Press Briefing: Tuesday, 31 October, 2017

Reducing the Incidence of Digestive Cancers

Introduction from the UEG Vice-President:
Paul Fockens

Long-term use of aspirin in reducing the incidence of digestive cancers
Kelvin Tsoi

Benefits of H. Pylori eradication in preventing gastric cancer in the older population
Wai K Leung

Questions and Close:
Paul Fockens
Long-term use of aspirin in reducing the incidence of digestive cancers

Kelvin Tsoi
Stanley Ho Big Data Decision Analytics Research Centre
Jockey Club School of Public Health and Primary Care
The Chinese University of Hong Kong

Felix Chan, Hoyee Hirai, Joseph Sung
The global cancer burden

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Male Cancers</th>
<th>Female Cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7,410,376</td>
<td>6,657,518</td>
</tr>
<tr>
<td>Lung</td>
<td>1,241,601</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>1,094,916</td>
<td></td>
</tr>
<tr>
<td>Colorectum</td>
<td>746,298</td>
<td>614,304</td>
</tr>
<tr>
<td>Stomach</td>
<td>631,293</td>
<td>320,301</td>
</tr>
<tr>
<td>Liver</td>
<td>554,369</td>
<td>583,100</td>
</tr>
<tr>
<td>Bladder</td>
<td>330,380</td>
<td></td>
</tr>
<tr>
<td>Oesophagus</td>
<td>323,008</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>213,924</td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>217,643</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>2,056,944</td>
<td>1,924,711</td>
</tr>
<tr>
<td>Digestive cancer</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

WHO GLOBOCAN 2012 (IARC)
Cancer prevention

- Healthy lifestyle:
  - No smoking
  - Healthy diet
  - Regular exercise
  - Low consumption of alcohol

- Regular screening

- Chemoprevention?
  - Aspirin?
Aspirin and NSAID* for cancer prevention

*non-steroidal anti-inflammatory drugs

“Aspirin might eventually be useful for the primary prevention of some cancers in patients who already qualify for prophylactic antiplatelet therapy…”

“Aspirin or other NSAIDs might also prove effective for secondary chemoprevention of gastrointestinal cancers in patients with no antecedent risk of gastrointestinal bleeding...”

Aspirin and colorectal cancer prevention

“USPSTF recommends initiating low-dose aspirin use for the primary prevention of CVD and CRC in aged 50 - 59 years...”
Aspirin and cancer risk

Original Investigation
Population-wide Impact of Long-term Use of Aspirin and the Risk for Cancer
Yin Cao, MPH, ScD; Reiko Nishihara, PhD; Kana Wu, MD, PhD; Molin Wang, PhD; Shuji Ogino, MD, PhD; Walter C. Willett, MD, DrPH; Donna Spiegelman, ScD; Charles S. Fuchs, MD, MPH; Edward L. Giovannucci, MD, MPH, ScD; Andrew T. Chan, MD, MPH

❖ Nurses’ Health Study (1980-2010) + Health Professionals Follow-up Study (1986-2012)

❖ 135 965 health care professionals
  ❖ 88,084 women
  ❖ 47,881 men

Regular Aspirin Users
Aspirin use at least 2 times per week, including standard and low dose

Non-regular Users
Aspirin use fewer than 2 times per week or used no aspirin

Use of aspirin for cancer incidences

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Regular User/Nonregular User</th>
<th>All Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td>All</td>
<td>8962/11 452</td>
<td>3748/3823</td>
</tr>
<tr>
<td>GI tract cancer</td>
<td>972/1404</td>
<td>889/1028</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>688/1040</td>
<td>511/656</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>124/154</td>
<td>162/167</td>
</tr>
<tr>
<td>Gastroesophageal cancer</td>
<td>61/109</td>
<td>142/138</td>
</tr>
<tr>
<td>Other GI tract cancer</td>
<td>99/101</td>
<td>72/67</td>
</tr>
<tr>
<td>Non-GI tract cancer</td>
<td>7 990/10 048</td>
<td>2 859/2 795</td>
</tr>
</tbody>
</table>

GI tract cancers: reduce 15%
Colorectal cancer: reduce 19%
Pancreatic cancer: insignificant
Gastroesophageal cancer: Reduce 29% (women only)
Other GI cancers: insignificant
Non-GI cancers: insignificant

Aim

To investigate whether long-term use of aspirin would reduce the incidences of common cancers

**Digestive Cancers**
- Colorectal Cancer
- Gastric Cancer
- Liver Cancer
- Oesophageal Cancer
- Pancreatic Cancer

**Non-digestive Cancers**
- Breast Cancer
- Bladder Cancer
- Kidney Cancer
- Leukaemia
- Lung Cancer
- Multiple Myeloma
- Prostate Cancer
Data Source

❖ The Hospital Authority (HA):
  ❖ Responsible for managing Hong Kong’s public hospital services since December 1991
  ❖ Covers 90% of local healthcare services:
    ❖ 42 hospitals and institutions
    ❖ 47 specialist out-patient clinics
    ❖ 73 general out-patient clinics
    ❖ 27,895 beds
    ❖ 75,000 staff

Population-based retrospective cohort study

Aspirin users: A cohort of patients who were prescribed aspirin between 2000 and 2004 were extracted from the electronic medical records and follow-up was undertaken until 2013

Non-aspirin users: The patients from the aspirin group were 1:2 age-sex matched – those who did not receive aspirin between 2000 and 2004

Exclusion criteria: Aspirin used or survival time <6 months
Outcomes & Statistical Analysis

The primary and secondary outcomes were the cancer incidences of the following cancers:

**Digestive Cancers**
- Colorectal Cancer (ICD 10: C18-C21)
- Gastric Cancer (ICD 10: C16)
- Liver Cancer (ICD 10: C22)
- Oesophageal Cancer (ICD 10: C15)
- Pancreatic Cancer (ICD 10: C25)

**Non-digestive Cancers**
- Breast Cancer (ICD 10: C50)
- Bladder Cancer (ICD 10: C67)
- Kidney Cancer (ICD 10: C64-C66, C68)
- Leukaemia (ICD 10: C91-95)
- Lung Cancer (ICD 10: C33-34)
- Multiple Myeloma (ICD 10: C88-C90)
- Prostate Cancer (ICD 10: C61)

❖ **Odds ratio (OR)** – for comparing the effect of aspirin on cancer incidences

❖ **Cumulative incidence function** – to present the different of cancer incidence rate by aspirin and non-aspirin use regarding the follow-up time
Patient Selection

Total number of patients between 2000 and 2004 (n = 4,564,100)

Patients prescribed Aspirin between 2000 and 2004 (n = 254,887)

Aspirin Group (n = 206,295)

Duration of Aspirin Prescribed less than 6 months (n = 48,592)

Median: 80mg/day

Non-Aspirin Group (n = 412,589)

Patients who never prescribed Aspirin between 2000 and 2013

1:2 matching with age, sex, and survival time on the duration of aspirin used

Demographics

<table>
<thead>
<tr>
<th>Age</th>
<th>Aspirin Group (n=206,295)</th>
<th>Non-Aspirin Group (n=412,589)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>17,653 (8.56%)</td>
<td>35,306 (8.56%)</td>
</tr>
<tr>
<td>50-64</td>
<td>54,287 (26.32%)</td>
<td>108,574 (26.32%)</td>
</tr>
<tr>
<td>65-79</td>
<td>103,797 (50.31%)</td>
<td>208,904 (50.42%)</td>
</tr>
<tr>
<td>&gt;=80</td>
<td>30,558 (14.81%)</td>
<td>60,663 (14.70%)</td>
</tr>
</tbody>
</table>

Duration of Aspirin Prescribed

<table>
<thead>
<tr>
<th>Duration</th>
<th>Aspirin Group</th>
<th>Non-Aspirin Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months - &lt; 3 years</td>
<td>44,515 (21.58%)</td>
<td>--</td>
</tr>
<tr>
<td>3 years - &lt; 5 years</td>
<td>23,437 (11.36%)</td>
<td>--</td>
</tr>
<tr>
<td>5 years - &lt; 10 years</td>
<td>60,027 (29.10%)</td>
<td>--</td>
</tr>
<tr>
<td>10 years or more</td>
<td>78,316 (37.96%)</td>
<td>--</td>
</tr>
</tbody>
</table>
Digestive cancers – colorectal cancer

Aspirin reduced incidence

OR: 0.76 (0.73 - 0.78)

Aspirin:
5,118 (2.48%)

Non-aspirin:
13,382 (3.24%)
Digestive cancers – liver and oesophageal cancer

Liver Cancer

Non-aspirin: 7,438 (1.80%)
Aspirin: 1,995 (0.97%)

OR: 0.53 (0.51 - 0.56)
Aspirin reduced incidence

Oesophagus Cancer

Non-aspirin: 2,097 (0.51%)
Aspirin: 561 (0.27%)

OR: 0.53 (0.49 - 0.59)
Aspirin reduced incidence
Digestive cancers – pancreatic and gastric cancer

Pancreas Cancer
- Aspirin: 691 (0.33%)
- Non-aspirin: 2,105 (0.51%)

Gastric Cancer
- Aspirin: 1,388 (0.67%)
- Non-aspirin: 4,489 (1.09%)

OR: 0.66 (0.60 - 0.71)
Aspirin reduced incidence

OR: 0.62 (0.58 - 0.65)
Aspirin reduced incidence
Non-digestive cancers – reduction in incidence

Lung Cancer

Non-aspirin: 18,951 (4.59%)
Aspirin: 6,220 (3.02%)
OR: 0.65 (0.63 - 0.66)
Aspirin reduced incidence

Prostate Cancer

Non-aspirin: 4,767 (1.16%)
Aspirin: 2,062 (1.00%)
OR: 0.86 (0.82 - 0.91)
Aspirin reduced incidence

Leukaemia

Non-aspirin: 1,285 (0.31%)
Aspirin: 487 (0.24%)
OR: 0.76 (0.68 - 0.84)
Aspirin reduced incidence
Non-digestive cancers – no reduction in incidence

Breast Cancer

Non-aspirin: 3,113 (0.75%)
Aspirin: 1,492 (0.72%)
OR: 0.96 (0.90 - 1.02)
Aspirin could NOT REDUCE incidence

Bladder Cancer

Non-aspirin: 3,597 (0.87%)
Aspirin: 1,744 (0.85%)
OR: 0.97 (0.92 - 1.03)
Aspirin could NOT REDUCE incidence

Kidney Cancer

Aspirin: 755 (0.37%)
Non-aspirin: 1,454 (0.35%)
OR: 1.04 (0.95 - 1.13)
Aspirin could NOT REDUCE incidence

Multiple Myeloma

Non-aspirin: 1,101 (0.27%)
Aspirin: 493 (0.24%)
OR: 0.90 (0.80 - 1.00)
Aspirin could NOT REDUCE incidence
## All cancer incidences

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Aspirin Users</th>
<th>Non-users</th>
<th>Odd Ratio 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GI Cancers</strong></td>
<td></td>
<td></td>
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<tr>
<td>Colorectal</td>
<td>5,118 (2.48%)</td>
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<td>Pancreas</td>
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<td>Gastric</td>
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<td></td>
<td></td>
<td></td>
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<td>Breast</td>
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<td>0.65 (0.63 - 0.66)</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>493 (0.24%)</td>
<td>1,101 (0.27%)</td>
<td>0.90 (0.80 - 1.00)</td>
</tr>
<tr>
<td>Prostate</td>
<td>2,062 (1.00%)</td>
<td>4,767 (1.16%)</td>
<td>0.86 (0.82 - 0.91)</td>
</tr>
</tbody>
</table>
## Compared with previous cohort

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>UNITED STATES JACOBS, 2007 (n = 18,127)</th>
<th>HONG KONG (n=618,884)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GI Cancers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorectal</td>
<td>0.68 (0.52 - 0.90)</td>
<td>0.76 (0.73 - 0.78)</td>
</tr>
<tr>
<td>Liver</td>
<td>N/A</td>
<td>0.53 (0.51 - 0.56)</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>N/A</td>
<td>0.53 (0.49 - 0.59)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.80 (0.45 - 1.44)</td>
<td>0.66 (0.60 - 0.71)</td>
</tr>
<tr>
<td>Gastric</td>
<td>N/A</td>
<td>0.62 (0.58 - 0.65)</td>
</tr>
<tr>
<td><strong>Non-GI Cancers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>0.83 (0.63 - 1.10)</td>
<td>0.96 (0.90 - 1.02)</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.83 (0.58 - 1.19)</td>
<td>0.97 (0.92 - 1.03)</td>
</tr>
<tr>
<td>Kidney</td>
<td>1.13 (0.69 - 1.87)</td>
<td>1.04 (0.95 - 1.13)</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>0.74 (0.43 - 1.27)</td>
<td>0.76 (0.68 - 0.84)</td>
</tr>
<tr>
<td>Lung</td>
<td>0.98 (0.76 - 1.25)</td>
<td>0.65 (0.63 - 0.66)</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>N/A</td>
<td>0.90 (0.80 - 1.00)</td>
</tr>
<tr>
<td>Prostate</td>
<td>0.81 (0.70 - 0.94)</td>
<td>0.86 (0.82 - 0.91)</td>
</tr>
</tbody>
</table>
Conclusion

Long-term use of aspirin (80mg daily) can significantly reduce digestive cancer incidence.

Similar benefits were observed in some other non-digestive cancers, such as leukaemia, lung and prostate cancer.
Thank you
Benefits of *H. Pylori* eradication in preventing gastric cancer in the older population: Results from a population-based study

Wai K Leung

Department of Medicine, University of Hong Kong, Hong Kong

Esther W Chan, Angel Wong, Equal Chen, Irene Ol Wong, Ian CK Wong, Michael KS Cheung
An introduction to *H. pylori*

- *H. pylori* has been classified by the International Agency for Research on Cancer (IARC) as a carcinogen in 1994.

- The prevalence of *H. pylori* infection varies, ranging from <20% in some European countries to >80% in some African countries.

- It is estimated that more than 4 billion people are infected with *H. pylori* in the world.
Global *H. pylori* prevalence
Gastric cancer: Global incidence and mortality

Overall incidence: 5th
Overall mortality: 2nd
Gastric cancer: Global incidence map

>70% cases in developing countries, 50% cases in East Asia

Source: GLOBOCAN 2012 (IARC)
*H. pylori* and gastric carcinogenesis

- *H. pylori*
- Chronic gastritis
- Glandular atrophy
- Intestinal metaplasia
- Dysplasia
- Carcinoma

*Host factors* (Cytokine gene polymorphism, low acid production)
Risk of gastric cancer in patients with premalignant gastric lesions: Netherlands

Annual incidence of GC:
- 0.1%
- 0.25%
- 0.6%
- 6%
Age and gastric pre-neoplastic changes: Netherlands

**HP eradication and gastric cancer development: asymptomatic individuals**

*H. pylori* eradication has been shown to reduce gastric cancer development by about 38%.
Baseline histology and gastric cancer development

GC prevention may only be achieved in those with no baseline atrophy, IM and dysplasia

Figure 3. Kaplan-Meier Analysis of Gastric Cancer Development With Respect to Treatment in Participants With No Atrophy, Intestinal Metaplasia, or Dysplasia

Figure 4. Kaplan-Meier Analysis of Gastric Cancer Development With Respect to Final \textit{Helicobacter pylori} Status in Participants With No Atrophy, Intestinal Metaplasia, or Dysplasia

Treatment allocation

Final HP status

Wong et al, JAMA 2004
Questions

Is there an optimal age of *H. pylori* eradication for gastric cancer prevention?

Is *H. pylori* still beneficial in older subjects?
Aims

To determine the risk of gastric cancer development after receiving *H. pylori* eradication therapy among different age groups in a large cohort of *H. pylori* infected subjects.

To compare the age-specific risk of gastric cancer development in this cohort of *H. pylori* eradicated subjects with the local general population.
Methods

DESIGN:
Retrospective cohort study

STUDY POPULATION:
All *H. pylori* subjects (aged >18) who had received a course of clarithromycin-based triple therapy for *H. pylori* infection in Hong Kong between January 2003 and December 2012
Gastric cancer risk in Hong Kong general population

- Age-specific gastric cancer incidence during the same period was obtained from the HK Cancer Registry:
  - Population-based registry

- Expected number of gastric cancer in different age groups were estimated

- Standardized incidence ratio (SIR) of the H. pylori eradicated cohort and the general population of the same age group was determined
Findings

73,237 *H. pylori* + subjects

63,396 successfully eradicated

153 (0.24%) developed gastric cancer

9,840 (13.4%) required re-treatment for *H. pylori*

Median time to GC: 4.9 (IQR: 2.7-7.2) years
Overall incidence: 3.2 per 10,000 person-years
Risk of gastric cancer according to age among those with successful *H. pylori* eradication
Observed number of gastric cancer cases in the *H. pylori* eradication therapy cohort and the expected number of gastric cancer cases in the general population as stratified by age groups

<table>
<thead>
<tr>
<th>Treatment outcome</th>
<th>HP eradication therapy cohort</th>
<th>General population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age group</td>
<td>Number of subjects</td>
</tr>
<tr>
<td>Results</td>
<td>&lt;40 yr</td>
<td>8,642</td>
</tr>
<tr>
<td></td>
<td>40-59 yr</td>
<td>32,125</td>
</tr>
<tr>
<td></td>
<td>≥60 yr</td>
<td>22,630</td>
</tr>
</tbody>
</table>

*Data on gastric cancer incidence in the general population are from the Hong Kong Hospital Authority’s Hong Kong Cancer Registry. The incidence tables gave annual incidence rates for each gender in 5-year age categories. For each 5-year category, the mean incidence rate between 2003 and 2014 (the latest available year) was used. The Standardized Incidence Ratio (SIR) is for the cohort as compared with the general population.*
Observed and expected incidence rates of gastric cancer in the *H. pylori* eradicated group and matched general population, according to age and follow-up durations.
Gastric cancer incidence in the *H. pylori* eradicated group as compared with gastric cancer incidence in the general population, stratified by age group and year of follow-up

<table>
<thead>
<tr>
<th>Age group</th>
<th>Year of follow-up</th>
<th>Number of subjects</th>
<th>Person-years at risk</th>
<th>Observed number of cases</th>
<th>Expected number of cases</th>
<th>SIR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>&lt;5</td>
<td>8,642</td>
<td>34,500</td>
<td>2</td>
<td>0.8</td>
<td>2.37 (0.40-7.84)</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>5-9</td>
<td>7,114</td>
<td>29,538</td>
<td>1</td>
<td>1.2</td>
<td>0.84 (0.04-4.12)</td>
<td>0.86</td>
</tr>
<tr>
<td></td>
<td>≥10</td>
<td>3,076</td>
<td>7,979</td>
<td>0</td>
<td>0.6</td>
<td>0.00 (0.00-5.30)</td>
<td>0.45</td>
</tr>
<tr>
<td>40-59 years</td>
<td>&lt;5</td>
<td>32,125</td>
<td>127,592</td>
<td>25</td>
<td>19.3</td>
<td>1.30 (0.86-1.89)</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>5-9</td>
<td>25,488</td>
<td>103,252</td>
<td>26</td>
<td>22.8</td>
<td>1.14 (0.76-1.65)</td>
<td>0.50</td>
</tr>
<tr>
<td></td>
<td>≥10</td>
<td>9,551</td>
<td>24,181</td>
<td>1</td>
<td>8.1</td>
<td>0.12 (0.01-0.61)</td>
<td>0.01</td>
</tr>
<tr>
<td>≥60 years</td>
<td>&lt; 5</td>
<td>22,630</td>
<td>85,519</td>
<td>51</td>
<td>59.8</td>
<td>0.85 (0.64-1.11)</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>5-9</td>
<td>15,510</td>
<td>59,648</td>
<td>42</td>
<td>52.1</td>
<td>0.81 (0.59-1.08)</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>≥ 10</td>
<td>4,685</td>
<td>11,586</td>
<td>5</td>
<td>13.3</td>
<td>0.37 (0.14-0.83)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Conclusion

The risk of gastric cancer was significantly lower among those who had received *H. pylori* eradication at age ≥60 than the matched population.

Our results support the potential benefits of *H. pylori* eradication on gastric cancer prevention in the aged population.
Thank you
Press Briefing: Tuesday, 31 October, 2017

Reducing the Incidence of Digestive Cancers

Questions?