



# Colorectal Cancer

## Screening

## 大腸癌篩查

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# Content

- 1) Epidemiology 趨勢
- 2) Risk factors for CRC 高危因素
- 3) Screening modality 篩查方法及準確程度
- 4) Updated Recommendations for CRC screening  
最新篩查指引
- 5) Local data 本地數據
- 6) Future perspectives 展望

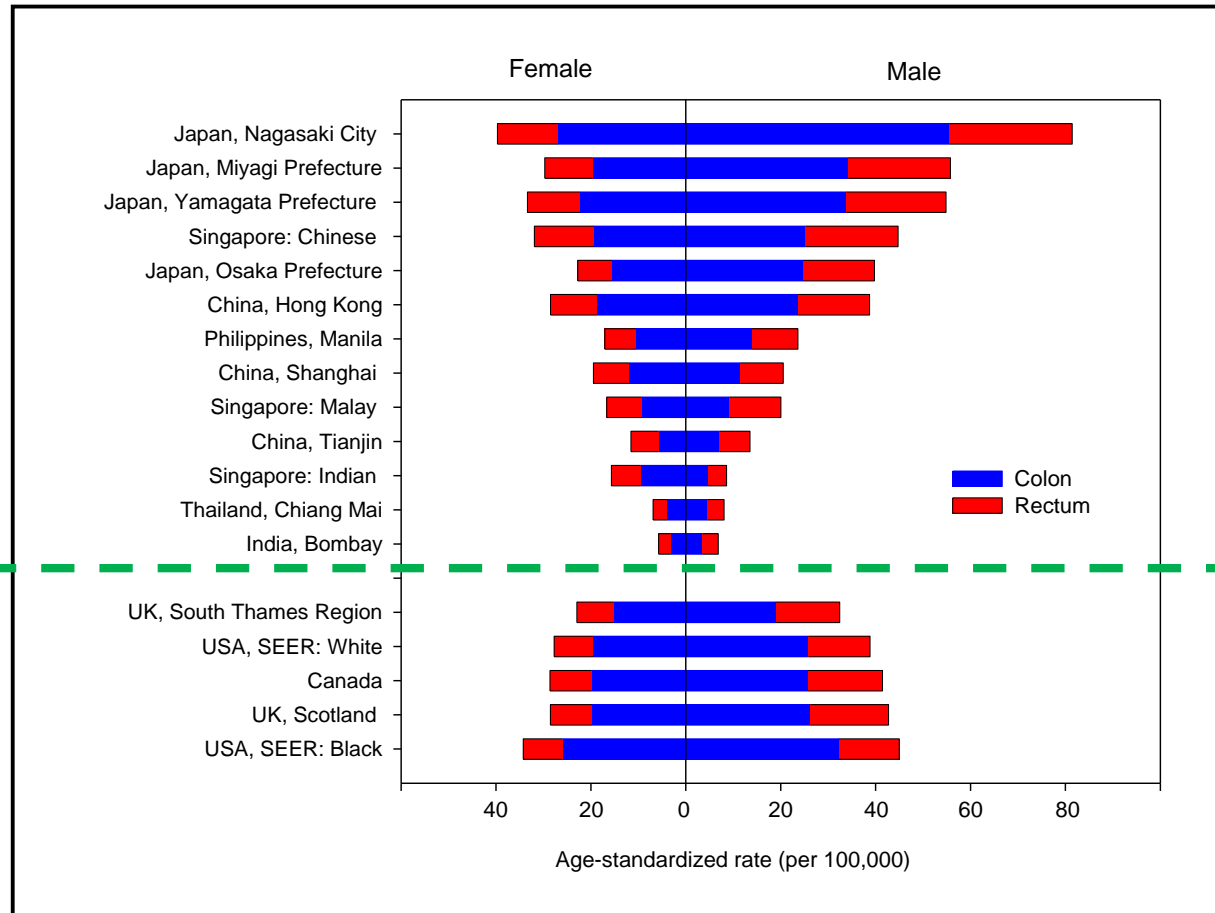


# Incidence of CRC in Asian populations is comparable to US and UK (1993-1997)

## 亞洲地區腸癌病發率

亞洲地區

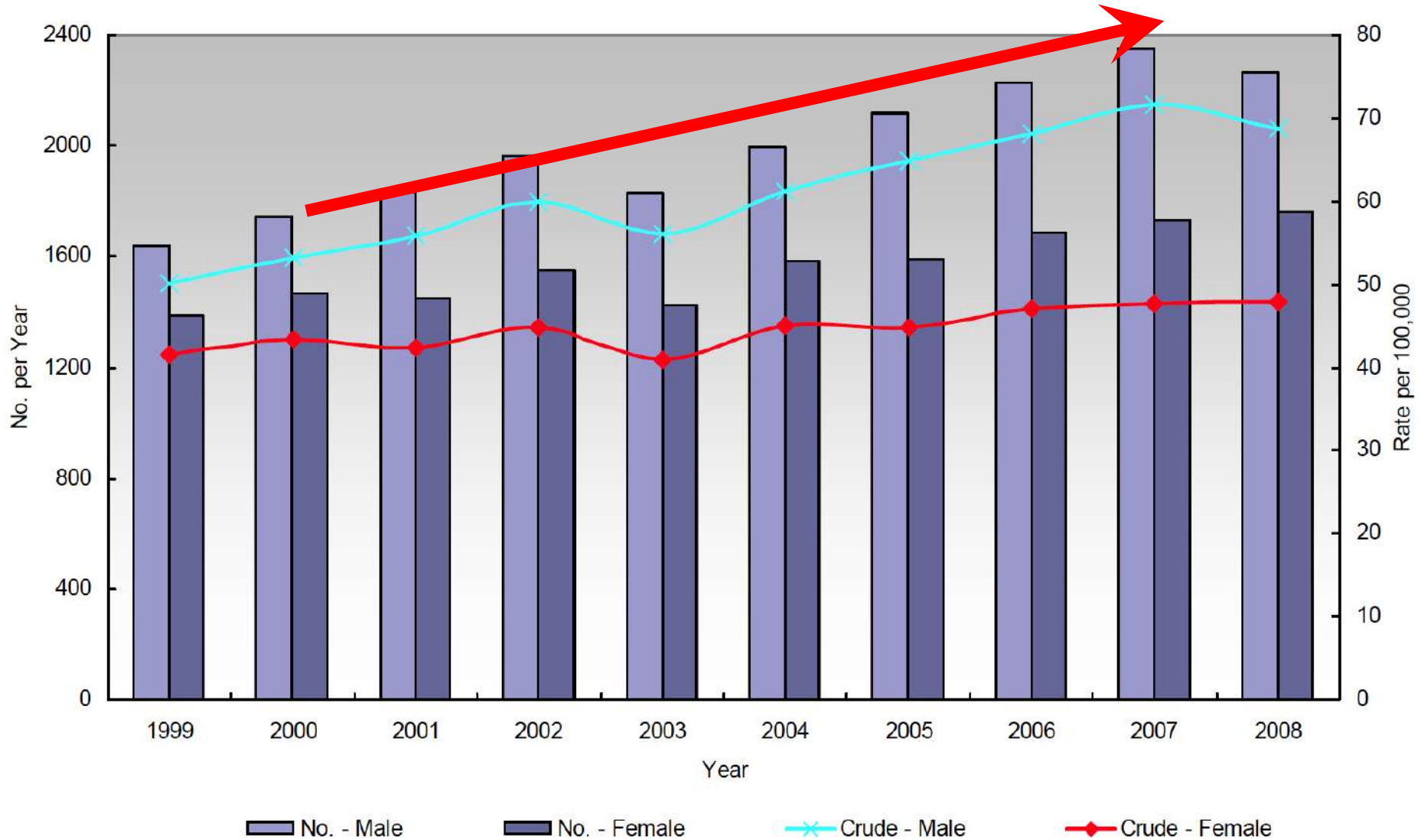
西方國家



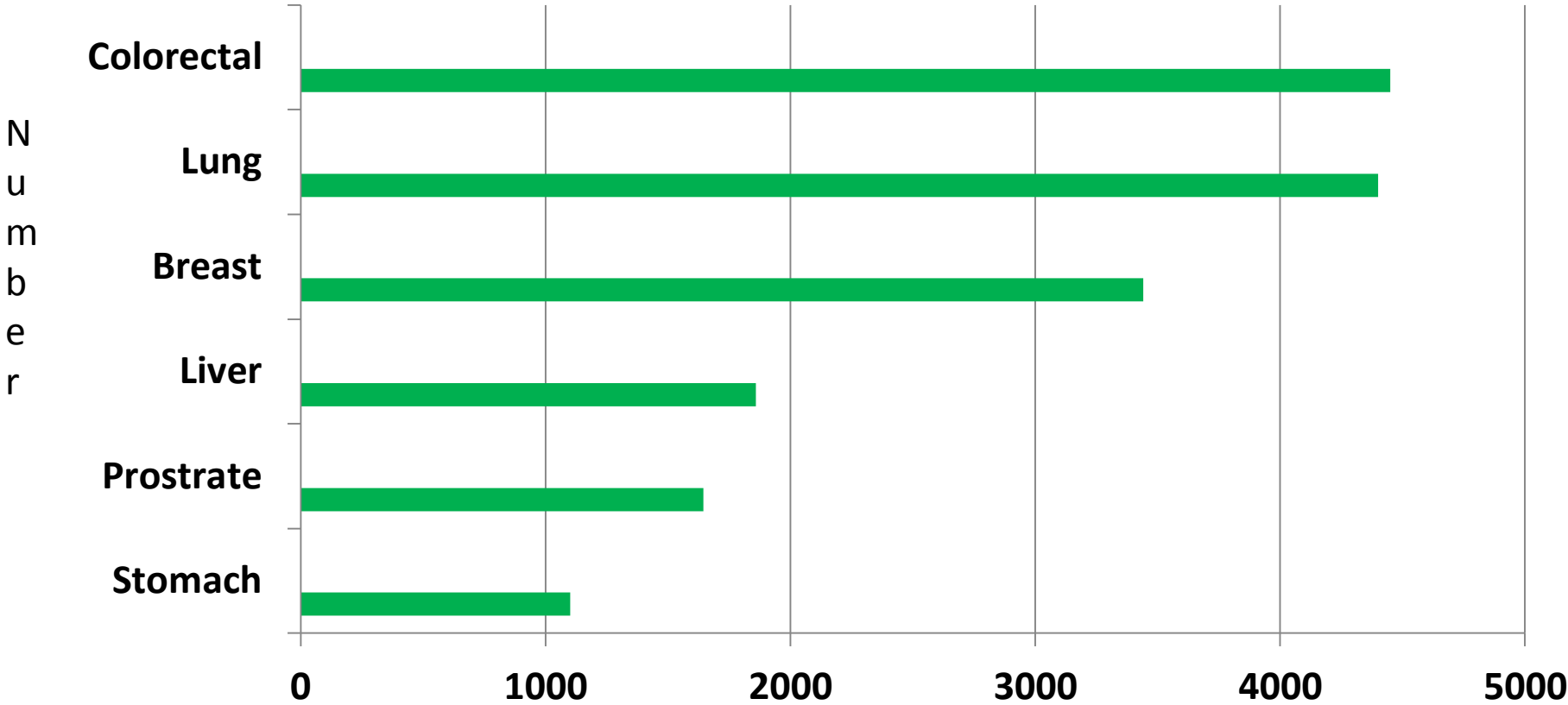


# Colorectal Cancer Incidence is rising

## 腸癌發病率不斷攀升



# Colorectal cancer has overtaken lung cancer for the first time to become the most common cancer in Hong Kong

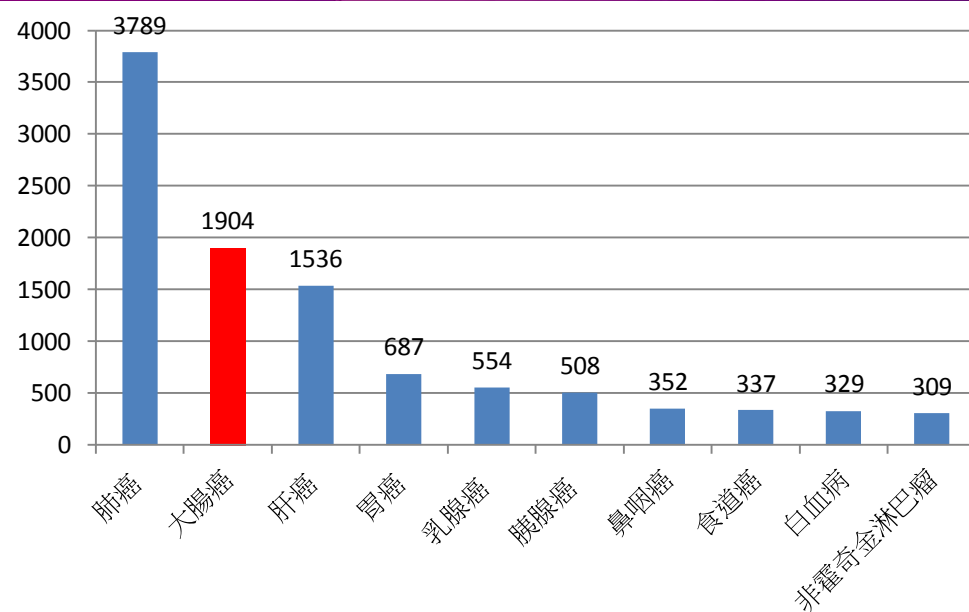
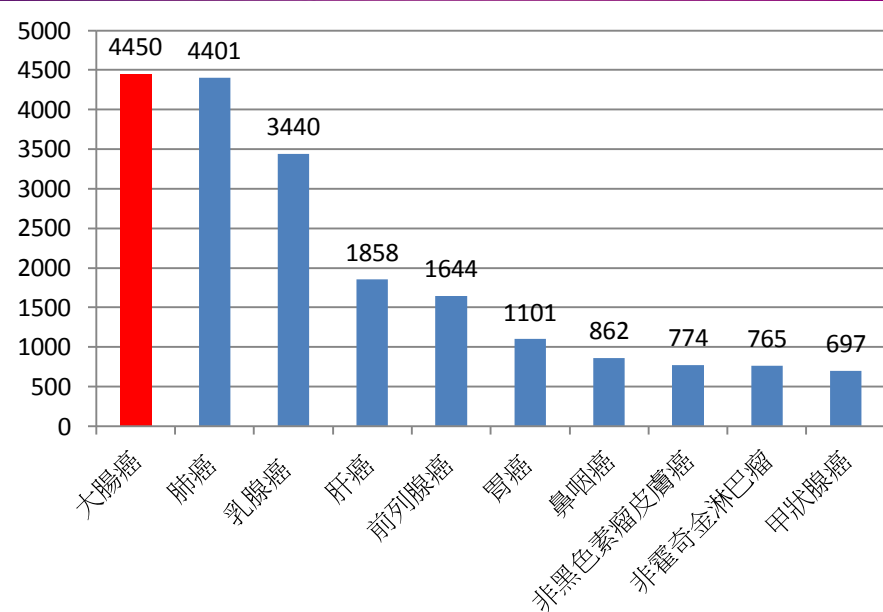


# Bowel cancer in Hong Kong: new cases and no. of deaths

## 香港大腸癌：新增與死亡個案

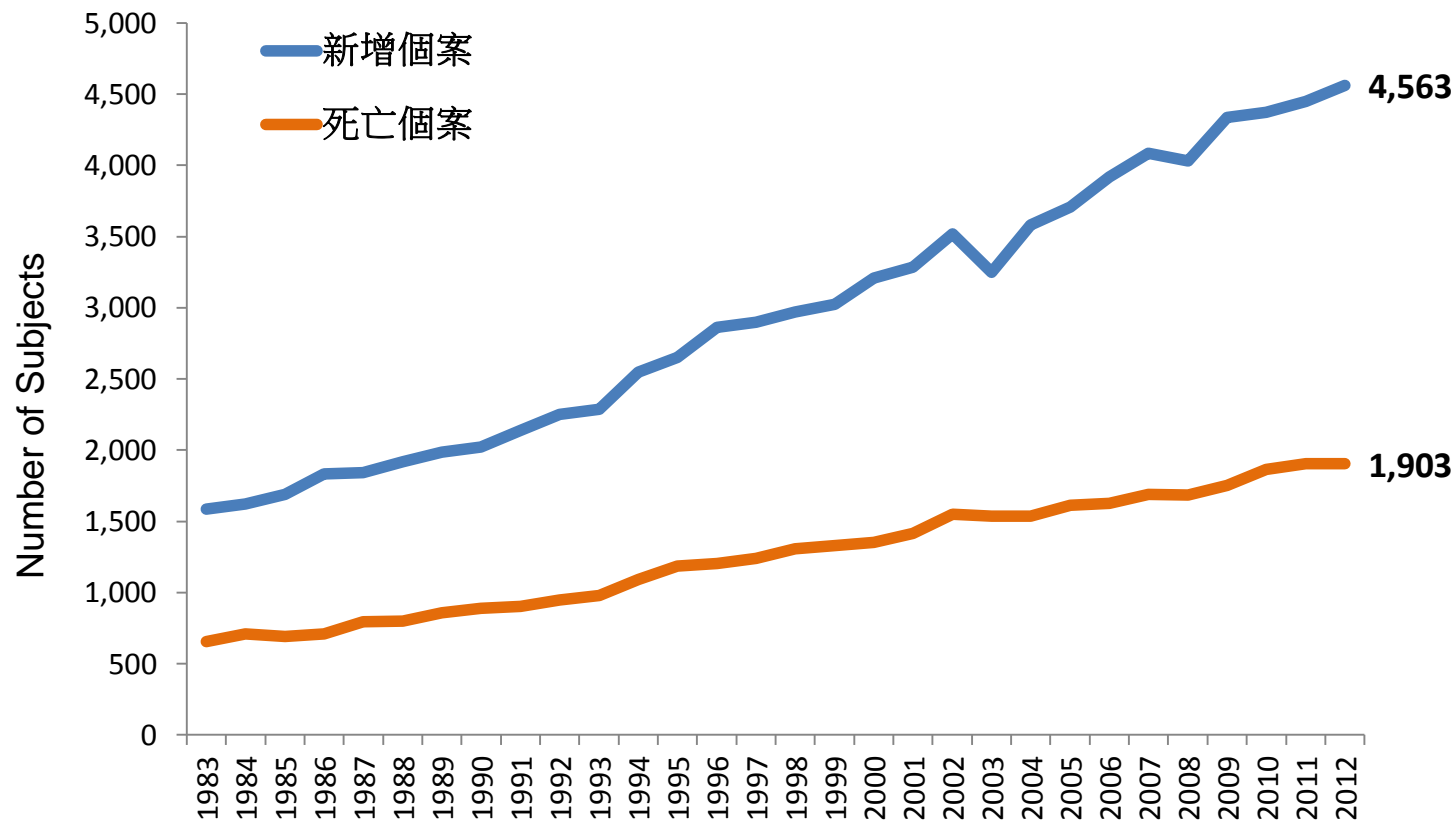
No. of new cases of top 10 cancers  
十大癌症新增個案

No. of deaths from top 10 cancers killers  
十大癌症死亡個案



# Mortality of CRC in Hong Kong is rising

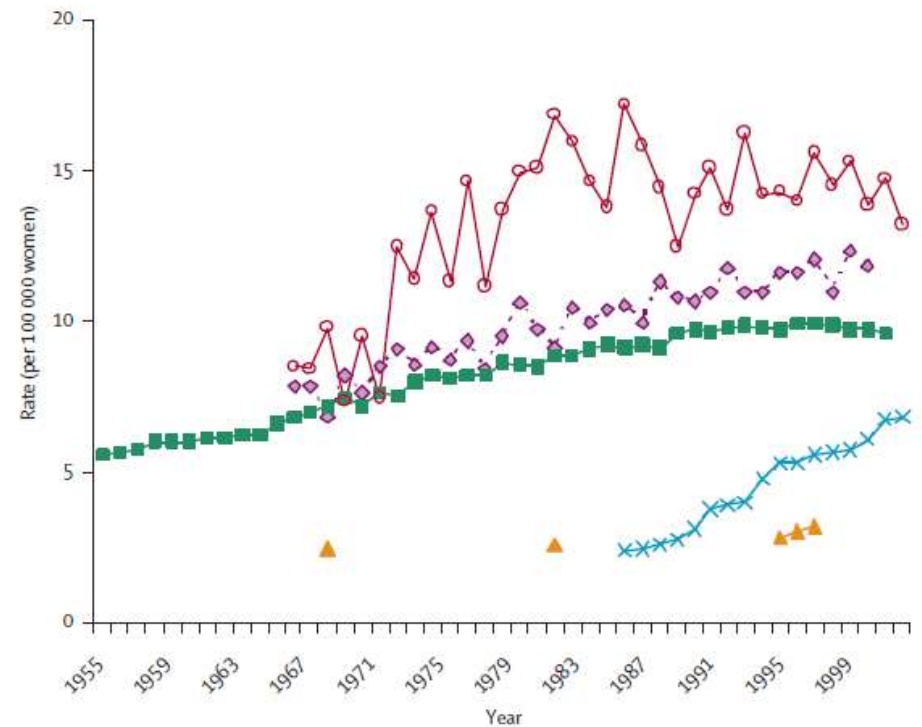
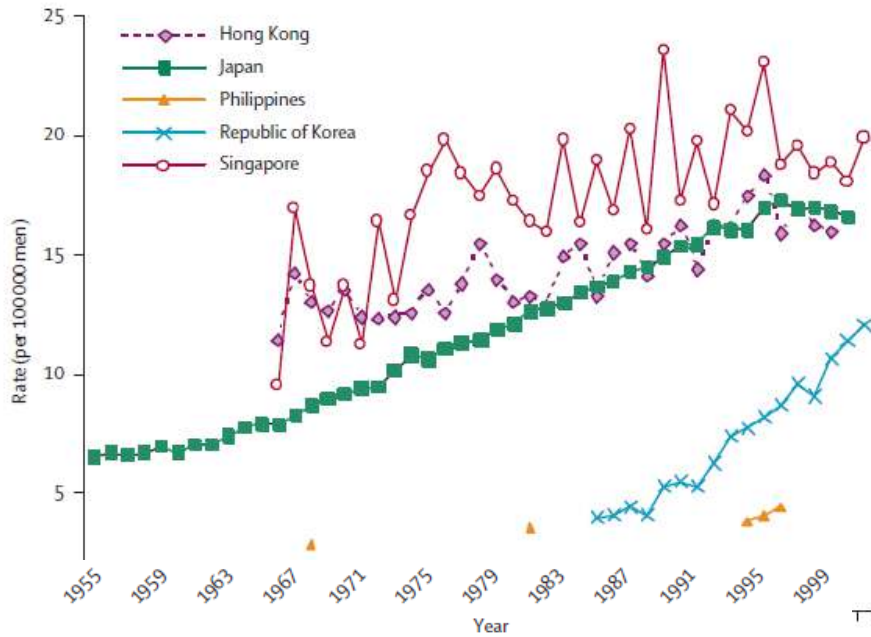
## 香港腸癌死亡率上升



\* Data from Hong Kong Cancer Registry, Hospital Authority. (2009)

# Rising colorectal cancer mortality in Asia

## 亞洲腸癌死亡率上升趨勢

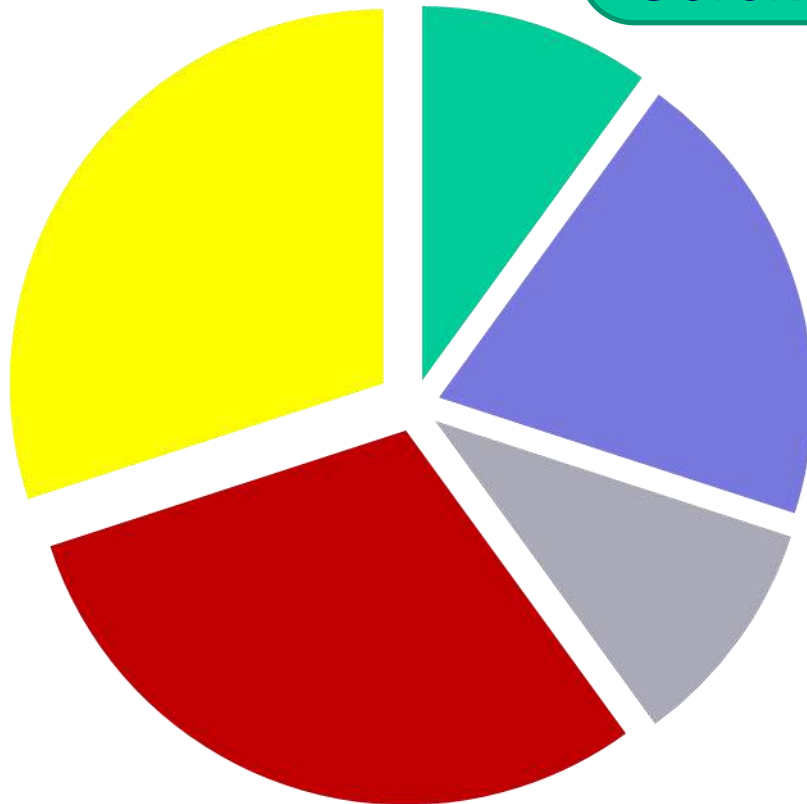




# Risk Factors for Colon Cancer

## 大腸癌高危因素

Obesity肥胖  
NAFLD非酒精性脂肪肝  
Diabetes mellitus糖尿病  
Coronary artery disease心血管疾病



Metabolic syndrome

Smoking

Family history of CRC

Sex

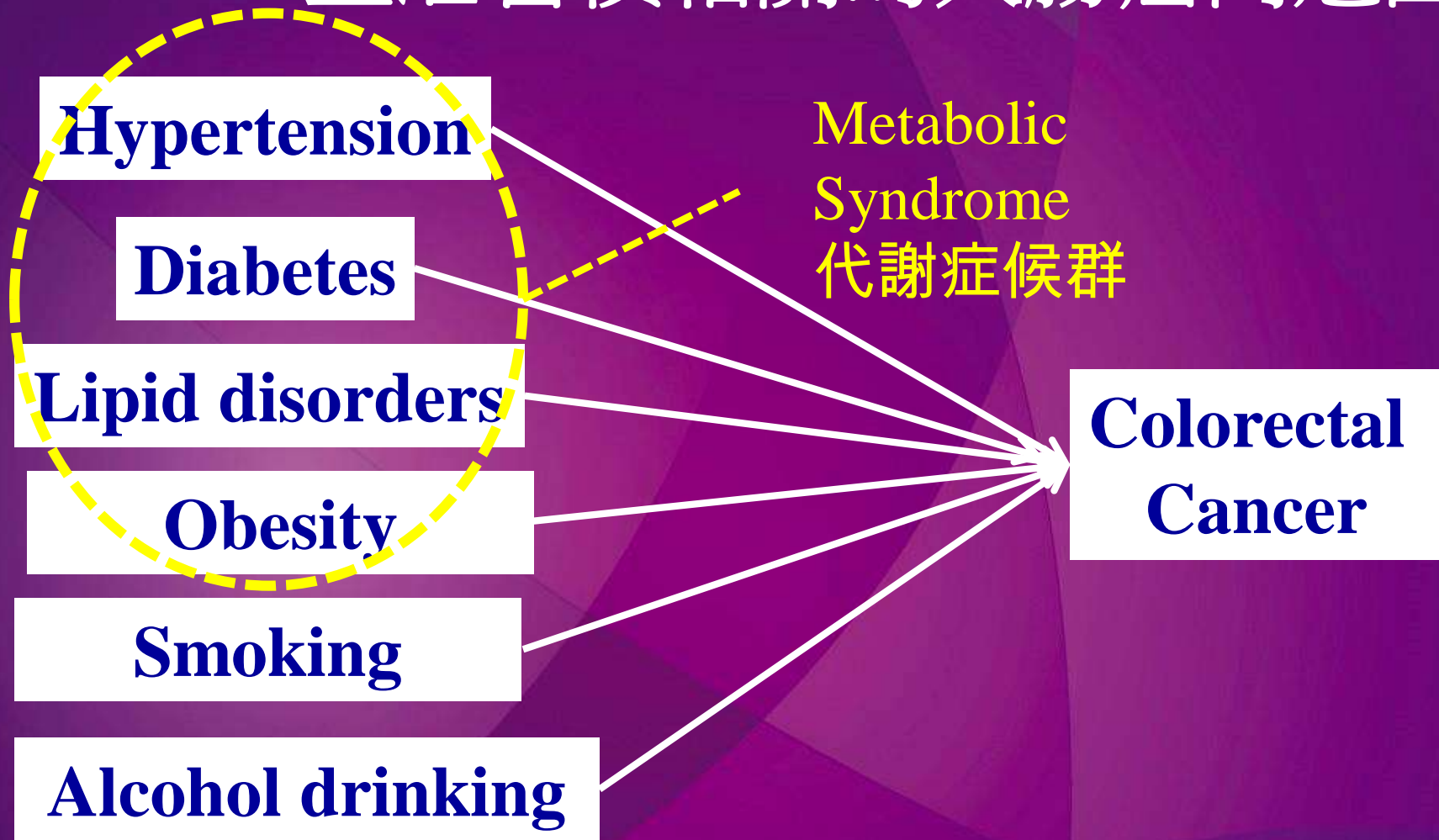
Age

Ng et al. Gastro 2013

Ng et al. Brit Med Bull 2013

Wong et al. Gut 2012; Lee et al CGH 2012

# 生活習慣相關的大腸癌高危因素



# Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies



*Andrew G Renehan, Margaret Tyson, Matthias Egger, Richard F Heller, Marcel Zwahlen*

Colon: HR1.24



## Increased Risk of Advanced Neoplasms Among Asymptomatic Siblings of Patients With Colorectal Cancer

SIEW C. NG,<sup>1</sup> JAMES Y. W. LAU,<sup>2</sup> FRANCIS K. L. CHAN,<sup>1</sup> BING YEE SUEN,<sup>1</sup> WAI-KEUNG LEUNG,<sup>3</sup> YEE KIT TSE,<sup>1</sup> SIMON S. M. NG,<sup>2</sup> JANET F. Y. LEE,<sup>2</sup> KA-FAI TO,<sup>4</sup> JUSTIN C. Y. WU,<sup>1</sup> and JOSEPH J. Y. SUNG<sup>1</sup>

<sup>1</sup>Department of Medicine and Therapeutics, Institute of Digestive Disease, Li Ka Shing Institute of Health Sciences, <sup>2</sup>Department of Surgery, <sup>4</sup>Department of Pathology, Prince of Wales Hospital, Chinese University of Hong Kong, Shatin, New Territories, Hong Kong SAR, China; and <sup>3</sup>Department of Medicine, Queenmary Hospital, University of Hong Kong, Hong Kong SAR, China

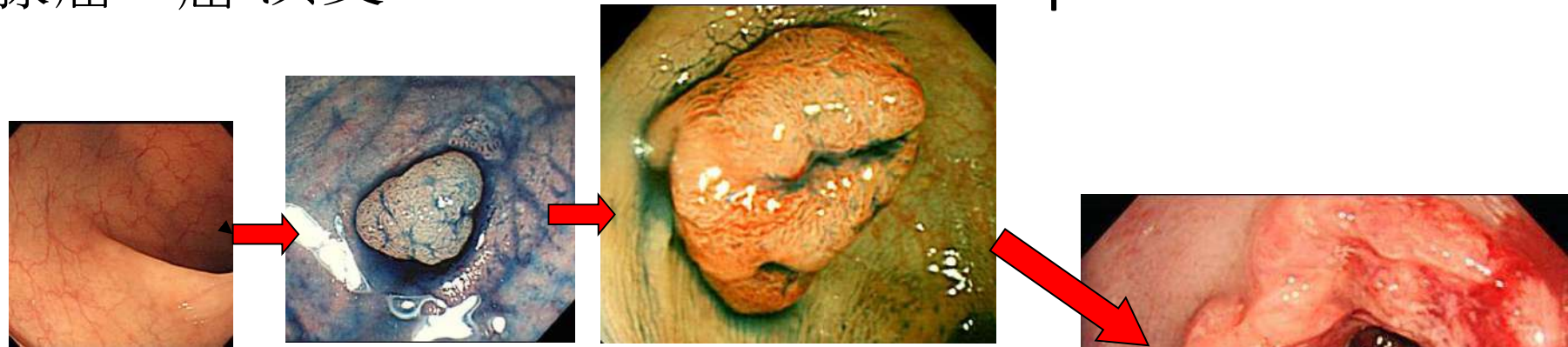
Siblings of patients with CRC has a more than **3-fold** increased risk of advanced neoplasms than siblings of healthy individuals



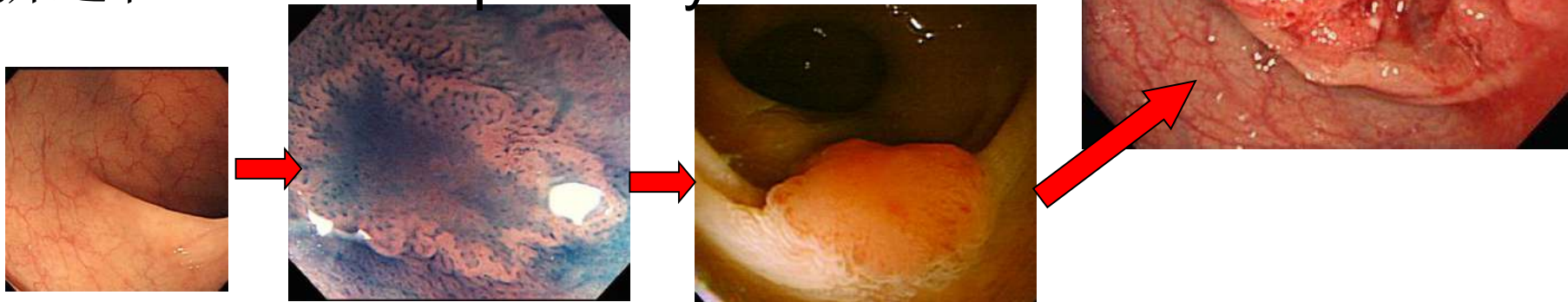
# 大肠癌的癌变过程

## Pathway of Colorectal Carcinogenesis

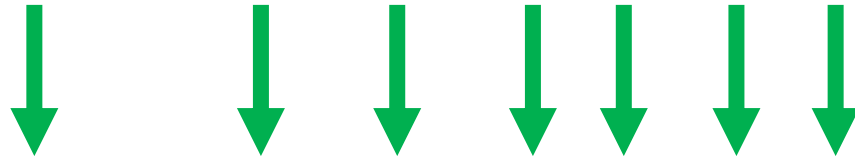
腺瘤 - 癌 演变 Adenoma-carcinoma sequence



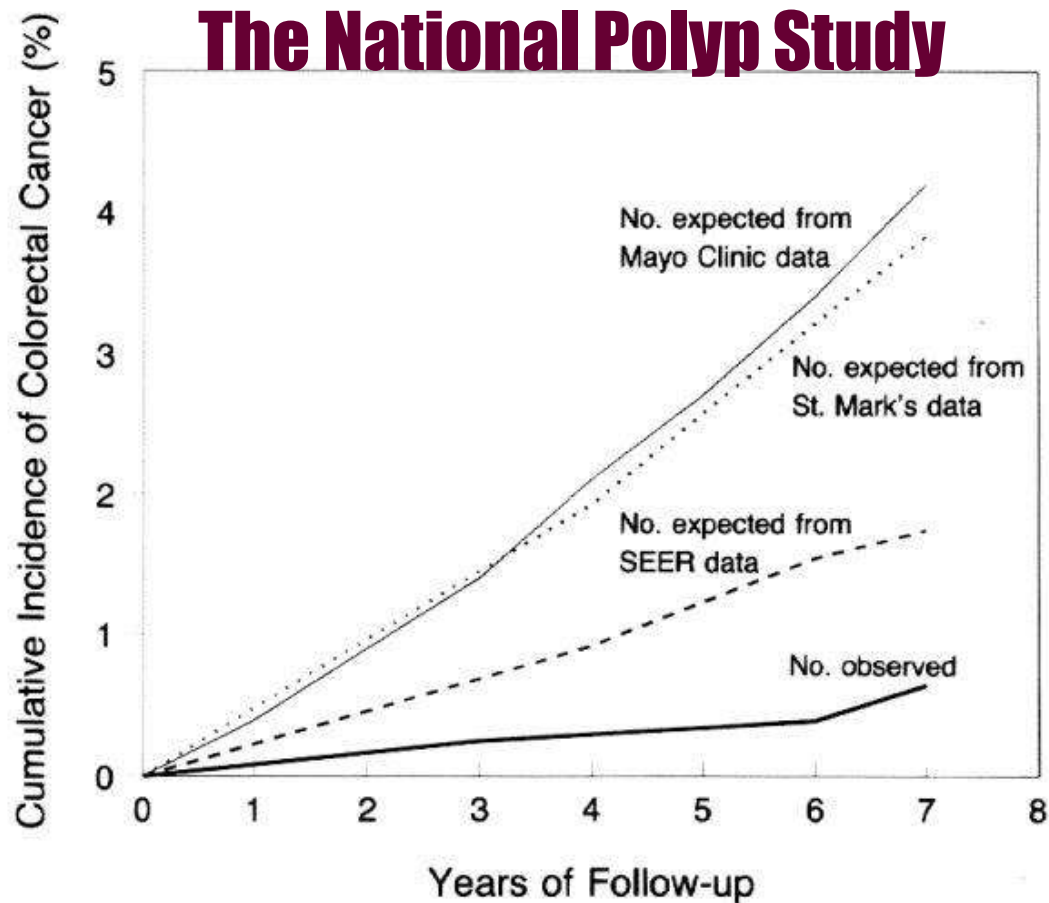
新途径 *De novo* pathway



# Can Screening Prevent Colorectal Cancer ?



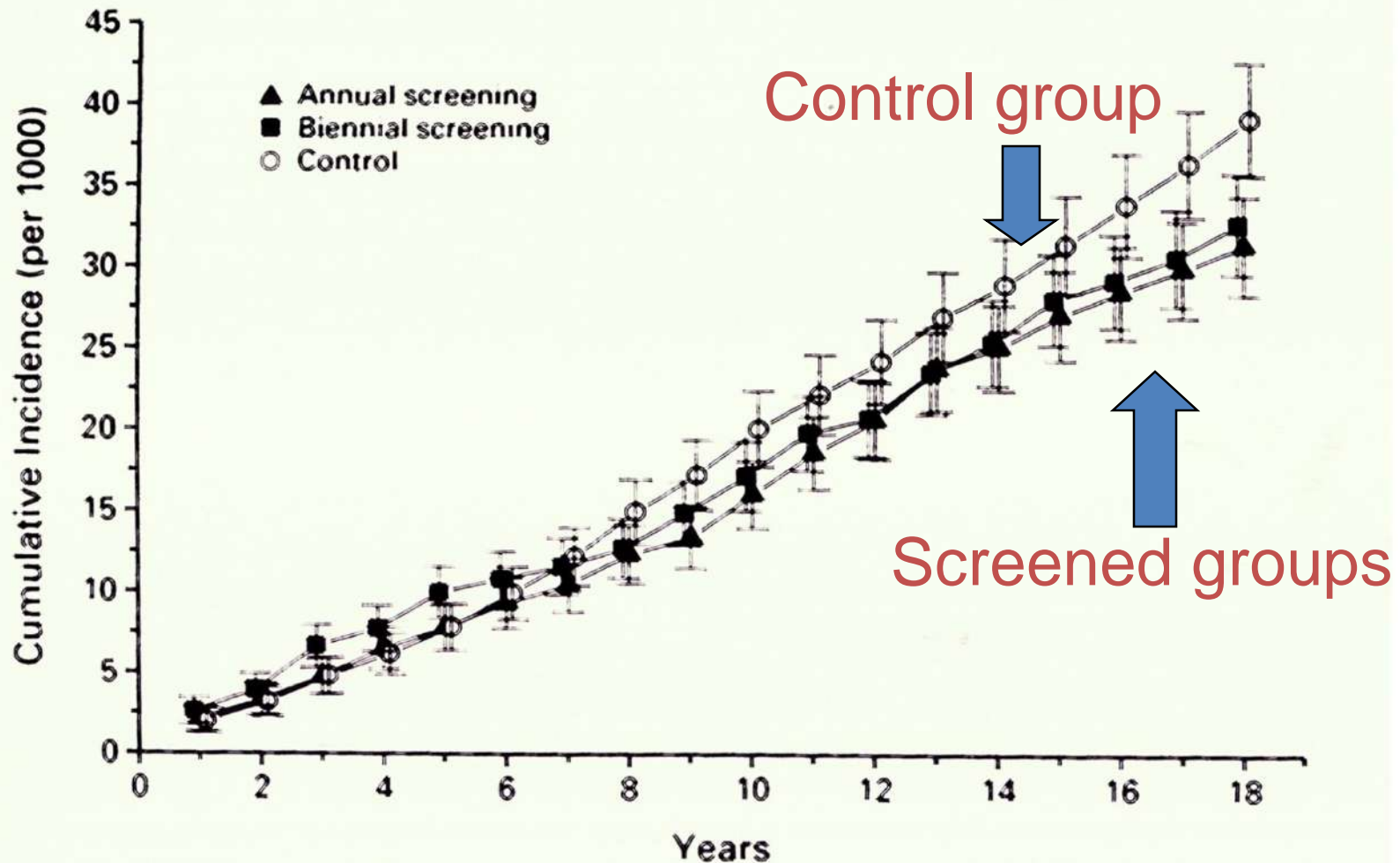
# Colonoscopy and Removal of polyps reduced CRC incidence by 76-90%



Winawer SJ et al. N Engl J Med 1993; 329: 1977-1981.

# Effect of FOBT Screening on CRC Incidence

## 大便隱血測試的功效





# CRC Screening reduces Mortality

## 大腸癌篩查減少死亡率

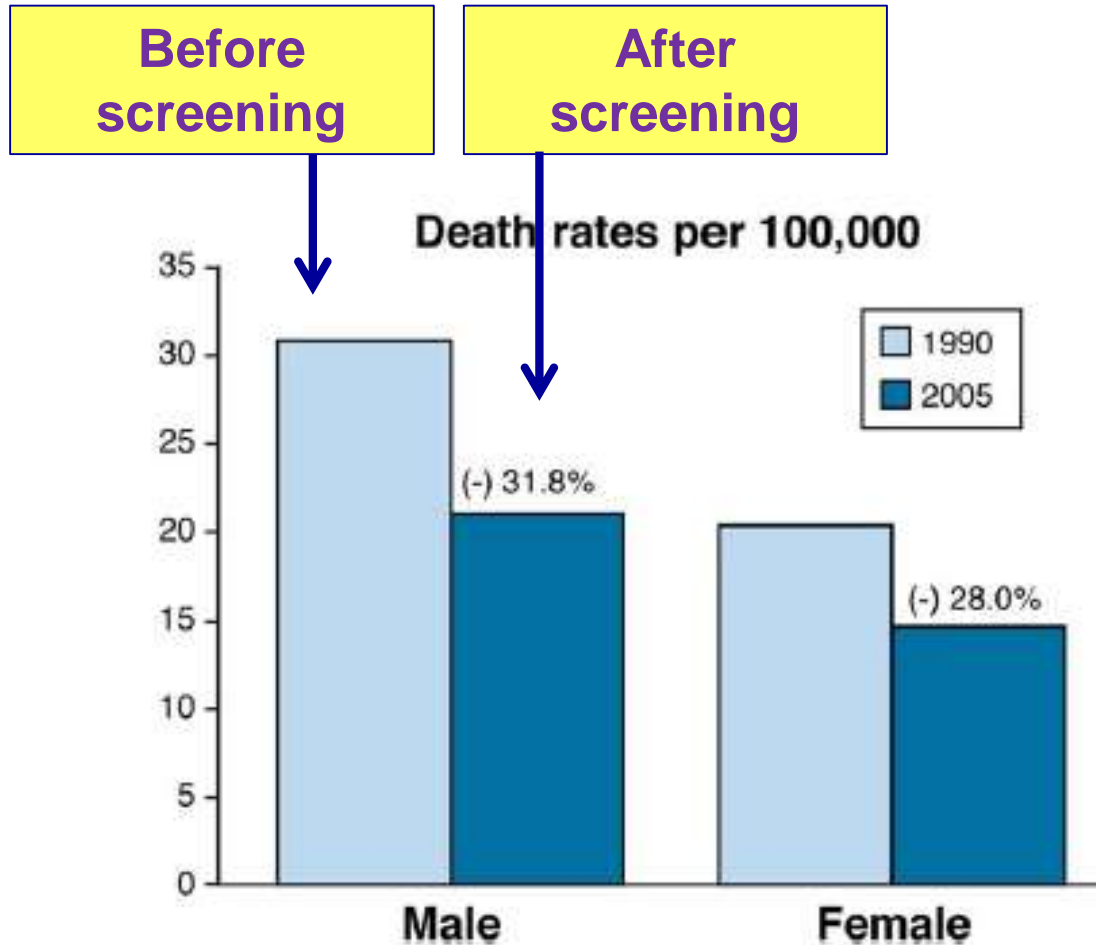
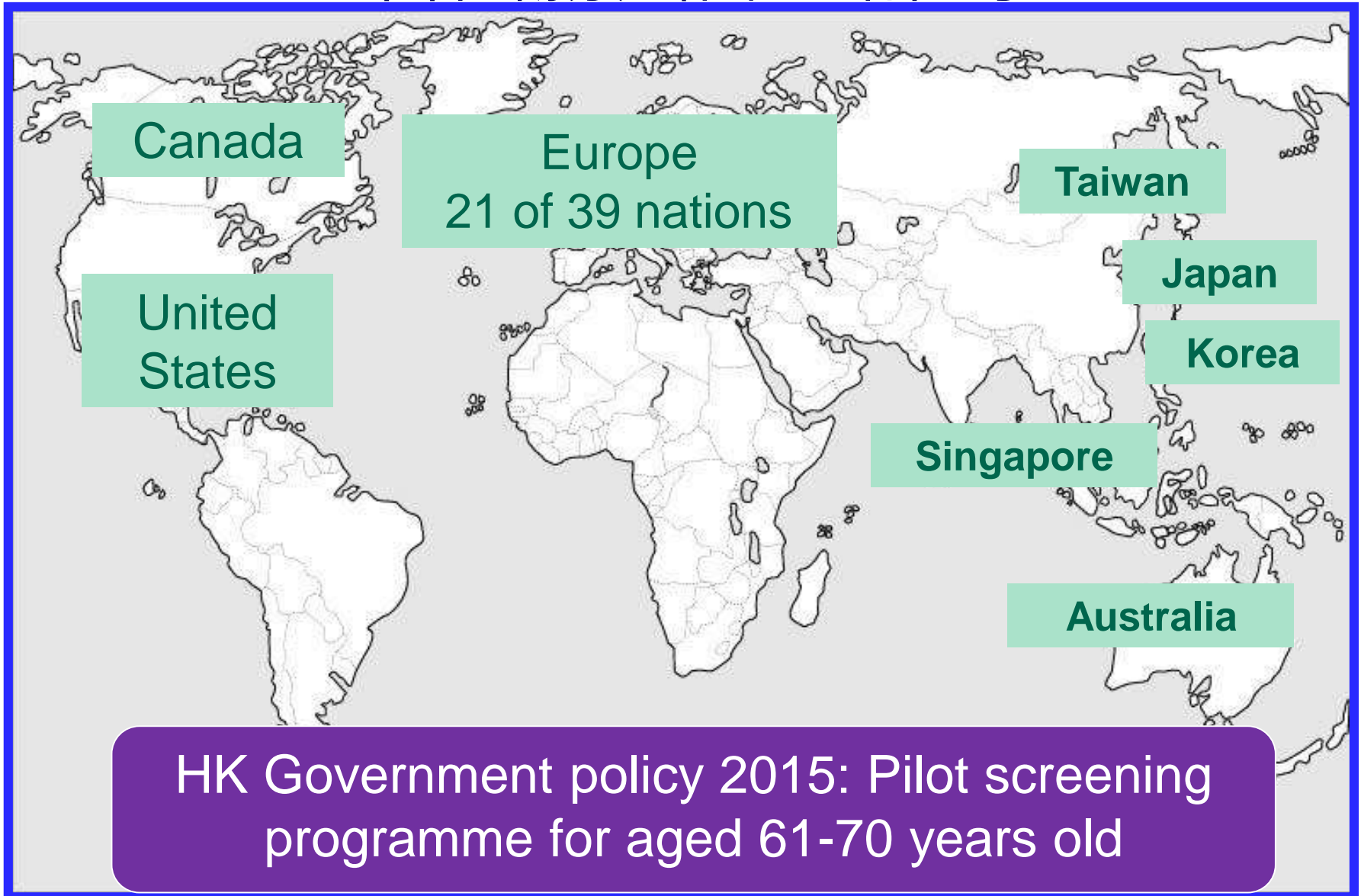


Figure 1. Death rates from CRC per 100,000 population.<sup>1</sup>

Jemal et al. Cancer J Clin 2008  
Zauber et al NEJM 2012

# National CRC Screening Programme

## 各國腸癌篩查計劃



HK Government policy 2015: Pilot screening programme for aged 61-70 years old



# The 2 most common methods for bowel cancer screening

Colonoscopy  
大腸鏡檢查



Faecal Occult Blood Test  
大便隱血測試



# Current Technologies

**Guaiac FOBT 愈創木脂測試**

**Fecal Immunochemical Test (FIT)**

**免疫化學測試**

**Sigmoidoscopy 乙狀結腸鏡檢查**

**Colonoscopy**



# Guaiac FOBT

*It works, but...*



**Imperfect specificity** 不全面特異性

**Limited sensitivity** 有限敏感度

**Moderate acceptability** 公眾未完全接受

Mandel et al. NEJM 1993  
Hardcastle et al. Lancet 1996  
Kronborg et al. Lancet 1996

# FIT are much better than gFOBT

## **BEHAVIOURAL:** Easier for the subject 容易使用 (受檢者)

- Remove need for diet and drug restriction 沒有任何飲食限制
- Easier stool-sampling methods 所需要的大便樣本相對較少

## **ACCURACY** 更準確

- Selectively target colonic bleeding 計對腸道出血
- Avoid diet and drug interference 避免飲食或藥物的幹擾
- More sensitive (including adenomas) but specificity is controlled 更準確，同時不會增加假陽性反應

## **LABORATORY:** Improved flexibility and quality

### 增加化驗靈活性及品質

- Easier-to-read endpoint 結果清晰
- Allow quantification, thus flexible 可量化結果

# Quantitative 數量化FIT



# Qualitative 質量化FIT





# Randomised Controlled Trial

## 隨機對照試驗

### GFOBT vs FIT

Population RCT comparing gFOBT with FIT in 20,623 individuals (intention-to-screen basis)

|                           | gFOBT      | FIT (OC-Sensor)*   |
|---------------------------|------------|--------------------|
| Participants              | 4836 (47%) | 6157 (60%, p<0.05) |
| Positivity rate<br>陽性反應   | 2.4%       | 5.5% (p<0.05)      |
| Advanced adenomas<br>後期腺瘤 | 46         | 121 (p<0.05)       |
| AA/participant            | 0.9%       | 2.0% (p<0.05)      |
| Cancer                    | 11         | 24                 |

\* 100ng/ml cut-off

Van Rossum et al. Gastroenterol 2008;135:82-90

# 另一挑戰:亞洲區低篩查率

## Low screening rate of population CRC screening program in Asia

| Country   | Screening or participation rate | Data source   |
|-----------|---------------------------------|---|
| Japan     | 18%                             | Saito H. J Med Screen. 2006;13 Suppl 1:S6-7.          |
| Korea     | 26.2%                           | WEO CRC meeting 2013                                  |
| Taiwan    | 33.7%                           | Bureau of Health Promotion, Taiwan                    |
| Australia | 40.1%                           | Flitcroft KL et al. J Med Screen 2011; 18: 193-203    |
| Hong Kong | 10%                             | Sung et al. AJG 2008; Wong et al. Preventive Med 2013 |

# Is Flexible Sigmoidoscopy 軟式乙狀結腸鏡檢查較 More Acceptable?

Office procedure 毋須在醫院進行

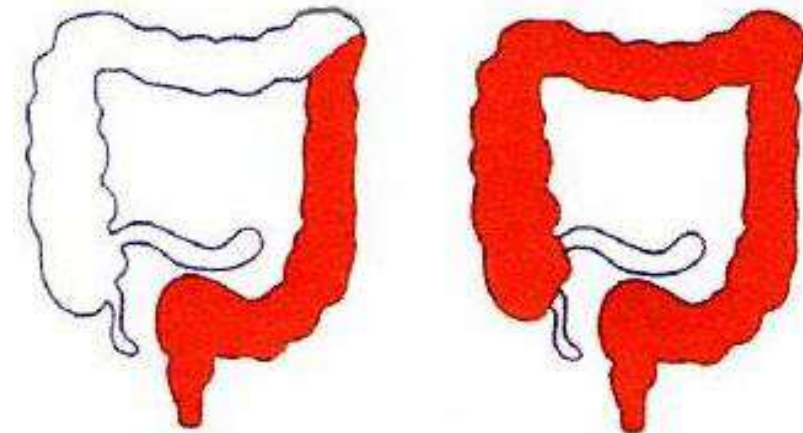
No sedation, easier preparation 毋須注射鎮藥或麻醉藥

Perforation rate 穿腸機會: 1/10,000

Can be done by nurse endoscopists 可由護士內鏡師進行檢查

**Supported by 4 Randomised controlled Trials**

- **NORCCAP**
- **UK FS**
- **SCORE**
- **PLCO**

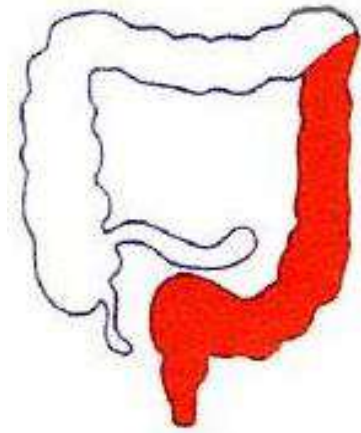


# Meta-Analysis of Flexible Sigmoidoscopy RCTs:

**High quality; 416,159 subjects**

**18% CRC incidence reduction**

**28% CRC mortality reduction**



**BUT.....No reduction in proximal CRC incidence**

**未能降低升結腸及橫結腸的發病率**

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Elmunzer BJ et al. PLOS Medicine 2012;9:1-9.

# Colonoscopy for CRC Screening

No randomization trial 非隨機試驗

- Large-scale cohort studies reduced incidence of colorectal cancers 大規模追蹤研究
- 降低腸癌發病率

**Table 1**

Major trials addressing a reduction in CRC mortality.

| Author                 | Year | Design       | N                                 | CRC Mortality Reduction                         |
|------------------------|------|--------------|-----------------------------------|---|
| Baxter <sup>12</sup>   | 2009 | Case-Control | 10,292 (Case)<br>51,460 (Control) | 67% - left sided<br>1% (NS) -right-sided        |
| Singh <sup>13</sup>    | 2010 | Cohort       | 54,803                            | 29% overall<br>47% left-sided<br>0% right-sided |
| Rabeneck <sup>14</sup> | 2010 | Cohort       | 2,412,077                         | 3% decrease/1% increase in colonoscopy          |
| Zauber <sup>15</sup>   | 2012 | Cohort       | 2602                              | 53% overall                                     |

# Is Colonoscopy the Best Test? Some Limitations .....

**Up to 25% have inadequate bowel preparation**

最高25%檢查前未完全清洗大腸

**Manpower is inadequate**

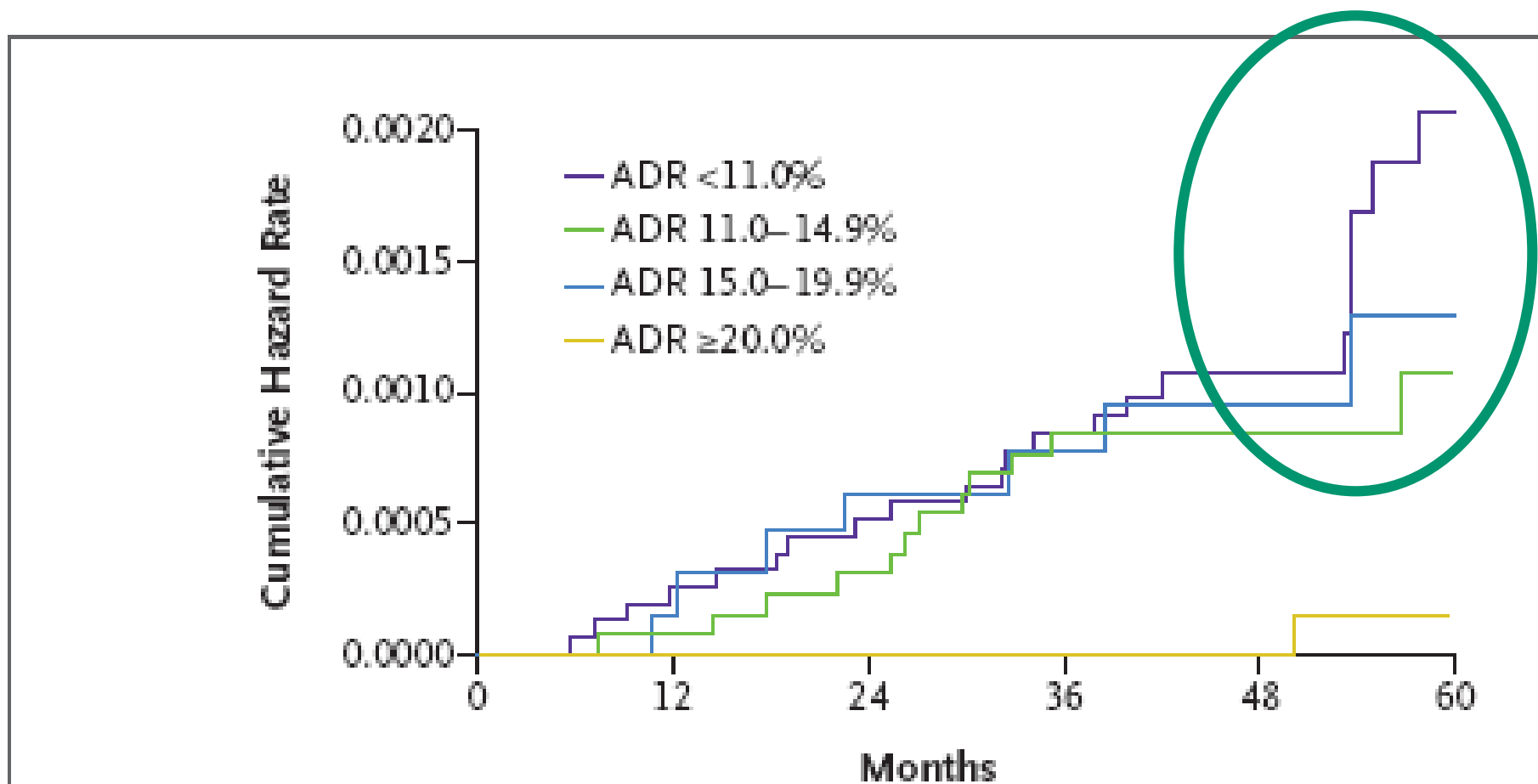
沒有足夠人手

**Fear of invasive procedure**

害怕侵入性檢查

# Adenoma Detection Rate <20% = Higher risk of Interval Cancer in next 5 years

Kaminskis et al. NEJM 2010



# Evidence for “Imperfect Colonoscopy”

## **Risk of interval cancer** 期間癌的風險

2-11% of all CRCs have a history of negative colonoscopy within 6-60 mos

## **Less or no protection in the right colon**

對升結腸及橫結腸很低或全無功效

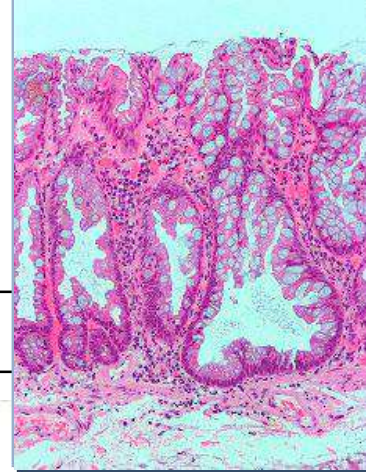
Colonoscopies missed almost all of the cancer-related deaths from the right CRC and 1/3 of the left CRC.

Pabby, GIE 2005, Robertson, Gastroenterol 2005, Bertagnolli, NEJM 2006, Bressler B et al. Gastro. 2007, Singh, Am J Gastro 2010, Baxter, Gastroenterol 2011, Baxter. Ann Int Med 2009



# An Emerging Entity: Serrated Polyps 鋸齒狀瘻肉

Leggett and Whitehall; Gastro 2010;138: 2088-2100



- Pathway may account for up to **20% of CRC**
- Genetic pathways are only partially characterized

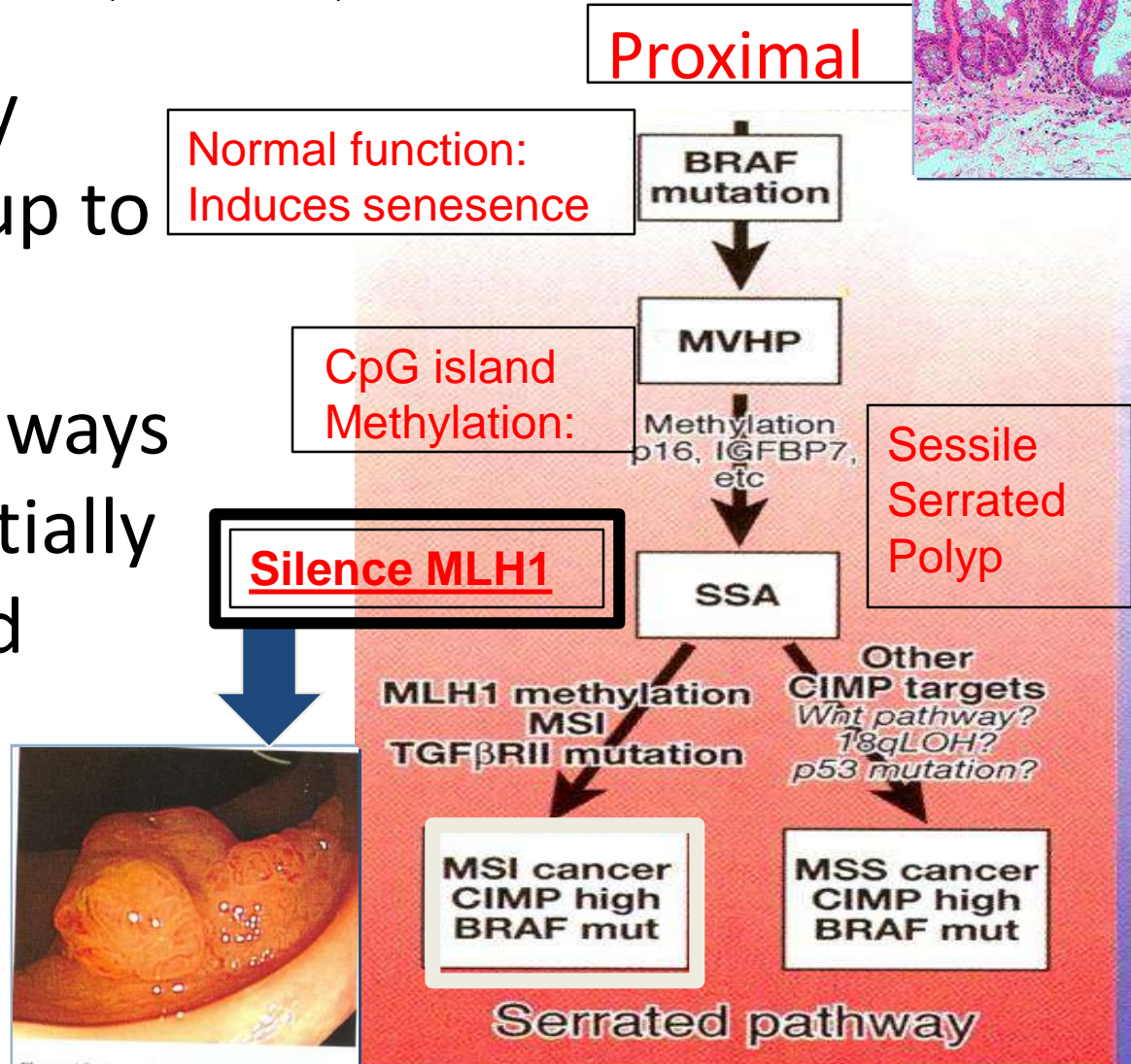
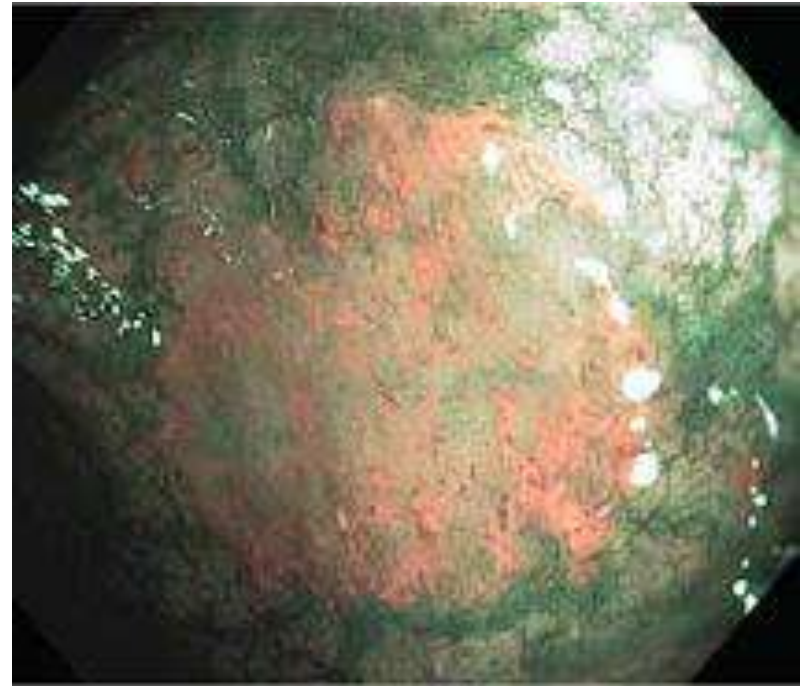


Figure 16. Serrated adenocarcinoma, subtype 1a.

# Sessile Serrated adenoma

## 無柄的鋸齒狀腺瘤



**Pathology: Misclassification**  
**Endoscopy: We miss them**

# 期間癌從何而來?

## Interval Cancer: WHY?

New, fast growing lesions

**Incomplete removal (19-27%)**

**Missed lesions**

**Up to 17% of polyps > 1cm are missed !!**

**Less protection in proximal colon**

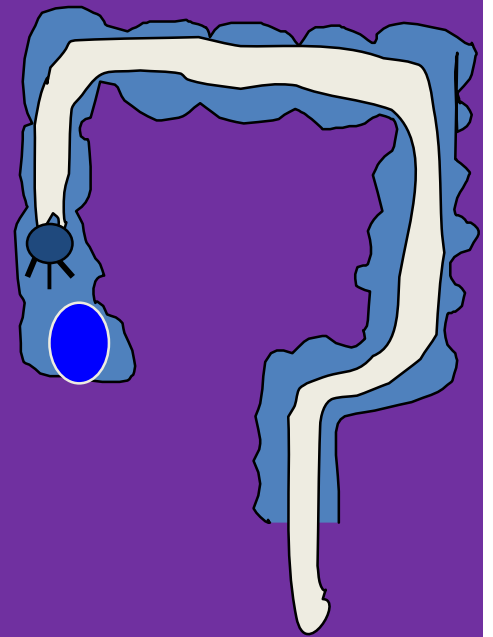


**Quality**

# How Good Is Your Dentist? How Good Is Your Endoscopist? The Quality Imperative

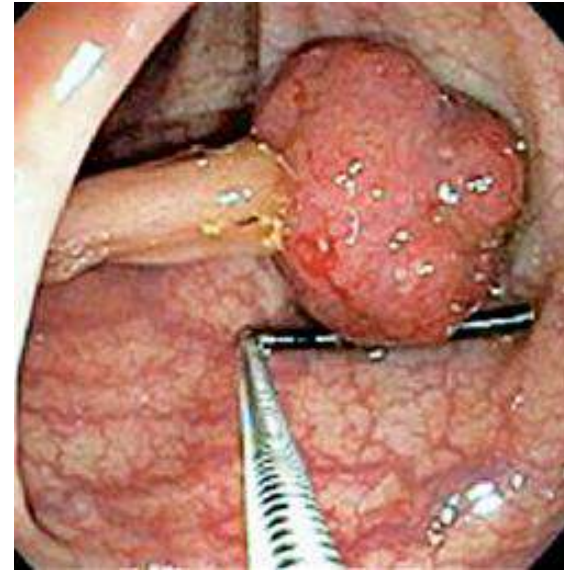
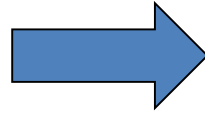
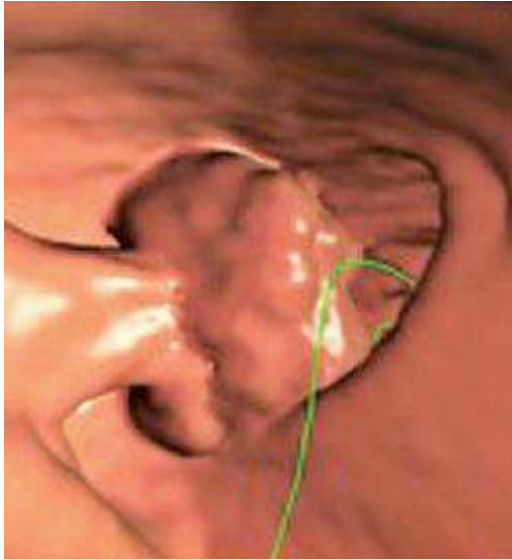
David Lieberman  
Gastroenterology 2012

High-quality exam to cecum  
Low rate of missed lesions  
Low rate of incompletely removed lesions  
Low rate of adverse events





# CT Colonography 腦斷層掃描結腸成像術



**Colon Capsule**  
大腸膠囊內鏡




# Sensitivity of “One time” CRC Screening Tests

## 一次性腸癌檢查方法比較: 敏感度

|                    | Sensitivity (%)    |                   |
|--------------------|--------------------|-------------------|
|                    | Colorectal Cancer  | Advanced Adenoma  |
| Guaiac FOB         | 50-75              | 20-25             |
| Immunochemical FOB | 60-85              | 20-50             |
| Barium Enema       | 50                 | 48                |
| CT colonography    | Uncertain<br>~ >90 | >90<br>(if >10mm) |
| Sigmoidoscopy      | >95                | 70                |
| Colonoscopy        | >95                | 88-98             |

Lieberman et al. NEJM 2010  
Quintero et al. NEJM 2012



An aerial photograph of a massive crowd of people, likely at a festival or public event. The crowd is densely packed and fills the entire frame. The people are wearing a variety of colorful clothing, creating a mosaic of reds, blues, greens, and whites. The perspective is from directly above, looking down on the sea of heads.

**Who should have  
CRC screening?**



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# **Cancer Screening is a Program**

**Not a test**

***Acceptance***

***Adherence***

***Quality control***

***Cost-effectiveness***



# 香港的结肠癌筛查计划

## Bowel Cancer Screening Programme in Hong Kong

Established in 2008

CRC screening for 10,000 asymptomatic individuals

Evaluate the preference of colonoscopy and compliance of annual iFOBT

**醫坊** 中大調查：17%現初期腺瘤  
**千名測試者 四人證患大腸癌**

一般人群會進行大腸癌檢查，但中文大學一項研究發現，一千多名無病徵的人當中，除有四人患有大腸癌外，有多達近一成七人患有可演變成大腸癌的腺瘤。中大呼籲，五十歲以上的患者，應每年檢查大腸及早預防大腸癌。 **本報記者**

**五**十八歲的王女士好愛運動，每周行山及游泳，而且更愛吃高纖低脂的食物，她一直自認為是健康一族，但早前參加中大的大腸癌篩查計劃後，才赫然發現大腸內有兩粒息肉，經化驗後確診患上初期的大腸癌。

王女士在檢查前，並無出現任何病徵，她坦言，對患上大腸癌感到震驚。

**健康一族赫見初期息肉**

中大在去年五月至八月間，替一千零三十七名，年齡介乎五十至七十歲和並無病徵的人，進行檢查大腸內鏡和大便隱血測試的檢查。

結果發現，有四人被確診患上大腸癌，另外分別有二十七人和一百五十一人，患有後期腺瘤和大腸腺瘤，佔受查人數的一成七，由於後期腺瘤和大腸腺瘤均可發展成大腸癌，但病人一般沒有病徵，猶如「隱形炸彈」。

**專家籲滿50歲每年驗腸**

中大消化疾病研究所主管沈祖堯表示，現時有很多病人，在持續腹痛及大便出血時，才前往檢查，但可能已經患上大腸癌。他建議，五十至七十歲人士即使沒有任何病徵，亦要接受每年做大腸鏡檢查，一旦發現有問題可以盡早治療。

■ 大腸癌病人王女士（右）生活健康，並無出現任何病徵，經檢查後才發現患上大腸癌。

■ 沈祖堯建議，五十至七十歲人士即使沒有任何病徵，也要接受每年做大腸鏡檢查。

# Bowel Cancer Education Centre

## 大腸癌教育中心

*The CUHK Jockey Club Bowel Cancer Education Centre has started its formal operation and service since 3<sup>rd</sup> May, 2008*

**Location:** 4/F, Lek Yuen Health Centre, Shatin, NT



# Major Findings CUHK CRC Screening

**Only 10%** of the respondents had undertaken a CRC screening test.

**Low knowledge** of CRC symptoms and risk factors.

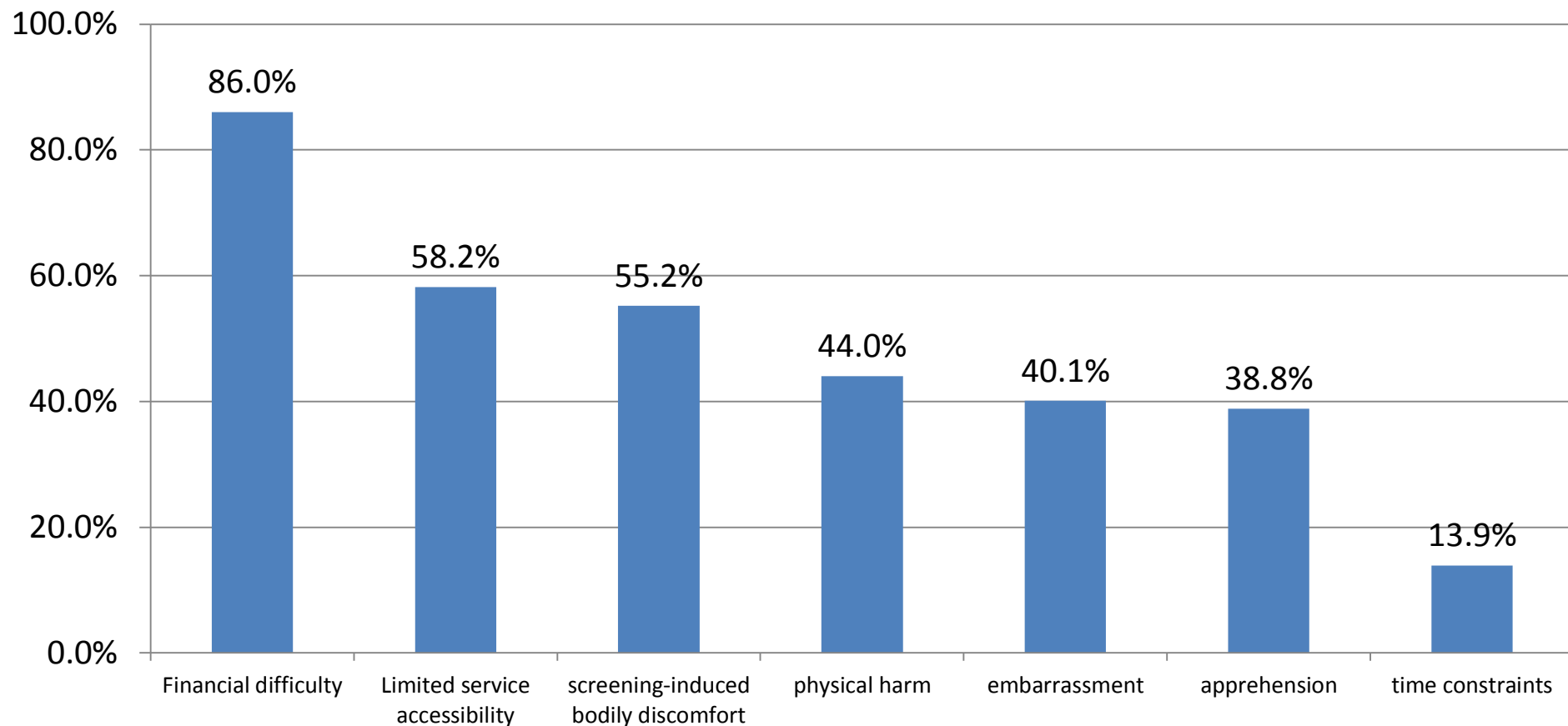
**Factors associated with CRC screening uptake:**

- physician's recommendation (aOR 23.50, 95% CI 10.66–51.80)



# Perceived Obstacles of Colorectal Cancer Screening and Their Associated Factors among 10,078 Chinese Participants

Martin C. S. Wong<sup>1,2\*</sup>, Jessica Y. L. Ching<sup>1</sup>, Hoyee H. Hirai<sup>1</sup>, Thomas Y. T. Lam<sup>1</sup>, Sian M. Griffiths<sup>2</sup>, Francis K. L. Chan<sup>1</sup>, Joseph J. Y. Sung<sup>1</sup>



## A comparison of the acceptance of immunochemical faecal occult blood test and colonoscopy in colorectal cancer screening: a prospective study among Chinese

M. C. S. Wong<sup>\*</sup>, K. K. F. Tsoi<sup>†</sup>, S. S. M. Ng<sup>†</sup>, V. W. Q. Lou<sup>‡</sup>, S. Y. P. Choi<sup>§</sup>, K. W. K. Ling<sup>†</sup>, F. K. L. Chan<sup>†</sup>, S. M. Griffiths<sup>\*</sup> & J. J. Y. Sung<sup>†</sup>

Colonoscopy vs. FIT = roughly equal preference  
**higher odds of choosing colonoscopy:**

Family history of CRC

self-perception of CRC risk

older age

married

positive perception of CRC screening

# Family doctors holds the key to success of a CRC screening program

|   | Bivariate LR |                  | Mutiple LR  |                  |
|---|--------------|------------------|-------------|------------------|
|   | aOR          | 95%CI            | aOR         | 95%CI            |
| Female  | 1.08         | 0.71-1.64        |             |                  |
| Age>50  | 1.94         | 1.28-2.94        |             |                  |
| Education: 1 <sup>o</sup> vs 2 <sup>o</sup> vs 3 <sup>o</sup> | 0.97         | 0.52-1.81        |             |                  |
| Income  | 1.31         | 0.78-2.16        |             |                  |
| Knowledge of CRC  | 2.66         | 1.40-5.05        | 2.22        | 1.22-9.11        |
| Knowledge of Screening  | 6.27         | 2.48-15.8        |             |                  |
| Perceived access  | 0.08         | 0.03-0.27        | 0.22        | 0.06-0.85        |
| Health insurance  | 1.45         | 0.95-2.22        | 2.06        | 1.01-4.19        |
| <b>Doctor's recommend</b>                                     | <b>21.8</b>  | <b>12.9-36.7</b> | <b>23.5</b> | <b>10.6-51.9</b> |



# Summary of the current issues

Low referral rates for CRC screening by physicians

Low level of knowledge

Enrolled participants uncertain of actual screening

Differential interest in different options

Compliance with screening declined over time

Especially with no screening choice

# Services 公共服務



# Multitarget stool DNA testing for CRC screening

## 多種目標大便DNA檢查(N=9,989)

Imperiale et al. NEJM 2014

Alquist et al. Gastroenterology 2012

### Good news

**Stool DNA has higher sensitivity than FIT for:**

- CRC (92 vs 74%)
- Advanced precancerous lesions (42% vs 23%)
- Serrated sessile lesions 1cm (42% vs 5%)

**The test is equally sensitive for right or left colonic lesions**

**此檢查對腸道不同位置有同等敏感度**

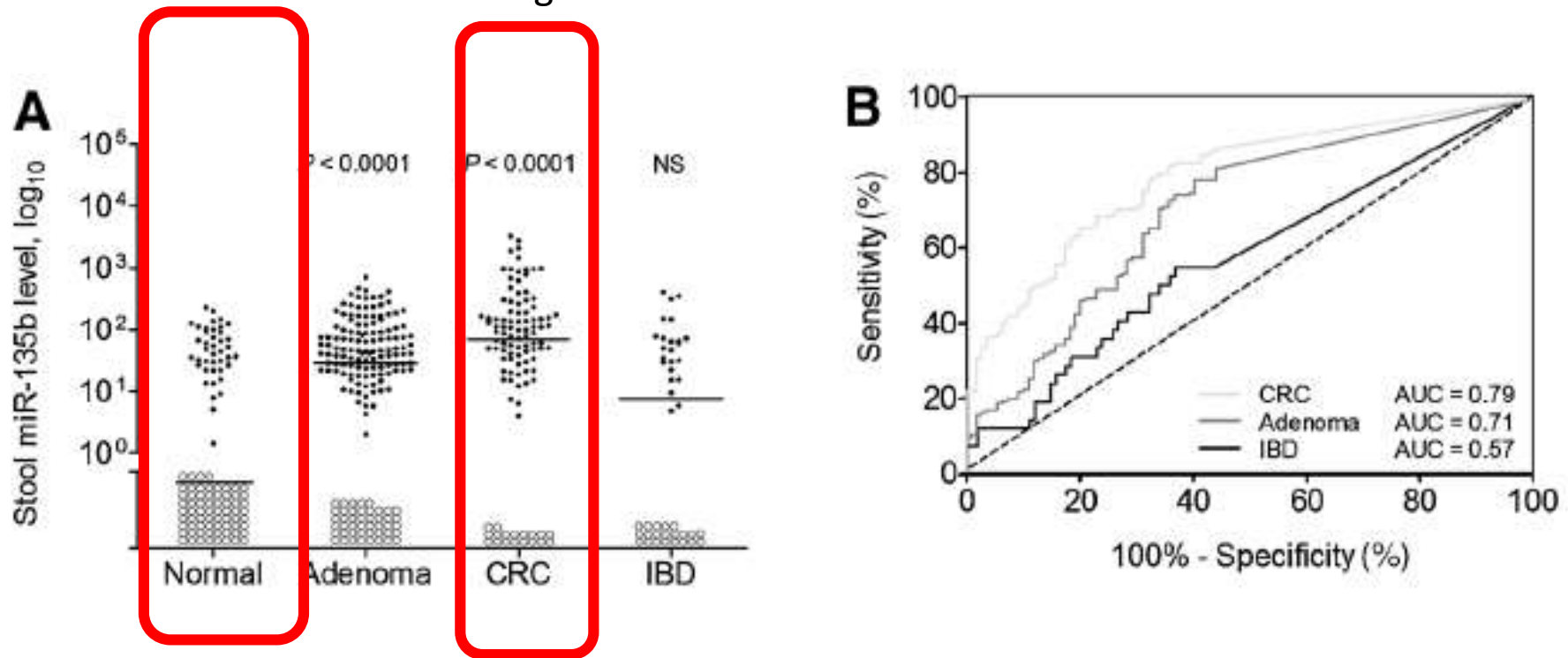


# MicroRNA 135b is a non-invasive fecal marker for CRC and adenoma

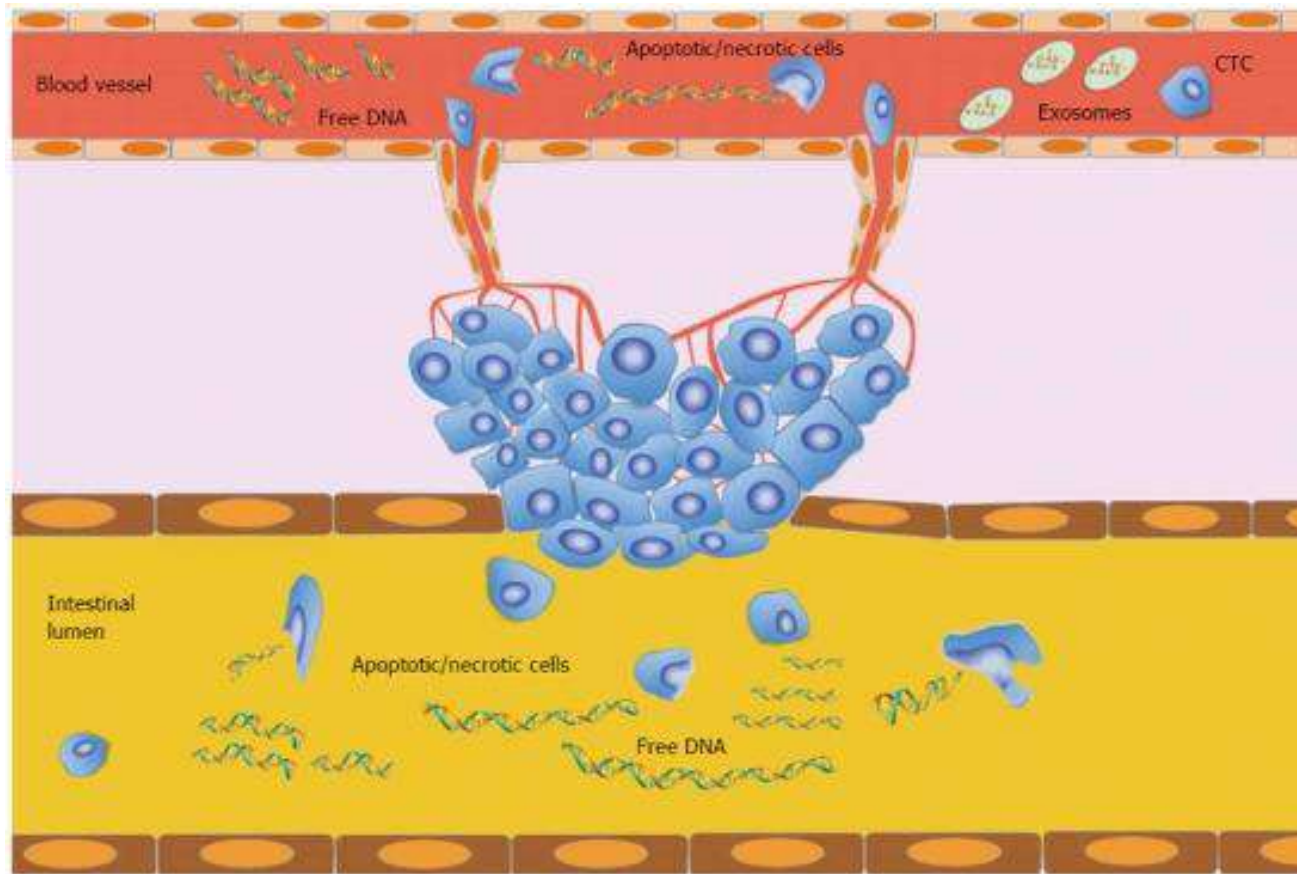
## 非侵入性的大便檢查

Ng SC et al. Clin Cancer Res 2014

Ng SC et al. Br Med Bull 2013



# The Future: Circulating free DNA The Principle works but it need confirmation in CRC diagnosis





# An updated Asia Pacific Consensus Recommendations on colorectal cancer screening

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J Y W Lau,<sup>6</sup> S Zheng,<sup>7</sup> S Adler,<sup>8</sup> N Reddy,<sup>9</sup> K G Yeoh,<sup>10</sup> K K F Tsoi,<sup>11</sup> J Y L Ching,<sup>2</sup>  
E J Kuipers,<sup>12</sup> L Rabeneck,<sup>13</sup> G P Young,<sup>14</sup> R J Steele,<sup>15</sup> D Lieberman,<sup>16</sup> K L Goh<sup>17</sup>

## **What are the new findings?**

In this updated Asia Pacific consensus recommendations:

- ▶ Age range for CRC screening is defined as 50–75 years.
- ▶ A risk-stratified scoring system is recommended to select high-risk patients for early colonoscopy.
- ▶ Quantitative FIT, but not gFOBT, is preferred for average-risk subjects.
- ▶ Quality control measures should be included in CRC screening programmes.

# The future is bright for CRC Screening





# Thank You!

