In What Asia-Pacific Populations is CRC Screening Justified?

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Chairman, National Colorectal Screening Programme, Ministry of Health, Singapore.
Outline

- CRC in the Asia-Pacific
- In which populations is screening justified?
- Risk-based algorithms for lower incidence countries
- Conclusion
Outline

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- Risk-based algorithms for lower incidence countries
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Colorectal Cancer Incidence in the Asia-Pacific

• 4th most common cancer in Asia, 600,000 new cases in 2012.
• ~300,000 deaths annually
• Wide variation in incidence
• More in developed regions
Burden of Colorectal Cancer in the Asia-Pacific


CRC incidence is increasing in many Asia-Pacific countries

- Aging population
- Change of life style, food
- Smoking
- Obesity

IARC, CI5plus
Burden of Colorectal Cancer in the Asia-Pacific

Top 20 in the world

- 5 countries from Asia-Pacific are among the top 20 highest incidence rates in the world.
Future Burden of CRC in Asia: Prediction by Globocan

- Incidence:
  - 2012: 600,000
  - 2035: 1,150,000

- Mortality:
  - 2012: 330,000
  - 2035: 320,000
Ratio of CRC Mortality to Incidence (M:I)

GLOBOCAN 2012 (IARC)
Screening reduces incidence & mortality

Decline in CRC incidence and mortality in the US.

Reasons
1. Effect of increased screening
2. Reduction of risk factors
3. Improved treatment

Cancer 2010;116:544–73

Siegel et al, CA Cancer J Clin. 2014; 64(2):104-17
Risk Factors for CRC

- Age
- Gender
- Ethnicity
- Smoking
- Heavy alcohol consumption
- Diet
- Obesity

- Personal or family hx of CRC, polyps
- Genetic syndromes (FAP, Lynch)
- Inflammable bowel disease (Crohn’s disease, or ulcerative colitis)
Risk Factors for CRC –
Red meat and processed meat

Carcinogenic for CRC recognized by IARC:
- Processed meat, Group
- Red meat, Group 2A

IARC Monographs evaluate consumption of red meat and processed meat

Lyon, France, 26 October 2015 – The International Agency for Research on Cancer (IARC), the cancer agency of the World Health Organization, has evaluated the carcinogenicity of the consumption of red meat and processed meat.

Red meat
After thoroughly reviewing the accumulated scientific literature, a Working Group of 22 experts from 10 countries convened by the IARC Monographs Programme classified the consumption of red meat as probably carcinogenic to humans (Group 2A), based on limited evidence that the consumption of red meat causes cancer in humans and strong mechanistic evidence supporting a carcinogenic effect.

This association was observed mainly for colorectal cancer, but associations were also seen for pancreatic cancer and prostate cancer.

Processed meat
Processed meat was classified as carcinogenic to humans (Group 1), based on sufficient evidence in humans that the consumption of processed meat causes colorectal cancer.
# Risk Factors for CRC – Ethnicity

## TABLE 4. Risk factors for colorectal neoplasm

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>1.5 (1.1-2.2)</td>
<td>0.019</td>
</tr>
<tr>
<td>Age</td>
<td>1.05 (1.03-1.07)</td>
<td>0.001</td>
</tr>
<tr>
<td>Family History</td>
<td>2.5 (1.5-4.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Chinese</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Japanese</td>
<td>4.2 (1.3—13.9)</td>
<td>0.019</td>
</tr>
<tr>
<td>Korean</td>
<td>2.0 (1.3-2.9)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Byeon JS et al., Colorectal neoplasm in asymptomatic Asians: a prospective multinational multicenter colonoscopy survey, Gastrointest Endosc, 2007 Jun;65(7):1015-22
Risk Factors for CRC – Ethnicity

- Chinese has the highest incidence of CRC compared with Malay and Indian in same environment in Singapore

<table>
<thead>
<tr>
<th>Ethnic Group</th>
<th>No.</th>
<th>CIR (95%CI)</th>
<th>ASIR (95%CI)</th>
<th>RR (95%CI)</th>
<th>RR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese</td>
<td>8,070</td>
<td>57.0 (55.7-58.2)</td>
<td>34.1 (33.3-34.8)</td>
<td>2.11 (2.34- 1.93)</td>
<td>1.31 (1.38 – 1.24)</td>
</tr>
<tr>
<td>Malay</td>
<td>776</td>
<td>30.4 (28.3-32.6)</td>
<td>26.1 (24.2-28.0)</td>
<td>-</td>
<td>Reference</td>
</tr>
<tr>
<td>Indian</td>
<td>307</td>
<td>17.5 (15.6-19.5)</td>
<td>16.1 (14.2-18.0)</td>
<td>Reference</td>
<td>-</td>
</tr>
<tr>
<td>Others</td>
<td>171</td>
<td>27.1 (23.1-31.2)</td>
<td>32.9 (27.5-38.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>All</td>
<td>9324</td>
<td>48.8 (47.8-49.8)</td>
<td>32.1 (31.5-32.8)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Crude and Age-standardised Incidence Rate for CRC by Ethnic Group in Singapore (2010-2014)

Singapore Cancer Registry, Trends in Cancer Incidence in Singapore 2010-2014
Risk Factors for CRC

Statement 2: There are ethnic differences in CRC risk and screening programme should take this into account.

<table>
<thead>
<tr>
<th>Accept completely (%)</th>
<th>Accept with some reservation (%)</th>
<th>Accept with major reservation (%)</th>
<th>Reject with reservation (%)</th>
<th>Reject completely (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>69.4%</td>
<td>27.8%</td>
<td>2.8%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Quality of Evidence: II-3
Classification of Recommendations: B

### SSA in Asian Population

**The Presence of Large Serrated Polyps Increases Risk for Colorectal Cancer**

Sakiko Hiraoka et al, Gastroenterology 2010;139:1503–1510

<table>
<thead>
<tr>
<th></th>
<th>Subjects w/o advanced neoplasia (n =8626)</th>
<th>Subjects with advanced neoplasia (n =1573)</th>
<th>Univariate analysis, OR (95% CI)</th>
<th>Multivariate analysis, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of small adenomas</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3</td>
<td>8537</td>
<td>1470</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>≥4</td>
<td>89</td>
<td>103</td>
<td>6.72 (5.03-8.97)</td>
<td>5.12 (3.80-6.88)</td>
</tr>
<tr>
<td>Large sessile polyps</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>8548</td>
<td>1511</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>78</td>
<td>62</td>
<td>4.50 (3.21-6.30)</td>
<td>4.01 (2.83-5.69)</td>
</tr>
</tbody>
</table>
Outline

- CRC in the Asia-Pacific
- In which populations is screening justified?
- Risk-based algorithms for lower incidence countries
- Conclusion
Asia Pacific Working Group for Colorectal Ca

An updated Asia Pacific Consensus Recommendations on colorectal cancer screening

- Modified Delphi process ((literature review, individual statement review, consensus meeting, voting and final consensus statement)
- Vote based on review of the literature on a Likert scale anchored by 1–5
- Consensus was achieved when >80% of the voting members indicated ‘accept completely’ or ‘accept with some reservation’
- Hong Kong, 9 - 10 June 2013
- Key opinion leaders, 14 countries
2015 Asia Pacific Consensus Recommendations for CRC screening


- Age range for CRC screening is defined as 50–75 years.
- Quantitative FIT, but not gFOBT, is preferred for average-risk subjects.
- A risk-stratified scoring system is recommended to select high-risk patients for early colonoscopy.
- Quality control measures should be included in CRC screening programmes.
Statement 1: Population screening for CRC is recommended in those Asia-Pacific regions where the incidence of CRC is high. In both genders, subjects aged 50 to 75 years are the target for CRC screening.

Level of agreement: A 69.4%, B=30.6%, C=0%, D=0%, E=0%.

Quality of evidence: II-2

Classification of recommendation: B

Statement 1: Population screening for CRC is recommended in those Asia-Pacific regions where the incidence of CRC is high.
Colorectal Cancer Incidence

Source: GLOBOCAN 2012 (IARC)
**Statement 1**: Population screening for CRC is recommended in those Asia-Pacific regions where the incidence of CRC is **high**.
Cost-Effectiveness of CRC Screening

Cost-effectiveness of Screening is related to the Incidence (ASR) of CRC

Cost-effectiveness analysis:

- ASR for CRC > 21/100,000, any screening modality is cost-effective.
- ASR for CRC < 14/100,000, FIT is not cost-effective.
- ASR for CRC < 21.7/100,000, colonoscopy once in 10 years is not cost-effective (ICER > USD 50,000/ QALY)
- When cost of colonoscopy < USD300, colonoscopy is the most cost-effective option.

### Population Risk for CRC & Cost Effectiveness

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>ASR (W)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korea</td>
<td>45.0</td>
</tr>
<tr>
<td>Taiwan</td>
<td>43.8</td>
</tr>
<tr>
<td>Australia/ NZ</td>
<td>38.2</td>
</tr>
<tr>
<td>Singapore</td>
<td>33.7</td>
</tr>
<tr>
<td>Japan</td>
<td>32.2</td>
</tr>
<tr>
<td>Brunei</td>
<td>25.0</td>
</tr>
<tr>
<td>Malaysia</td>
<td>18.3</td>
</tr>
<tr>
<td>China</td>
<td>14.2</td>
</tr>
<tr>
<td>Philippines</td>
<td>13.1</td>
</tr>
<tr>
<td>Indonesia</td>
<td>12.8</td>
</tr>
<tr>
<td>Thailand</td>
<td>12.4</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>10.1</td>
</tr>
<tr>
<td>India</td>
<td>6.1</td>
</tr>
<tr>
<td>Mongolia</td>
<td>6.0</td>
</tr>
<tr>
<td>Pakistan</td>
<td>4.0</td>
</tr>
</tbody>
</table>

- **ASR > 21**: any modality is cost-effective
- **ASR < 14**: FIT is **not** cost-effective

Dan YY, Yeoh KG. Screening based on risk for colorectal cancer is the most cost-effective approach. Clin Gastroenterol Hepatol 2012; 10(3):266-71.

Source: GLOBOCAN 2012, IARC; Taiwan Cancer Registry, 2011
Burden of Health in Developing Countries

- CRC incidence is low in developing countries
- Communicable disease has heavier weight as the cause of death compared with cancer
- Among cancers, CRC is less common compared to liver and cervical cancer

Outline

- CRC in the Asia-Pacific
- In which populations is screening justified?
- Risk-based algorithms for lower incidence countries
- Conclusion
Statement 4: The Asia Pacific Risk Score is useful to identify subjects with a high risk of colorectal advanced neoplasia

Level of agreement: A= 55.6%, B=38.9%, C=5.5%, D=0%, E=0%
Quality of evidence: II-2
Classification of recommendation: B
Asia Pac Risk Score (APCS) Identifies High Risk Group

Risk Stratification Tool

Gut 2011; 60(9):1236-41

The Asia-Pacific Colorectal Screening score: a validated tool that stratifies risk for colorectal advanced neoplasia in asymptomatic Asian subjects

Khay-Guan Yeoh,1 Khek-Yu Ho,1 Han-Mo Chiu,2 Feng Zhu,1 Jessica Y L Ching,3 Deng-Chyang Wu,4 Takahisa Matsuda,5 Jeong-Sik Byeon,6 Sang-Kil Lee,7 Khean-Lee Goh,8 Jose Sollano,9 Runsun Rerknimitr,10 Rupert Leong,11 Kelvin Tsoi,3 Jaw-Town Lin,2 Joseph J Y Sung,3 for the Asia-Pacific Working Group on Colorectal Cancer

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>50-69</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>≥70 yrs</td>
<td>3</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>1</td>
</tr>
<tr>
<td>Family History</td>
<td>1st degree</td>
<td>2</td>
</tr>
<tr>
<td>Smoking</td>
<td>Current / Ex</td>
<td>1</td>
</tr>
</tbody>
</table>

Score 0 to 7
### Prevalence and relative risk of colorectal adv neoplasia by Risk score

<table>
<thead>
<tr>
<th>Risk Tier</th>
<th>Risk Score</th>
<th>No. of subjects (%</th>
<th>Colorectal Adv neoplasm (%)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>0 – 1</td>
<td>559 (29.5)</td>
<td>7 (1.3)</td>
<td>Reference</td>
</tr>
<tr>
<td>Intermediate</td>
<td>2 – 3</td>
<td>966 (51.1)</td>
<td>31 (3.2)</td>
<td>2.6 (1.1-6.0)</td>
</tr>
<tr>
<td>High risk</td>
<td>4 – 7</td>
<td>367 (19.4)</td>
<td>19 (5.2)</td>
<td>4.3 (1.8-10.3)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1892 (100)</td>
<td>57 (3.0)</td>
<td></td>
</tr>
</tbody>
</table>

The high risk group has 4.3 x more advanced neoplasm vs low-risk group.

Gut 2011; 60(9):1236-41
Countries with a low incidence rate for CRC

- **ASR > 21**: any modality is cost-effective
- **ASR > 14**: FIT is cost-effective

References:
- Ferlay et al, GLOBOCAN 2002, IARC Cancerbase 2.0, 2004
- Dan et al, Clin Gastroenterol Hepatol 2012
Using APCS Risk Score to Select High Risk Individuals, in countries with low incidence.

- Using the APCS risk score, the high risk group has 4x risk vs AR.
- absolute risk
- individualise management according to risk.

ASR > 21 any modality is cost-effective

ASR > 14 FIT is cost-effective
### Prevalence and relative risk of colorectal adv neoplasia by Risk score

<table>
<thead>
<tr>
<th>Risk Tier</th>
<th>Risk Score</th>
<th>No. of subjects (%)</th>
<th>Colorectal Adv neoplasm (%)</th>
<th>RR (95% CI)</th>
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</table>

The high risk group has 4.3 x more advanced neoplasm vs low-risk group.

Gut 2011; 60(9):1236-41
Guidance Statement 1: ACP recommends that clinicians perform individualized assessment of risk for colorectal cancer in all adults.

Guidance Statement 2: ACP recommends that clinicians screen for colorectal cancer in average-risk adults starting at the age of 50 years and in high-risk adults starting at the age of 40 years or 10 years younger than the age at which the youngest affected relative was diagnosed with colorectal cancer.

Guidance Statement 3: ACP recommends using a stool-based test, flexible sigmoidoscopy, or optical colonoscopy as a screening test in patients who are at average risk. **ACP recommends using optical colonoscopy as a screening test in patients who are at high risk.** Clinicians should select the test based on the benefits and harms of the screening test, availability of the screening test, and patient preferences.

Guidance Statement 4: ACP recommends that clinicians stop screening for colorectal cancer in adults over the age of 75 years or in adults with a life expectancy of less than 10 years.
Asia Pacific CRC Screening Score (APCS)

- Include important risk factors in the population
- Able to differentiate risk groups
- Easy to use
- Can be replicated

**APCS score**
- Age
- Gender
- Family Hx
- Smoking
- BMI
Modified APCS risk score

Modified Asia-Pacific Colorectal Screening (APCS) Score to Stratify Risk for Colorectal Advanced Neoplasia in Asymptomatic Population in Asian subjects

Joseph J. Y. Sung, Martin C. Wong, Kelvin K. Tsoi

<table>
<thead>
<tr>
<th>Risk category</th>
<th>No. of subjects (%)</th>
<th>Colorectal Adv neoplasm (%)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk (0)</td>
<td>110 (2.0)</td>
<td>1 (0.9)</td>
<td>1.00</td>
</tr>
<tr>
<td>Intermediate (1-3)</td>
<td>4148 (75.9)</td>
<td>169 (4.1)</td>
<td>4.48 (0.63-31.7)</td>
</tr>
<tr>
<td>High risk (4-6)</td>
<td>1205 (22.1)</td>
<td>126 (10.5)</td>
<td>11.5 (1.62-81.5)</td>
</tr>
<tr>
<td>Total</td>
<td>5463 (100)</td>
<td>296 (5.4)</td>
<td></td>
</tr>
</tbody>
</table>

# Scoring Systems Published Recently

<table>
<thead>
<tr>
<th>Study, Yr</th>
<th>Population</th>
<th>Risk Factors</th>
<th>Scores</th>
<th>Risk for Adv Neo</th>
<th>% of adv neo (100%)</th>
</tr>
</thead>
</table>
| Yeoh et al, 2011 | Asian 860 1892 | Age, sex, first-degree relative with CRC, Smoking (4) | 0 - 7  
0, 1 = average  
2, 3 = moderate  
3 to 7 = high | 1.3%  
4.4%  
7.9% | 12%  
55%  
33% |
| Cai et al. 2012  | Chinese 5229 2312 | Age,sex,diabetes,smoking,green vegetables, pickled food, fried food, white meat (7) | 0 - 13  
0 to 3 = low  
>3 = high | 2.6%  
10.2% | 20%  
80% |
| Tao et al, 2014  | German 7891 3519 | Age, sex, FHx,smoking, ethanol,NSAID use, prior colono, polyp history, red meat consumption (8) | Risk quintiles: very low, low, Intermediate, high, very high | 4.9%, 9.2%, 10.1%, 14.6%, 18.9% | 10%  
18%  
20%  
25%  
27% |
| Kaminski et al, 2014 | Poland 17979 17939 | Age, sex, FHx, smoking, BMI (5) | 0 – 8  
0 = low  
7-8 = high | 1.32%  
19.1% | 0.2%  
2% |
| Kim et al, 2015  | Korean 3561 1316 | Age, sex, first-degree relative with CRC, smoking, BMI (5 ) | 0 – 8  
0, 1 = average  
2, 3 = moderate  
3 to 8 = high | 2.0%  
3.7%  
10.9% | 14%  
46%  
40% |
| Imperiale et al, 2015 | US, 94% white 2993 1467 | Age, sex, first-degree relative with CRC, smoking, waist circumference (5) | 0 - 12  
0 = very low  
1 to 3 = low  
4 to 6 = intermediate  
>6 = high risk | 1.7%  
3.3%  
11%  
22% | 2%  
18%  
41%  
39% |
Other Risk Scores


- Caucasian population in US, split-sample validation
- Five risk factors with 0-12 points
- Four risk categories with highest risk of 22% of advanced neoplasia, compared with lowest one of 1.7%
- Use different screening method in different risk categories
- Save resources
Outline

- CRC in the Asia-Pacific
- In which populations is screening justified?
- Risk-based algorithms for lower incidence countries
- Conclusion
Conclusions (1)

1. CRC screening unequivocally improves survival and reduces mortality from colorectal cancer. (Saquib et al. Int. J. Epidemiol 2015: 44 (1): 264-277)


   - Age range for CRC screening is defined as 50–75 years.
   - Quantitative FIT, but not gFOBT, is preferred for average-risk subjects.
   - A risk-stratified scoring system is recommended to select high-risk patients for early colonoscopy.
Conclusions (2)

4. **In What Asia-Pacific Populations is CRC Screening Justified?**

   Population screening is recommended for communities where the incidence of CRC is high. *(Sung JJY, et al. Gut 2015)*

5. In countries with low incidence of CRC, where population screening is not cost-effective, a risk-based algorithm may be helpful on identifying high-risk individuals for screening.

6. The Asia Pacific CRC Risk Score (APCS) is useful in identifying subjects with a high risk of colorectal advanced neoplasia. *(Gut 2015)*
Conclusions (3)

7. The Asia Pacific CRC Risk Score (APCS) enables an individualized assessment of risk for advanced neoplasia, it is simple & easy to use, and modelling suggests this approach is cost-effective.

• In low incidence countries, it can be used to identify high-risk individuals for screening.

• In high incidence countries, prioritise high risk individuals for colonoscopy (Gastroenterol 2015, in press).
## Population Risk for CRC & Cost Effectiveness

<table>
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<tr>
<th>COUNTRY</th>
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<td>Pakistan</td>
<td>4.0</td>
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</tbody>
</table>

Source: GLOBOCAN 2012, IARC; Taiwan Cancer Registry, 2011

#### ASR > 21
- any modality is cost-effective
- Population screening by FIT.
- Colonoscopy for high-risk.

#### ASR < 14
- Population screening not cost-effective.
- High-risk groups can be screened.

FIT is cost-effective
Using APCS to select HR group for Early Colonoscopy

A Risk-scoring System Combined with a Fecal Immunochemical Test Is Effective in Screening High-risk Subjects for Early Colonoscopy to Detect Advanced Colorectal Neoplasms

Han-Mo Chiu, MD, Jessica YL. Ching, MPH, Kai Chun Wu, MD, Rungsun Rerknimitr, MD, Jingnan Li, MD, Deng-Chiang Wu, MD, Khean Lee Goh, MD, Takahisa Matsuda, MD, Hyun-Soo Kim, MD, Rupert Leong, MD, Khay Guan Yeoh, MD, Vui Heng Chong, MD, Jose D. Sollano, MD, Furqaan Ahmed, MD, Jayaram Menon, MD, Joseph JY. Sung, MD for the Asia-Pacific Working Group on Colorectal Cancer

• Total 5657 subject from 12 AP regions

• LR, MR – FIT while HR – early colonoscopy

• Advanced neoplasia in LR, MR and HR were 1.5%, 5.1% and 10.9% respectively

• 70.6% of advanced neoplasia were in HR and asked to go for early colonoscopy

• Use of the APCS score-based algorithm in triaging subjects for FIT or colonoscopy can substantially reduce colonoscopy workload