



# Research and Clinical Practice of Integrative Medicine in Digestive Diseases

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# Questions

- Is there a scientific basis for TCM?
- How do we INTEGRATE TCM with conventional healthcare?

# Systematic review and meta-analysis

## Is it a viable solution?

AP&T Alimentary Pharmacology and Therapeutics

### Systematic review: the efficacy of herbal therapy in inflammatory bowel disease

S. C. Ng, Y. T. Lam, K. K. F. Tsoi, F. K. L. Chan, J. J. Y. Sung & J. C. Y. Wu

#### Common conclusions

- Flawed methodology
- Heterogeneity
- Publication bias
- Need of randomized controlled trials

# Challenges in searching for the BEST of TCM

- Lack of high quality evidence
- Non-English literature
- Individualized treatment (for both patients and physicians)
- Heterogeneity in herb combinations

# A Different Paradigm!

## Modern Medicine

Disease entities

Anatomical injury &  
Pathophysiology

3 main perspectives

- Genetic makeup of host
- Environmental factors including diet
- Infective agents

## Chinese Medicine

Holistic approach

Disease is caused by disharmony

5 main theories

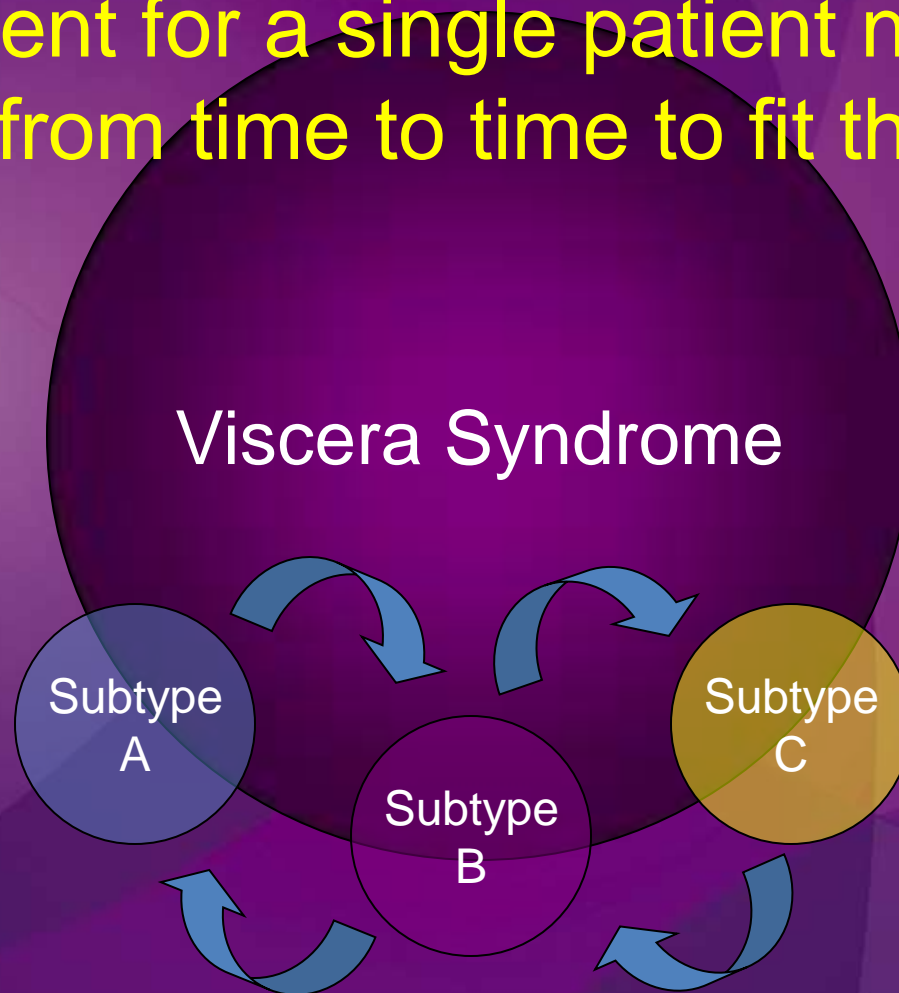
- Ying and Yang
- 5 paths of energy
- “Viscera” and syndromes
- Qi & fundamental sub.
- Meridians

# “Using a Western ruler to measure Eastern distances”

<b>Unique aspect of TCM</b>	<b>Challenge to evaluation by conventional EBM</b>
TCM diagnosis based on practitioner’s subjective assessment of patient’s state of disharmony, unlike technologically driven WM dx	RCT eligibility requires consistent diagnosis, traditionally based on WM diagnostic criteria
Individualized treatment based on TCM syndrome; treatment may vary by patient or by visit	Traditional RCTs involve treatment standardized to WM diagnosis
TCM involves complex array of treatments including (e.g. acupuncture, herbs, Tai Chi, etc...)	Traditional RCTs evaluate an isolated component (e.g. single drug), controlling for all non-specific effects

# Individualized Treatment

Treatment for a single patient needs to be adjusted from time to time to fit the “syndrome”



# Irritable Bowel Syndrome

**Abdominal Pain**

**relieved by defecation**

**altered frequency**

**altered consistency**





# Rome II criteria (1999)

≥12 weeks of continuous or recurrent symptoms  
(in the preceding 12 months)

Abdominal pain/discomfort  
that has 2 of 3 features:

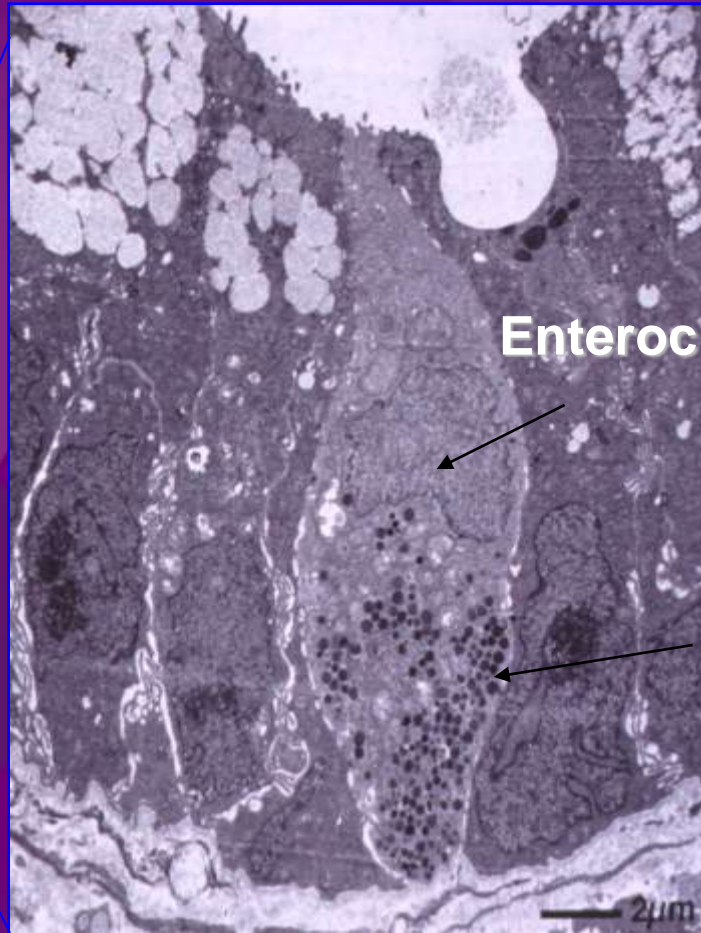
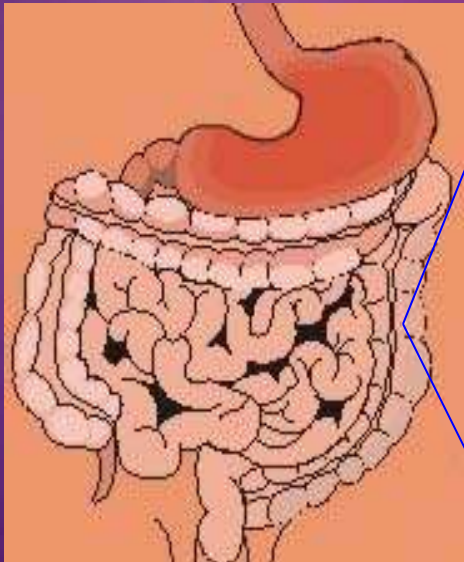
- relieved with defecation  
and/or
- associated with change  
in stool frequency  
and/or
- associated with change  
in form (appearance) of  
stool

+

Supportive symptoms:

- altered stool frequency
- altered stool form
  - lumpy/hard
  - loose/watery
- altered stool passage
  - urgency
  - incomplete evacuation
  - straining
- passage of mucus
- bloating or abdominal distension

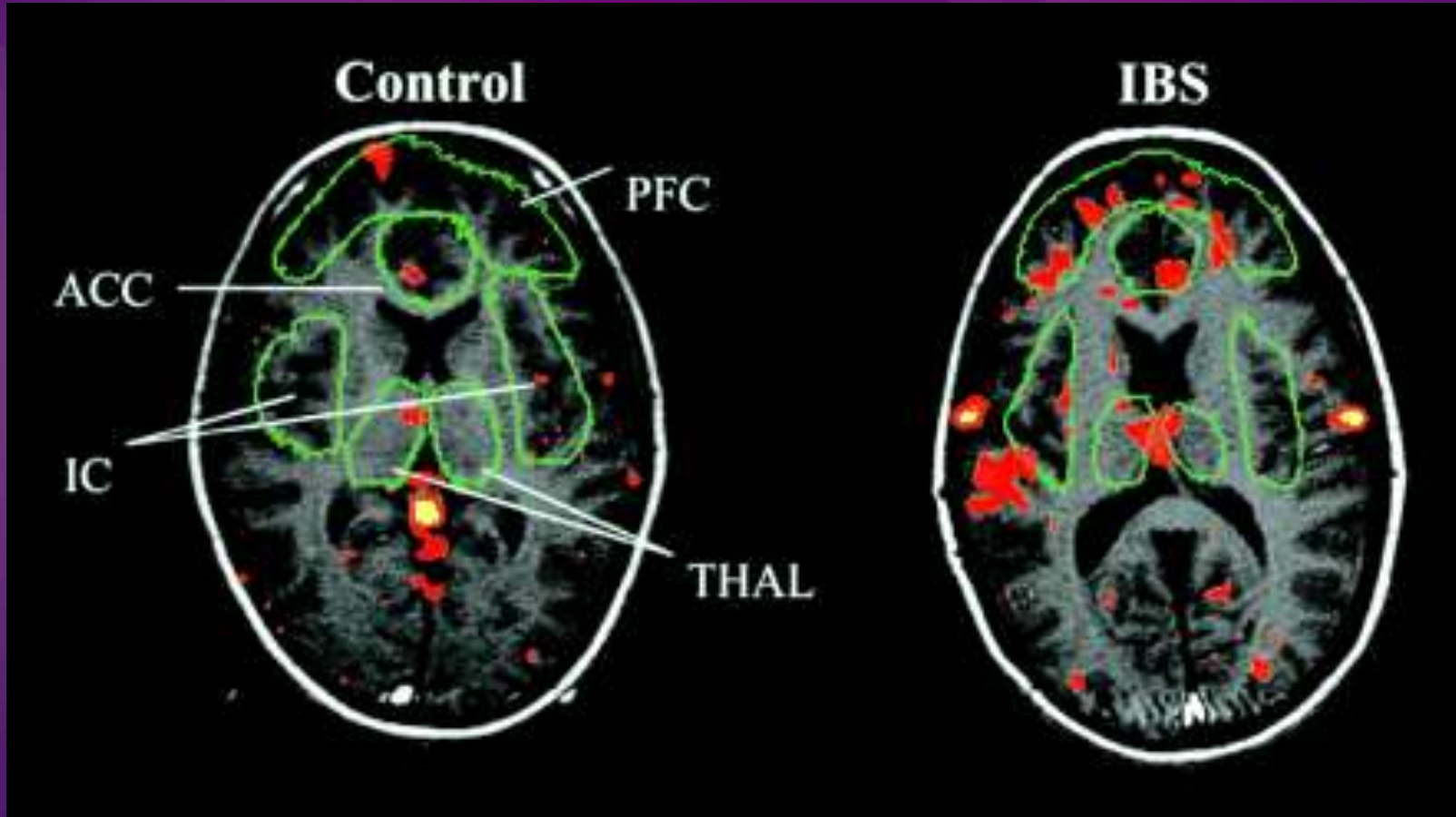
# Serotonin (5-hydroxytryptamine): Potential Therapeutic Target for IBS?



Enterochromaffin cells

Secretory granules

# Increased activity at Anterior Cingulate, Prefrontal Cortex, Insular Cortex & Thalamus



# Do we have a common language?



Aliment Pharmacol Ther 2004; 20: 1205–1210.

doi: 10.1111/j.1365-2036.2004.02242.x

## *Agreements among traditional Chinese medicine practitioners in the diagnosis and treatment of irritable bowel syndrome*

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# What does IBS mean among TCM practitioners?

Phase I

**Blinded consultation  
40 patients with IBS**

Learning

Phase II

**Blinded consultation  
40 patients with IBS  
20 patients without IBS**

**TCM Practitioners  
1 University in China  
1 Northern China  
1 Southern China  
1 Hong Kong**

**Diagnosis**

**Principle of treatment**

**Prescription**

# Structured Questionnaire

## 辨証分型 (Diagnosis)

肝氣鬱結

脾氣虧虛

中焦濕阻

脾腎陽虛

## 治則 (Principle Of Treatment)

抑肝扶脾

健脾助肝

清熱祛濕

溫補脾腎



## 首選方劑 (Prescription)

痛瀉要方

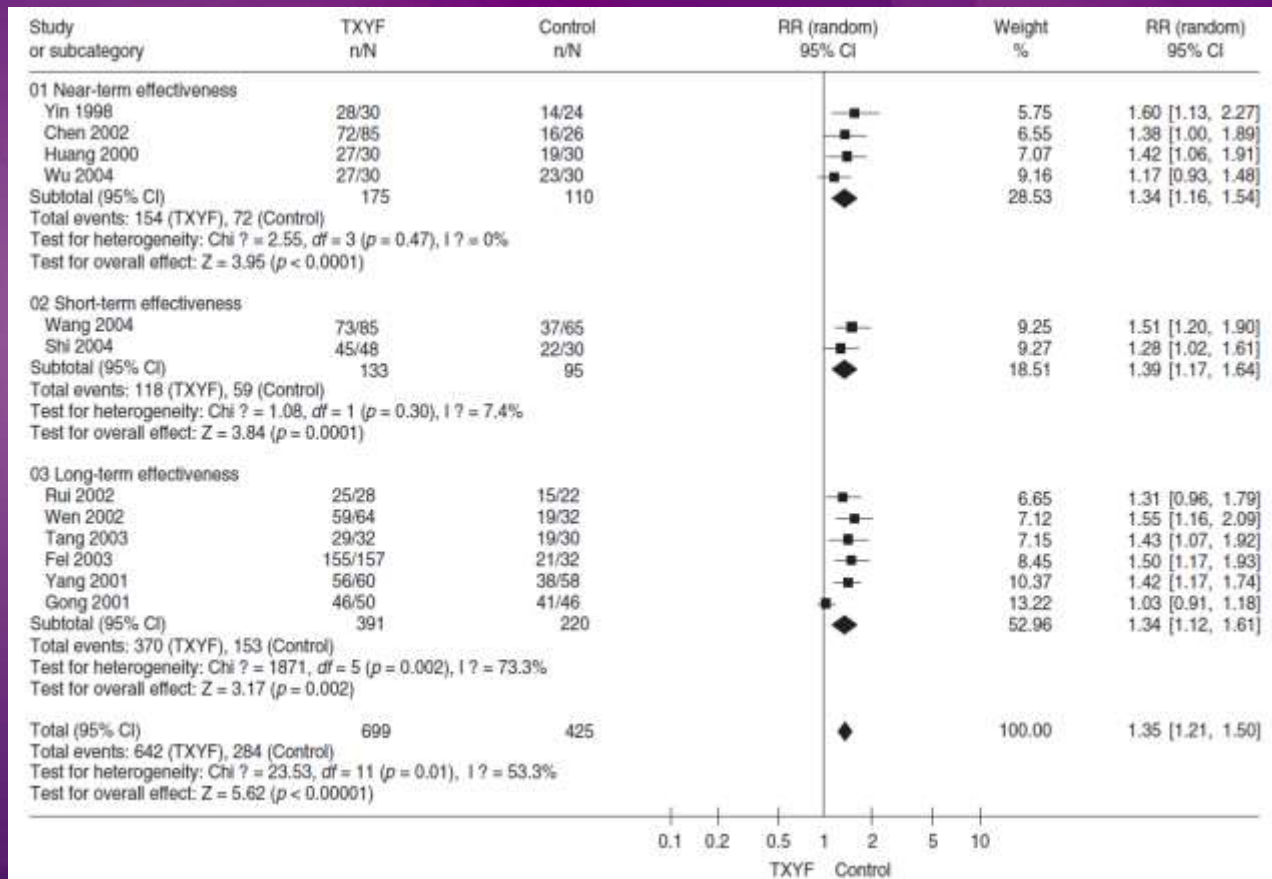
參苓白朮散

葛根芩連湯

四神丸合附子理中湯

# Tong Xie Yao Fang (痛瀉要方): a promising formula for treatment of irritable bowel syndrome

12 controlled trials (N=1125) on the effectiveness of TXYF in IBS symptom control



# Herbal medicine for digestive disorders



Tong Xie You Fang 痛瀉要方

He Zi 訶子  
Bai Zhu 白朮  
Hou Po 厚朴  
Bai Shao 白芍  
Yi Yi Ren 薏苡仁  
Yan Hu Suo 延胡索  
Huo Tan Mu 火炭母

Irritable bowel syndrome



Hemp Seed Pill 麻仁丸

Zhi Shi 枳實  
Hou Po 厚朴  
Xing Ren 杏仁  
Bai Shao 白芍  
Da Huang 大黃  
Huo Ma Ren 火麻仁

Constipation

Qi Wei Bai Zhu Powder  
七味白朮散

Fu Lin 茯苓  
Ge Gen 葛根  
Gan Cao 甘草  
Bai Zhu 白朮  
Ren Shen 人參  
Mu Xiang 木香  
Huo Xiang 藿香

Chemotherapy-related  
diarrhea



# Combo therapy of Curcumin and Mesalamine is more effective in treating patients With mild-to-moderate ulcerative colitis

50 patients with active mild-to-moderate ulcerative colitis who failed maximum treatment of mesalamine randomized to curcumin Vs placebo as combo treatment with mesalamine

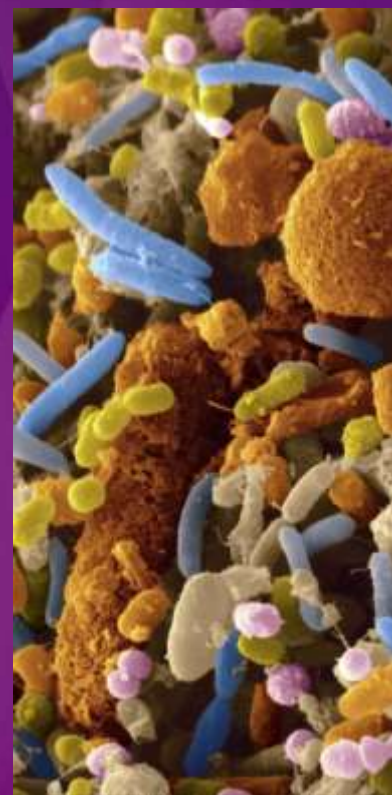


<b>Outcome at 4 weeks</b>	<b>Curcumin 3g capsule N=26</b>	<b>Placebo N=24</b>	<b>P value</b>
Clinical Remission	54%	0%	0.01
Clinical Response	65%	13%	<0.001
Endoscopic Remission	43%	0%	0.043

# Can Chinese herbal medicine be used as prebiotics?



**Tong Xie Yao Fang**  
痛瀉要方



**Gut microbiota composition and  
mucosal immune activation**

# When surgeons meet the acupuncturists.....



# Electroacupuncture Reduces Duration of Postoperative Ileus After Laparoscopic Surgery for Colorectal Cancer

SIMON S. M. NG, WING WA LEUNG, TONY W. C. MAK, SOPHIE S. F. HON, JIMMY C. M. LI, CHERRY Y. N. WONG, KELVIN K. F. TSOI, and JANET F. Y. LEE

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Zusanli (stomach meridian ST-36)



Sanyinjiao (spleen meridian SP-6)



Zhigou (triple energizer meridian TE-6)



Hegu (large intestine meridian LI-4)

- ↓ Length of hospitalization
- ↓ Procedure cost
- Cost-effectiveness analysis underway

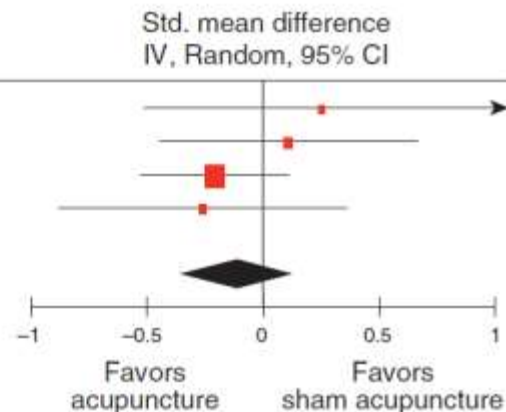
# Meta-analysis: Efficacy of Acupuncture is not more effective than sham acupuncture

## 1. Symptom severity

Study	Acupuncture Total	Sham acupuncture Total	Weight	Std. mean difference IV, Random, 95% CI
Anastasi <i>et al.</i> (34)	12	15	9.9%	0.25 (-0.51, 1.01)
Forbes <i>et al.</i> (37)	22	29	18.6%	0.11 (-0.45, 0.66)
Lembo <i>et al.</i> (38)	78	75	56.7%	-0.21 (-0.53, 0.11)
Lowe <i>et al.</i> (42)	28	22	14.9%	-0.26 (-0.88, 0.36)
Total (95% CI)	140	141	100.0%	-0.11 (-0.35, 0.13)

Heterogeneity:  $\text{Tau}^2 = 0.00$ ;  $\chi^2 = 2.05$ , d.f. = 3 ( $P = 0.56$ );  $I^2 = 0\%$

Test for overall effect:  $Z = 0.91$  ( $P = 0.36$ )

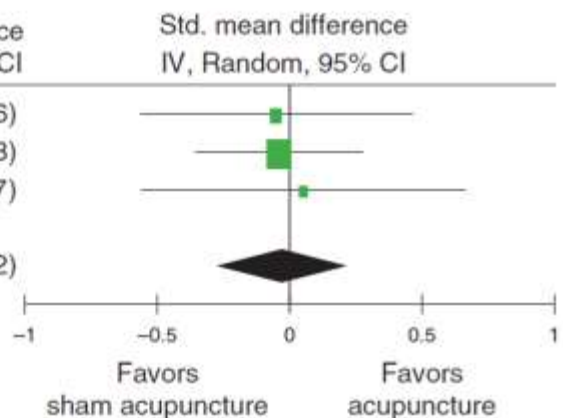


## 2. Quality of life

Study	Acupuncture			Sham acupuncture			Weight	Std. mean difference IV, Random, 95% CI
	Mean	s.d.	Total	Mean	s.d.	Total		
Forbes <i>et al.</i> (37)	64.6	19.8	27	65.6	19.8	32	23.2%	-0.05 (-0.56, 0.46)
Lembo <i>et al.</i> (38)	73.1	17.3	78	73.8	17.6	75	60.6%	-0.04 (-0.36, 0.28)
Schneider <i>et al.</i> (44)	64	82.1	21	60	64.2	20	16.2%	0.05 (-0.56, 0.67)
Total (95% CI)			126			127	100.0%	-0.03 (-0.27, 0.22)

Heterogeneity:  $\text{Tau}^2 = 0.00$ ;  $\chi^2 = 0.08$ , d.f. = 2 ( $P = 0.96$ );  $I^2 = 0\%$

Test for overall effect:  $Z = 0.22$  ( $P = 0.83$ )

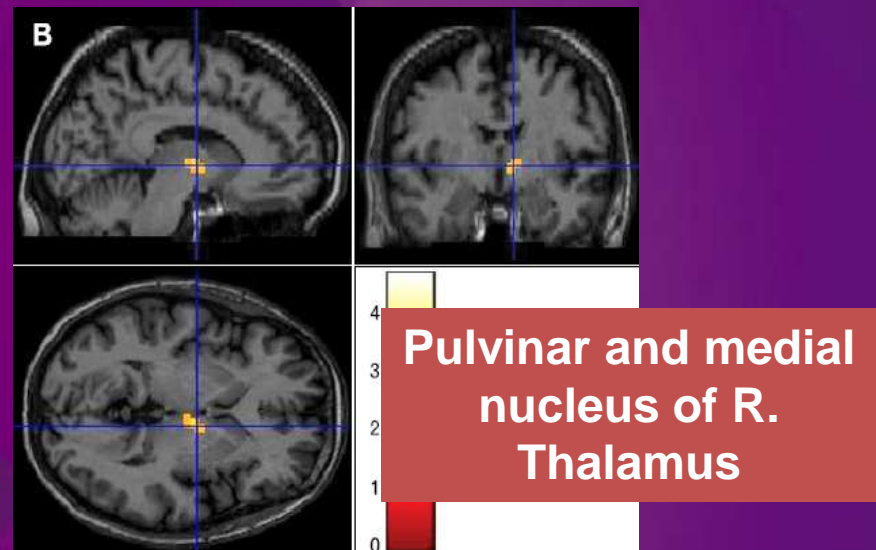
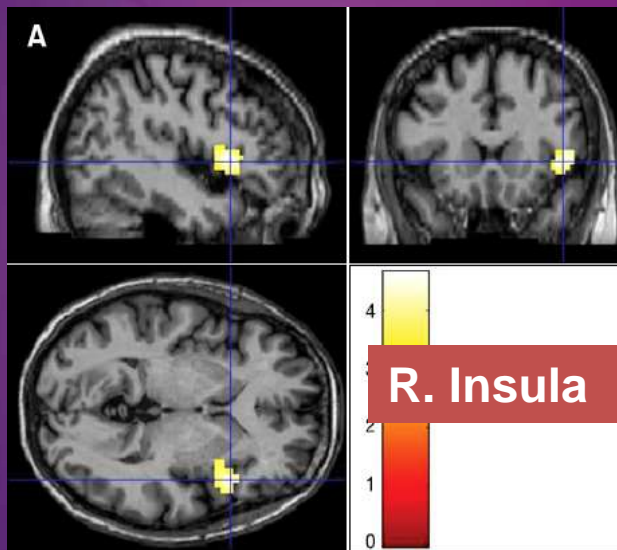


# Acupuncture as an adjunct for IBS: An enhanced therapist-based placebo?

Comparator	No. of studies	No. of subjects	Relative risk (95% C.I.) of improved IBS symptoms
Acupunctures Vs Medications	5	220 (control: 229)	1.28 (1.12-1.45)
Acupuncture + Chinese medicine Vs CM alone	4	284 (control: 182)	1.17 (1.02-1.33)
Acupuncture Vs psychotherapy	1	50 (control: 50)	1.05 (0.87-1.26)
Acupuncture + psychotherapy Vs psychotherapy alone	1	50 (control: 50)	1.2 (1.03-1.39)
Acupuncture Vs no specific treatment	2	87 (control: 94)	2.11 (1.18-3.79)

# Electro-acupuncture leads to higher activation at R. insula and R. thalamus than sham acupuncture

- 30 IBS-diarrhea patients were randomized to true electroacupuncture or sham acupuncture
- Functional MRI done during rectal distension after acupuncture treatment



Acupuncture-mediated pain modulation in IBS by (1) modulation of serotonin pathway at insula and (2) modulation of mood and affective response at the pulvinar and medial nucleus of the thalamus

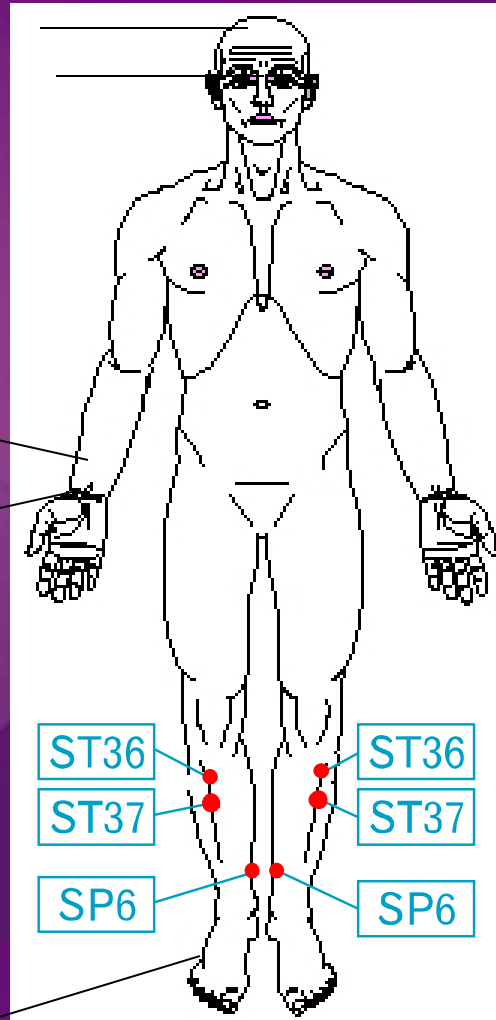
# Sham-controlled RCT for acupuncture treatment of IBS and generalized anxiety disorder

GV20 baihui 百會

Yintang 印堂

PC6 Neiguan 內關

HT 7 Shenmen 神門



LR3 Taichong 太沖

Comorbid non-depressed  
IBS + GAD patients

Real  
acupuncture

Sham  
acupuncture

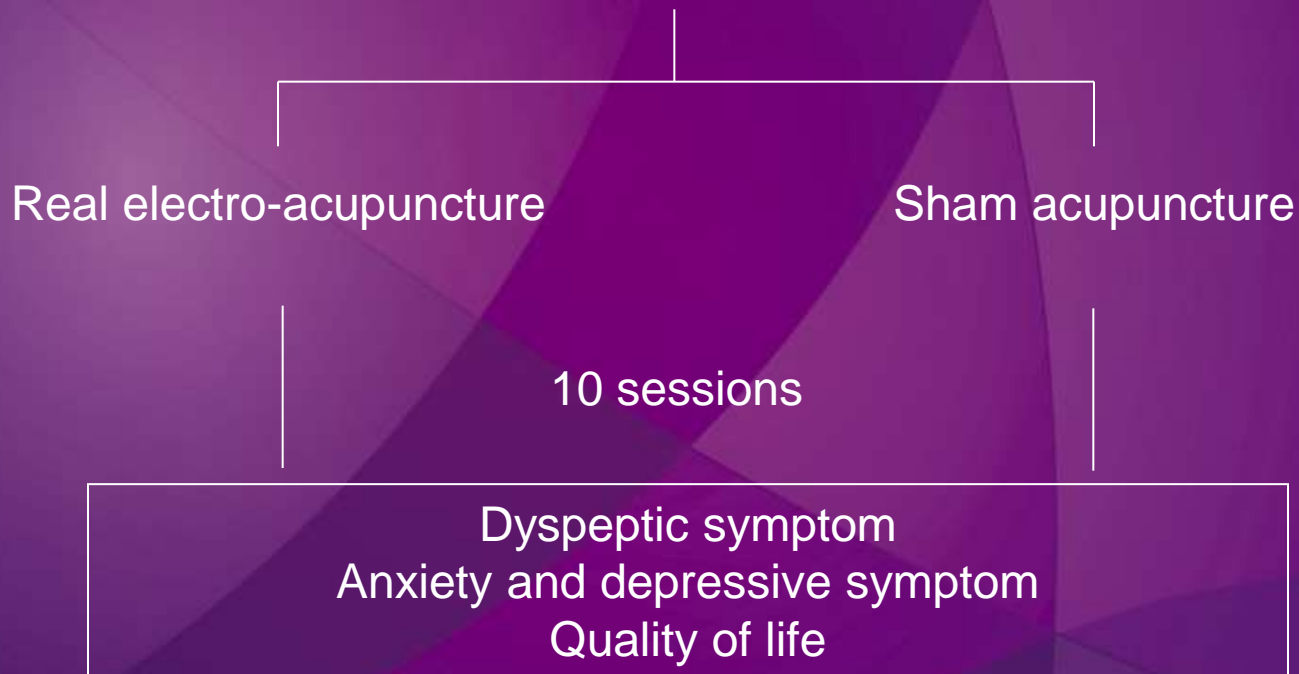
10 sessions

IBS symptom  
Anxiety symptom  
Quality of life  
Functional MRI



# Acupuncture treatment for refractory functional dyspepsia

Functional dyspepsia patients who fail to have adequate symptom relief with proton pump inhibitor



# What are the unmet needs of our patients?

- Communication between TCM and Western physicians
- Combo treatment with monitoring of safety and herb-drug interaction
- TCM physicians with good credentials

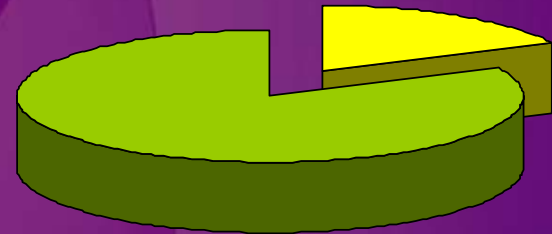
# A consumer-driven health-care system

Institute for Public  
Opinion in Allensback

Germany survey 2005  
772 subject interviewed

“If you were sick, would  
you prefer a therapy  
consisting of Western  
medicine or a  
combination of Chinese  
and Western medicine?”

■ Western ■ Combo



# Where is our patient load?

## Elderly

- Musculo-skeletal pain e.g. OA knee, low back pain
- Dementia

## Chronic non-infectious diseases

- Psychiatric disorders
- DM, Cardiovascular diseases
- Gastrointestinal problems
- Skin conditions

## Cancer

- No effective chemotherapy
- As an adjuvant

# Hong Kong Institute of Integrative Medicine

- Established in 2012 by CU Medicine, Hong Kong
- East-West Centre for Research and Education
- Integrative Medical Clinic
  - Clinical platform for research, education and practice of integrating TCM with conventional healthcare system



# Choose the “right” place

Integrative Medical Clinic in Prince of Wales Hospital, teaching hospital of CU Medicine Hong Kong



- 140,000 hospital admissions and 710,000 outpatient visits/ year
- 4 Chinese FDA Clinical Trial Centres (Oncology, Digestive, Cardiovascular, Endocrine)
- Only National Cancer Institute Clinical Trial Centre in HK
- 3 National State Key Laboratories (Oncology, Digestive, Chinese Medicine)

# Choose the “right” diseases

- Common, chronic or recurrent in nature
- No effective treatment,
- Serious side effects or high costs in conventional medicine
- Well accepted TCM treatment with high demand in the public

# Registration requirements of proprietary Chinese medicine in HK

## Product safety

- Heavy metals, pesticide residues, microbial, toxicity, mutagenicity, carcinogenicity, teratogenicity

## Product efficacy

- Pharmacodynamics; clinical trial data

## Product quality

- Manufacturing method; physiochemical properties of crude drugs; product specification, method and certificate of analysis; stability test reports



# Other research in Integrative Medicine

## Public health issues

- Jockey Club School of Public Health and Primary Care
- Policy, financing and healthcare delivery model

## Branch of Cochrane Center on TCM and CAM

- Systematic reviews and meta-analysis

## Basic science

- Drug mechanism and development

# Education and training: Highlights

## Postgraduate training in Chinese Medicine

- Clinical research methodology
- English speaking setting
- Overseas experience

## Non-Chinese medicine streams

- MBChB, BSc (Public Health), BPharm

## International networking

- Visiting scholarships
- Exchange program
- Conferences and workshop

# Development of Integrative Medical Care

## Stage 1

- Communication, transparency, safety monitoring
- Risk management, clinical governance and quality assurance

## Stage 2

- Cross validation of Western and TCM diagnosis
- Pragmatic trials, outcome and cost-effectiveness research

## Stage 3

- Evidence-based, protocol-driven diagnosis and management algorithm supported by pragmatic trials and outcome research
- Credentialing of training and qualification

# Education in Integrative Medicine

- Mutual understanding and communication
- Elective clinical attachment for undergraduates of healthcare related disciplines and international exchange students
- Clinical research training for graduates of Chinese medicine



# Integrating TCM with Modern Conventional Healthcare: Challenges

- Clinical governance
- Quality assurance
- Risk and safety management
- Liability
- Credentialing
- Sharing of patient records
- Reimbursement

# Integration of Chinese Medicine and Western Medicine should not be a dream

- New tools to identify the best TCM
  - Microbiome studies
  - Pragmatic Trial
  - Clinical Outcome and Cost-effectiveness studies
- Modernized integrative model
  - Patient-centered
  - Practice of modern healthcare administration
  - Protocol-based approach

