

# 兒童用藥

台大兒童醫院

李秉穎

# 常見的兒科處方箋

※本次收據共計： 50 元

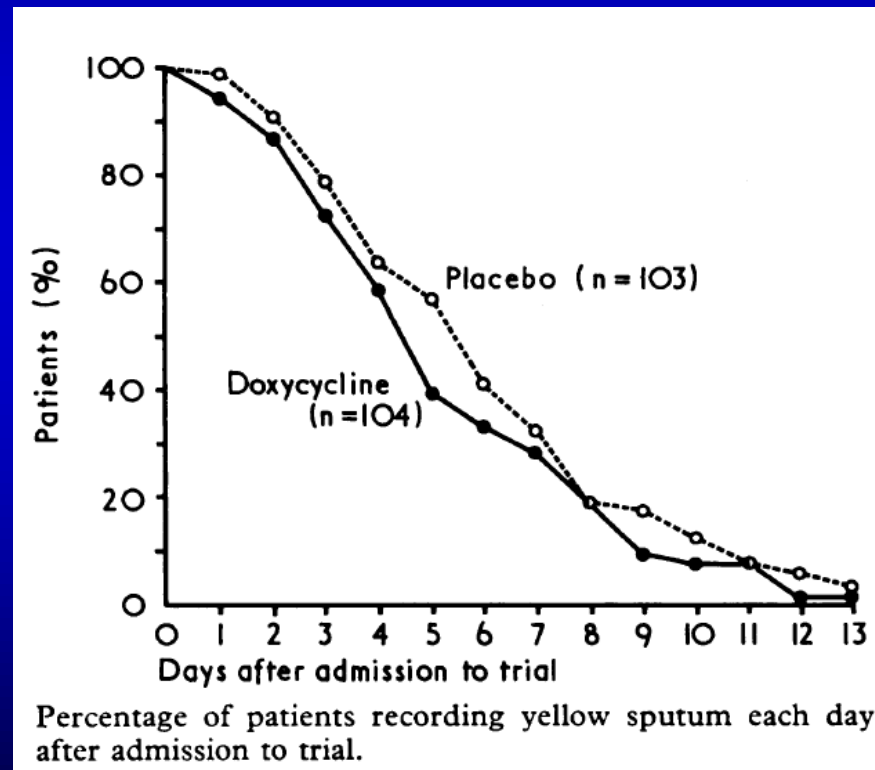
N 藥品名稱	用法	服法*天數	劑量	總數	單
1 methylprednisolone	口服	一天4次 * 3		6.	
適應症:緩解發炎及過敏性症狀					
Trimethoprim	口服	一天4次 * 3		4.5	
適應症:治療各種感染症					
AMOX (250)	口服	一天4次 * 3		4.5 #	
適應症:扁桃腺炎、咽喉炎、中耳炎					
Ketotifen	口服	一天4次 * 3		6.	
適應症:過敏性鼻炎、皮膚炎					
Periatin會想睡,頭?	口服	一天4次 * 3		4.5 #	
適應症:過敏及搔癢症					
Amatadine	口服	一天4次 * 3		3.5 #	
適應症:預防及治療A型流行性感冒					
2 VENTOL LIQUID 5.34	口服	一天4次 * 3		1.	DT
適應症:氣喘、支氣管痙攣					
3 Diprophyllin supp	外用	一天1次		1.	B
適應症:氣喘及支氣管痙攣					
警語:請照醫師指示服用!!					

※本次收據共計： 100 元

N 藥品名稱	用法	服法*天數	劑量	總數	單
1 methylprednisolone	口服	一天4次 * 3		6.	
適應症:緩解發炎及過敏性症狀					
Bacidal	口服	一天4次 * 3		5	
適應症:表淺性皮膚感染、泌尿道感染					
Ketotifen	口服	一天4次 * 3		6	
適應症:過敏性鼻炎、皮膚炎					
Periatin會想睡,頭?	口服	一天4次 * 3		5	
適應症:過敏及搔癢症					
Amatadine	口服	一天4次 * 3			
適應症:預防及治療A型流行性感冒					
Panadol gr.	口服	一天4次 * 3			
適應症:退燒止痛					
2 VENTOL LIQUID 5.34	口服	一天4次 * 3			
適應症:氣喘、支氣管痙攣					
3 Diprophyllin supp	外用	一天1次			
適應症:氣喘及支氣管痙攣					
警語:請照醫師指示服用!!					

# Judicious use of antimicrobial agents

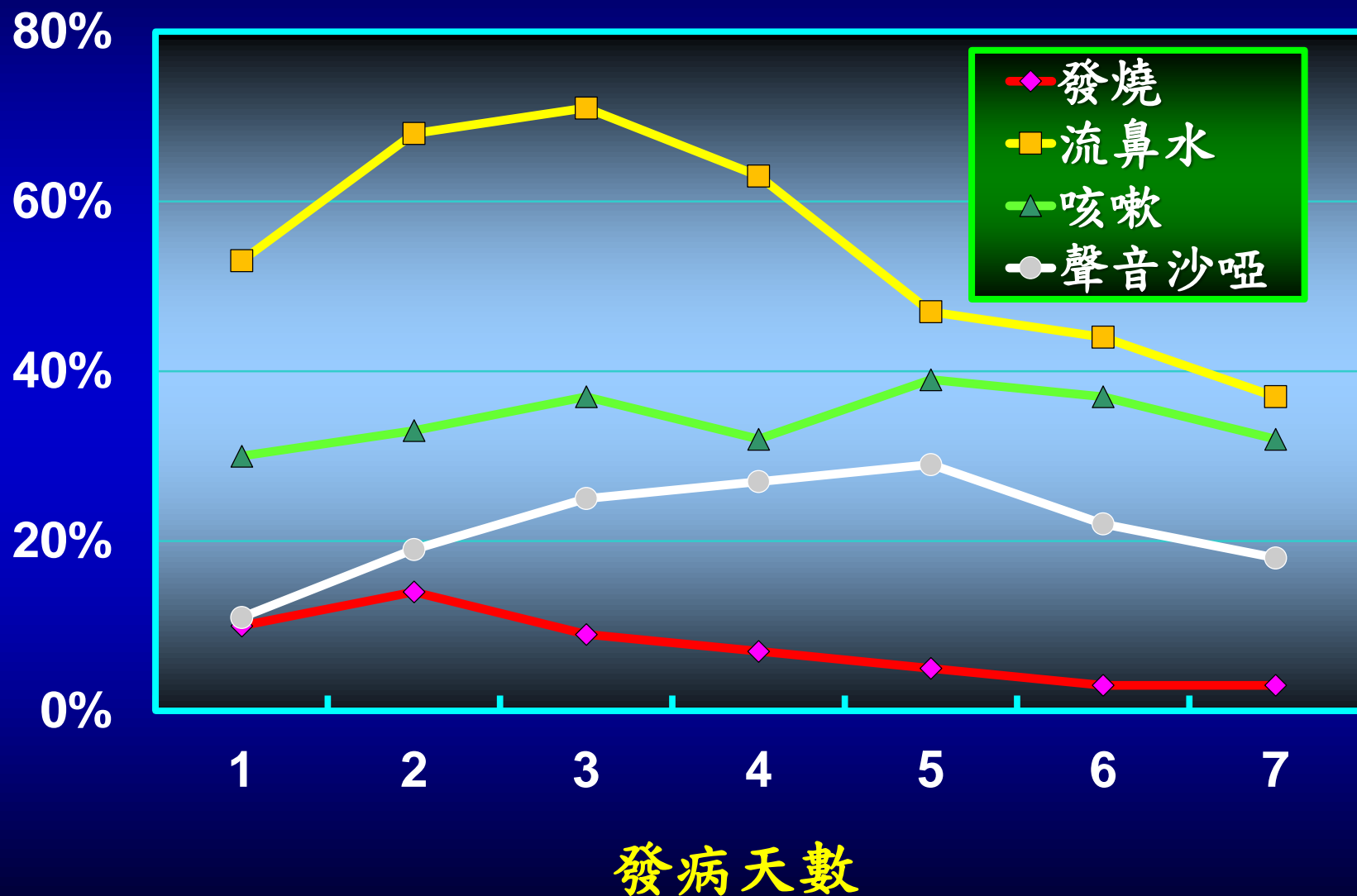
- AAP, AAFP, CDC, 1998: **Mucopurulent rhinitis ... is not an indication for antimicrobial treatment.**



O'Brien KL. Pediatrics 1998;101:178.

Stott NCH. Br Med J 1976;2:556.

# 鼻病毒感染症狀的變化





# 口服類固醇對志願者鼻病毒感染的影響

Prednisone 20 mg tid X 5 days

N=47, Baltimore, 1996

— steroid — placebo

分數

噴嚏



鼻水



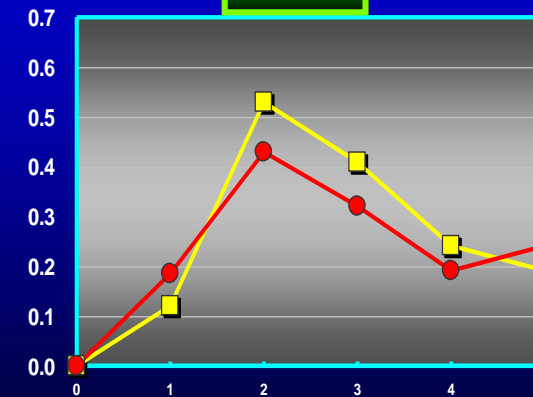
鼻塞



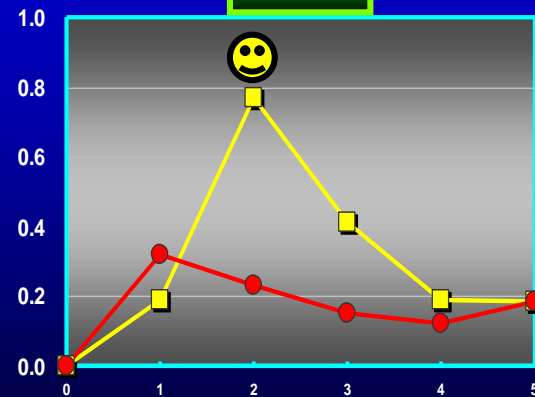
咳嗽



倦怠



頭痛

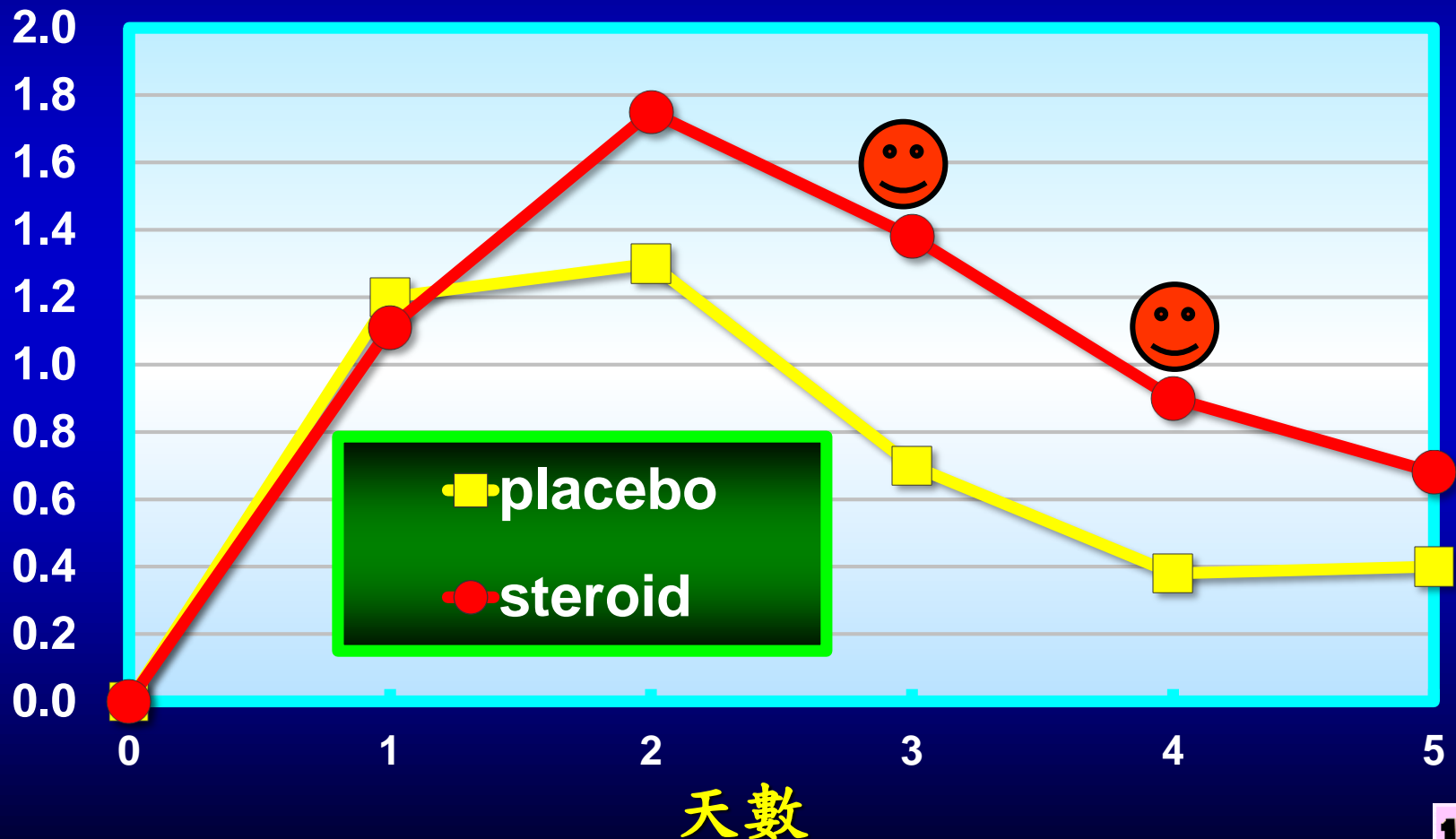


# 口服類固醇對志願者鼻病毒病毒量的影響

Prednisone 20 mg tid X 5 days

N=47, Baltimore, 1996

## 病毒量 TCID 50



# 台灣健保資料庫中類固醇使用狀況

## N=15,859,129，20-64歲，2013-2015

Characteristic	Steroid Bursts, n (%)
<b>ICD-9-CM code (diagnosis)</b>	
692.xx (contact dermatitis and other eczema)	410 518 (15.6)
465.xx (acute upper respiratory tract infections of multiple or unspecified sites)	248 035 (9.5)
708.xx (urticaria)	221 851 (8.5)
466.xx (acute bronchitis and bronchiolitis)	130 982 (5.0)
461.xx (acute sinusitis)	123 595 (4.7)
463.xx (acute tonsillitis)	99 291 (3.8)
698.xx (pruritus and related conditions)	95 768 (3.7)
460.xx (acute nasopharyngitis [common cold])	71 067 (2.7)
464.xx (acute laryngitis and tracheitis)	55 873 (2.1)
462.xx (acute pharyngitis)	54 272 (2.1)
<b>Physician specialty</b>	
Dermatology	808 162 (30.8)
Otolaryngology	537 546 (20.5)
Family practice	482 196 (18.4)
Internal medicine	294 477 (11.2)
Pediatrics	164 884 (6.3)

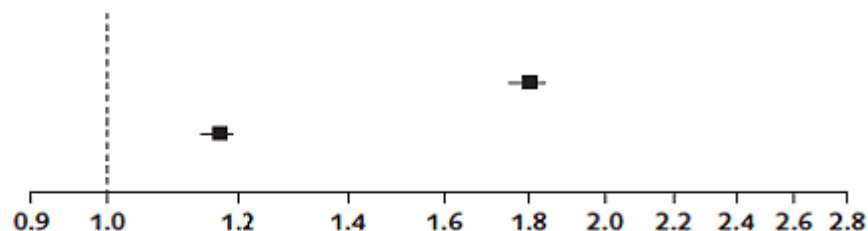
ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

# 台灣健保資料庫中類固醇使用狀況

## N=15,859,129，20-64歲，2013-2015

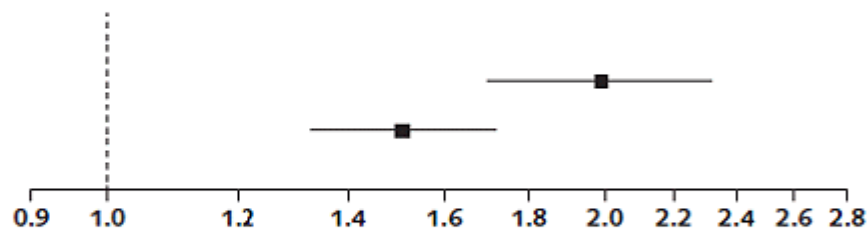
### Gastrointestinal bleeding

Period	IRR (95% CI)
5-30 d	1.80 (1.75-1.84)
31-90 d	1.17 (1.14-1.19)



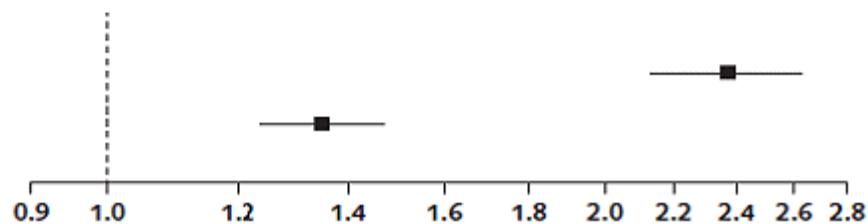
### Sepsis

Period	IRR (95% CI)
5-30 d	1.99 (1.70-2.32)
31-90 d	1.51 (1.33-1.72)



### Heart failure

Period	IRR (95% CI)
5-30 d	2.37 (2.13-2.63)
31-90 d	1.35 (1.24-1.47)



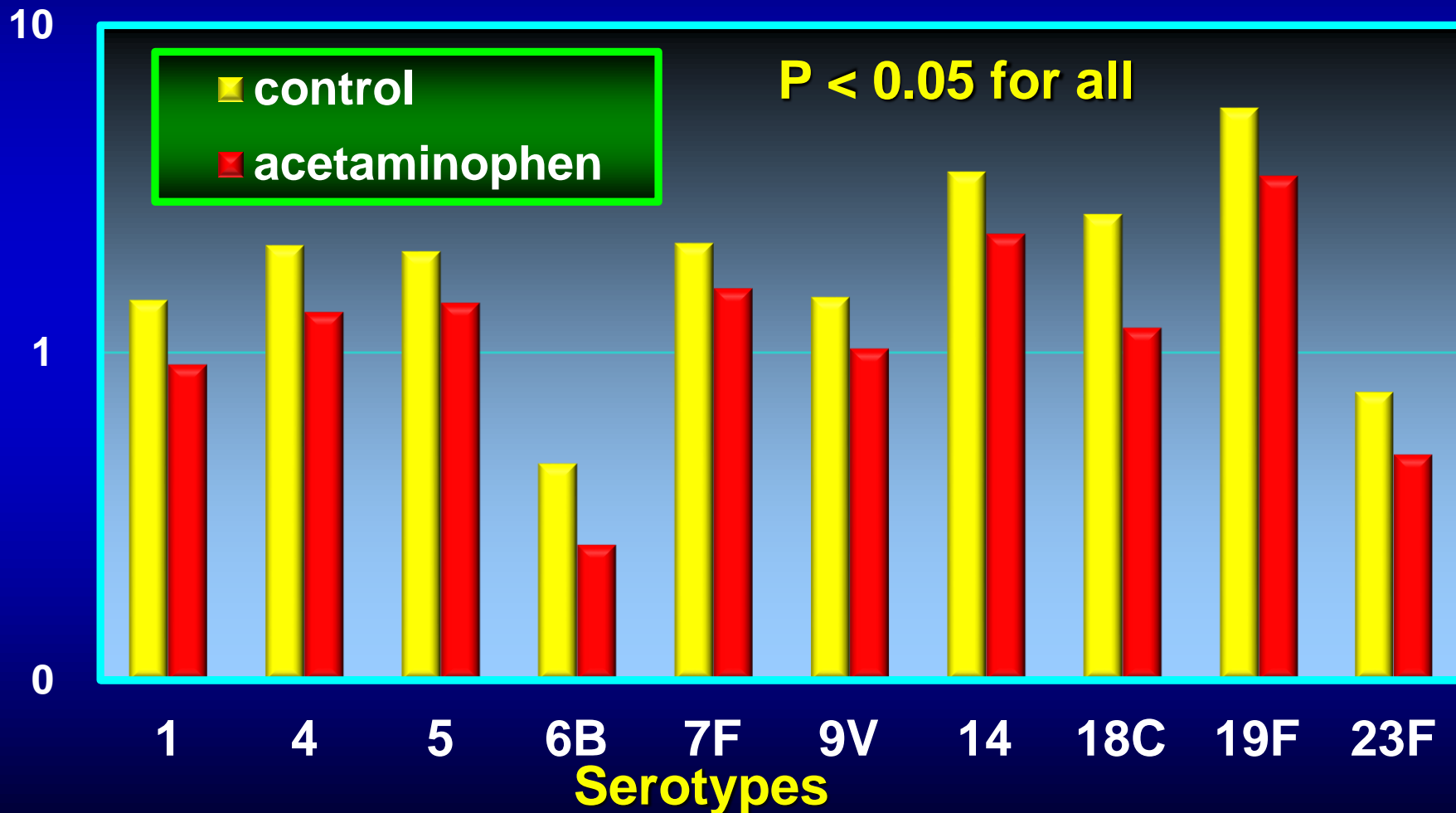
IRR: incidence rate ratio

IRR (95% CI)

# 常規給acetaminophen以預防發燒

11-valent pneumococcal conjugate vaccine, Synflorix, 2009

GMC of pneumococcus antibody ( $\mu\text{g/ml}$ ) post-dose 3



# 退燒對於動物敗血症的影響

死亡率 (動物總數)

動物	病原	退燒藥	治療組	對照組
Mice	Pneumococcus	aspirin	47% (120)	23% (120)
Rabbits	Rinderpest	aspirin	50% (22)	17% (12)
Goats	Trypanosoma	flurbiprofen	100% (5)	6% (17)
Rabbits	P multocida	salicylate	22% (46)	20% (45)
Rabbits	P multocidat	salicylate	100% (9)	29% (7)

# 該不該使用退燒藥？

- WHO recommendation
  - No evidence shows that paracetamol is beneficial.
  - Health professionals **should not be encouraged to give antipyretics routinely to febrile children.**
- 台灣兒科醫學會
  - 發燒不一定需要使用退燒藥，尤其體溫並未超過**39°C**以上時。
  - 以下情形的發燒病患，體溫超過**38°C**以上時建議退燒：
    - 慢性肺病、成人型呼吸窘迫症候群
    - 有心臟衰竭之心臟病或發紺性心臟病
    - 慢性貧血
    - 糖尿病與其他代謝異常
    - 有熱性痙攣既往歷或伴有癲癇發作的神經系統疾病
    - 孕婦
    - 其他因為發燒而有不適症狀者



# 感冒藥物無效

- Cough and cold preparations < 12 yrs: all 6 randomized placebo-controlled studies - **ineffective**
- **American Academy of Pediatrics, 1997:** cough medications - “indications for their use in children **have not been established.**”
- **American College of Chest Physicians, 2006:** “literature regarding over-the-counter cough medications **does not support** the efficacy of such products in the pediatric age group.”
- > 750,000 calls of concern related to cough and cold products since January 2000.<sup>2</sup>



# 感冒藥物的危險性

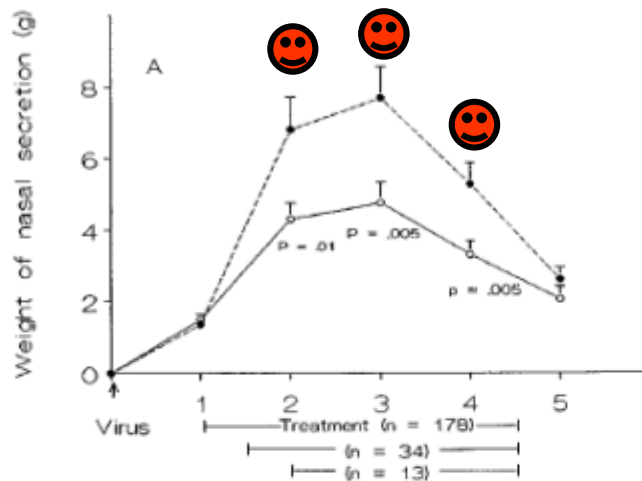
- < 6 yrs
  - **Decongestants:** cardiac arrhythmias and other cardiovascular events
  - **Antihistamines:** hallucinations
  - **Antitussives:** depressed levels of consciousness and encephalopathy.
- **FDA: 123 deaths** related to the use of such products in children **under 6** during the past several decades.
  - **Accidental overdose**
  - Inadvertent misuse
  - Drug–drug or drug–host interactions in children

# Brompheniramine 對感冒的療效

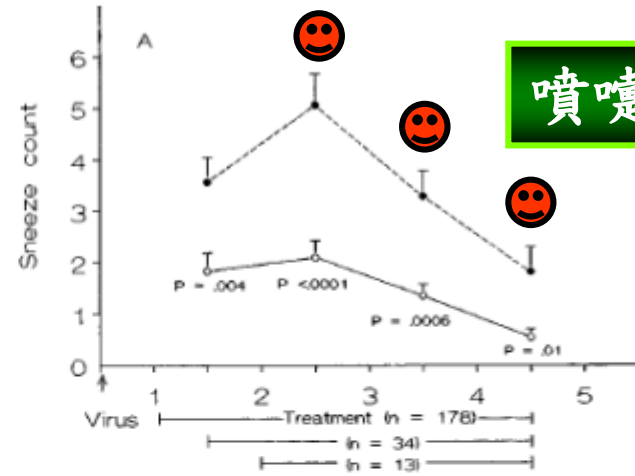
第一代抗組織胺, 抗體陰性受試者

rhinovirus challenge,  $\geq 18$  yrs, N=250

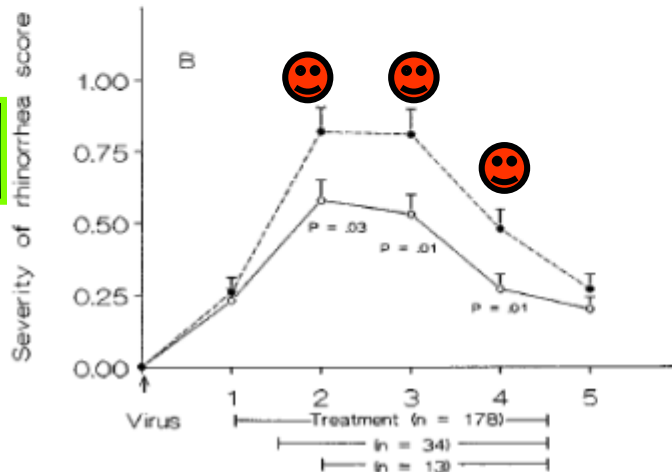
鼻涕重量



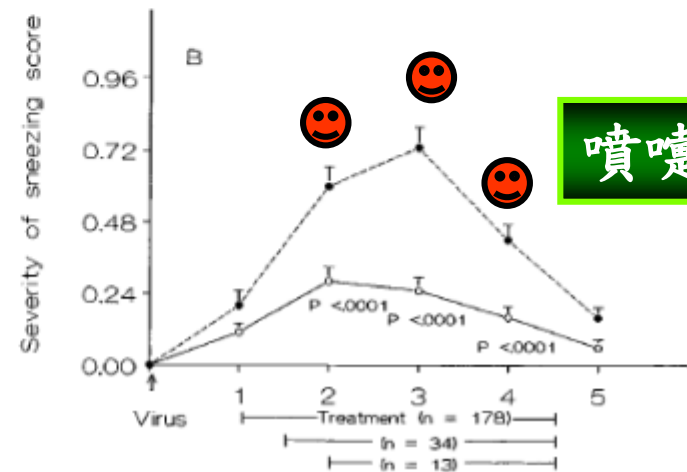
噴嚏次數



鼻涕分數



噴嚏分數

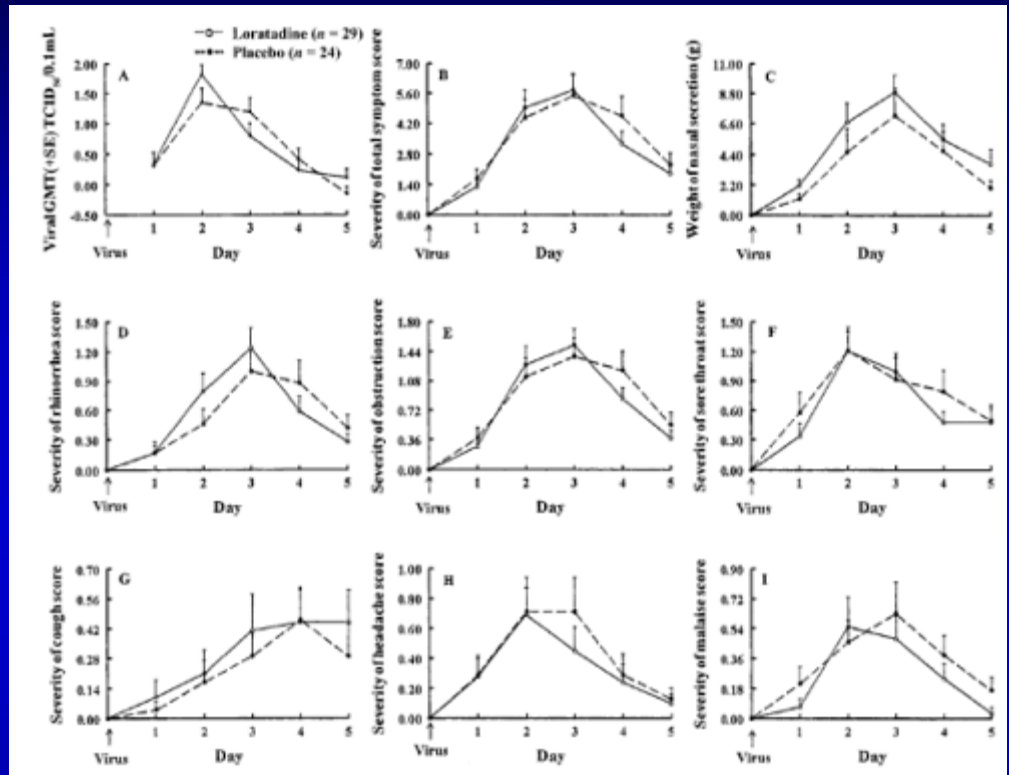


☺ P < 0.05

# Loratadine (Clarytine) 對感冒的療效

第二代抗組織胺, rhinovirus challenge

成人, N=60



- **1<sup>o</sup> antihistamine**: block histaminic and **muscarinic receptors + pass BBB**
- 2<sup>o</sup> generation antihistamine: block histaminic receptors

# PPA藥品明年七月禁用 二百多種感冒藥要回收

中央社 2005.3.25

- 衛生署決定，明年七月全面禁用含**PPA**（**phenylpropanolamine**）藥品，包括「斯斯」、「克風邪」等鼻炎膠囊產品在內的二百多種感冒藥，必須把握時間回收或更改配方。
- 在羅氏鮮、諾美婷上市前，PPA曾經是衛生署唯一核准用於減肥的藥物，但在國外出現**中風及死亡**的報告後，衛生署已於前年底禁止用於減肥。
- 由於PPA也有**血管收縮**的作用，可以解除鼻充血以及腫脹，多半以低劑量、複方形式存在於綜合感冒藥或是抗過敏藥中，用來治療鼻炎或是鼻塞，目前市面約有二百多種綜合感冒藥含PPA。

Hutton N. J Pediatr 1991;118(1):125.

Clemens CJ. J Pediatr 1997;130(3):463.

# Mucolytics

## Cochrane Database of Systematic Reviews

- COPD
  - **Significant reduction** in the number of exacerbations per patient with oral mucolytics (20% reduction).
  - The number of days of disability also fell
  - Conclusion: **should be considered for use**
- Acetylcysteine/carbocysteine for RTI in children
  - **Some benefit** from mucolytic agents, although differences were of little clinical relevance.
- Overall **safety** was good

Poole P. Cochrane Database Syst Rev 2006;(3):CD001287.

Duijvestijn YCM. Cochrane Database Syst Rev 2009;(1): CD003124.

# Brown mixture

- **Glycyrrhiza fluid extract**
- **Opium camphor tincture:** pain relief, **sedation**, antidiarrhea
- **Antimony potassium tartrate (酒石酸銻鉀) :**  
**expectorant (FDA)**
  - 副作用：salivation, cough, metallic taste, nausea, vomiting, bloody diarrhea, dizziness, irritability, and muscular pains, **arrhythmia**.
  - 與opium混合物會引起噁心、嘔吐之不良反應，用於預防過量服用產生生理依賴。(2006.3.8 藥政處公告)
- Spirit ethyl nitrite, glycerin



# 鎮靜安神藥物

院所名稱: [REDACTED] 診所: [REDACTED] 【藥品明細及收據】

院所地址: 台北市 [REDACTED]

姓名: 張 [REDACTED] 生日: 93.07.04 年齡: 3歲5月男 就醫序號: 0050

日期: 96.12.22 證號: 044112 發藥 3日份 身份證: [REDACTED]

調劑藥師: [REDACTED] 醫師姓名: [REDACTED]

藥品名稱 單位 含量 用法 次量 x次x天 總量 診察費: 220

1 Panadol (500mg) 內服 0.38錠x4x3 4.5 藥服費: 30

2 Noscapine (20mg) 內服 0.38錠x4x3 4.5 藥費: 85

3 Cabosistin 內服 0.38錠x4x3 4.5 診療費: 0

4 Berotec (2.5mg) 內服 0.18錠x4x3 2.1 合計: 335

有人會心悸

5 Valium (5) 內服 0.33錠x1x3 1.0 部份負擔: 50

易昏昏欲睡, 痛門診: 0

6 Tapal 內服 1.50錠必要時 3.0 藥費自付: 0

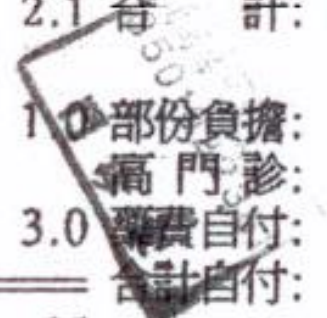
合計自付: 50

合計藥費: 85

健保申請: 285

掛號費: 100

實收金額: 150



# Codeine: CNS suppression and death of infants

- **Codeine: slower metabolism in infants**
- Magnani B, 1999: 29 days old boy
  - 1.26 mg/kg codeine -> **expired**
  - Toxic blood level: 0.34 mg/L
- von Muhlendahl KE. 1976: **2 deaths with > 5 mg/kg of codeine**
- Karen G, 2005:
  - **Mother**: taking codeine 30mg q12h X 2 weeks for episiotomy pain
  - Infant with **breast feeding, sudden death** on day 13
  - Blood concentration of morphine (the active metabolite of codeine): 70 ng/mL

Magnani B. Pediatrics 1999 ;104(6):e75.

Koren G. Lancet 2006; 368: 704.



# 兒童避免使用嗎啡類製劑抑制咳嗽

- 九個月大女嬰：發燒、咳嗽 6天，2012.7.31 因嚴重咳嗽一天兩度至診所就醫
  - 第一次：cefixime, levofloxacin, chlorpheniramine, carbinoxamine-pseudoephedrine, cyproheptadine、tretoquinol、methylprednisolone
  - 第二次：cefixime, dexchlorpheniramine, terbutaline, **noscipine**
- 晚上服藥兩小時後，家人發現女嬰活力差、嗜睡
- 住院：心跳慢(85次/分)，瞳孔對稱性縮小，腦部電腦斷層正常，troponin I些微上升(1.2 ng/mL)
- 給予naloxone靜脈注射後，女嬰意識短暫恢復幾秒，又再度呈現嗜睡狀態
- 痰液檢查發現呼吸道融合病毒陽性反應
- 兩天後女嬰轉至普通病房，觀察一天後狀況穩定出院。

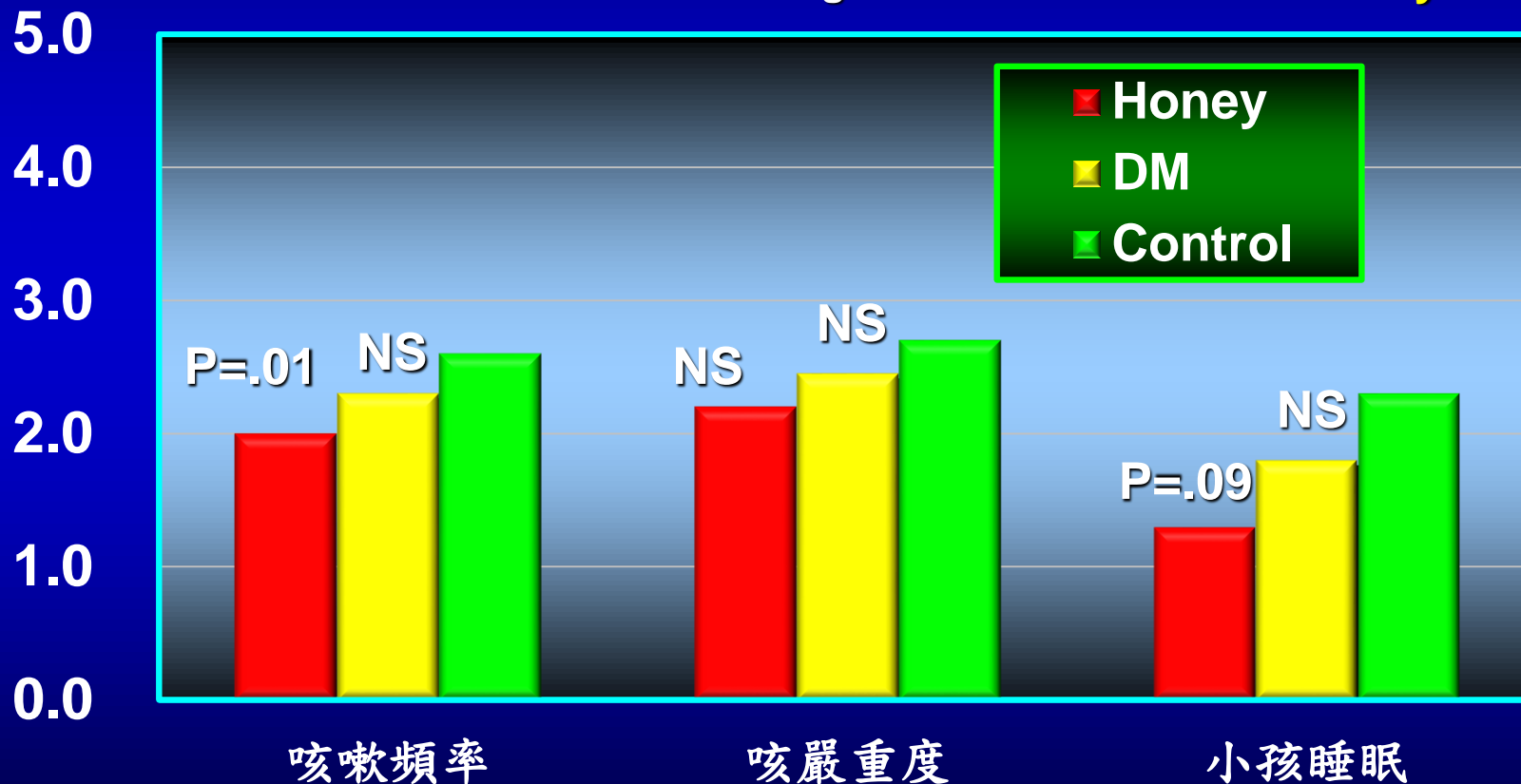
# 蜂蜜可以治療咳嗽

2-18 yrs with nocturnal cough, N=105

2007, Pennsylvania

- Treated for 1 day
- This work was supported by an unrestricted research grant from the **National Honey Board**

Likert scale score



# Complementary and alternative medicine in children with asthma

## Turkey, 2004

- 304 asthmatic children, 49% had used some form of complementary and alternative medicine
  - Quail eggs: 79%
  - Herbal medicine: 31%
  - Turkish wild **honey**: 26%
  - Speleotherapy: 5%
  - Royal jelly: 5%

# 止咳藥的使用原則

- 不同原因的咳嗽，治療方法不一樣，必須找到病因，才能對症下藥。
- **刺激型咳嗽**：可以使用藥物壓抑咳嗽反應，例如百日咳。
- **氣喘型咳嗽**：早晚較厲害，必須使用支氣管擴張劑、過敏抑制藥物。
- **排痰型咳嗽**：是正常生理反應，不需要用藥物壓抑。



# Oral rehydration therapy

## 兒童急性腸胃炎最重要的治療

- AAP, CDC, ESPGN, WHO: 除了嚴重脫水，**oral rehydration therapy**為第一線治療
- **Cochrane meta-analysis: 1982-2005, 17 trials**
  - 口服與靜脈治療沒有重大臨床差異
  - 口服治療住院時間較短
  - 靜脈治療有2.5%靜脈炎
- **1970's WHO推廣oral rehydration therapy**
  - 1970's 全世界腸胃炎死亡 4.6 million/year
  - 1980's 全世界腸胃炎死亡 3.3 million/year
  - 1990's 全世界腸胃炎死亡 2.5 million/year

# 兒童腹瀉是否應該禁食

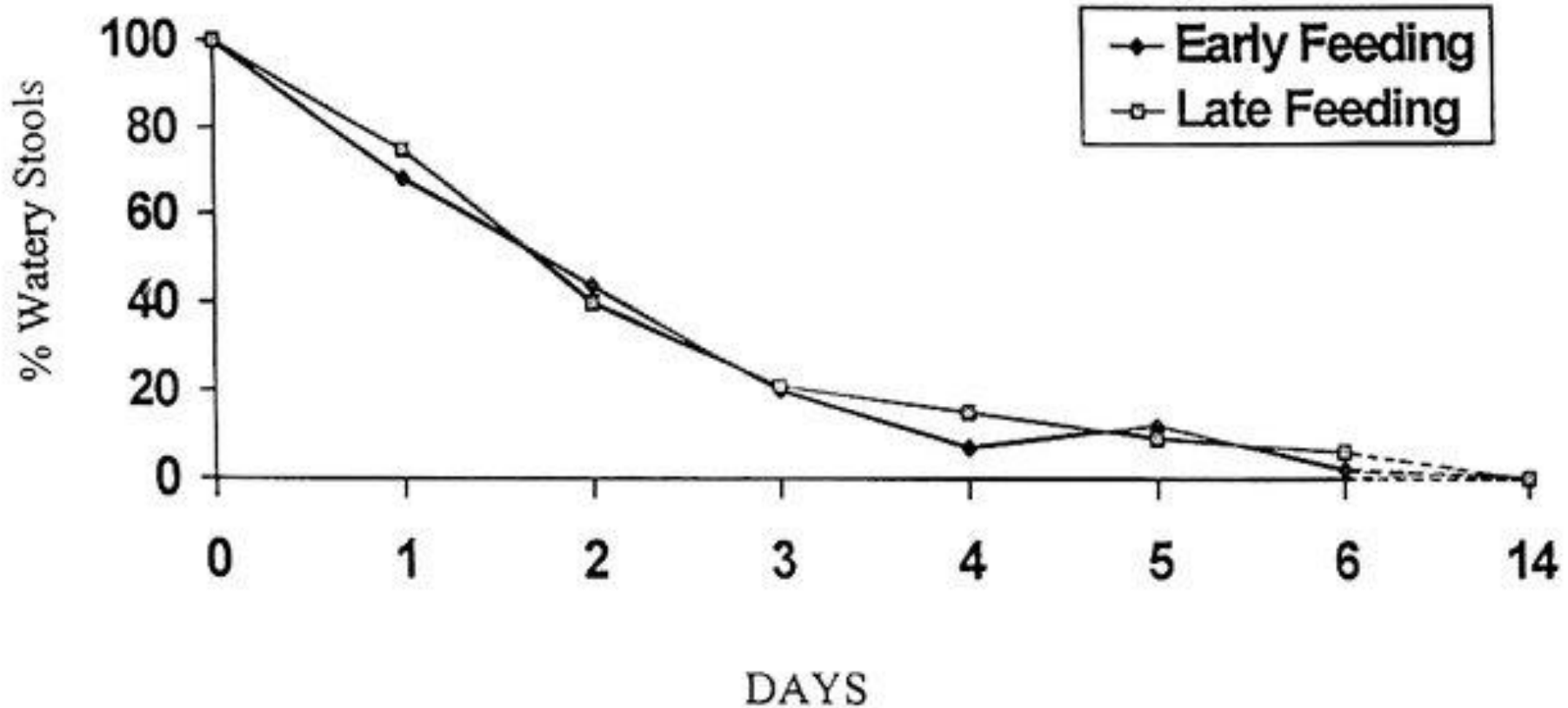
Sandhu BK. J Pediatr Gastroenterol Nutr 2001;33:S13.

- 1930s以前：並未常規禁食
- Powers, 1926: treatment for “intestinal intoxication” – 補充水分、輸血、禁食，禁食一段時間以後慢慢增加進食量
- 1940s-1950s: 有研究顯示持續進食可有較高之體重與較少之慢性腹瀉
  - 但，兒童仍被持續禁食24-48小時



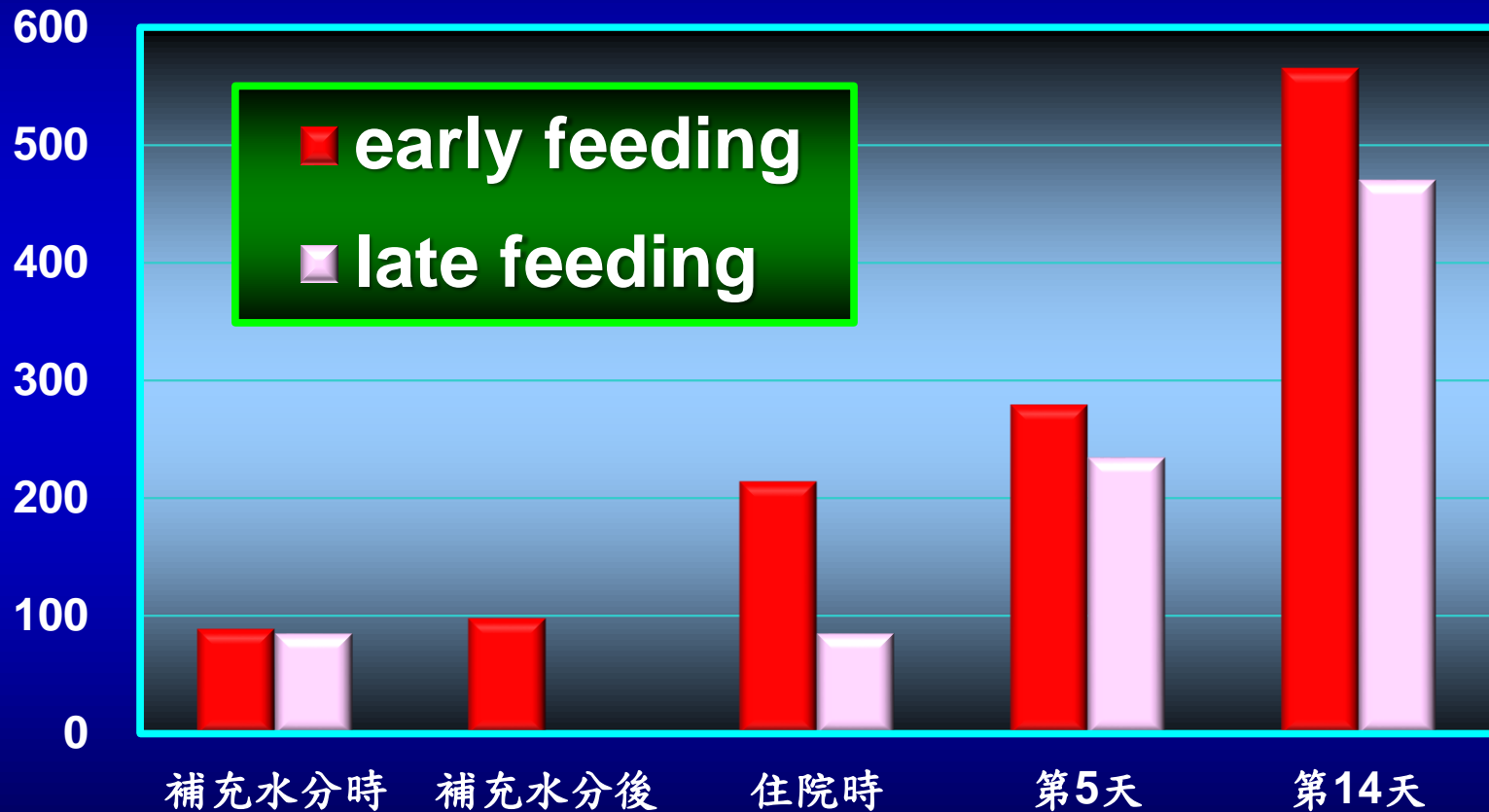
# 禁食與否的糞便變化

Sandhu BK. J Pediatr Gastroenterol Nutr 1997;24:522



# 兒童禁食與否的體重變化

體重增加量(公克)





# 止吐藥

- **Dopamine receptor antagonists**
  - **Metoclopramide**: extrapyramidal reactions, 促進胃部與小腸排空
  - **Domperidone**: 沒有 extrapyramidal reactions, 副作用包括 QT prolongation、ventricular arrhythmias
  - Prochlorperazine: extrapyramidal reactions、QT prolongation
    - 應用最低有效劑量
- **Antihistamine**
  - Dimenhydrinate: 第一代
- **Serotonin 5HT<sub>3</sub> receptor antagonists**
  - **Ondansetron (Zofran)**:
    - No antidopaminergic properties
    - 價格高

# Antiemetics for acute gastroenteritis in children and adolescents Poole P. Cochrane Database Syst Rev 2011, Issue 9. Art.No.: CD005506.

- 口服ondansetron
  - 減少嘔吐
  - 減少靜脈注射補充水分的需要
  - 減少立即住院的必要性
- 靜脈ondansetron與metoclopramide
  - 減少嘔吐
  - 減少住院
- 有些報告惡化腹瀉

# Antimotility agents

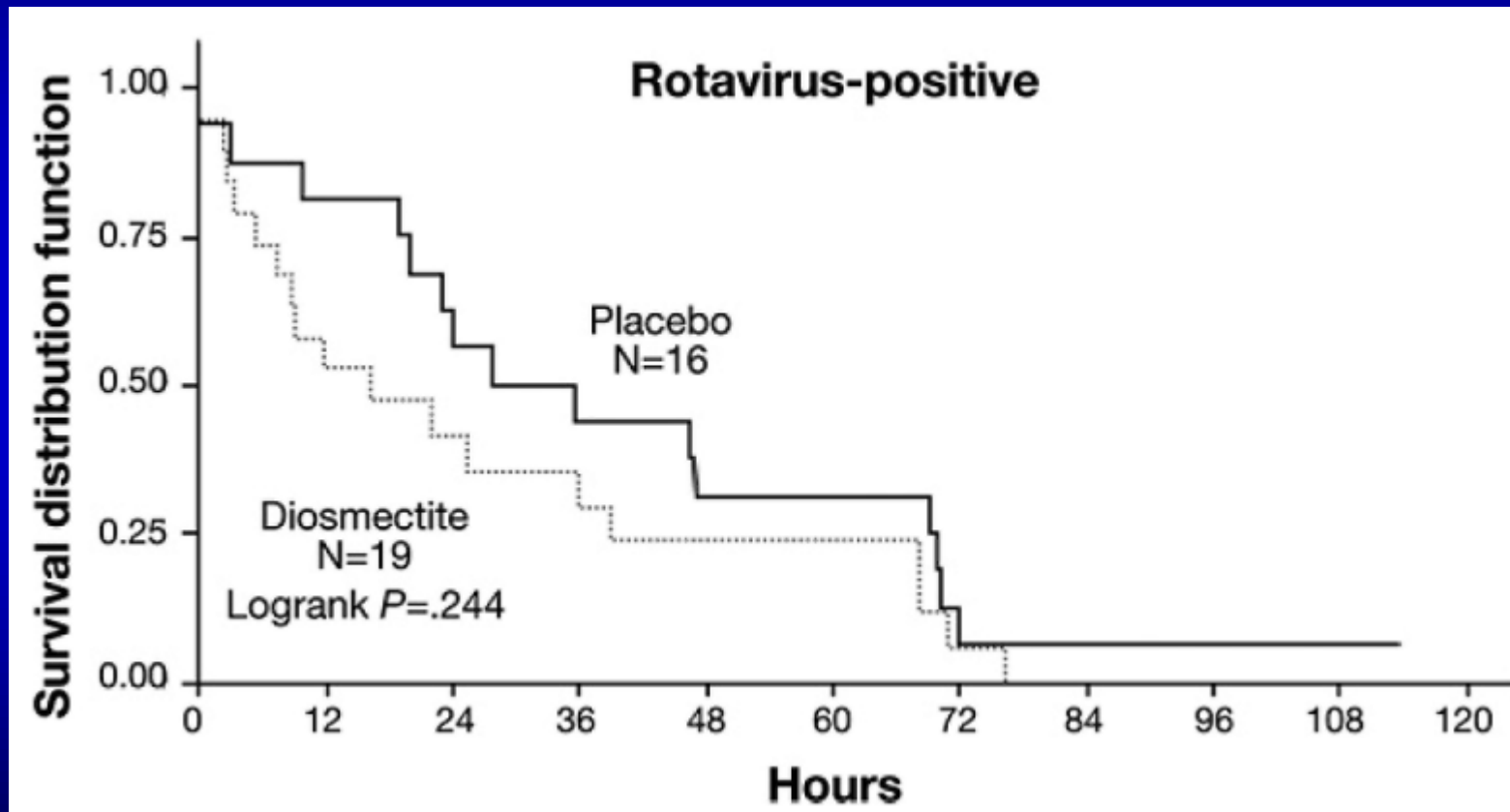
- **Loperamide (Imodium):** 綜合分析 (NICE2009)
  - 24小時腹瀉發生率較低 RR 0.66 (95% CI 0.57 - 0.78).
  - 48小時腹瀉發生率較低 RR 0.59 (95% CI 0.45 - 0.78).
  - 腹瀉時間較短 -0.80 days (95% CI -0.87 to -0.74 days).
  - 不良反應
    - 腹脹、嗜睡、腸阻塞、死亡：治療組明顯較多 (21/927 vs. 4/764)
    - **腸阻塞、死亡等嚴重不良反應只發生於 loperamide組** 8/927 vs. 0/764.

# Diosmectite 治療兒童腹瀉

秘魯、馬來西亞，N=602，2009

Adsorbent

- 減少腹瀉次數，尤其輪狀病毒感染



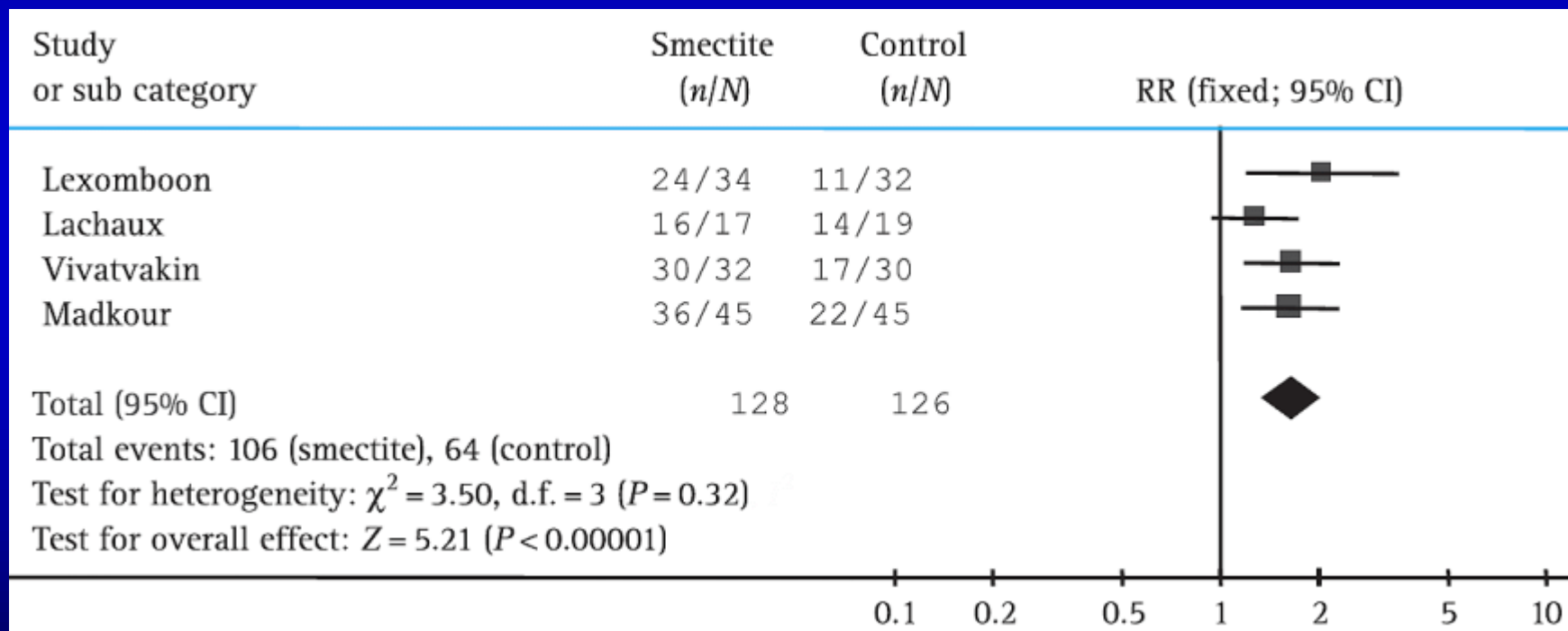
腹瀉持續時間

# Smectide治療兒童腹瀉

## Meta-analysis, 2006

Adsorbent

- 減少腹瀉天數，三天痊癒率增加，不良反應相同



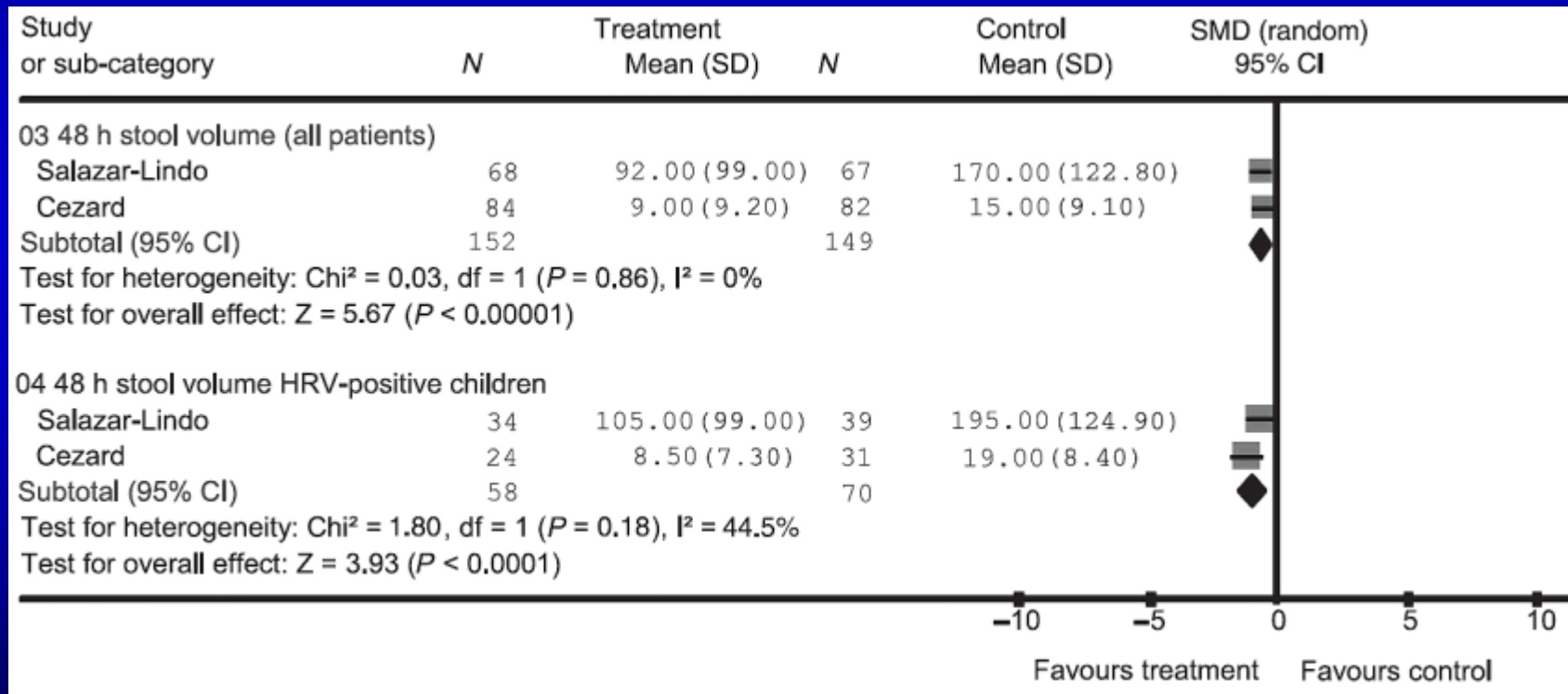
三天痊癒率

# Racecadotril治療兒童腹瀉

## Meta-analysis, 2006

Anti-secretory

- 減少腹瀉天數，5天痊癒率相同，不良反應相同



48小時糞便量

# Probiotics治療兒童腹瀉

## Cochrane Database of Systematic Reviews

### ● 急性感染性腹瀉

- 縮短腹瀉時間：平均差異24.76小時 (95%CI: 15.9-33.6小時)
- 減少腹瀉 $\geq 4$ 天：RR 0.41 (95%CI: 0.32-0.53)
- 減少第2天排便次數：平均差異0.80 (95%CI: 0.45-1.14)

### ● 持續腹瀉 ( $\geq 14$ 天)

- 縮短腹瀉時間：平均差異4.02天 (95%CI: 4.61-3.43天)
- 減少糞便次數
- 縮短住院天數



# Managing acute gastroenteritis among children

七大原則，CDC, 2003

- Oral rehydration solutions (ORS) should be used for rehydration.
- Oral rehydration should be performed rapidly (i.e., within 3–4 hours).
- An age-appropriate, **unrestricted diet** is recommended as soon as dehydration is corrected.
- For **breastfed** infants, nursing should be continued.
- If formula-fed, **diluted formula is not recommended**, and **special formula usually is not necessary**.
- Additional ORS should be administered for ongoing losses through diarrhea.
- No unnecessary laboratory tests or medications should be administered.



# Evidence-Based Guidelines for the Management of Acute Gastroenteritis in Children in Europe

European Society of Pediatric Gastroenterology, Hepatology and Nutrition, 2014

- **Oral rehydration solution:** hypo-osmolar solution
- **Early resumption of feeding** after rehydration therapy is recommended.
- **Lactose-free formulas**
  - **Can be considered in hospitalized children age <5 years**
  - The routine use of is not recommended in outpatient setting
- Beverages with a high **sugar** content should not be used

# Evidence-Based Guidelines for the Management of Acute Gastroenteritis in Children in Europe

European Society of Pediatric Gastroenterology, Hepatology and Nutrition, 2014

- Selected **probiotics** can be used
- **Antiemetic**
  - Ondansetron may be effective in young children
- **Antimotility**: Loperamide is **not recommended**
- **Adsorbents**:
  - Diosmectite can be considered
  - Smectite plus Lactobacillus GG and Lactobacillus GG alone are equally effective
- **Antisecretory**:
  - Racecadotril can be considered
  - Bismuth subsalicylate is not recommended

# NICE guideline 2009

## National Collaborating Centre for Women's and Children's Health

- **Antiemetics:** 嚴重時可考慮ondansetron，但可能惡化腹瀉，不建議metoclopramide與dexamethasone
- **Antidiarrheal agents**
  - Loperamide: 減少腹瀉，但可能嚴重副作用
  - Kaolin-pectin: 可能有效，證據較少
  - **Smectite:** 可能有效
  - **Racecadotril:** 可能有效
  - 都需要更多研究

# Summary

## ● 呼吸道感染

- 宜避免：類固醇、充血抑制藥物、止咳藥、嗎啡類（含codeine）、安神劑
- 不宜常規使用：退燒藥、抗生素
- 可能有幫助：抗組織胺、化痰藥

## ● 腸胃道感染

- 不需要：禁食、稀釋配方奶
- 宜避免：antimotility agents
- 可能有幫助：probiotic、antiemetic、antidiarrheal agents（除了antimotility）

**Thanks....**

