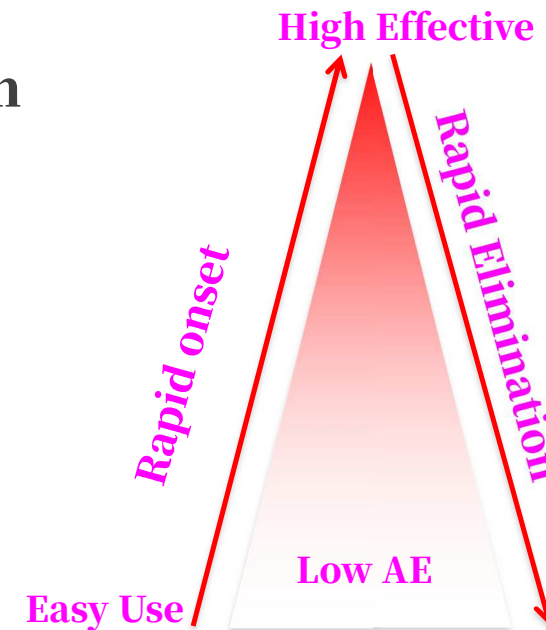
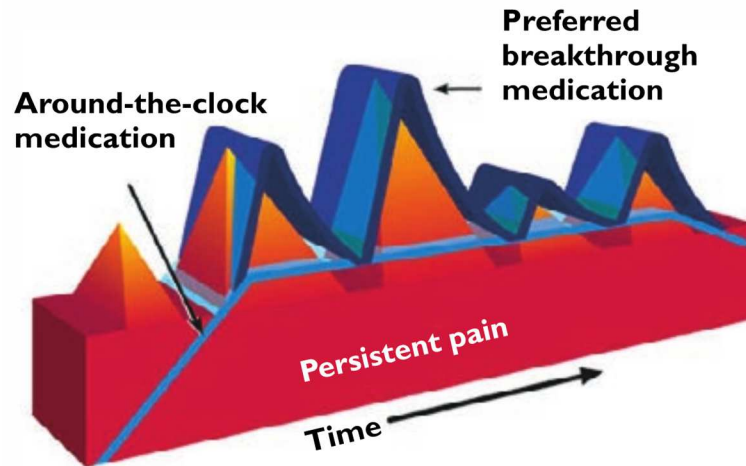


病人有突發性疼痛嗎?

病人沒有突發性疼痛
而是背景疼痛控制不佳

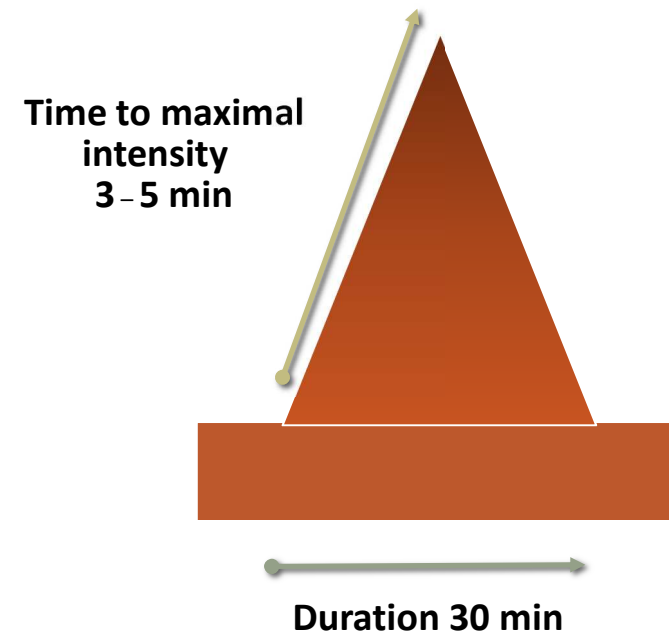
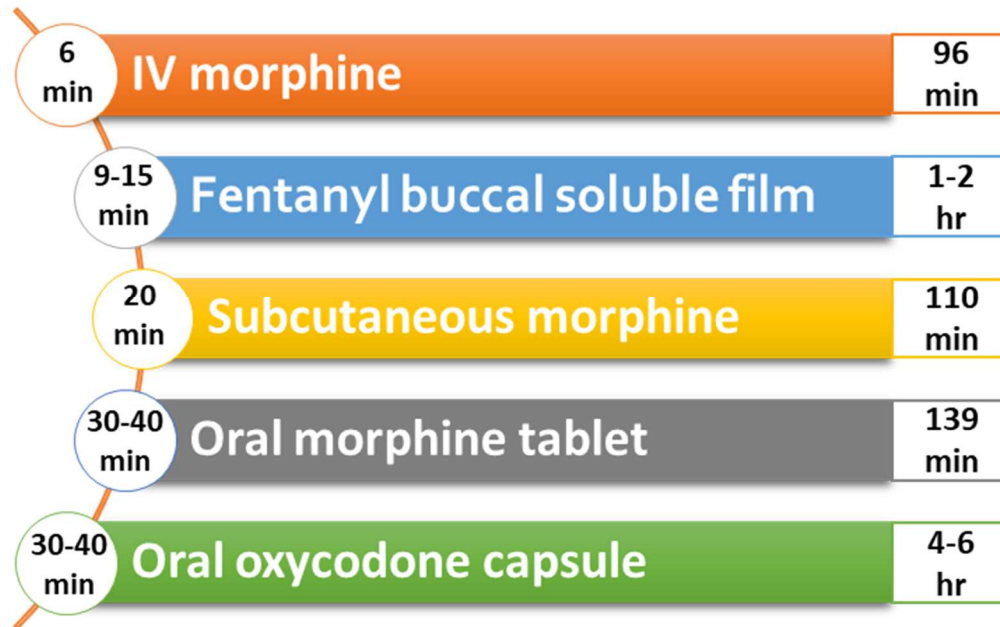
The Gold Standard Treatment for BTcP

1. **Rapidly** effective
2. To avoid accumulation and long-lasting side effects: **rapid elimination**
3. Well tolerated with **few side effects**
4. **Easy to use**, even in case of bowel occlusion
5. Superior to conventional treatments



Onset of Different Opioid Formulations

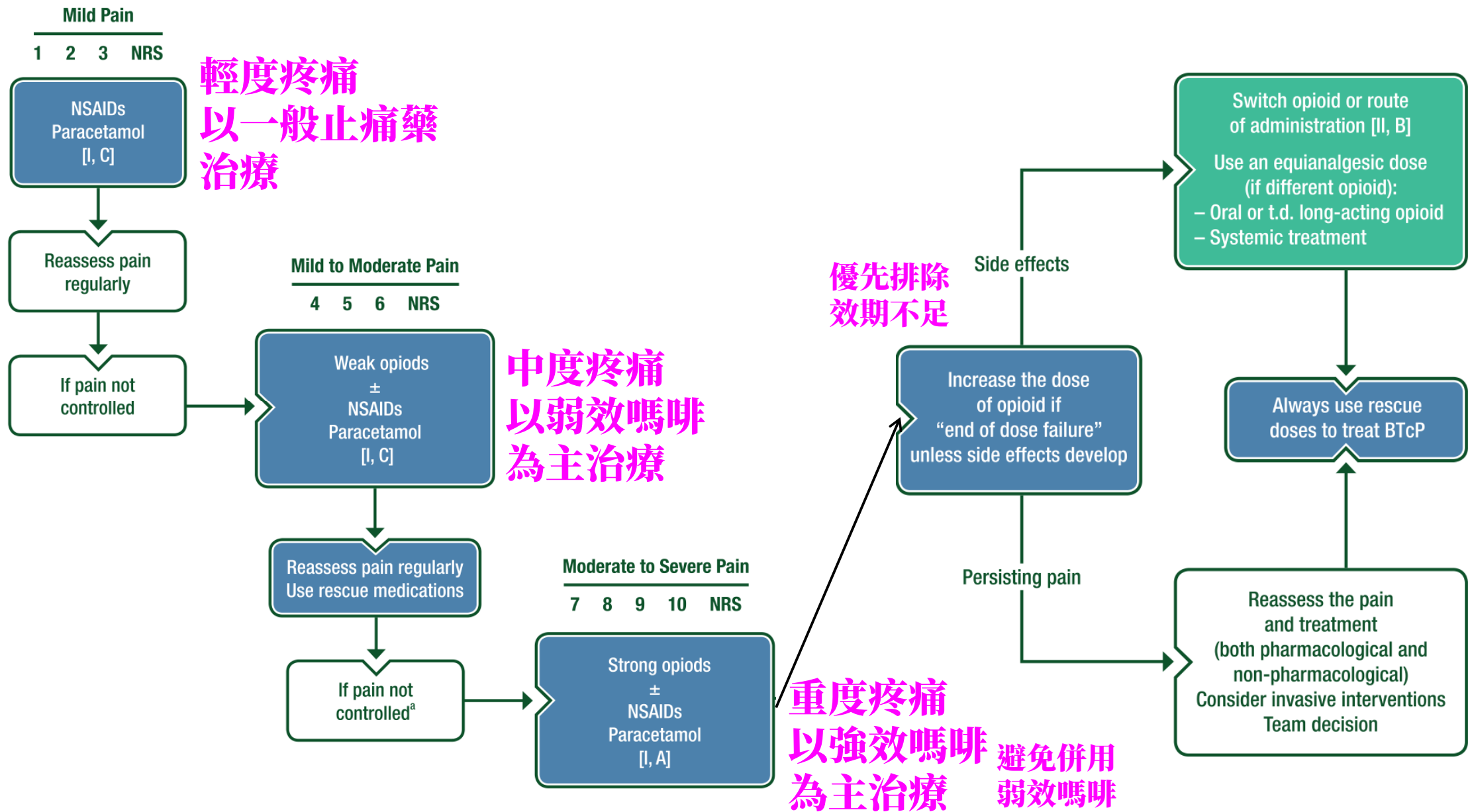
The slow onset of oral morphine does not correlate with the sudden onset and short time to maximum severity of BTcP¹.

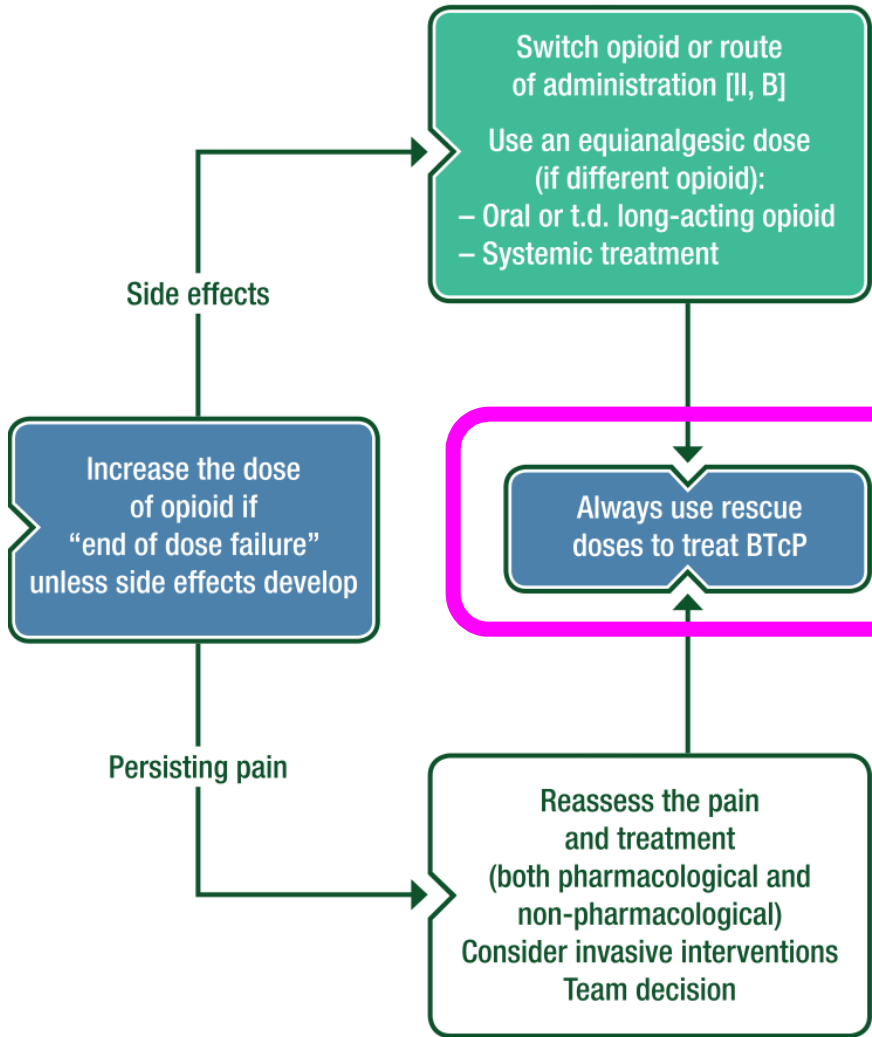


BTcP=breakthrough cancer pain; IV=intravenous; ROO=rapid-onset opioid.

1. Smith H. CNS Drugs. 2012;26(6):509-35. 2. Upton RN, et al. Clin Pharmacokinet. 1997;33(3):225-44.

3. Vasisht N, et al. Clin Drug Investig. 2009;29(10):647-54. 4. Mercadante S. Drugs. 2012;72(2):181-90.





轉換藥物或使用途徑
但效果有限
配合輔助藥物

Buccal and sublingual administration

FENTORA® PROVIDES FLEXIBILITY FOR EACH PATIENTS

使用新一代RRO
(rapid onset opioids)

重新評估疼痛種類劑量
考慮介入性治療

e.g.: nerve block,
bone cement...

BUCCAL



Between the cheek and the gum

SUBLINGUAL



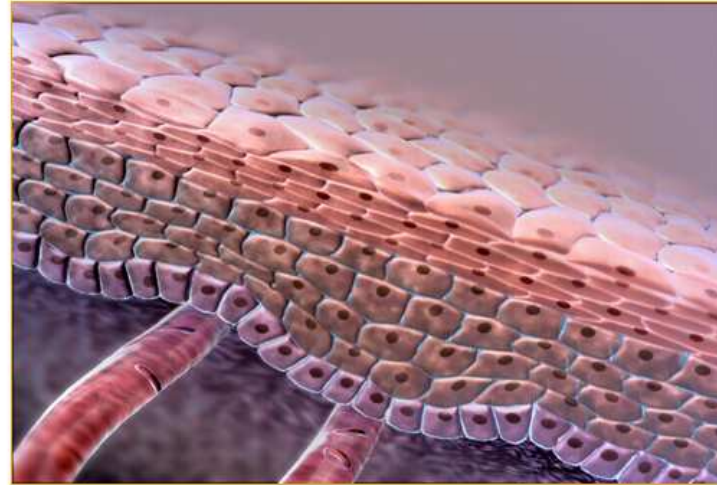
Under the tongue



Most Rapid Onset Opioids are Administered via Buccal Mucosa

Characteristics of Buccal Mucosa

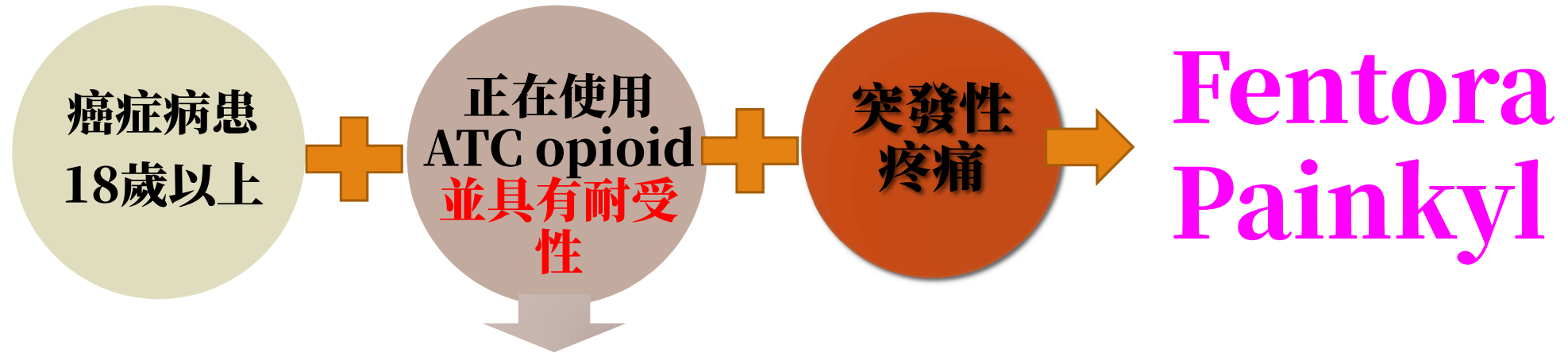
- Large surface area
- Uniform temperature
- High permeability
- Well vascularized



Advantage of transmucosal absorptions

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

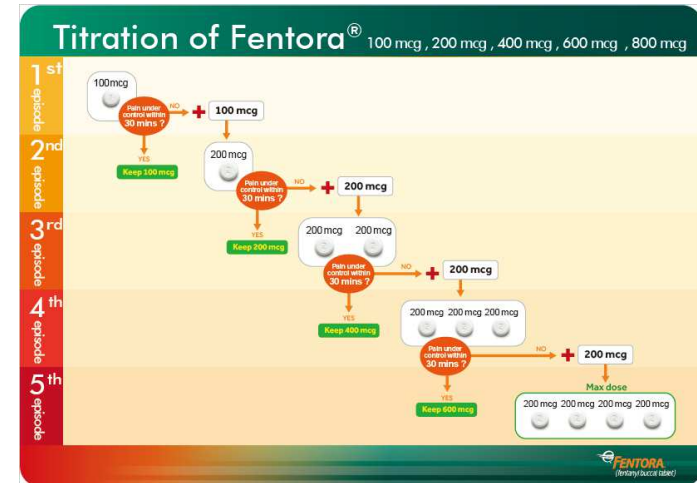
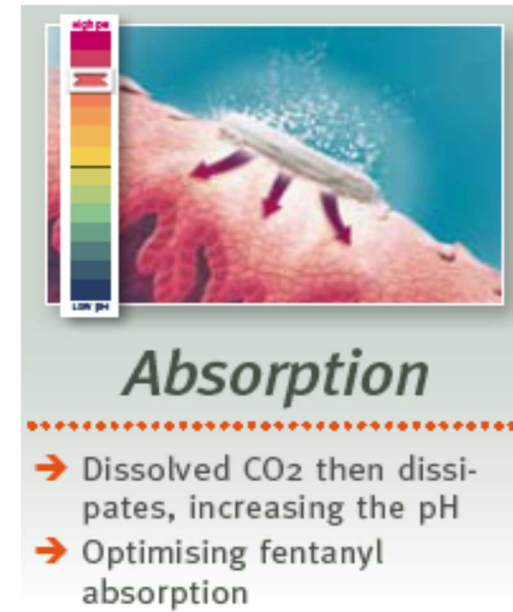
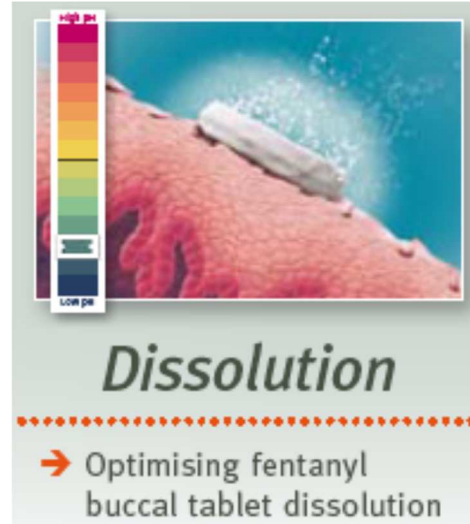
衛福部食藥署適應症



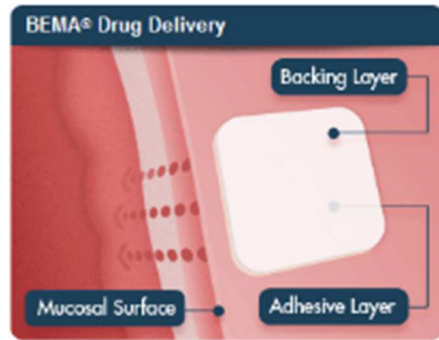
at least 60 mg of oral morphine daily,
at least 25 mcg/hr. of transdermal fentanyl,
at least 30 mg of oral oxycodone daily,
at least 8 mg of oral hydromorphone daily,

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

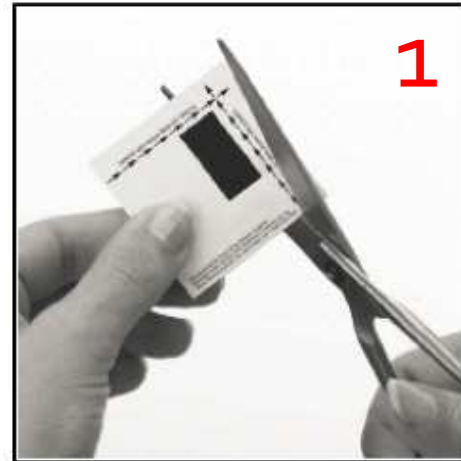
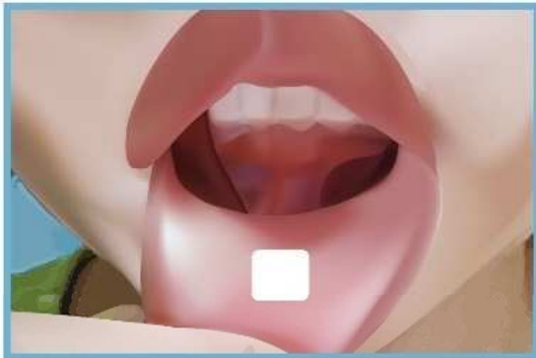
FENTORA, which employs the OraVescent drug delivery technology, is a potent opioid analgesic intended for buccal administration. FENTORA is formulated as a flat-faced, round, beveled-edge, white tablet.



The Instruction of Painkyl®



BDSI's "BEMA" technology



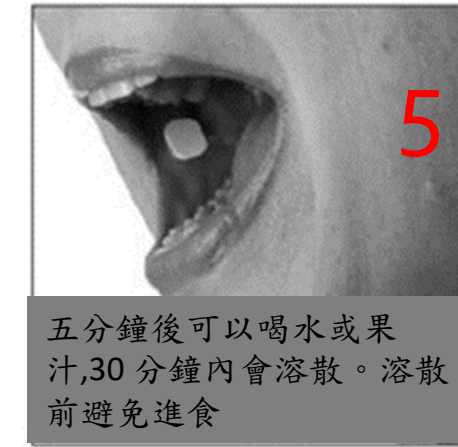
使用前用舌頭潤濕您的口腔黏膜或以清水漱口



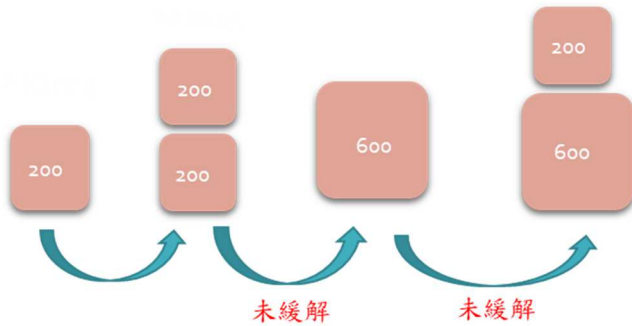
貼片置於一清潔、乾燥的手指近指尖處，粉紅面朝上



粉紅面貼附到口腔黏膜，並按壓貼片5秒。



五分鐘後可以喝水或果汁，30分鐘內會溶散。溶散前避免進食



口訣:手乾，口濕，粉紅對粉紅，按壓5秒鐘

**Responder ($\geq 33\%$
improvement in pain intensity)**

10 mins

15 mins

30 mins

Painkyl

Rauck et
al. 2010

ND

26% vs 21%

47%* vs 38%

Fentora

Slatkin et
al. 2007

16%* vs 10%

29%* vs 14%

51%* vs 26%

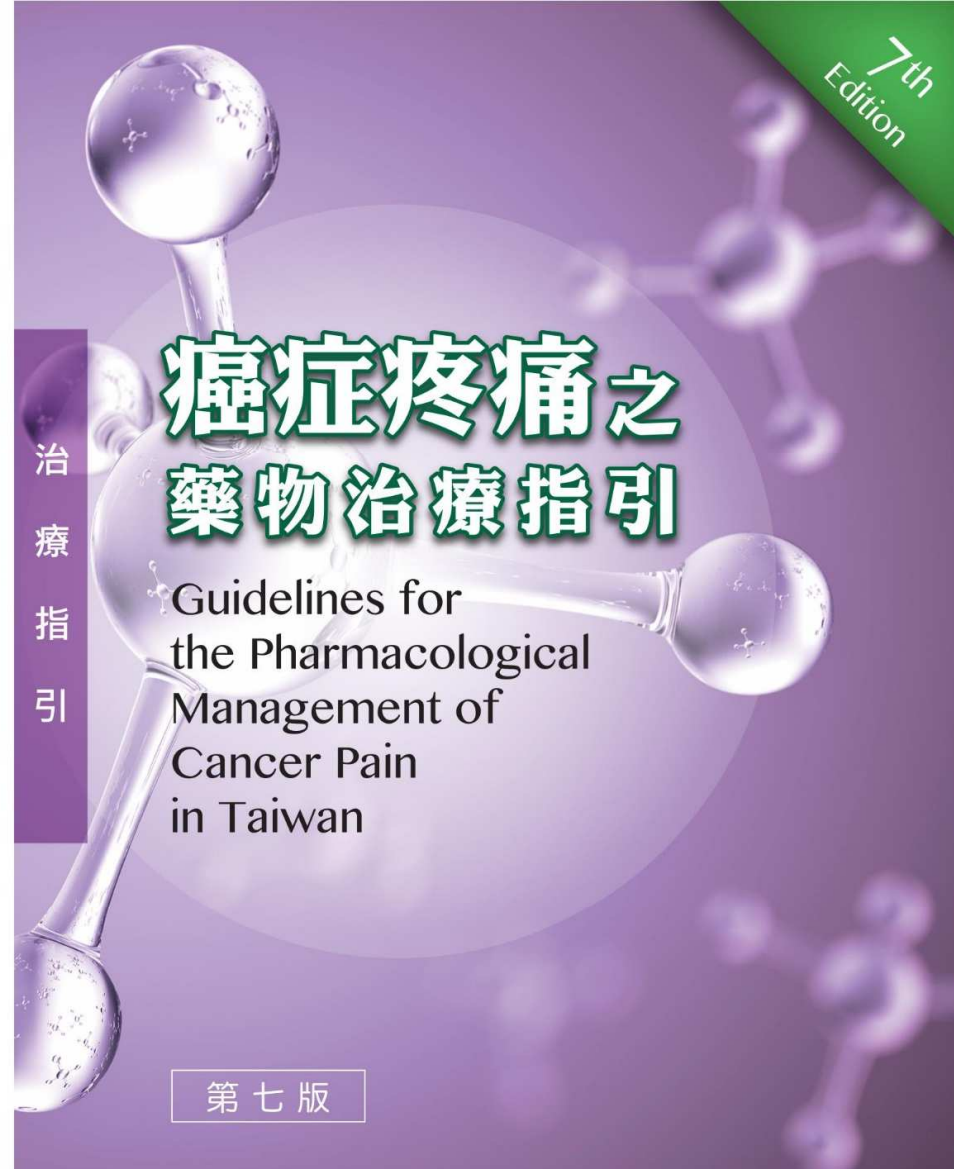
*significant different from placebo ; ND = not determined

	Fentora	Painkyl
劑型	fentanyl buccal soluble tab 口頰錠	fentanyl buccal soluble film 口頰溶片
劑量 (mcg)與健保價	100 mcg: 220 200 mcg: 250	200 mcg: 275 600 mcg: 395
口腔黏膜給藥技術	OraVescent® drug delivery Technology	BEMA® (BioErodible MucoAdhesive) Film Technology
達到統計學意義的 ”止痛起始時間” (Pivotal Study)	10 mins	30 mins
Tmax	40 mins (200 mcg) 46.8 mins (400 mcg)	60 mins (200 mcg) 120 mins (400 mcg)
Cmax	0.25 ng/ml (100 mcg) 0.4 ng/ml (200 mcg) 1.02 ng/ml (400 mcg)	- 0.38 ng/ml (200 mcg) 0.7 ng/ml (400 mcg)
Absolute Bioavailability	65%	71%
藥物投與方式	口頰 & 舌下 兩種投與方式	僅能由口頰投與

- (1) 病人是否有背景疼痛（過去一週每天疼痛持續 12 小時以上）？
 - (2) 背景疼痛是否充分控制（疼痛於過去一週，每天有 12 小時以上處於緩解或輕微狀態）？
 - (3) 病人的疼痛是否有惡化？
- 若三項皆為「是」即可診斷為突發性疼痛。



**本人小心願：未來不再出現
Morphine 15mg 2-4# Q4-6H PO 這類處方
醫療團隊請互相提醒**





腫瘤內科

江佳駿 醫師

Chia-Chun Chiang, M.D.
Internal Medicine
Medical Oncology

+886 982918185
nwosaga@gmail.com

謝謝參與
歡迎指教

Thank You for you attention
Your comments are very welcome

