

胃食道逆流治不好怎麼辦？

一難治性胃食道逆流症症狀的 診斷與治療

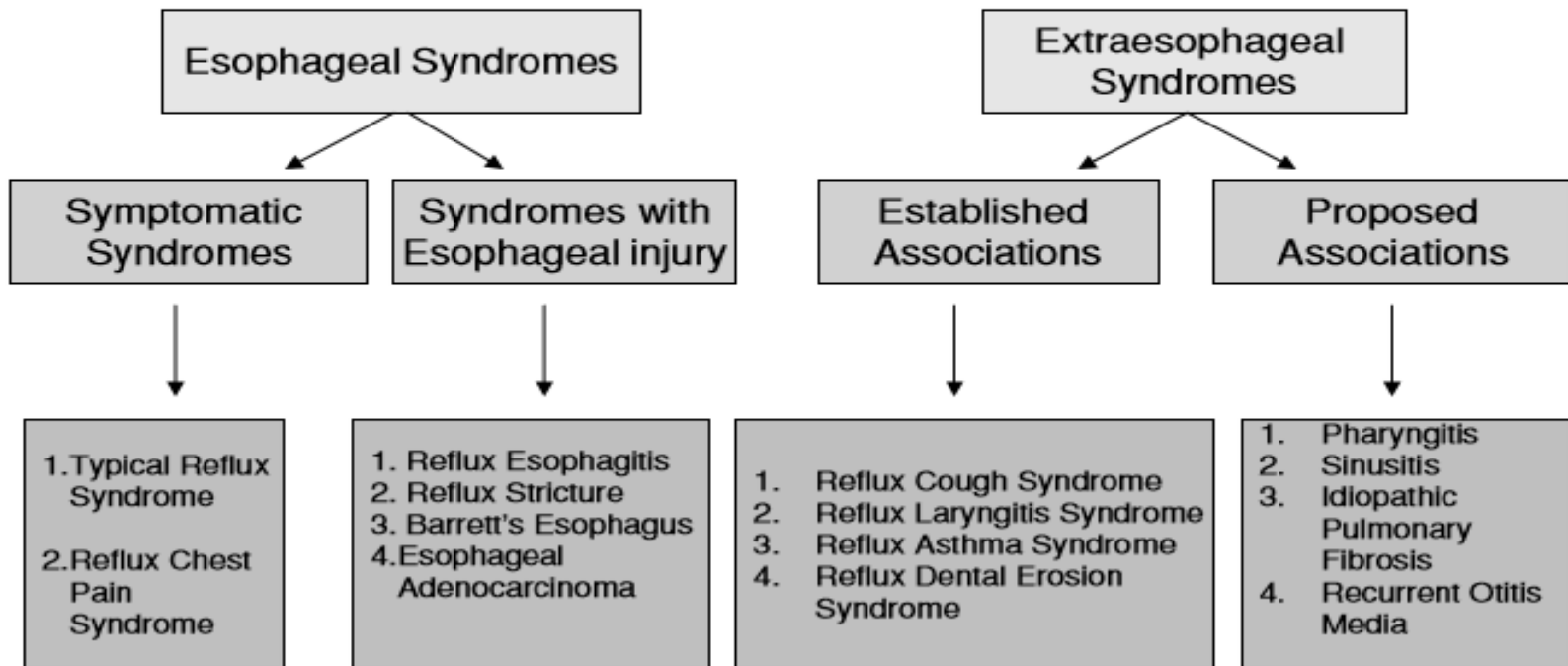
臺中榮總胃腸肝膽科主治醫師
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大綱

- 難治性胃食道逆流症症狀的臨床特徵：
 - 定義
 - 流行病學
 - 風險因素
 - 可能的病因
- 診斷
- 治療

2006年蒙特婁國際共識定義 胃食道逆流以困擾症狀為主

GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms or complications



2023年國際里昂共識提出「可執行的胃食道逆流」定義,增加內視鏡和逆流檢測

Recent advances in clinical practice



OPEN ACCESS

Updates to the modern diagnosis of GERD: Lyon consensus 2.0

Recent advances in clinical practice

Table 1 Justification of update of the Lyon Consensus

Key areas in need for update identified by the steering committee

Entities not covered in original Lyon Consensus

Entities covered in update of Lyon Consensus

Modern definition of actionable GERD in the context of presenting symptoms

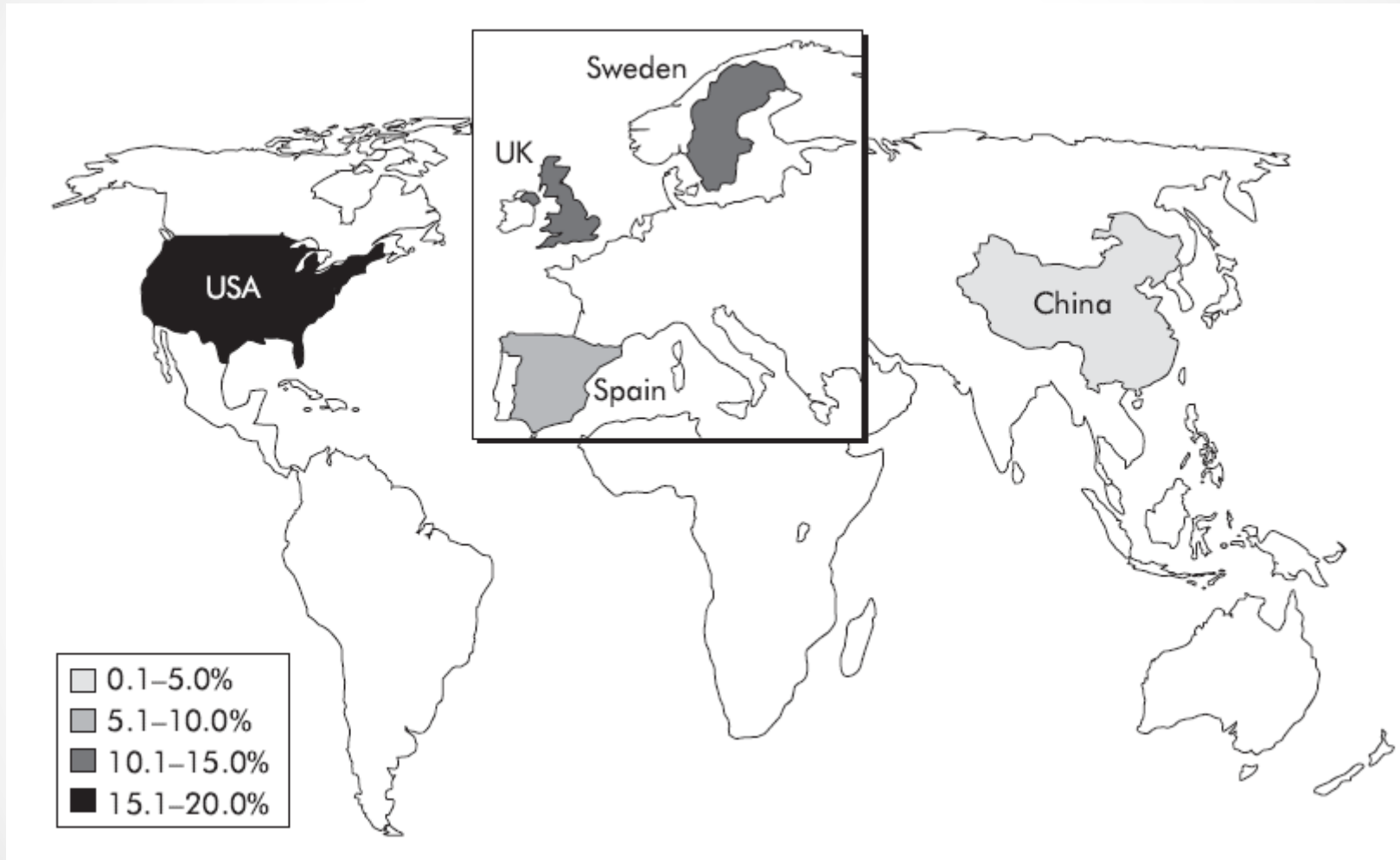
Concept of 'actionable GERD'

Description of conclusive GERD where oesophageal testing supports revising, escalating or personalising GERD management

Modern definition of GERD

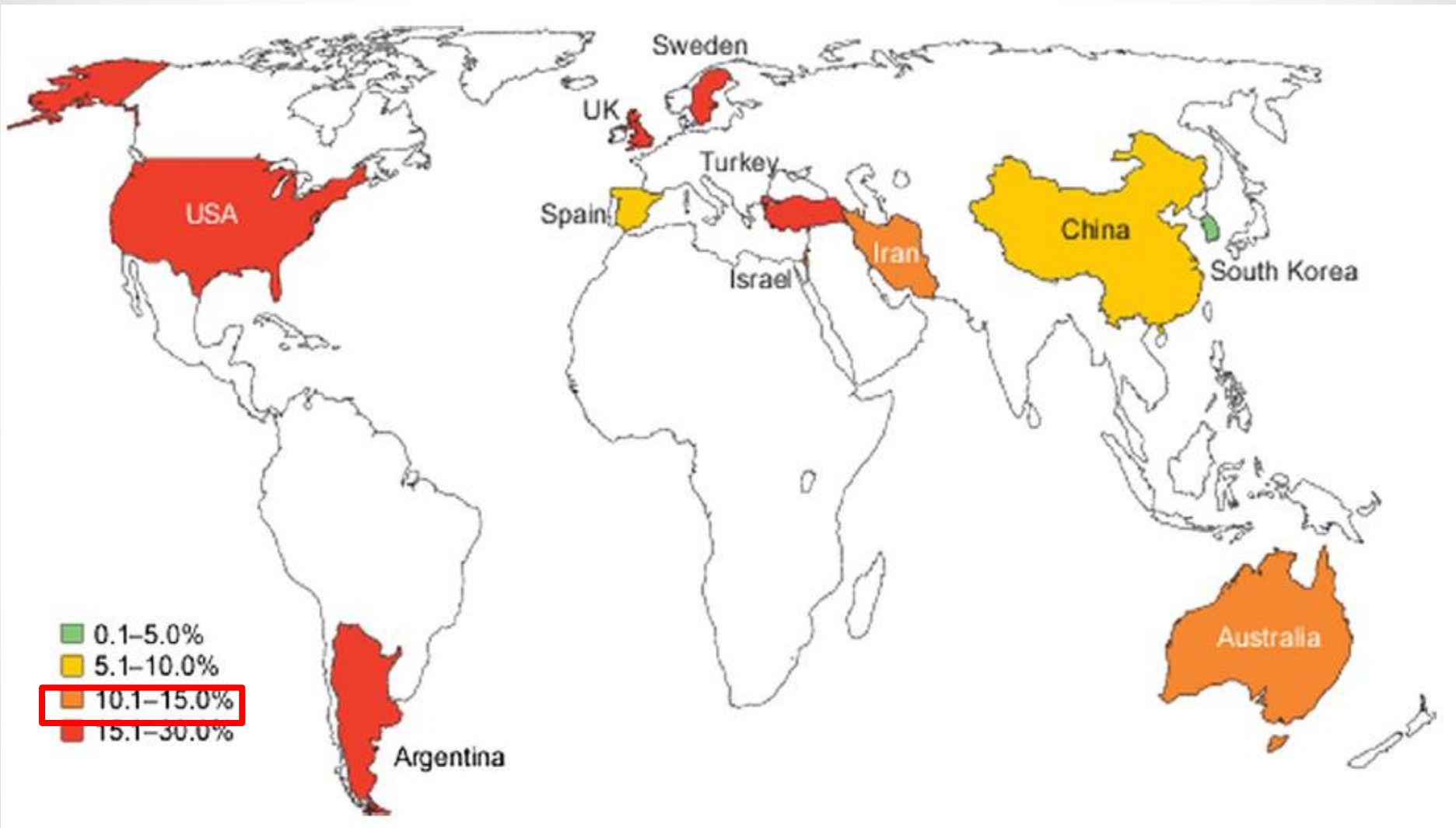
Definition of GERD that takes both troublesome symptoms and oesophageal test results into consideration; criteria that rule out GERD are also defined, for use in diagnostic criteria for disorders of gut-brain interaction

2005年全球盛行率調查, 以每週至少一次心灼熱或胃酸逆流症狀估計, 台灣約5%的人口有胃食道逆流



Dent, 2005 Gut

2013年全球盛行率調查, 以每週至少一次心灼熱或胃酸逆流症狀估計, 台灣約5-10%有胃食道逆流



2020年全球盛行率調查, 以心灼熱或胃酸逆流症狀估計, 台灣約20-25%有胃食道逆流

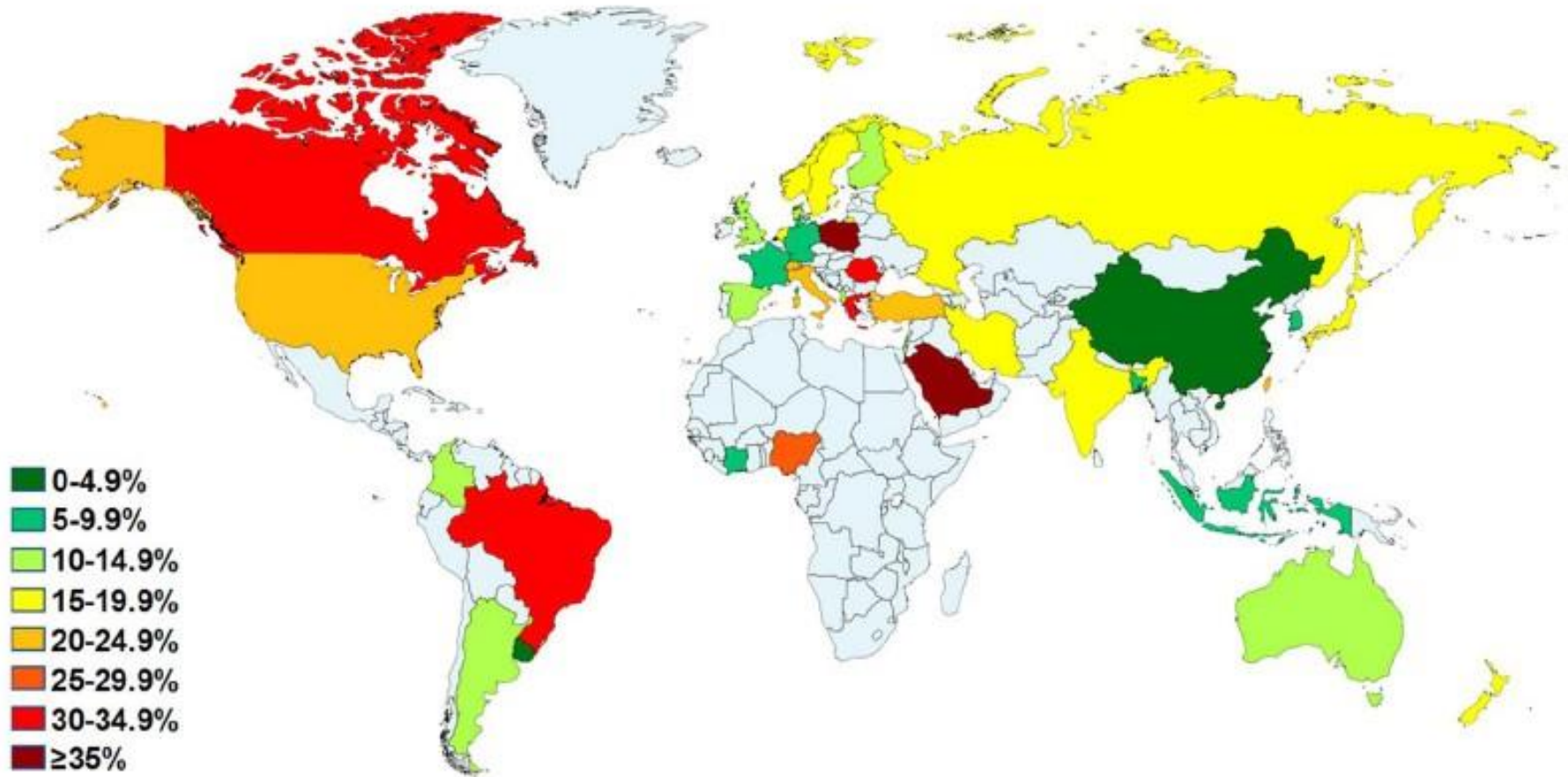
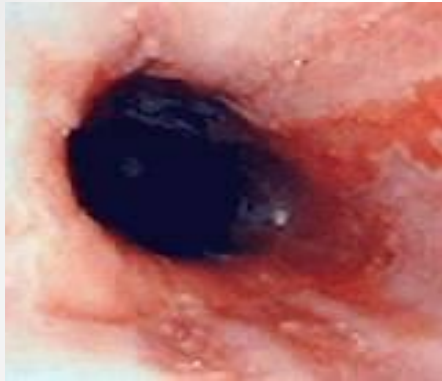


Figure 2. Distribution of GORD prevalence according to country.

臺中榮總健檢也發現逆流性食道炎盛行率在七年間從5%增加到12%，尤其是中年人

糜爛性食道炎



非糜爛性食道

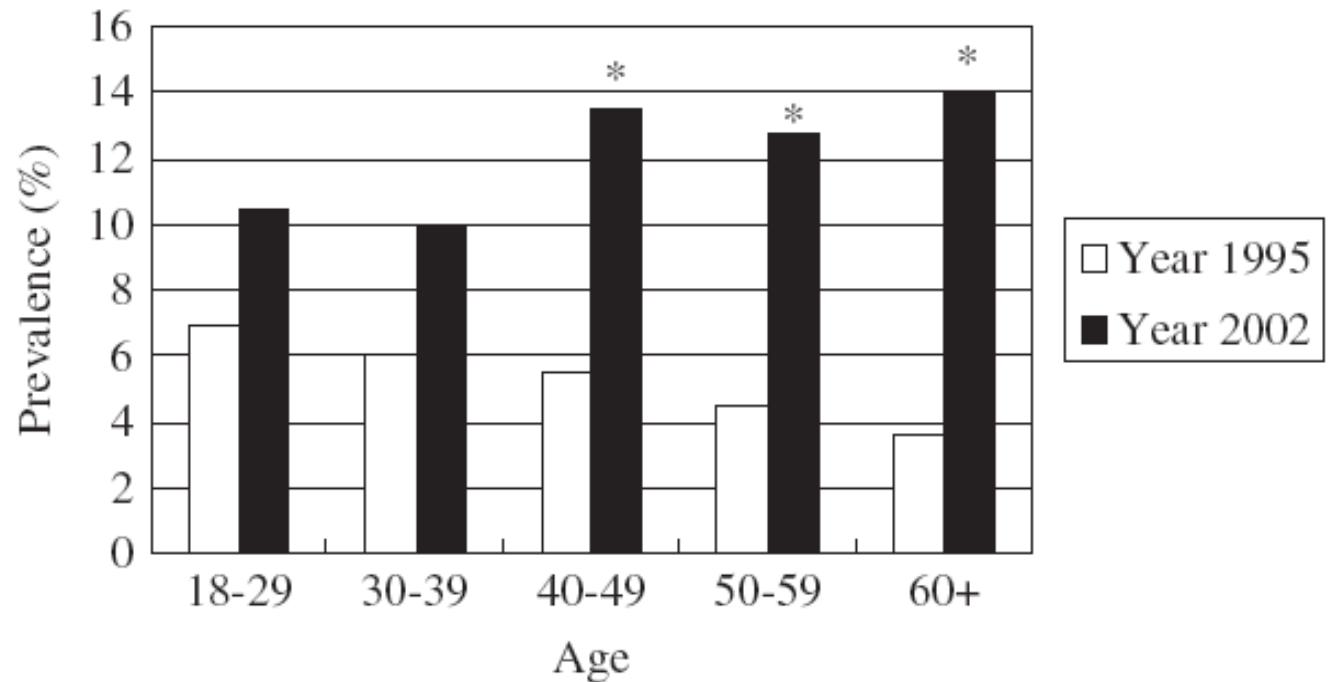


FIGURE 1. Age-specific prevalence of erosive esophagitis in apparently healthy Taiwanese adults in 1995 and 2002. * $P < 0.0001$ compared with 1995.

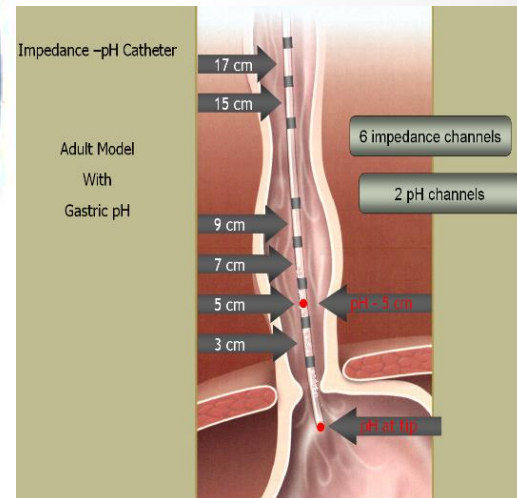
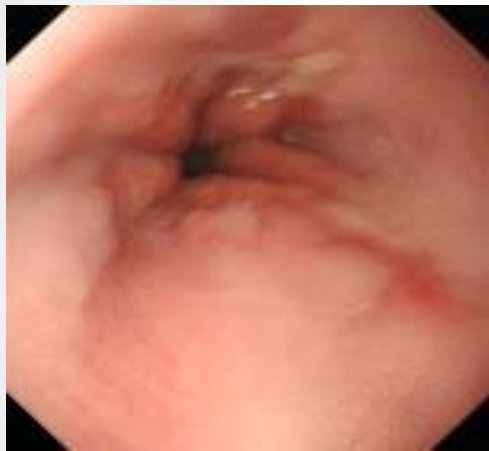
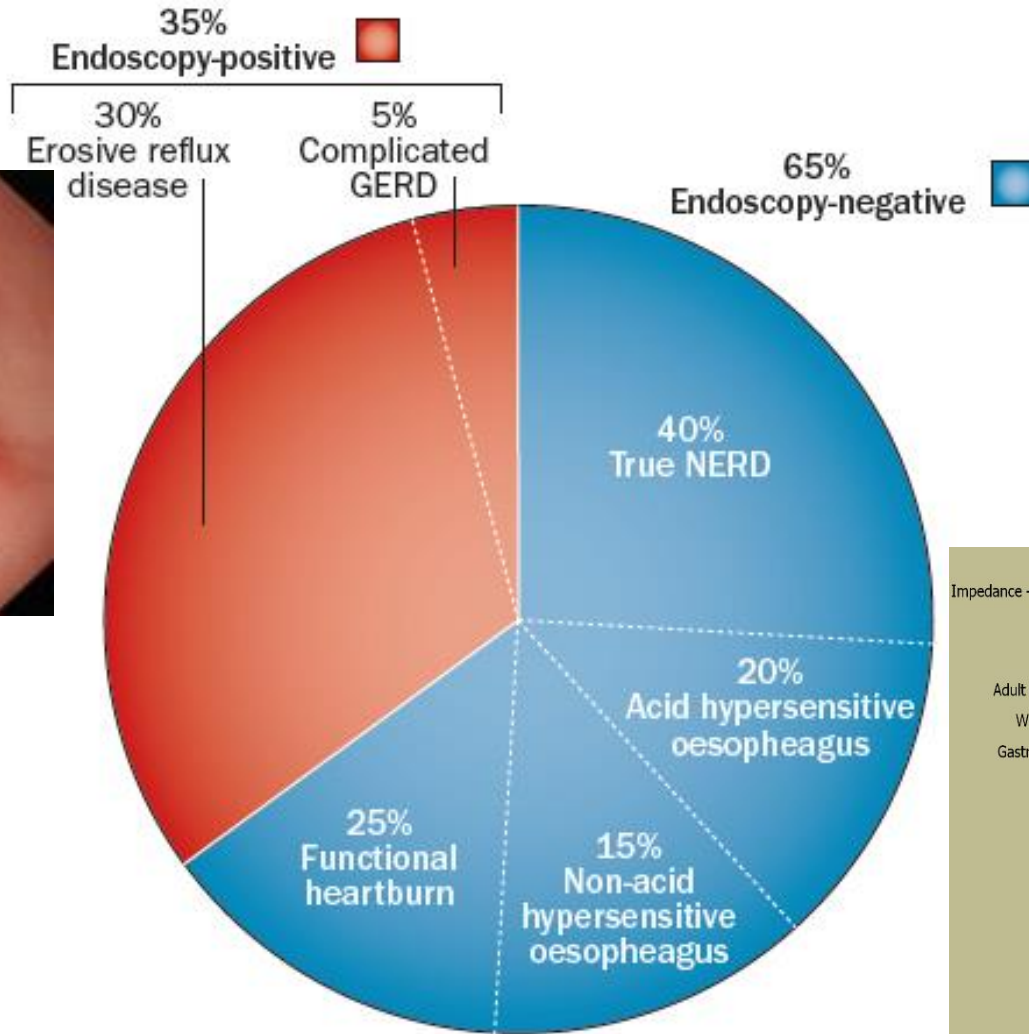
同時期,亞洲國家包括新加坡、菲律賓、馬來西亞、與韓國,逆流性食道炎也都呈現倍數增加

Table 4. Time trend studies for erosive esophagitis in asian regions

Study	Time Interval	Prevalence rates of Erosive esophagitis (first-second, %)
Singapore; Ho <i>et al.</i> ⁶⁶	9 years (1992–2001)	4.3 to 10.0
Philippines; Sollano <i>et al.</i> ⁶⁷	6 years (1994/7–2000/3)	2.9 to 6.3
Malaysia; Goh <i>et al.</i> ⁶⁸	10 years (1989/1990–1999/2000)	2.0 to 8.4
Taiwan; Lien <i>et al.</i> ⁶⁹	7 years (1995–2002)	5.0 to 12.6
Kim <i>et al.</i> 2009 ⁷⁰	10 years (1995–2005)	1.8% (1995), 5.9% (2000), 9.1% (2005)

Goh KL, 2011 J Gastroenterol Hepatol

事實上,僅1/3逆流病人內視鏡胃呈現糜爛性 食道炎,其餘診斷有賴生理性的逆流檢測



美國調查7萬多人,發現四成有逆流症狀,服用質子幫浦抑制劑中,半數效果不好

Results of a Survey of 71,812 Persons in the United States

Ever had GERD symptoms



Had GERD symptoms in the past week



Persistent GERD symptoms in persons taking daily PPIs



Factors associated with GERD symptoms in past week

- Female sex
- Non-Hispanic white race
- Comorbidities

Factors associated with PPI-refractory GERD symptoms

- Female sex
- Latino race
- Younger age

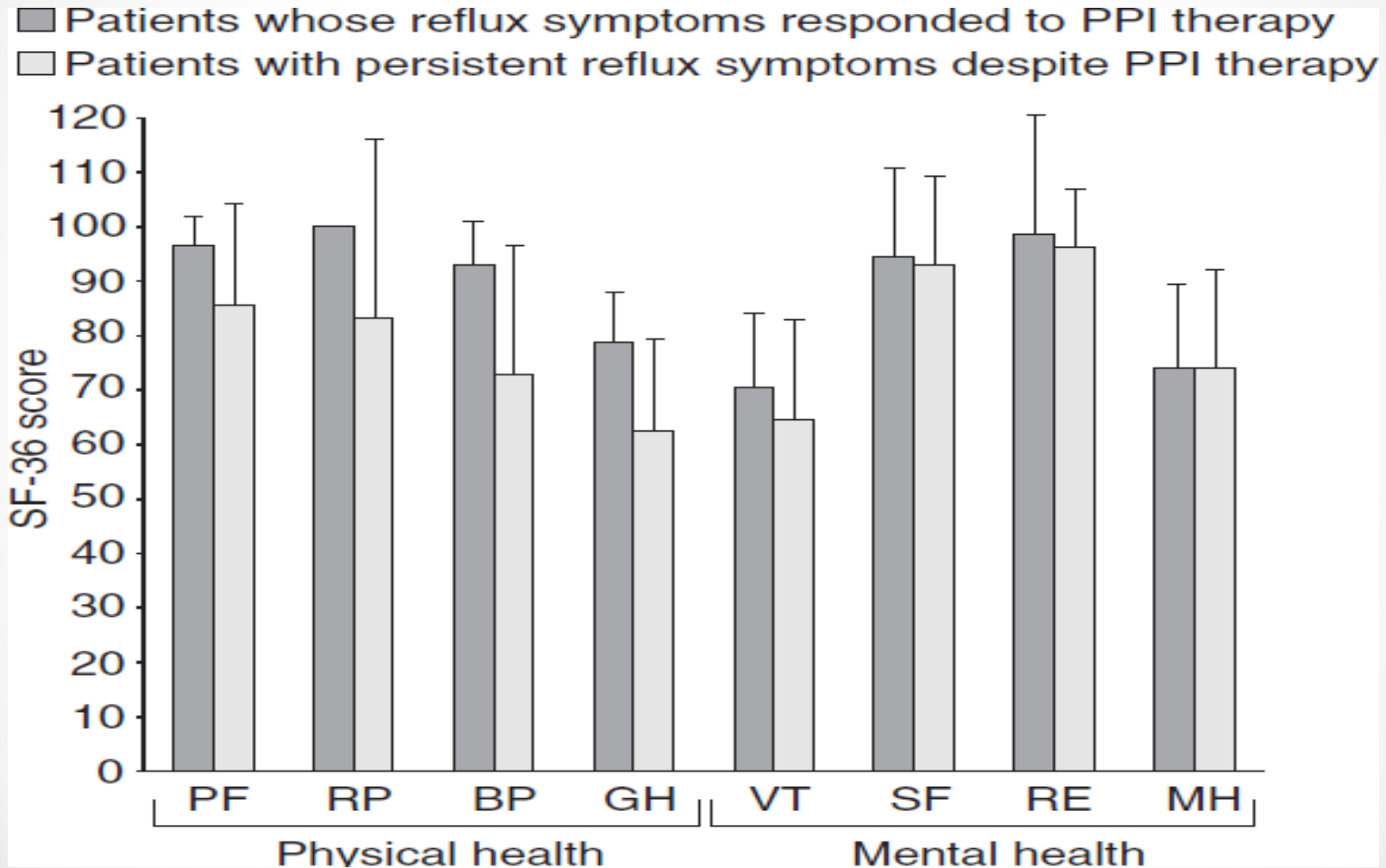
Delshad 2020 Gastroenterol

何謂難治型胃食道逆流？

東、西方的定義略有不同

- Symptoms (heartburn and/or regurgitation) not responding to a double dose of a PPI during a treatment period of at least 12 weeks. Sifrim 2012 Gut
- Persistent and troublesome GERD symptoms after at least 8 weeks of a standard dose of PPI. ([Asia-Pacific consensus](#)) Fock KM 2006 Gut
 - * Troublesome= impairment of patients' quality of life

系統回顧發現:困難型胃食道逆流者的生活品質不如服藥有效者 (n= 14774)



困難型胃食道逆流的風險因子 —病例對照研究 (n = 245)

- Poor compliance.
- Obesity (BMI>30),
- Lack of performed lifestyle interventions,
- Atypical GERD symptoms (cough, chest pain),
- Long disease duration,
- Hiatal hernia,
- EE LA grade C & D,
- positive *H. pylori* status,

困難型胃食道逆流的風險因子 — 跨國多中心縱向觀察 (n = 1888)

Table 3 Factors influencing treatment response

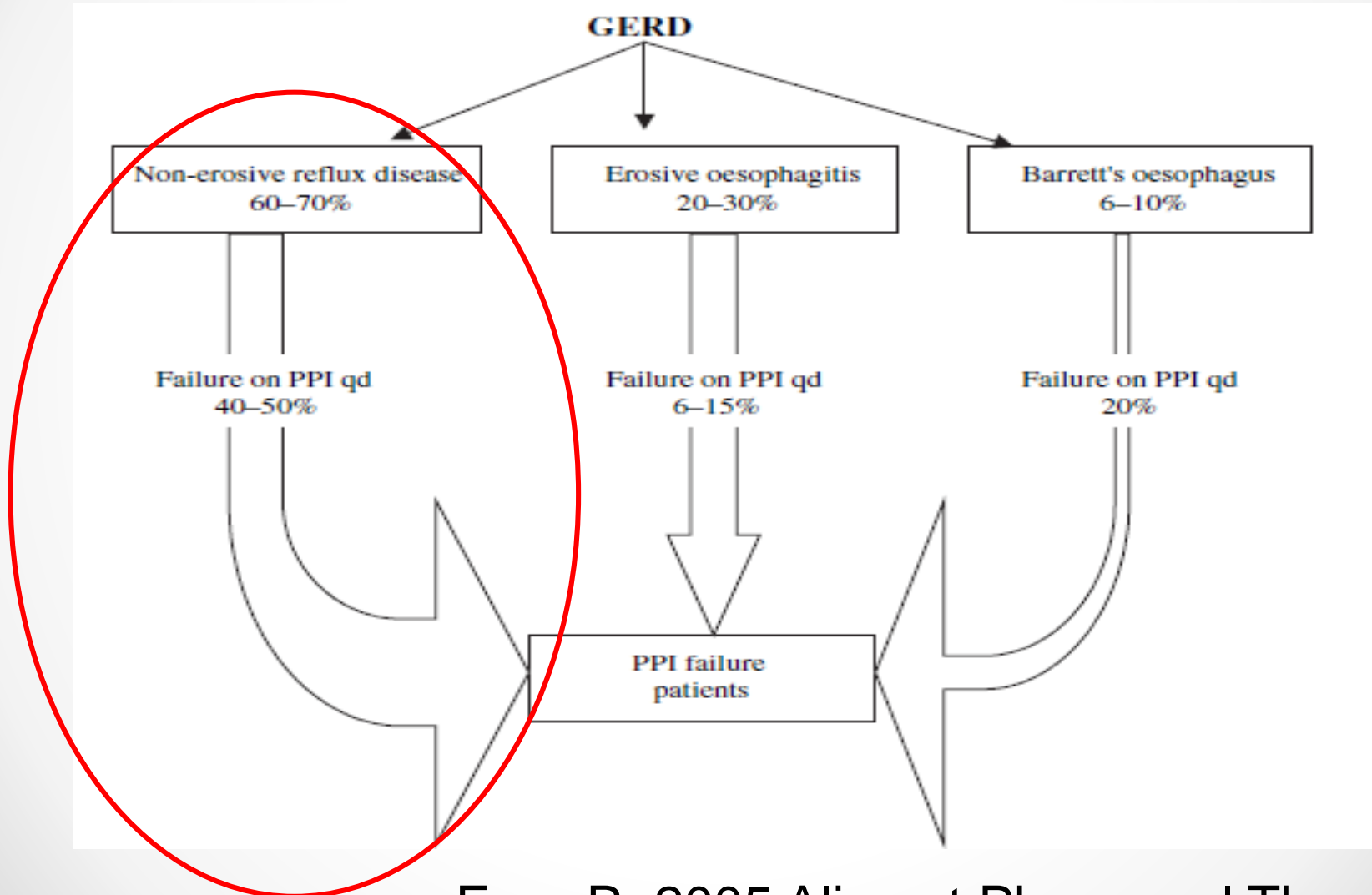
Factor	Logistic regression p-value
ERD/NERD NERD	<0.0001
HADS total score	<0.0001
• Anxiety sub-score	<0.0001
• Depression sub-score	<0.0001
IBS	<0.0001
BMI Low BMI 25.7 NR vs. 26.8 R	<0.0001
Gender Female	0.0011
Geography	0.0052
<i>H. pylori</i>	Not significant
Age	Not significant
Oesophagitis grade (A-D)	Not significant

亞洲人困難型胃食道逆流似乎 較高(n = 1888)

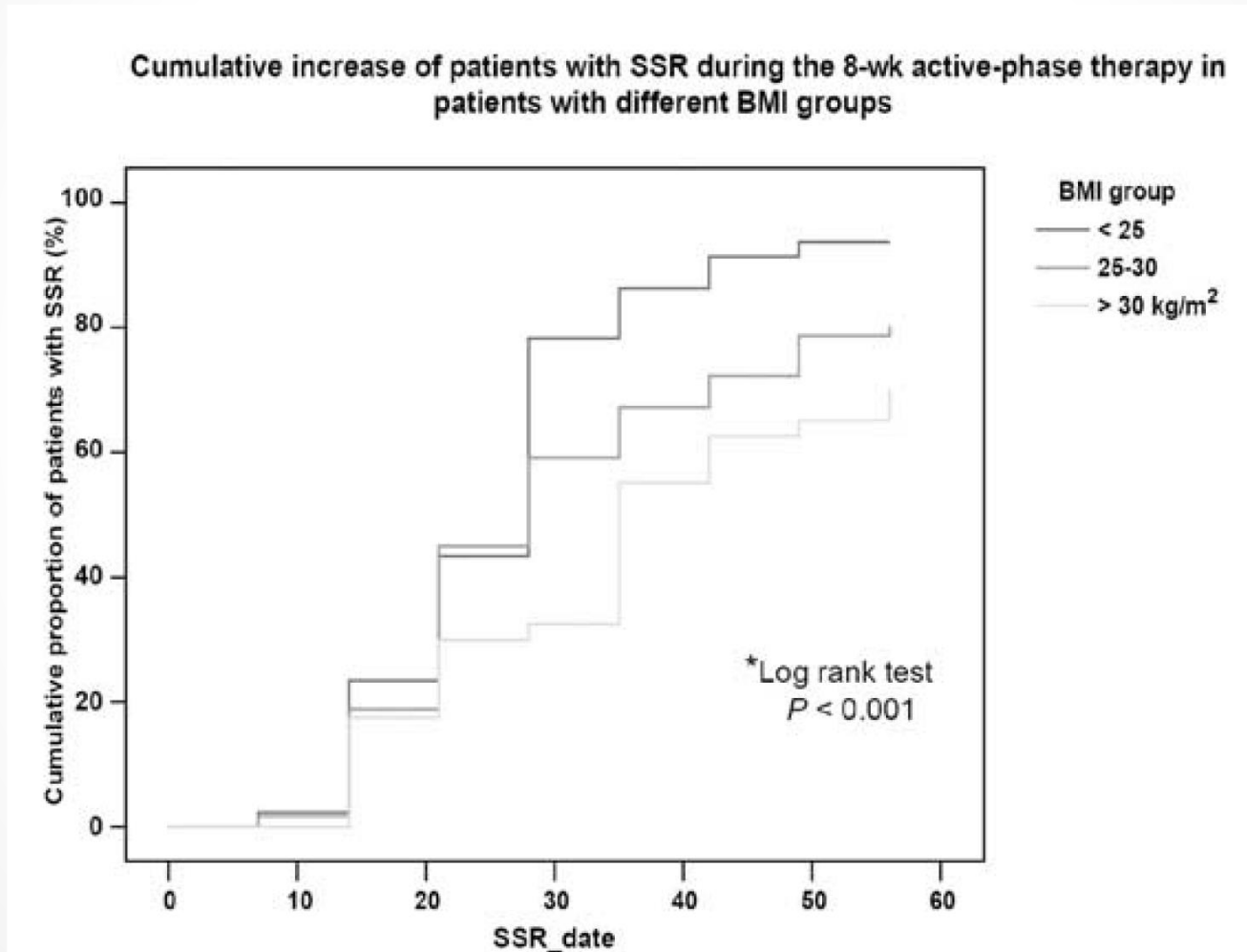
- REAL LIFE study (n=1888) a multicentre, multinational, prospective, open study of 8 weeks pantoprazole treatment, 40 mg daily
- Non-response rates: South Africa (17.5%), Western Europe, South America and Canada (~28%), Australia (38.3%) and Asia (39.2%) .

Heading 2011 BMC Gastroenterol

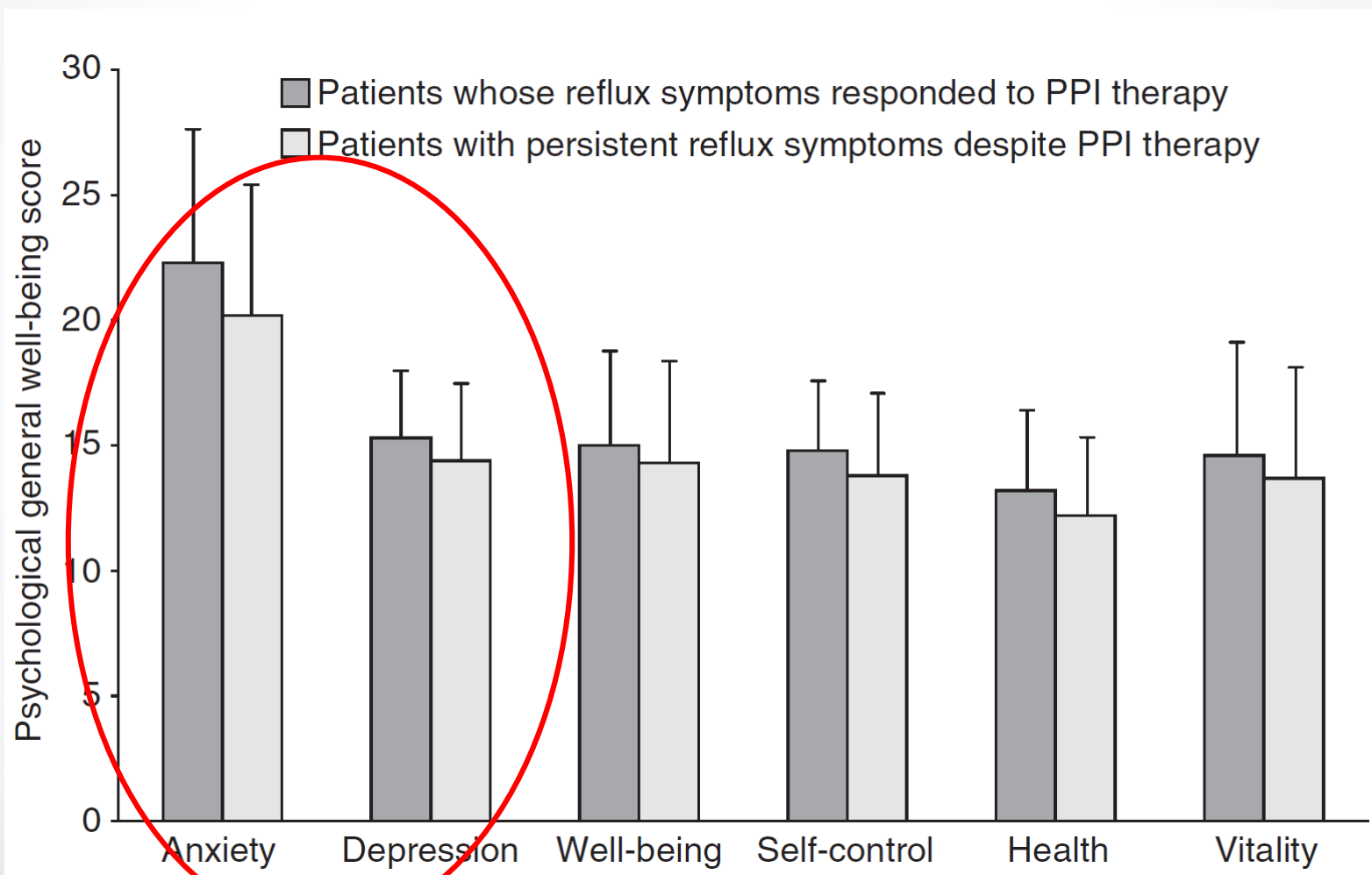
系統回顧發現:困難型胃食道逆流多數來自非糜爛性胃食道逆流, 因此內視鏡的診斷角色有限



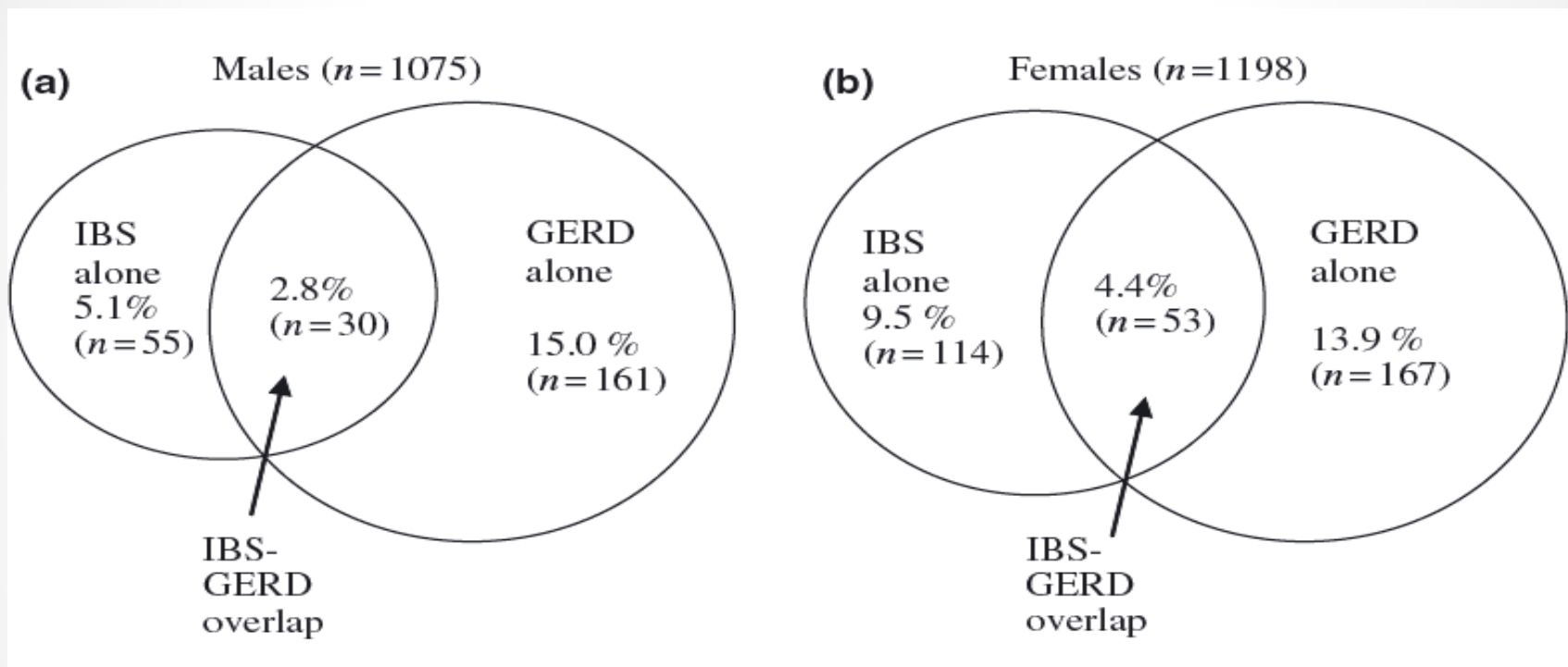
成大醫院一前瞻性縱向觀察研究發現： 體重過重者較易是困難型胃食道逆流



系統回顧發現:焦慮憂鬱者較易成為困難型胃食道逆流 (n = 14774)



約1/4胃食道逆流病人會伴隨腸躁症,此類病人女性較多



- Predictors of overlap vs. GERD alone were **insomnia** (OR 1.5; 1.13-1.90), frequent **abdominal pain** (OR 1.8; 1.02-3.2), a higher **somatization** (OR 1.7; 1.1-2.4).

一個前瞻性世代研究中發現胃食道逆流病人伴隨腸躁症、功能性消化不良者、無糜爛性食道炎、與BMI<25者皆較易是困難型胃食道逆流

Table 3 Independent predictive factors of PPI failure in three groups of patients with gastro-oesophageal reflux symptoms (multivariate analysis)

Factor	OR (95% CI)	p Value*
Whole population (n=100)		
BMI \leq 25 kg/m ²	5.33 (1.88 to 15.07)	0.002
Functional dyspepsia	5.61 (1.99 to 15.79)	0.001
No oesophagitis	4.19 (1.00 to 17.64)	0.050
Patients with symptoms (n=85)		
BMI \leq 25 kg/m ²	5.03 (1.66 to 15.23)	0.004
Functional dyspepsia	4.46 (1.46 to 13.68)	0.009
Irritable bowel syndrome	3.65 (1.03 to 12.98)	0.044
Patients with documented GORD (n=67) by pH-impedance		
Functional dyspepsia	7.95 (2.00 to 31.60)	0.003
No oesophagitis	6.96 (1.09 to 44.30)	0.040
Irritable bowel syndrome	6.51 (1.51 to 28.08)	0.012
BMI \leq 25 kg/m ²	4.51 (1.17 to 17.38)	0.029

Patients with documented GORD had 24 h oesophageal acid exposure $>$ 5% and/or positive SI/SAP.

小結

1. 近二十來，包括台灣在內的許多國家，胃食道逆流盛行率快速上升，其中近半數服用質子幫浦抑制劑效果不佳，影響生活品質。
2. 困難型胃食道逆流的風險因子，包括非糜爛性逆流症狀、精神狀態、伴隨非典型症狀、或功能性胃腸疾病、生活型態、藥物順從性、女性、較長病史、亞洲人等因素。
3. 體重、幽門桿菌、及食道炎嚴重度的數據在困難型胃食道逆流較不一致。

診斷

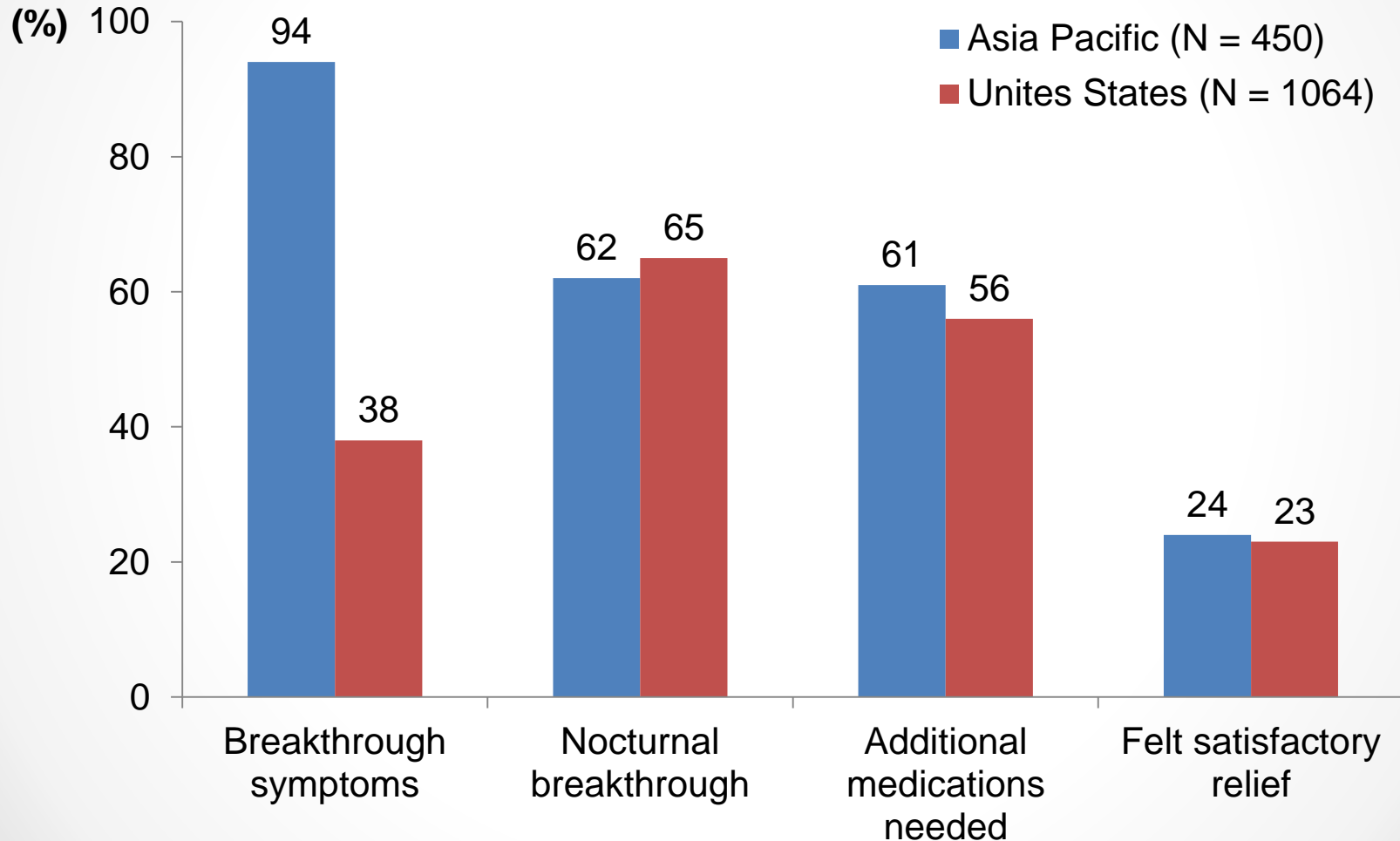
1. 治療失敗的可能原因
2. 非逆流的病因
3. 客觀逆流檢測

困難型胃食道逆流的可能原因

Table 1. Putative mechanisms for failure of proton pump inhibitor (PPI) treatment

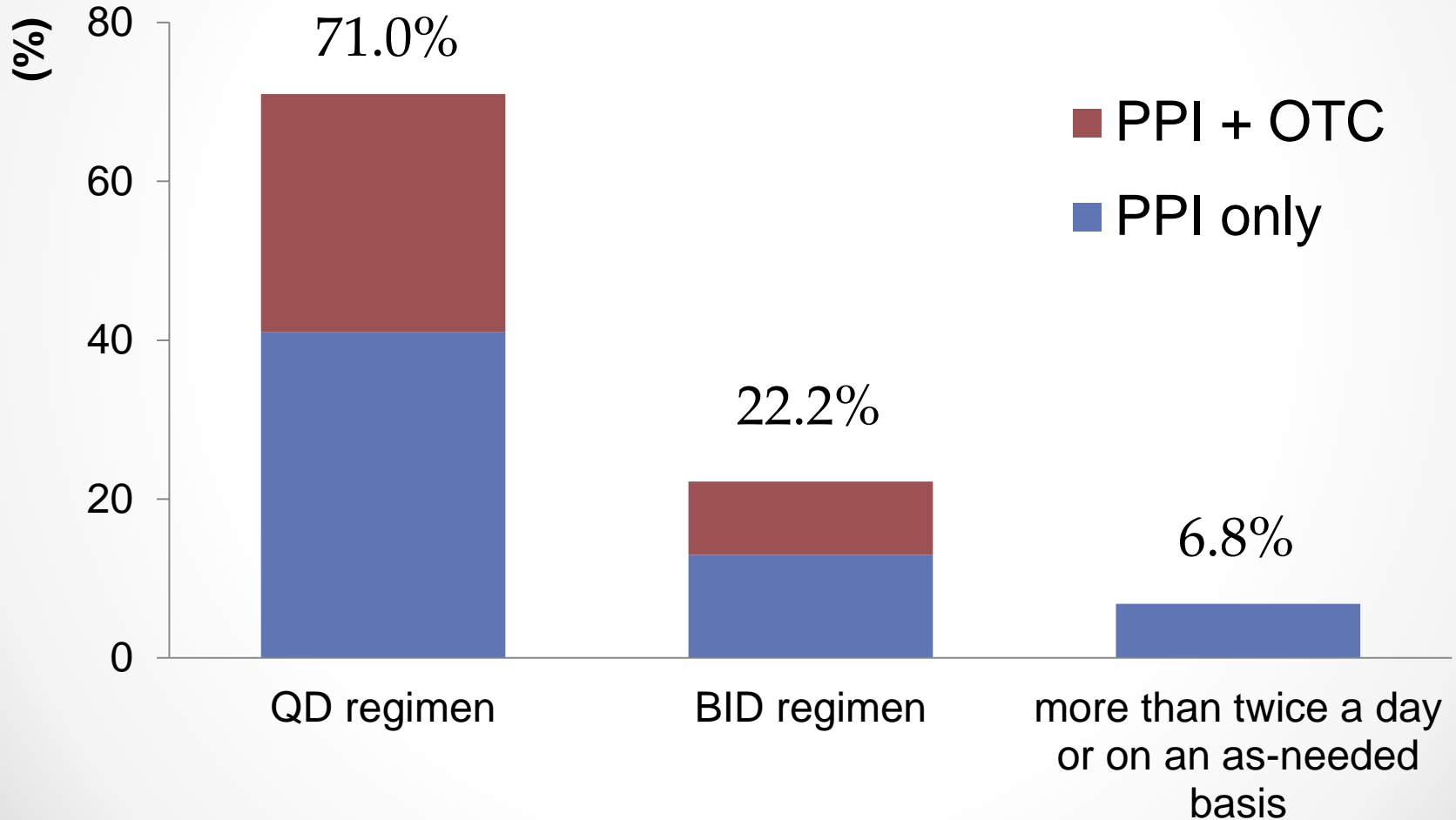
- Compliance
- Improper dosing time
- Weak acidic reflux
- Duodenogastroesophageal/bile reflux
- Esophageal hypersensitivity
- Delayed gastric emptying
- Psychological comorbidity
- Concomitant functional bowel disorder
- Reduced PPI bioavailability
- Rapid PPI metabolism
- PPI resistance
- Nocturnal reflux
- *Helicobacter pylori* infection status
- Eosinophilic esophagitis

亞洲人比美國人更容易有 困難型胃食道逆流？

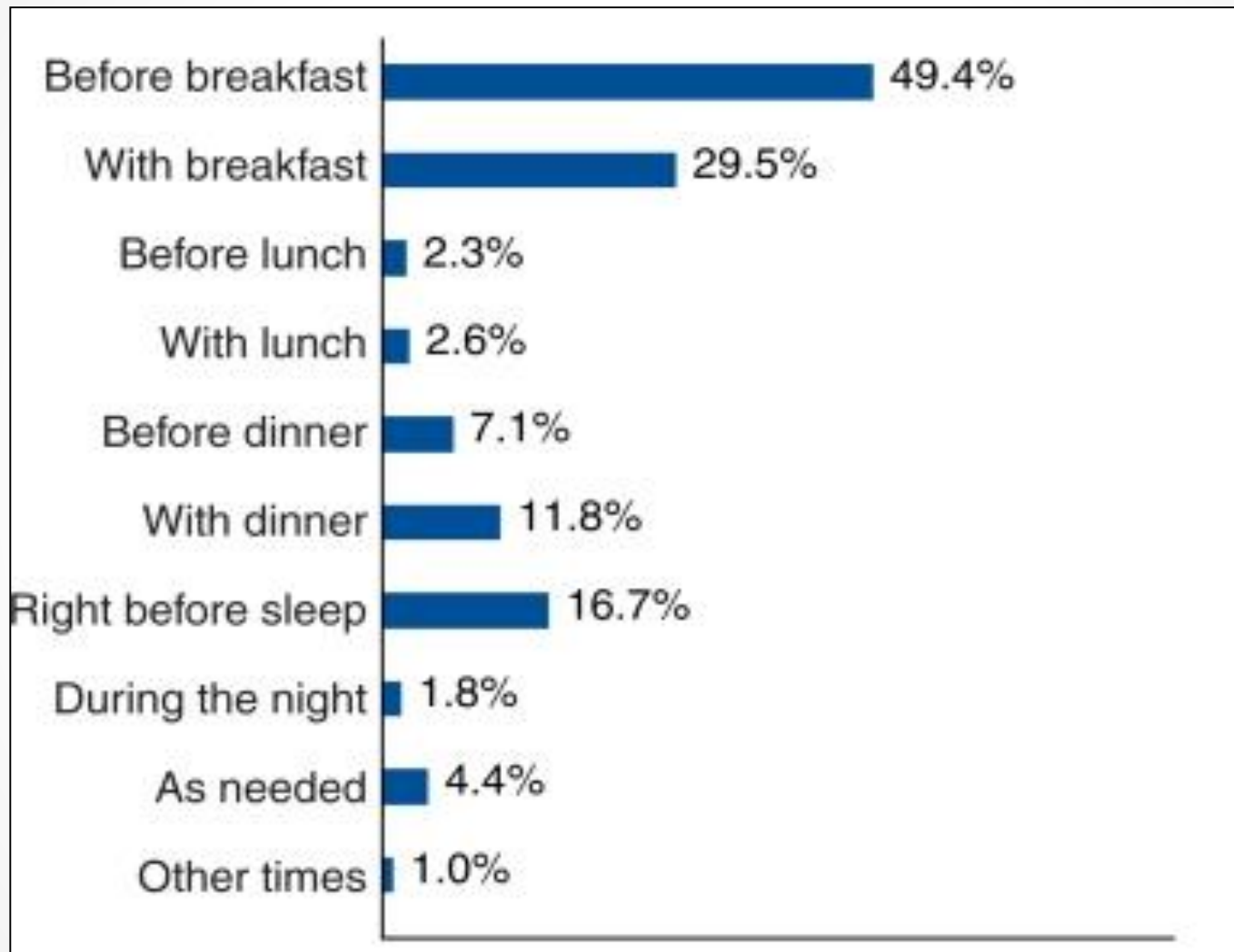


Goh KL, 2014 J Gastroenterol Hepatol (Asia Pacific Survey, GAPs)
AGA Survey. Harris Interactive Inc; 2008.

美國一社區型調查發現：使用質子幫浦抑制劑者，22%每日需服用兩次，41%每日服用一次或兩次者仍需額外胃藥 (n = 617)

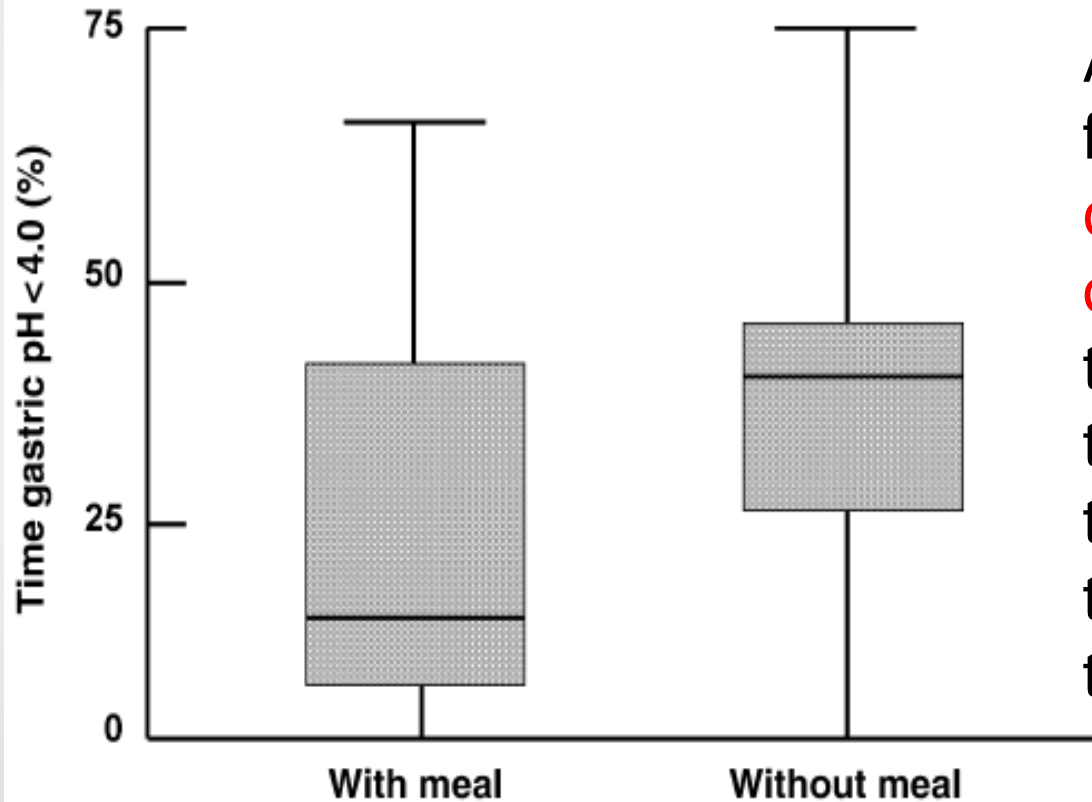


調查也發現: 50% 病人服藥的時間不恰當



Chey WD 2009 Curr Med Res Opin
Gunaratnam NT 2006 Aliment Pharmacol Ther
The Gallup Study 2000

早餐前服用質子幫浦抑制劑者,較沒吃早餐者,胃酸控制較佳,但七成美國基層醫師未如此建議病人



A survey of 491 physicians found that **70% of primary care physicians** and **20% of gastroenterologists** in the US advised patients to take the PPI dose at bed time or **did not believe** that the relationship to meals was important

僅55%病人遵從處方醫囑：症狀嚴重度、個人偏好、疾病知識、藥物口感、副作用、年齡、共藥、個性、社經地位、保險給付都可能是影響因素

- According to a large population-based survey, only **55%** of the GERD patients **took their PPIs as prescribed** (complete relief of heartburn at a rate of 11.5%/week).
- The presence & **severity** of **symptoms**, and **personal preference** to take PPIs affect the adherence.
- **Knowledge** about GERD, **desire for personal control**, the prescribed drug (**taste, consistency**, etc), **side effects**, **number of pills** per day, **concomitant therapies**, **age**, **personality**, **socioeconomic status** and **healthcare coverage**.

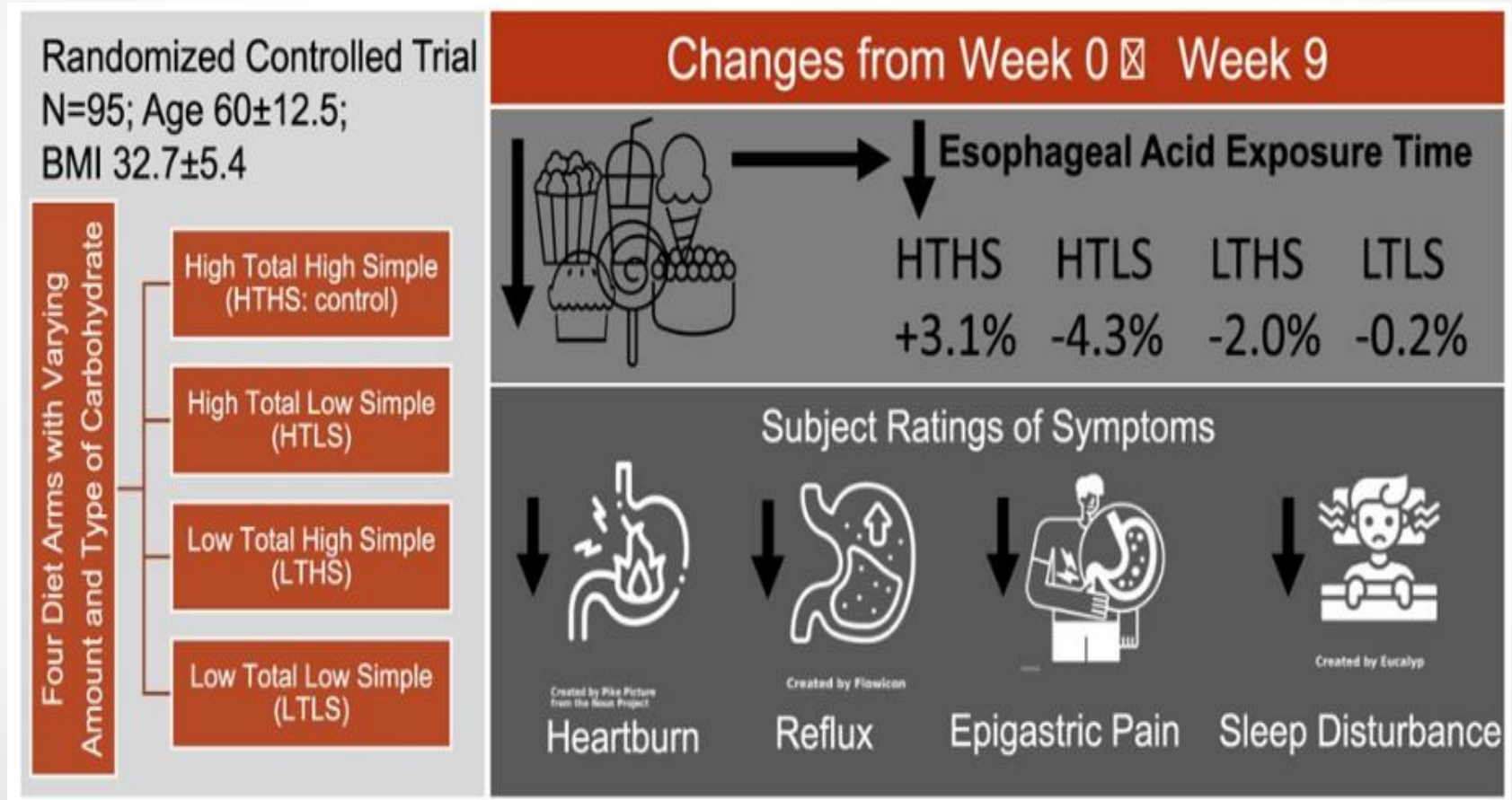
The Gallup Study 2000,
Chiba 1997 Gastroenterol
Hungin AP, 1999 Br J Gen Pract
Fass, 2005 Aliment Pharmacol Ther

美國臨床指引建議:體重過重者減重,睡前2-3小時避免進食,床頭搖高,戒菸,避免促發逆流症狀的食物

ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease

1. We recommend weight loss in overweight and obese patients for improvement of GERD symptoms (strong recommendation, moderate level of evidence).
2. We suggest avoiding meals within 2–3 hours of bedtime (conditional recommendation, low level of evidence).
3. We suggest avoidance of tobacco products/smoking in patients with GERD symptoms (conditional recommendation, low level of evidence).
4. We suggest avoidance of “trigger foods” for GERD symptom control (conditional recommendation, low level of evidence).
5. We suggest elevating head of bed for nighttime GERD symptoms (conditional recommendation, low level of evidence).

隨機臨床試驗發現:減少每日簡單糖62克可以減少逆流，改善症狀



Gu 2022 Am J Gastroenterol

檢查排除非逆流病因: 大於40歲,非慢性症狀, 出血,貧血,體重減輕,胃口不佳,吞嚥困難或疼痛,持續嘔吐,家人癌症病史

- New onset dyspepsia in pts ≥ 40 years
- Evidence of GI bleeding (hematemesis, melena, hematochezia, occult blood in stool)
- Iron deficiency anemia
- Anorexia
- Unexplained weight loss
- Dysphagia
- Odynophagia
- Persistent vomiting
- GI cancer in a first-degree relative

困難型胃食道逆流胃鏡檢查結果與未曾治療者類似

TABLE 4. Comparison of endoscopic and histologic findings in the PPI treatment failure group and the no-treatment group

N=105 **N=91**

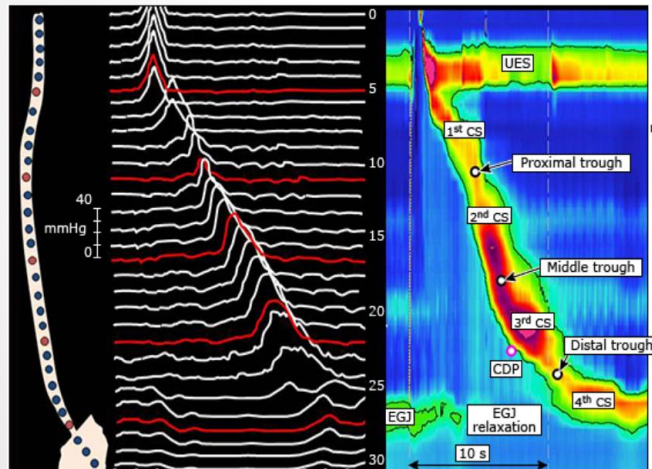
Endoscopic findings	PPI treatment failure, N (%)	No treatment, N (%)	P value
Normal	58 (55.2)	37 (40.7)	.04
Erosive esophagitis	7 (6.7)	28 (30.8)	<.001
Grades A/B	7 (6.7)	26 (28.6)	
Grades C/D	0	2 (2.2)	
Barrett's esophagus	4 (3.8)	3 (3.3)	1.0
Eosinophilic esophagitis	1 (0.9)	0	1.0
Hiatal hernia	14 (13.3)	13 (14.3)	.85
Esophageal ring	11 (10.5)	10 (11)	.91
Esophageal candidiasis	1 (0.95)	1(1.1)	1.0
Esophageal webs	1 (0.95)	0	1.0
Esophageal angiodysplasia	1 (0.95)	0	1.0

A US case-control study

Endoscopic findings	PPI treatment failure, N (%)	No treatment, N (%)	P value
Achalasia*	1 (0.95)	0	1.0
Gastric bezoar	1 (0.95)	0	1.0
Gastric ulcer	1 (0.95)	0	1.0
Gastric cancer	0	1 (1.1)	.46
Erosive gastritis	6 (5.7)	12 (13.2)	.07
Erosive duodenitis	2 (1.9)	4 (4.4)	.4
Duodenal ulcer	0	3 (3.3)	.09
Gastric/duodenal polyps	11 (10.5)	6 (6.6)	.34

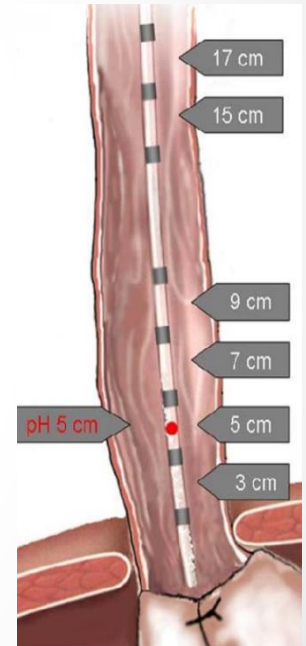
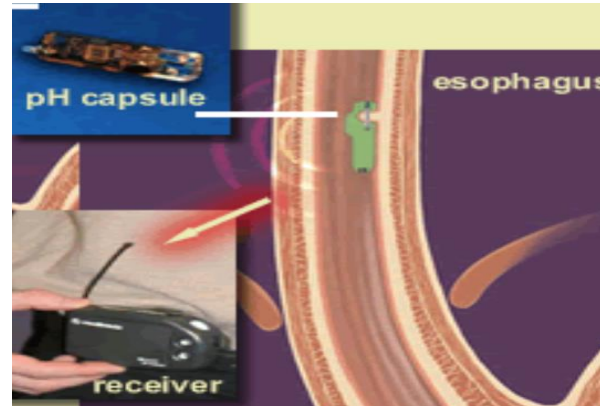
2018年國際里昂共識推薦的三種食道 生理功能檢測診斷胃食道逆流

高解析度食道壓力
阻抗檢測



多通道食道內阻抗酸鹼
偵測計

96h無線電食道
酸鹼值監控檢測



逆流測試可評估困難型胃食道逆流病人是否真有逆流

Diagnosis of GERD based on EGD and esophageal function testing (HRM & reflux monitoring)

- 1. Inadequate acid suppression:
 - PPI compliance, dosing, timing, residual acid
- 2. esophageal hypersensitivity for acidic and/or non-acid reflux
- 3. non-GERD causes

The Lyon Consensus, Gyawali, 2018 Gut

逆流測試可評估無逆流性食道炎病人是,胃酸過度暴露, 對酸過度敏感,或功能性心灼熱

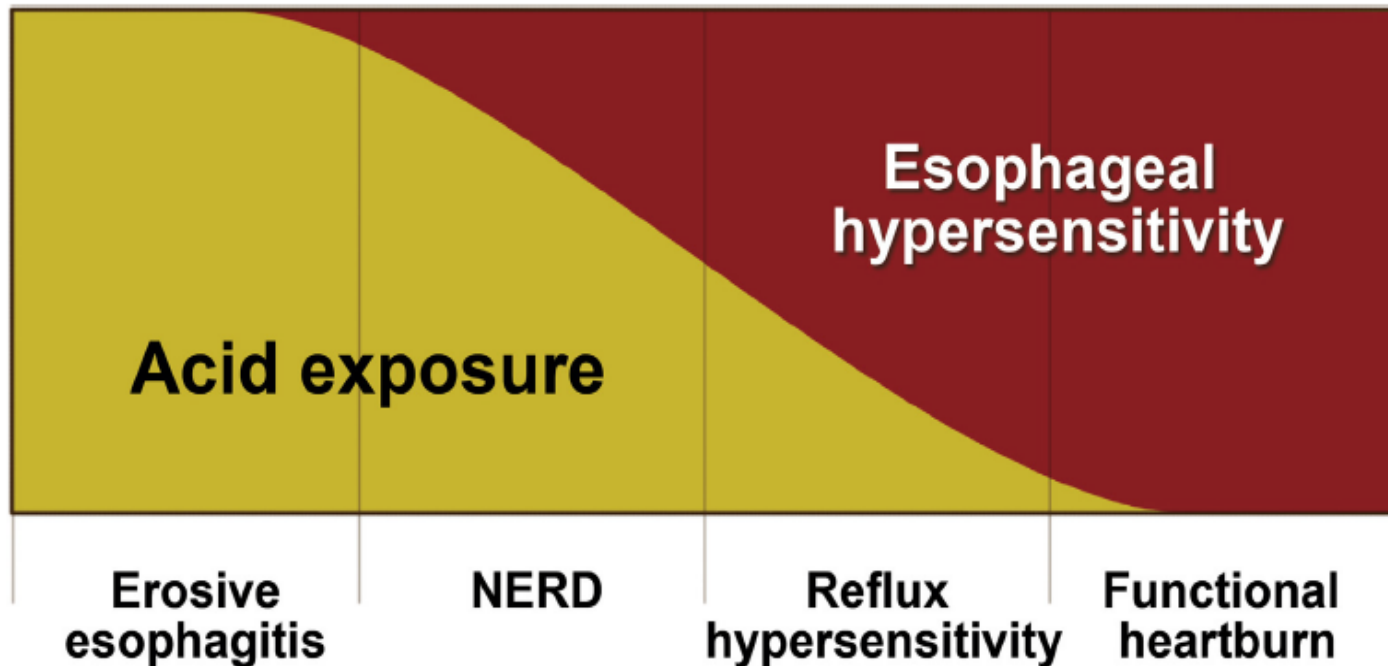
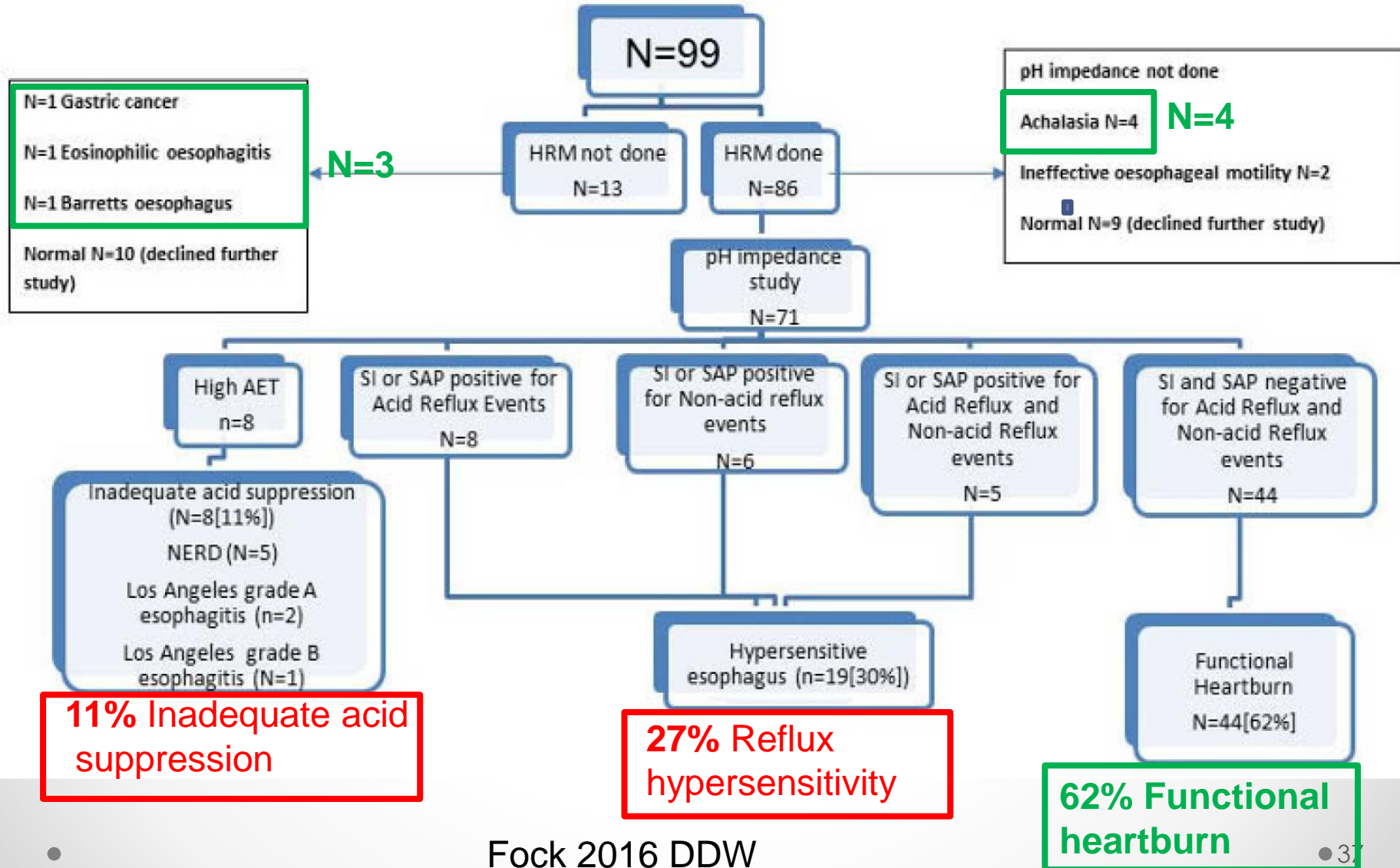


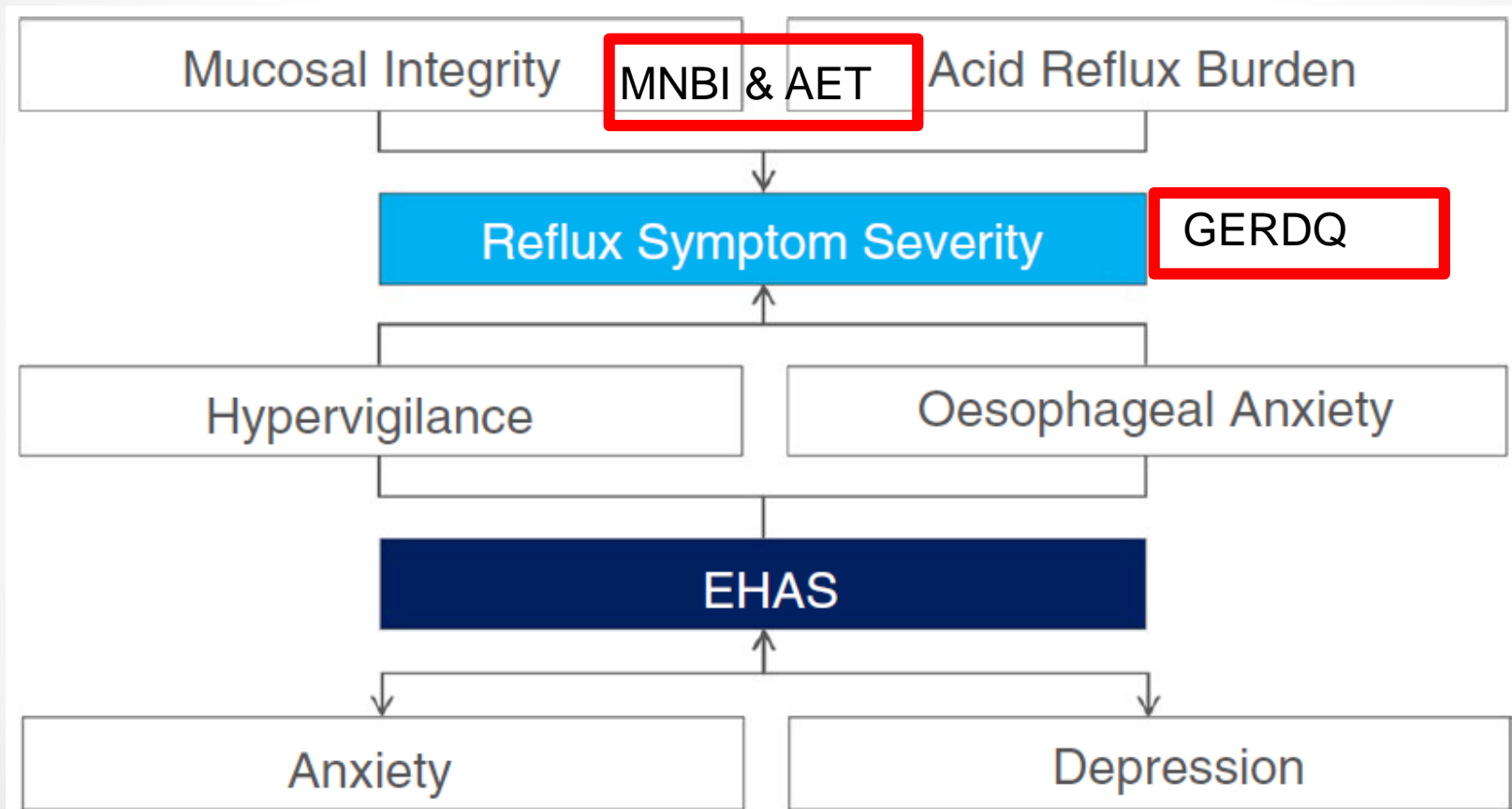
Figure 2. The interplay between esophageal hypersensitivity and acid exposure in the reflux symptom spectrum. Symptoms in erosive esophagitis are dominated by abnormal acid exposure whereas symptoms in functional heartburn are dominated by hypersensitivity. Symptoms in NERD and reflux hypersensitivity are related to a combination of both acid exposure and hypersensitivity, with a shift reflecting a more pronounced effect of acid exposure along the NERD diagnostic spectrum and a more pronounced effect of esophageal hypersensitivity along the reflux hypersensitivity diagnostic spectrum.

Aziz Q, 2016 Gastroenterology

使用多通道食道內阻抗酸鹼偵測計發現,約六成屬於功能性心灼熱,三成屬於食道過度敏感



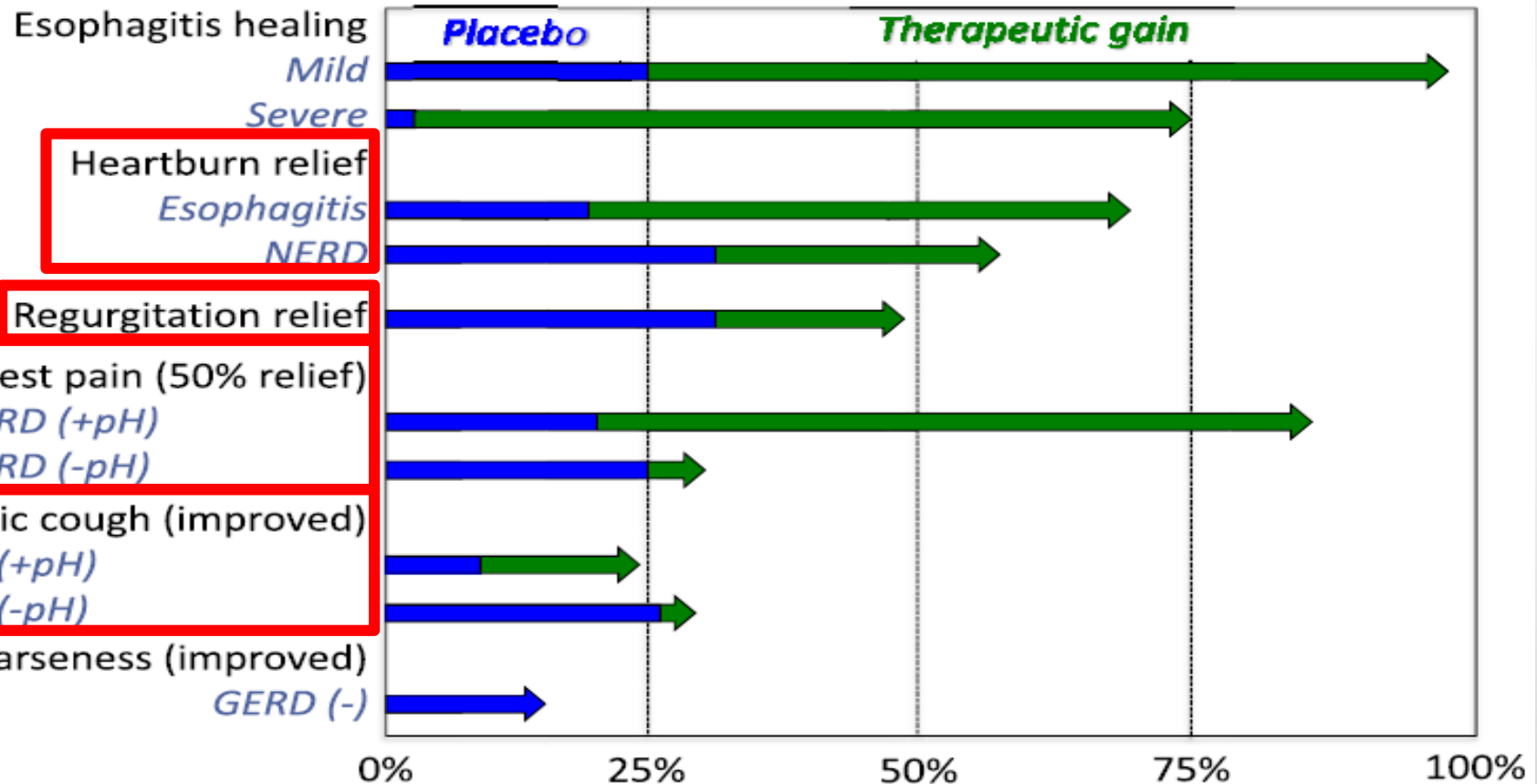
症狀的嚴重度取決於胃酸暴露與 食道過度警覺及中樞神經的焦慮



質子幫浦抑制劑效果依次: 輕度食道炎>中重度 食道炎>心灼熱>胃酸異常的胸痛>逆流症狀 咽喉症狀治療反應普遍不佳

PPI efficacy for potential manifestations of GERD

Estimates based on available RCT data



咽喉逆流症狀機轉,來自咽喉逆流直接刺激,與食道迷走神經受酸刺激的間接反射

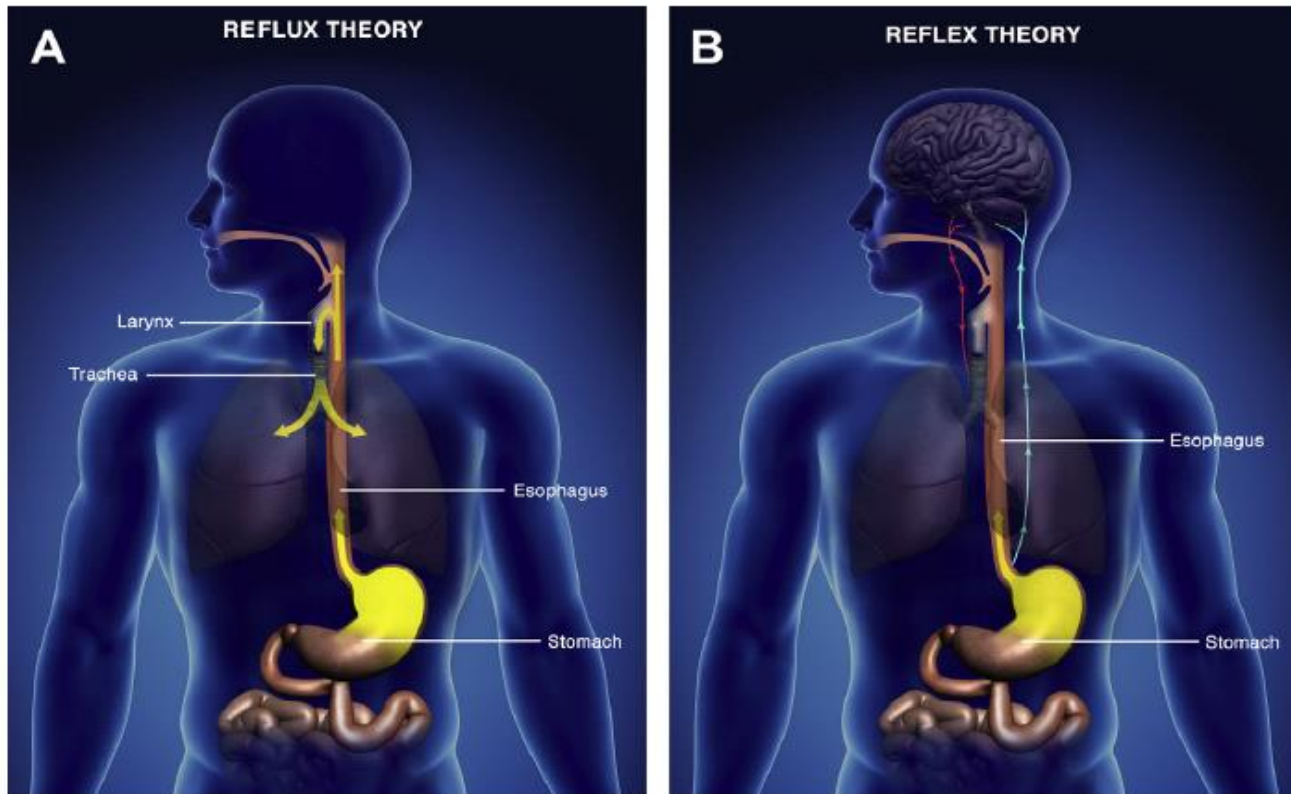
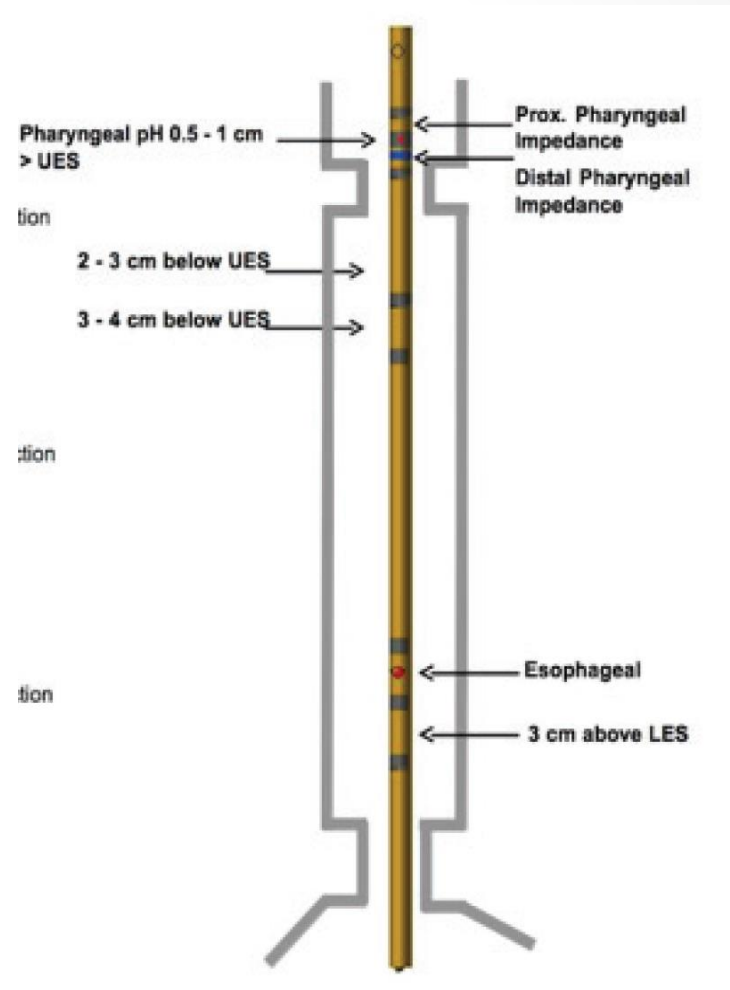


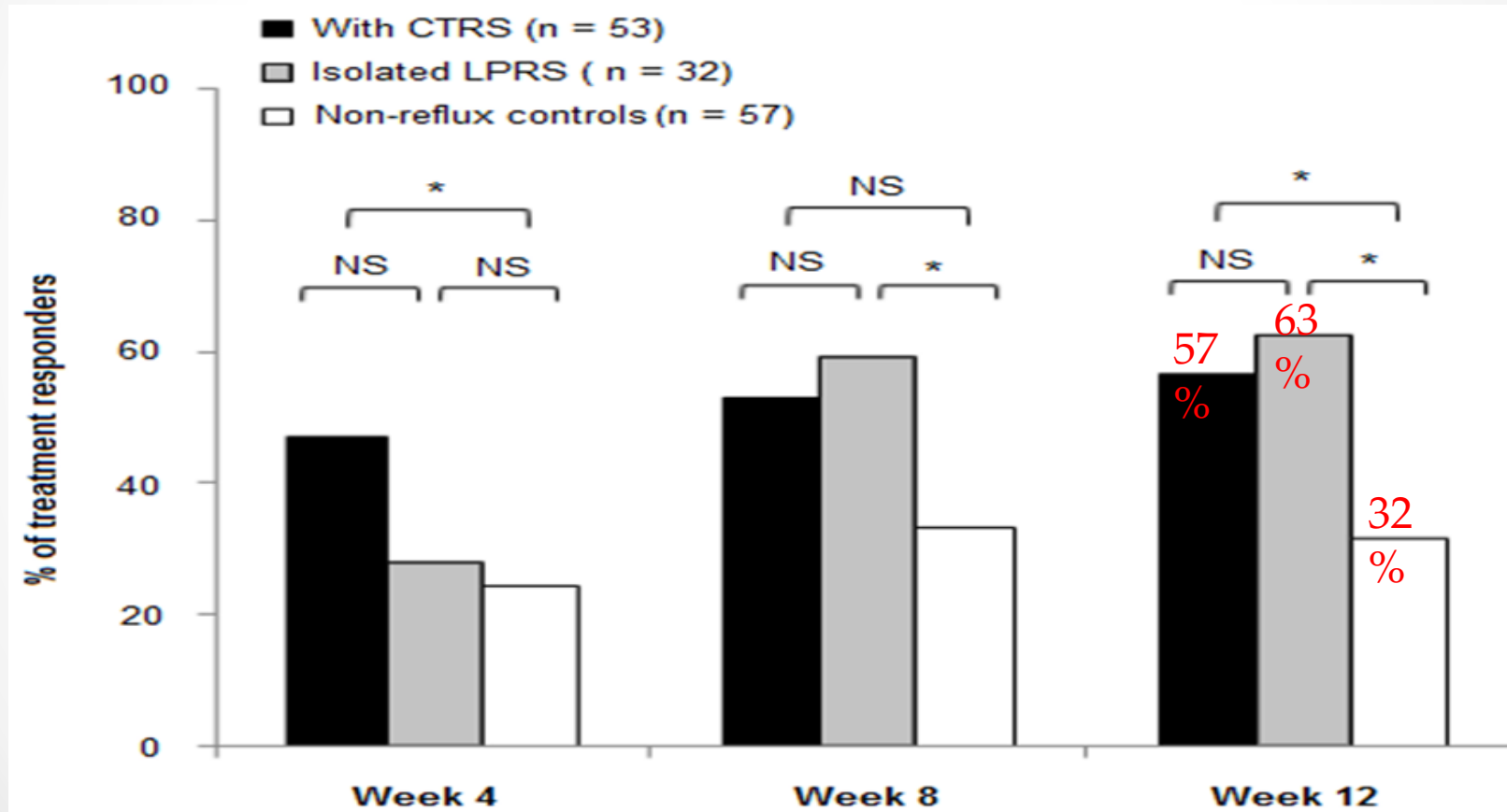
Fig. 6. The two mechanisms, reflux (A) and reflex (B) theories, underlying the pathophysiology of the extraesophageal manifestations of GERD including LPR.

利用下咽多通道食道內阻抗酸鹼偵測計， 可同時偵測咽喉與食道胃酸暴露

- 我們提出組合 pH(composite pH)參數:
 - 1)24小時內咽喉酸逆流次數 ≥ 2 ;
 - 2)遠端食道胃酸暴露過多

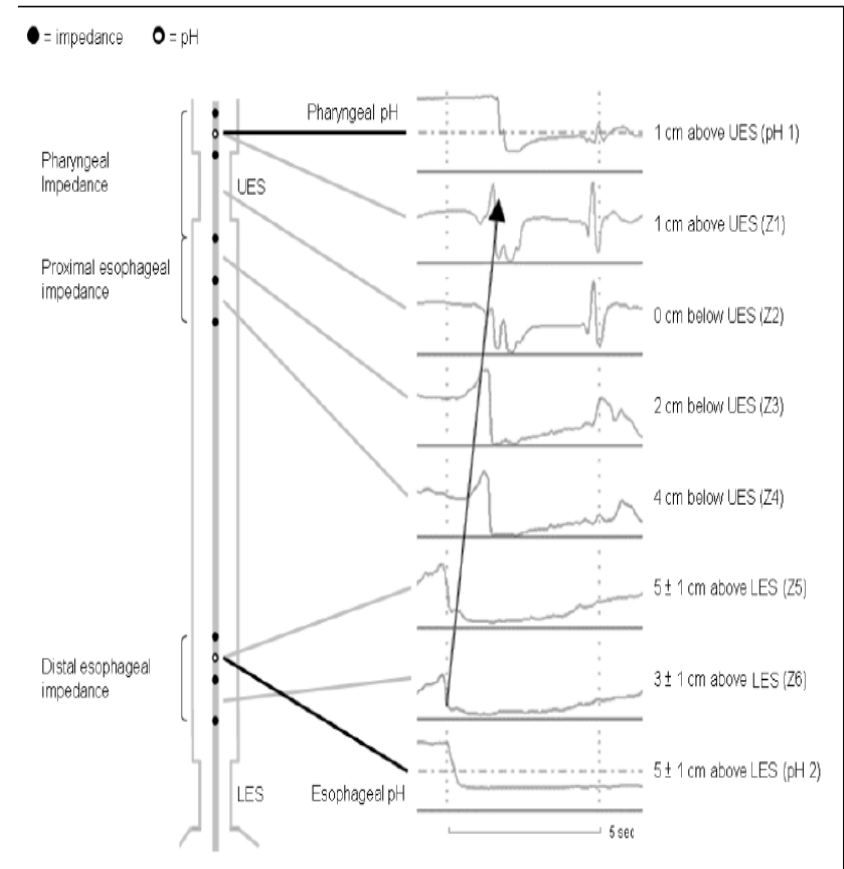
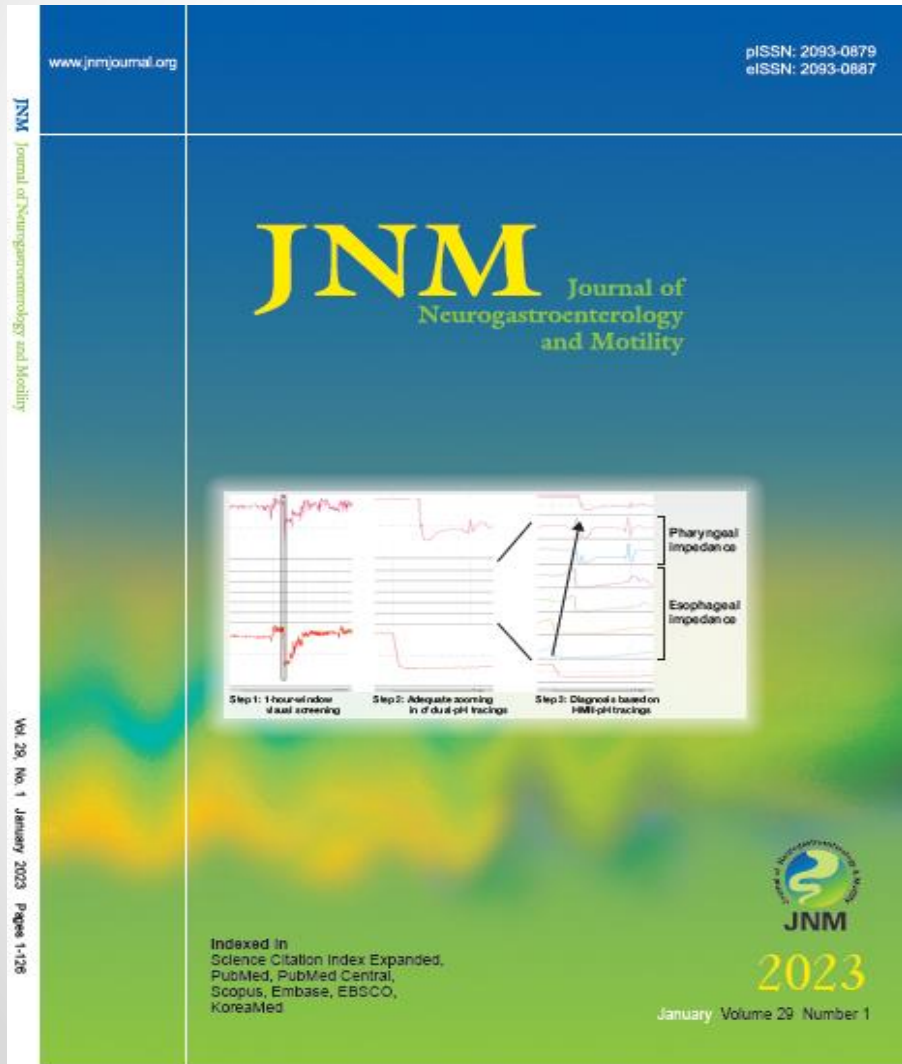


服用12週 PPI質子幫浦抑制劑後,合併典型
症狀者(57%)與單獨咽喉症狀者(63%)療
效均較組合pH檢查陰性者(32%)明顯改善



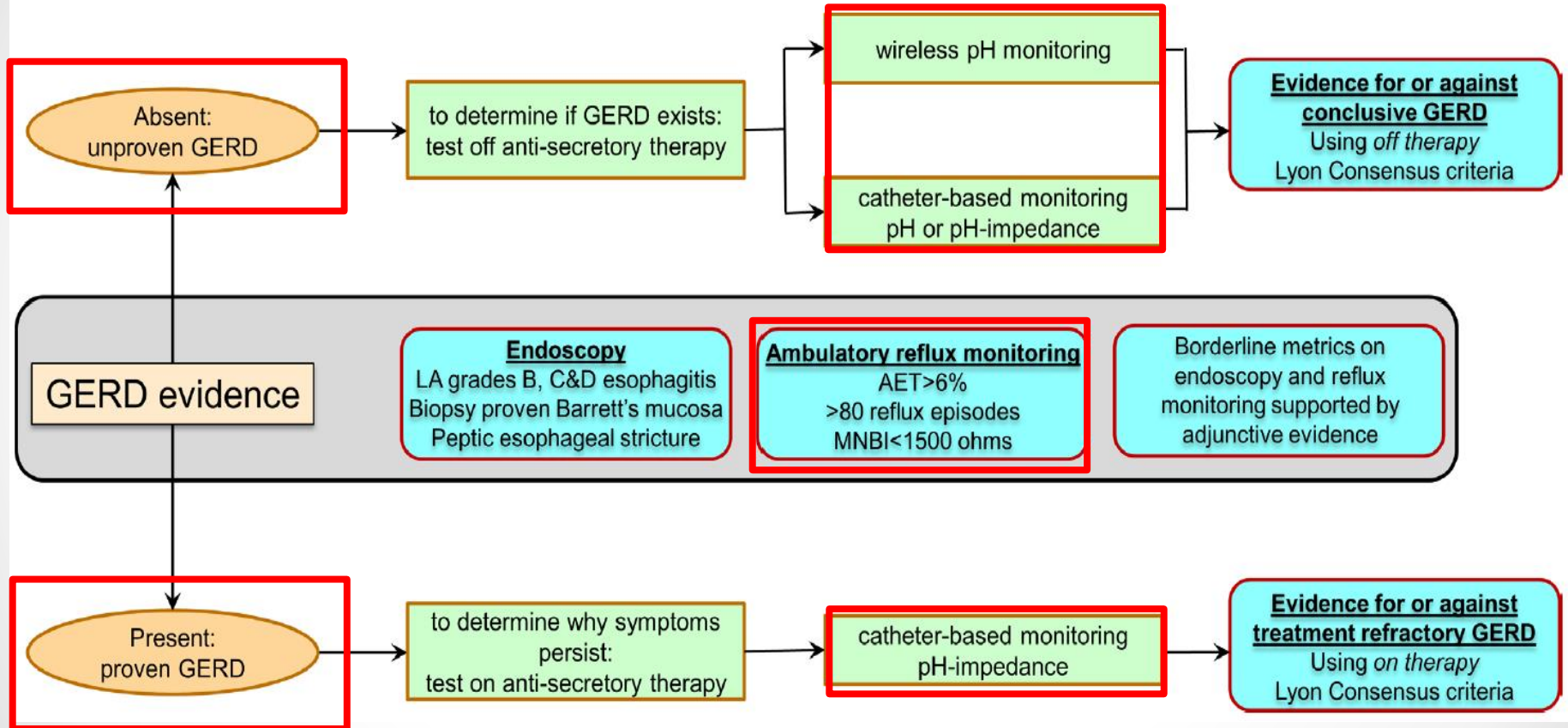
Lien HC, 2020 Clin Gastroenterol Hepatol.

三步驟驗證咽喉逆流診斷標準,登在 亞洲蠕動學會官方雜誌JNM封面



Chen YY, Lien HC 2023 JNM

最新第二版國際里昂共識提出,內視鏡與逆流檢測 關於,確診與未確診逆流的檢驗方式與診斷標準



國際里昂共識將檢測後病人分為, 確診有逆流, 確診無逆流, 與不確定有無逆流等三類

	UNPROVEN GERD ENDOSCOPY, WIRELESS pH STUDY, 24 HOUR pH OR pH IMPEDANCE, HRM <i>off therapy</i>			PROVEN GERD ENDOSCOPY, 24 HOUR pH IMPEDANCE <i>on therapy</i>
	ENDOSCOPY	pH or pH-IMPEDANCE	HRM	ENDOSCOPY pH-IMPEDANCE
CONCLUSIVE EVIDENCE FOR PATHOLOGIC REFLUX	LA grades B, C&D esophagitis Biopsy proven Barrett's mucosa Peptic esophageal stricture	AET>6% on 24 hour studies AET>6% on ≥2 days on wireless studies		LA grades B, C&D esophagitis Peptic esophageal stricture AET>4%, reflux episodes>80
BORDERLINE OR INCONCLUSIVE EVIDENCE	LA grade A esophagitis	AET 4-6% on 24 hour studies AET 4-6% on ≥2 days on wireless studies Total reflux episodes 40-80/day		LA grade A esophagitis AET 1-4% Total reflux episodes 40-80/day MNBI 1500-2500 Ω
ADJUNCTIVE OR SUPPORTIVE EVIDENCE*	Hiatus hernia Histopathologic scoring systems Electron microscopy of biopsies	Reflux-symptom association Total reflux episodes >80/day MNBI<1500 Ω	Hypotensive EGJ Hiatus hernia IEM/absent contractility	Hiatus hernia MNBI <1500 Ω Reflux symptom association
EVIDENCE AGAINST PATHOLOGIC REFLUX		AET<4% each day of study** Total reflux episodes<40/day MNBI>2500 Ω		AET<1% Total reflux episodes <40/day MNBI>2500 Ω

小結

- 診治困難型胃食道逆流病人,需先考慮病人服藥時間、劑量、順從性、與飲食習慣等生活方式，並排除其他可能的非逆流病因，特別是有警訊時。
- 評估病人主要症狀後，安排內視鏡與逆流測試，有助於病人後續治療。
- 逆流生理測試為有效的檢驗工具。

治療

案例分享與個人化治療

案例分享一：48歲 蔡先生

- C.C.: Lump throat sensation, cough and chest tightness for 3 years, AR:+, UE: LA Gr A EE in Dr. Wu's clinic, but refractory to PPI therapy.
- PHx: a mechanic, ex-SMK, ex-ALC for 4 years, BMI: 24.2
- P.I.: He underwent imp-pH off PPI, reporting borderline AET, SI(-)/SAP(-)

報告日期：2021/01/11

頁次：1 / 3

多管腔食道內阻抗及酸鹼度測定(打報告用)

According to the findings including 1) DeMeester Score is 16 (<14.7), 2) acid exposure time 4 % (upright: 6.1 %) (< 4.2%), 3) SI/SAP: insignificant and 4) reflux number : 38 (acid reflux: 29, weak acid: 9), the impression is suspected pathologic GERD based on the Lyon Consensus 2018. besides, the proximal reflux up to 20 with 15 acid reflux, the LPR is also impressed. Please correlate with clinical presentation.

蔡先生停止使用質子幫浦抑制劑一周後,接受多通道食道內阻抗酸鹼偵測計



胃酸暴露時間雖然小於4%,但逆流次數超過80次

REFLUX MONITORING SUMMARY

[pH]Acid Exposure Summary	Total	Normal
Ch 1 Prox.		
Acid exposure time (%)	0.0	
Longest reflux (min)	N/A	
Ch 2 Dist.		
Acid exposure time (%)	2.7	<4.2
Longest reflux (min)	7.6	<9.2
DeMeester Score	12.3	<14.7

REFLUX ANALYSIS BASED ON Z MEASUREMENT AND CLASSIFIED BASED ON pH

[Z]Reflux Episode Activity	Total	Upright	Supine	Post-prandial
Acid reflux	52	51	1	26
Weakly acidic reflux	38	37	1	6
Non-acid reflux	3	3	0	2
All reflux	93	91	2	34

症狀與酸或弱酸逆流相關度極高

[Z]Symptom Association Summary	Regurg.
Number of occurrences	9
Acid reflux	6
Weakly acidic reflux	3
Non-acid reflux	0
All reflux	9
Symptom Index (SI)	100.0
Symptom Association Probability (SAP)	100.0

[Z]Reflux Symptom Index	Regurg.
Acid reflux	66.7
Weakly acidic reflux	33.3
Non-acid reflux	0.0
All reflux	100.0

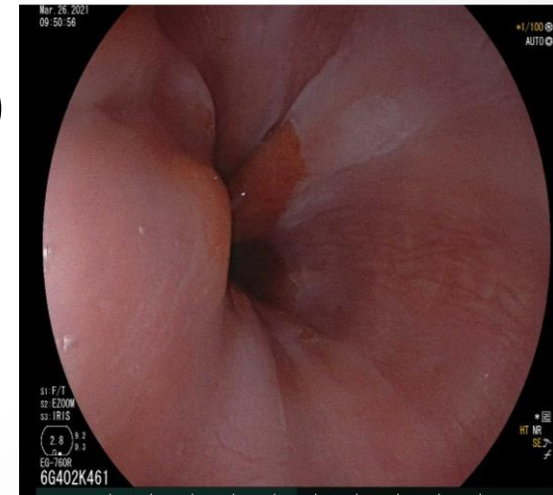
[Z]Reflux Symptom Association Probability*	Regurg.
Acid reflux	100.0
Weakly acidic reflux	99.1
Non-acid reflux	0.0
All reflux	100.0

診斷為食道過度敏感

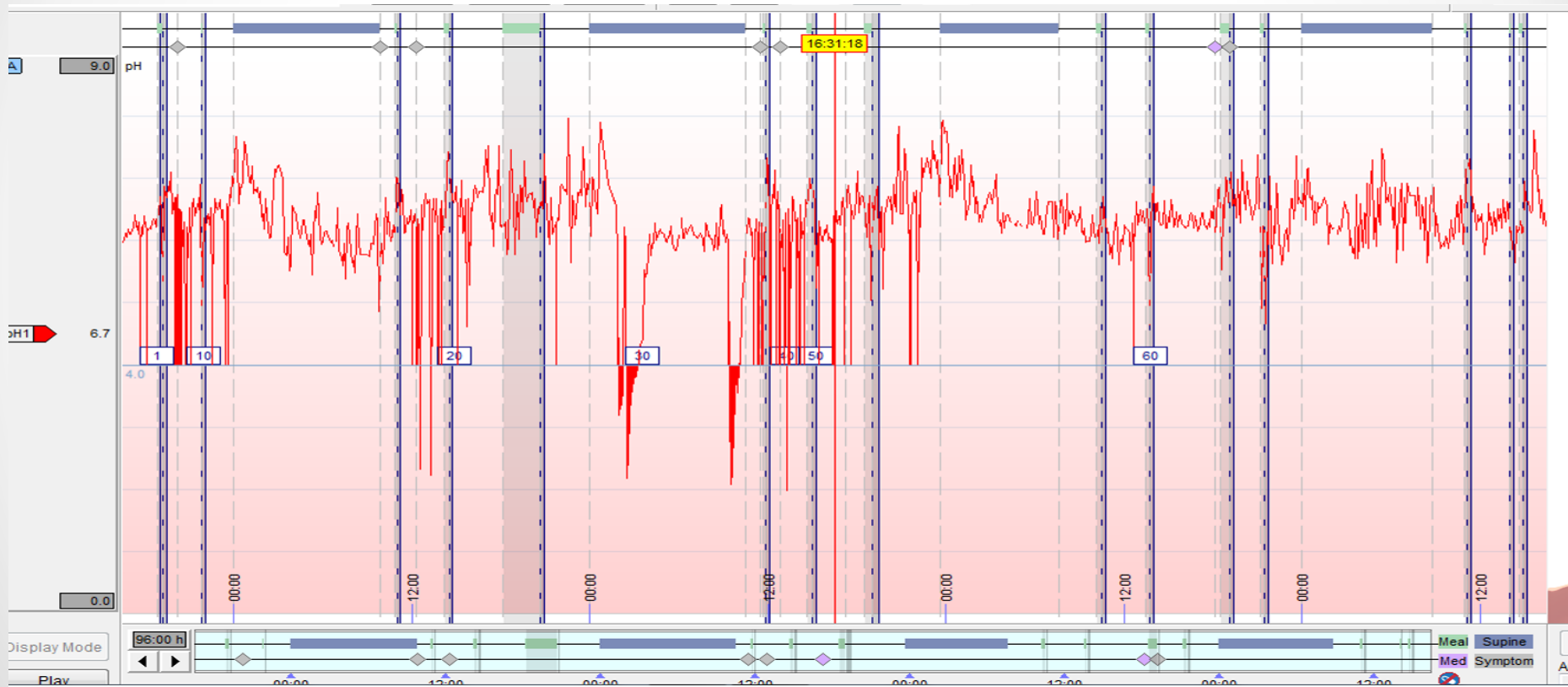
- 1. There is a **day to day variation** for AET based on catheter-based recording.
- 2. There is also a **day to day variation** for symptom-reflux association.
 - Tseng D, 2005 J Gastrointest Surg

案例分享二:莊先生 51 歲男性

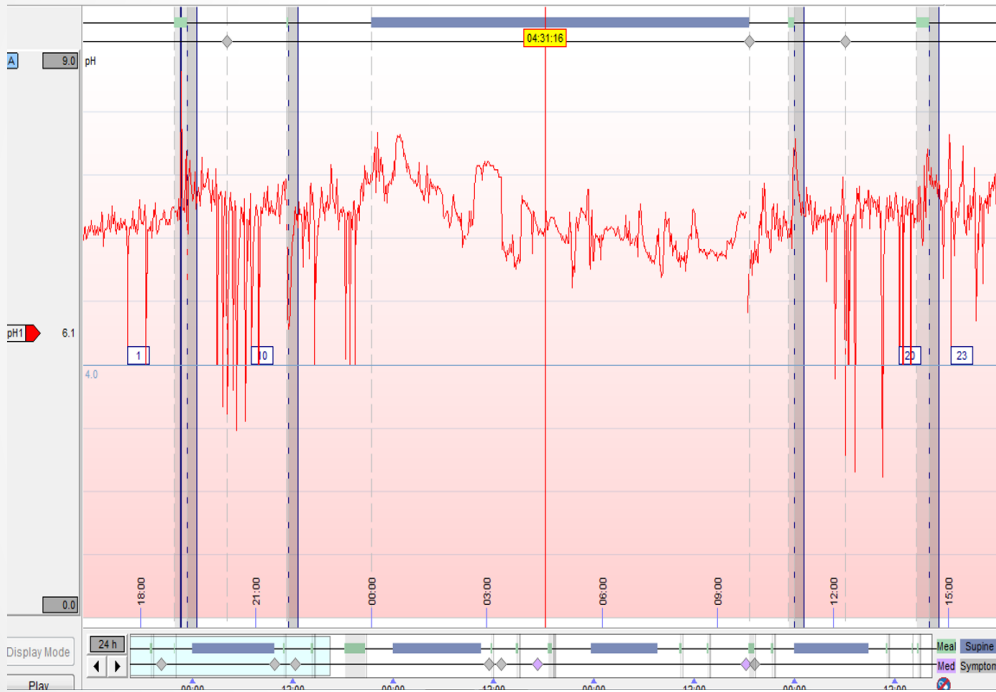
- C.C: AR, acid in mouth & lump throat for 1 year, refractory to Nexium therapy, ref from Dr. Liao's clinic ; recent UE: minimal change
- PHx. HBV carrier, SMK:+, ALC: social drinker ;
- Insomnia with hypnotics use
- HT: 160 cm, BW: 69 kg (BMI: 26.9)



莊先生停藥後,接受96h無線電食道 酸鹼值監控檢測



第一天胃酸暴露正常,但症狀與逆流相關

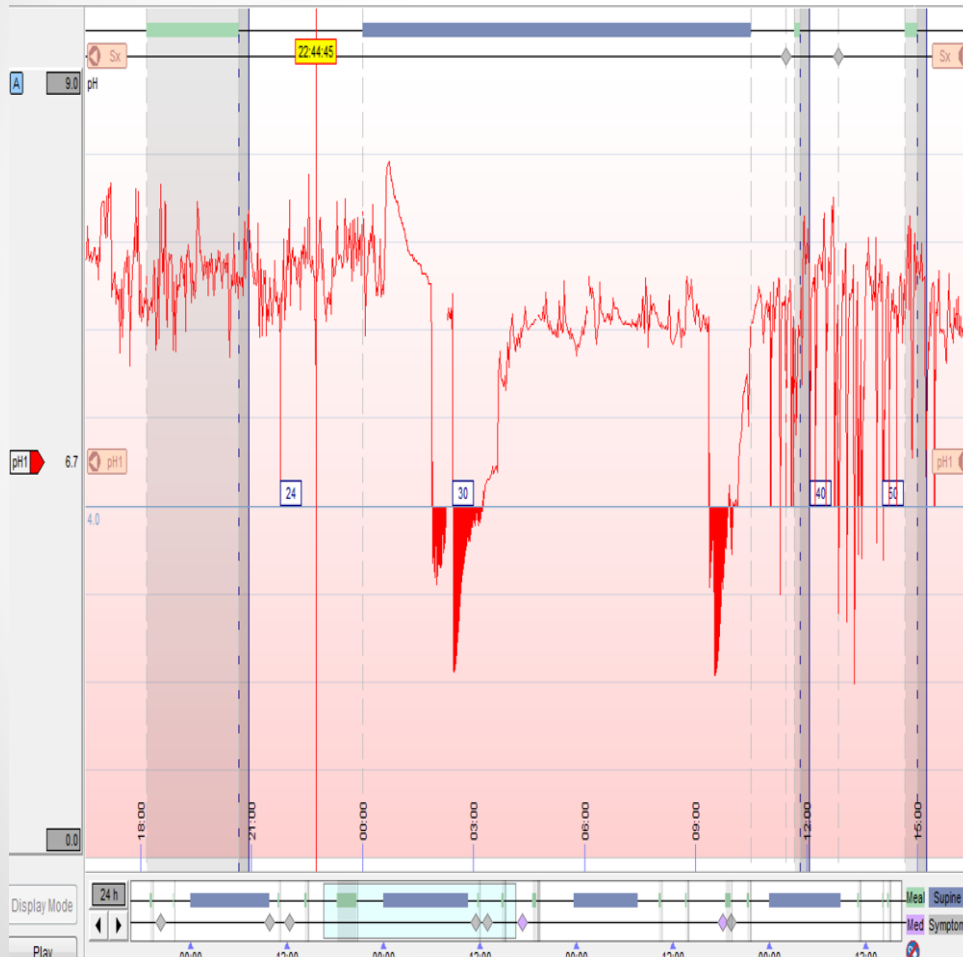


Acid Reflux Analysis	Total	Upright	Supine
Acid exposure time (HH:MM)	00:13	00:13	00:00
Acid exposure time (%)	1.0	1.8	0.0
Number of refluxes	23	23	0
Number of long refluxes	0	0	0
Longest reflux (min)	2.4	2.4	N/A

DeMeester Score	Score	Normal*
Ch 1	4.0	<14.7

Symptom Analysis	Acid sensation
Number of occurrences	3
Symptoms related to reflux	2
Symptoms not related to reflux	1
Reflux periods	23
Symptom Index (SI)	66.7
Symptom Association Prob. (SAP)*	99.2

第二天胃酸暴露異常， 且症狀與逆流相關



Acid Reflux Analysis	Total	Upright	Supine	Post-prandial
Acid exposure time (HH:MM)	02:05	00:16	01:49	00:11
Acid exposure time (%)	10.4	2.7	17.6	3.8
Number of refluxes	32	22	10	13
Number of long refluxes	4	0	4	0
Longest reflux (min)	48.7	2.4	48.7	2.4

DeMeester Score	Score	Normal*
Ch 1	39.9	<14.7
95th percentile		

Symptom Analysis	Acid sensation
Number of occurrences	2
Symptoms related to reflux	2
Symptoms not related to reflux	0
Reflux periods	32
Symptom Index (SI)	100.0
Symptom Association Prob. (SAP)*	97.0

診斷由第一天的食道過度敏感， 改為第二天的確診胃食道逆流

- 48-hour wireless pH study increases the proportion of patients with a pathological AET by 12.4% and, doubling the symptoms reported, leading to a change in symptom association in 20% of patients.
 - Prakash 2005 Clin Gastroenterol Hepatol
- One-third of patients classified as functional heartburn at 24-hour pH-monitoring can be re-classified as true NERD after a more prolonged pH recording period.
 - Penagini R, 2015 JNM

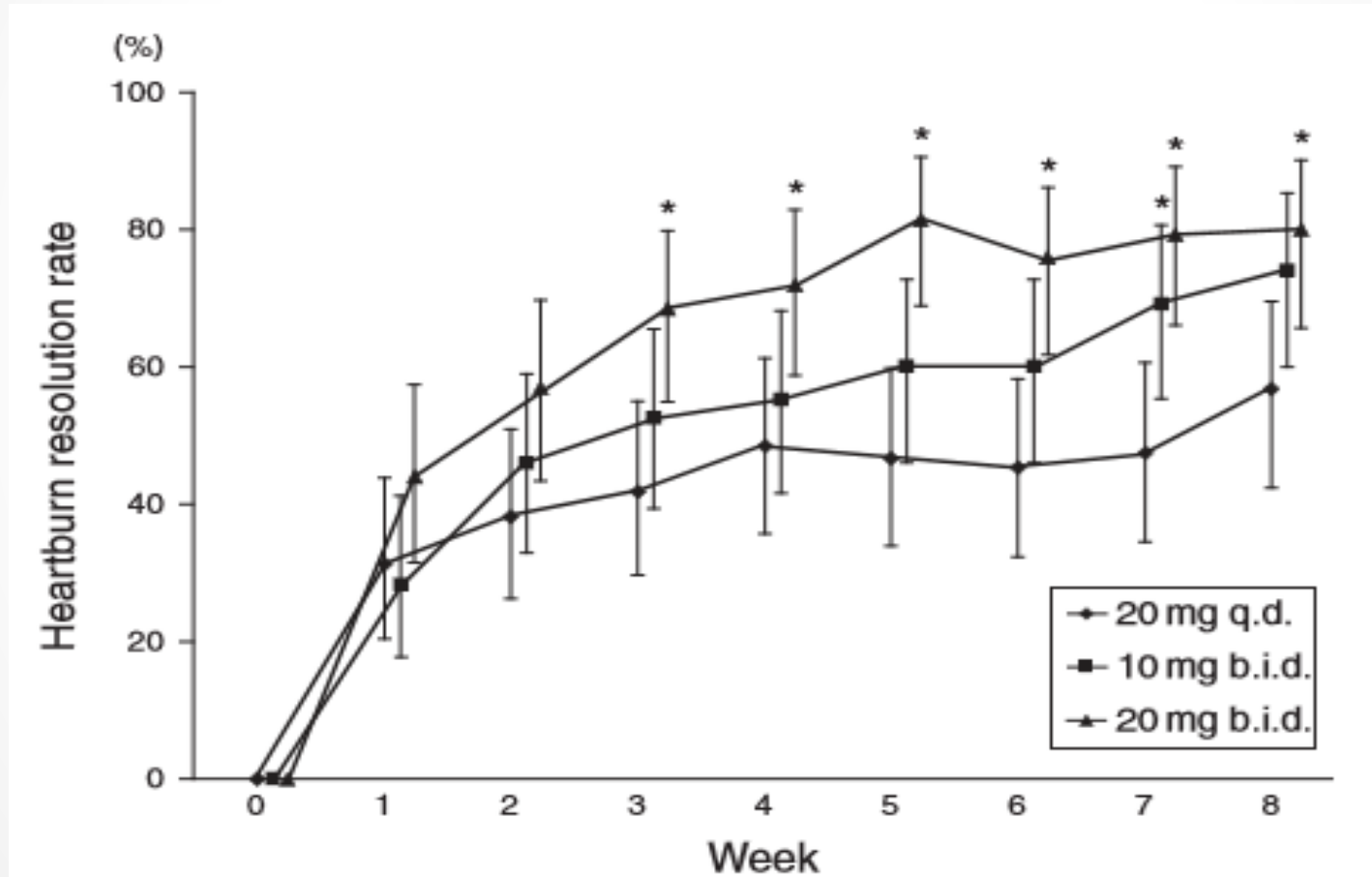
逆流檢查後的診斷

- 1. Off PPI (24h pH, impedance-pH, or 96 h wireless pH)
 - GERD
 - Reflux Hypersensitivity (RH)
 - Functional Heartburn (FH) or alternative Dx
- 2. On bid PPI: (impedance-pH only)
 - Truly refractory GERD
 - Overlap between GERD and RH
 - Overlap between GERD and FH

治療困難型胃食道逆的選擇

- Check compliance, dosing times, and duration with PPI; Lifestyle modification
- Double or split the PPI dose,
- Add on H2RA, alginate
- Add on prokinetics?
- Add on TLESR reducers (Baclofen)
- Visceral pain modulators (e.g. TCA, SSRI)
- Anti-reflux surgery, endoscopic anti-reflux therapy

隨機臨床試驗顯示分次劑量與加倍(早晚各一次) 比較單一劑量治療效果好 (n = 304)



Kinoshita Y 2012 Am J Gastroenterol

必要時晚上增加一顆 H2RA 對夜間 症狀有幫助,但長期使用會無效

- **Acute H2R blockade** improved control of nocturnal gastric pH and improvement of GERD symptoms.

Mainie 2008 J Clin Gastroenterol; Peghini, 1998 Gastroenterology

- **No difference** in gastric acid control between long term treatment (**28 days**) with PPI twice daily vs PPI twice daily plus H2RA.

Fackler 2002 Gastroenterol.

小型隨機臨床試驗顯示: 增加alginate 30ml qid 使用四週,比單獨使用PPI效果好 (n = 76)

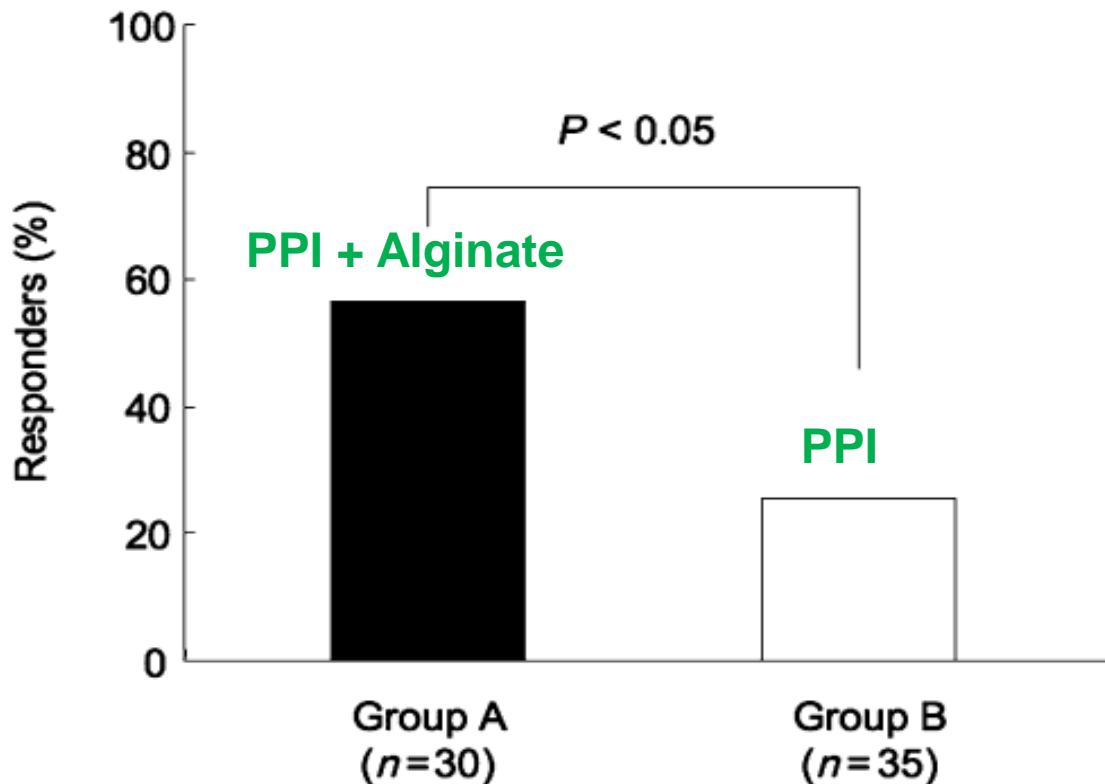


Fig. 2 Rate of complete resolution of heartburn for 7 consecutive days up to the last day of medication. There were significantly more responders in group A than in group B.

綜合分析顯示: 增加促進蠕動藥物對逆流症狀沒有幫助, 卻可能增加副作用, 不建議常規使用

- Twelve RCTs .
- Combined therapy was **not** associated with significant **relief of symptoms** or endoscopic response relative to single therapy.
- Although there was a reduction in the number of reflux episodes in GERD, there was **no** significant **effect on acid exposure time**.
- The proportion of patients with **adverse effects** undergoing combined therapy was **higher** than for PPI therapy.

綜合分析顯示: 增加Baclofen對症狀有幫助,但副作用也增加

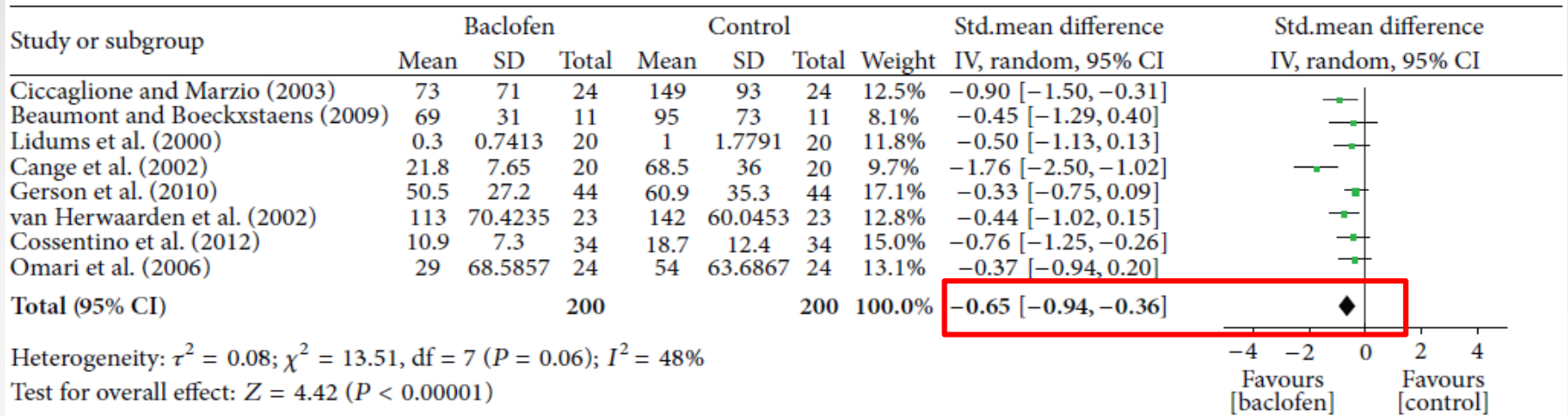


FIGURE 2: Meta-analysis of the incidence of GER in the PP population given either baclofen or placebo for the treatment of GERD.

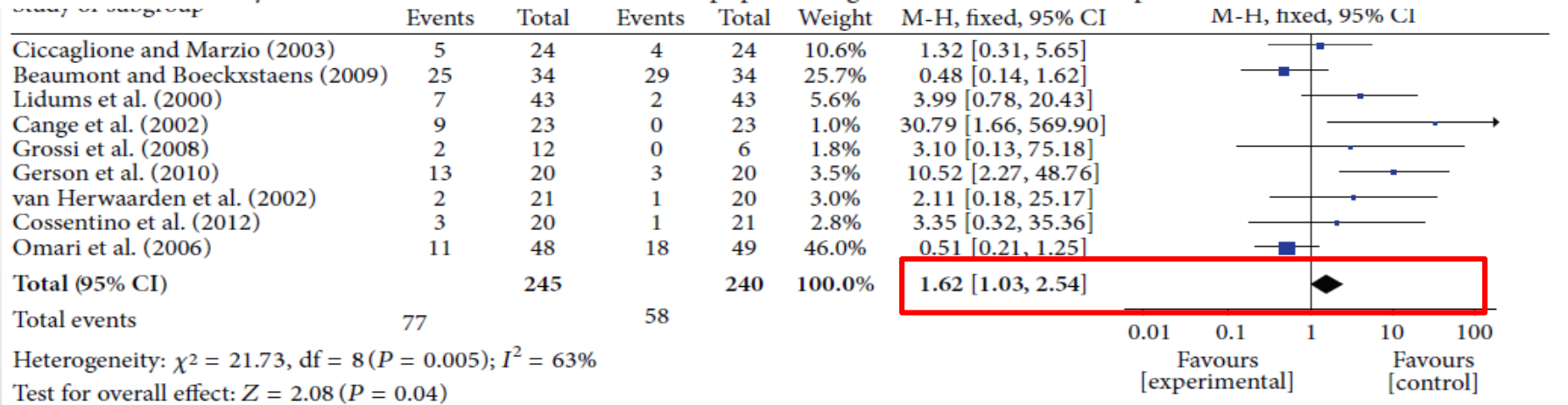


FIGURE 5: Meta-analysis of the overall adverse events in the PP population given either baclofen or placebo for the treatment of GERD.

綜合分析顯示:低劑量抗憂鬱症藥物對功能性胸痛有幫助

Table 2. Characteristics of RCTs Examining the Effect of Antidepressants on Functional Chest Pain

Study, year	Design	Jadad score	Total, N	Patients, n	Controls, n	Female, %	Mean age, y	Drug class	Drug	Dose	Duration, wk	Symptom evaluation	Symptom reduction	
													Drug	Placebo
Cannon et al, ¹⁸ 1994	Parallel	3	40	20	20	73	49.5	TCA	Imipramine	25–50 mg	3	Diary	52% ^a	1%
Cox et al, ²³ 1998	Cross-over	3	18	18	18	100	53	TCA	Imipramine	50 mg	5	Diary	11 episodes ^a	21 episodes
Varia et al, ¹⁹ 2000	Parallel	4	30	15	15	Unreported	Unreported	SSRI	Sertraline	50–200 mg	8	VAS	62.6% ^a	15.4%
Spinhoven et al, ²¹ 2010	Parallel	3	46	23	23	48	57.4	SSRI	Paroxetine	10–40 mg	16	VAS	18.6%	18.6%
Keefe et al, ²⁴ 2011	Parallel	5	58	30	28	67	Unreported	SSRI	Sertraline	50–200 mg	10	Diary	67.2% ^a	44.2%
Lee et al, ²² 2010	Cross-over	5	50	50	50	14	23.5	SNRI	Venlafaxine	75 mg	4	Diary	52% had >50% reduction ^a	4% had >50% reduction
Clouse et al, ¹⁷ 1987	Parallel	4	19	11	8	76	48	SARI	Trazodone	100 mg	3	Likert scale	Exact data not extractable	Exact data not extractable
Doraiswamy et al, ²⁰ 2006	Parallel	3	50	27	23	42	53.3	SSRI	Paroxetine	5–50 mg	8	VAS	Exact data not extractable	Exact data not extractable

SARI, serotonin antagonist and reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; VAS, visual analogue scale.

^aP < .05 vs placebo.

綜合分析顯示:低劑量抗憂鬱症藥物對逆流 症狀效果不一致

Table 3. Characteristics of RCTs Examining the Effect of Antidepressant GERD Symptoms

Study, year	Jadad score	Design	Subjects	Total, Patients, Controls,				Mean age, y	Drug class	Drug	Dose, mg	Duration	Symptom evaluation	Symptom reduction	
				N	n	n	Female, %							Drug	Placebo
Viazis et al, ²⁶ 2012	5	Parallel	Hypersensitive esophagus	75	39	36	Unreported	Unreported	SSRI Citalopram	20	26 wk	Physician visit	61.5% symptom-free ^a	33.3% symptom-free	
Ostovaneh et al, ²⁹ 2014	5	Parallel	PPI-refractory GERD	96	48	48	58	37.1	SSRI Fluoxetine	20	6 wk	Diary	37% heartburn-free days ^a	7% heartburn-free days	
Forcelini et al, ²⁸ 2014	5	Cross-over	NERD	20	20	20	75	36.1	TCA Nortriptyline	10-25 ^b	3 wk	Heartburn questionnaire	2.5 points	2.5 points	
Hershcovici et al ²⁷ (abstract only), 2011	3	Parallel	PPI-refractory GERD	140	NA	NA	29	55.6	TCA Nortriptyline	50	6 wk	Diary	23.1% symptom-free	27.1% symptom-free	

No studies included patients with functional heartburn

藥物治療失敗者接受抗逆流手術的失敗率約高出四倍 (n=115)

Resp to PPI vs. Non-resp HR:3.85 (2.05–7.22)

Primary typical vs. EER HR:2.34 (1.31–4.17)

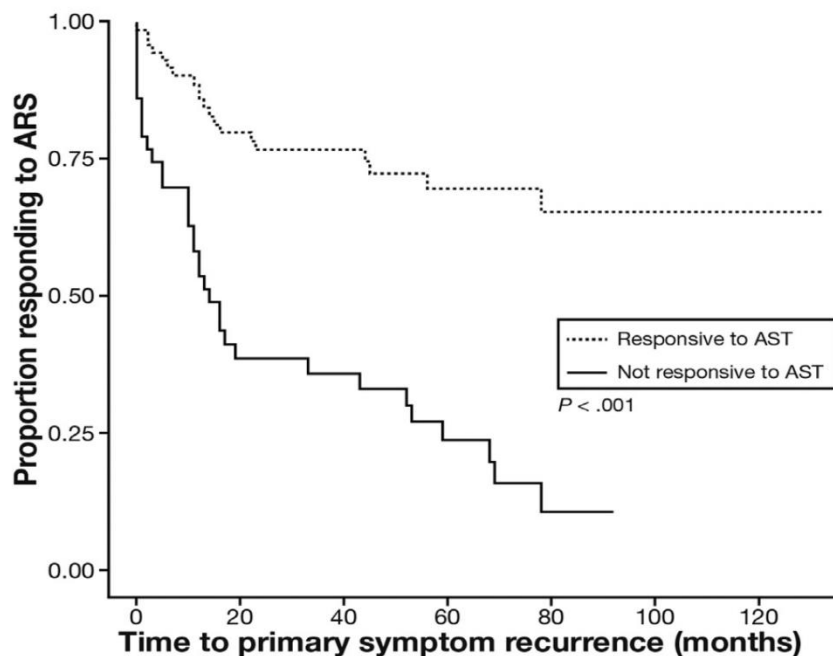


Figure 3. Time to primary symptom recurrence by preoperative response to AST.

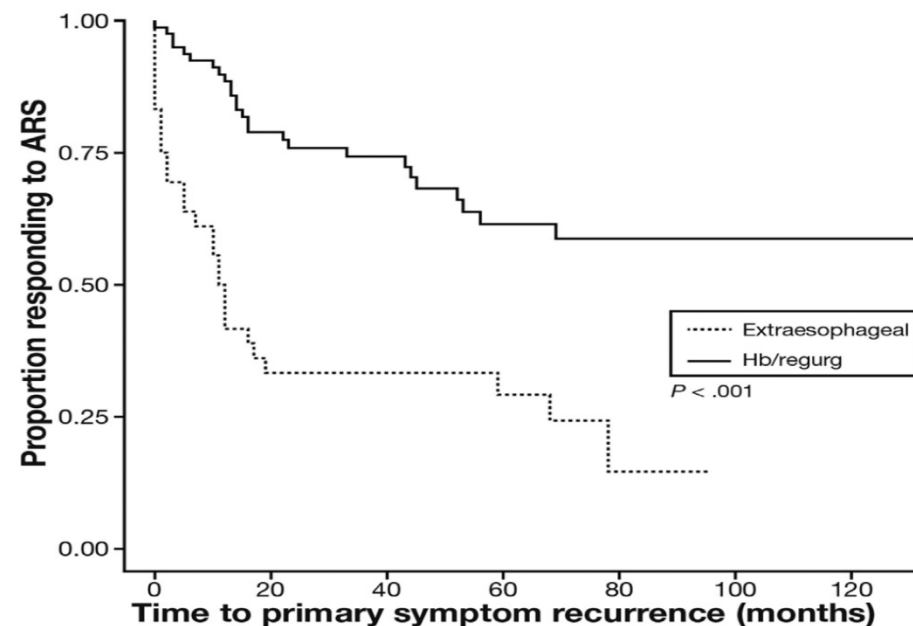


Figure 2. Time to primary symptom recurrence after fundoplication by primary presenting symptom. Hb/regurg, heartburn/regurgitation.

結論

- 困難型胃食道逆是一群異質性高的病人,仔細評估病人困擾症狀,藥物順從性,生活型態,對治療很有幫助。
- 多數困難型胃食道逆症狀病人是由非逆流因素引起。
- 逆流測試有助於釐清症狀與逆流間的關係,並引導後續包括外科手術在內的治療決策。

臺中榮總2023年1月成立功能性食道疾病中心， 服務中部地區病人



**謝謝聆聽，敬請指教!!
祝大家新年快樂 平安健康**