# Appendix

Lee YC, Chen HH, Chiu HM, et al; The Benefit of Mass Eradication of *Helicobacter pylori* Infection: A Community-Based Study of Gastric Cancer Prevention.

**Appendix Table 1.** Estimated treatment effectiveness for prevention of gastric atrophy and intestinal metaplasia using an extrapolation method based on Poisson regression models, after adjustment for the declining incidence rates related to improved sanitation and hygiene.

**Appendix Table 2.** Histological severity scores obtained before (2004) and after (2008) *Helicobacter pylori* treatment of the study participants ($n$ = 841), based on the updated Sydney classification.

**Appendix Table 3.** Individual factors associated with changes in histological severity scores before and after chemoprevention.

**Appendix Table 4.** Number of subjects at risk, number of incident cases, incidence rates of gastric cancer per 100,000 subjects, and standardized incidence ratios in the reference population in Taiwan per year of the study period.

**Appendix Figure 1.** Location of Matsu Island.

This supplementary material has been provided by the authors to give readers additional information about their work.

**Appendix Table 1: Estimated treatment effectiveness for prevention of gastric atrophy and intestinal metaplasia using an extrapolation method based on Poisson regression models, after adjustment for the declining incidence rates related to improved sanitation and hygiene.**

| | Gastric atrophy | Intestinal metaplasia | Gastric cancer | Gastric cancer mortality |
|---|---|---|---|---|
| Observed number (*O*) | 7 | 130 | 15 | 13 |
| Expected number (*E*) | 18 | 68 | 10.7 | 3.3 |
| *O*/*E* (95% CI) | 0.39 (0.185 to 0.815) | 1.91 (1.608 to 2.268) | 1.40 (0.845 to 2.325) | 3.94 (2.288 to 6.785) |
| 1 – *O*/*E* (95% CI) | 0.61 (0.185 to 0.815) | -0.91 (-0.608 to -1.268) | -0.40 (-1.325 to 0.155) | -2.94 (-1.288 to -5.785) |

Using data on endoscopic examinations to detect gastric atrophy and intestinal metaplasia that developed between 1995 and the end of 2003, two Poisson regression models were used to estimate regression parameters pertaining to the natural course of gastric atrophy, intestinal metaplasia, gastric cancer, and gastric cancer mortality, with adjustment for the declining incidence possibly related to improved sanitation and hygiene by using the calendar year as a proxy variable.

The formula for a Poisson regression model for the premalignant lesions is expressed as follows:

Gastric atrophy: log (μ) = log (py) – 1.8217 + 0.2525 × calendar year (during two-stage screening) – 0.5788 × calendar year (prior to chemoprevention),

Intestinal metaplasia: log (μ) = log (py) – 2.8778 + 1.1692 × calendar year (during two-stage screening) – 0.5798 × calendar year (prior to chemoprevention),

where μ indicates the expected number of new cases with gastric atrophy or intestinal metaplasia and log (py) is the natural logarithm of person-year at risk, so-called offset (multiplier). By taking the year 1995 as the reference group, the calendar year is dummied to specify the two-stage screening period (1996–1998) and the year prior to chemoprevention (2003), respectively. The expected numbers after chemoprevention in the year 2008 can be extrapolated by applying these Poisson regression models. The effectiveness of *H. pylori* treatment in reducing these precursor lesions can be calculated as: (1 – observed/expected number) × 100%. The results are shown in Table 1. Note that both gastric atrophy and intestinal metaplasia showed annual decline of 6%, on average, during the wash-out period, which was possibly related to improved sanitation and hygiene.

For gastric cancer and gastric cancer specific death, the calculation is identical except that the calendar year was taken as a continuous variable to specify the pre-chemoprevention period (1995–2003). The number of subjects at risk, number of incident gastric cancer cases, and the number of gastric cancer mortality cases are shown in the following table (note that the number of subjects at risk also included those who were less than 30 years of age):

| Year | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study periods | Before chemoprevention | | | | | | | | | After chemoprevention | | | | |
| No. of subjects | 5,711 | 5,959 | 7,240 | 7,536 | 6,560 | 6,733 | 8,851 | 8,763 | 8,806 | 9,359 | 10,345 | 9,786 | 9,965 | 9,961 |
| No. of gastric cancers | 4 | 5 | 5 | 4 | 4 | 2 | 6 | 1 | 3 | 9 | 1 | 2 | 2 | 1 |
| No. of gastric cancer deaths | 2 | 3 | 3 | 1 | 2 | 3 | 3 | 0 | 0 | 3 | 3 | 3 | 2 | 2 |

The formula for a Poisson regression model for gastric cancer and death from gastric cancer is expressed as follows:

Gastric cancer: $\log(\mu) = \log(py) - 6.9591 - 0.1244 \times$ calendar year (pre-chemoprevention period),

Gastric cancer mortality: $\log(\mu) = \log(py) - 7.3710 - 0.1895 \times$ calendar year (pre-chemoprevention period),

where $\mu$ indicates the expected number of new cases with gastric cancer or death from gastric cancer and log (py) is the natural logarithm of person-year at risk, so-called offset (multiplier). The expected value of gastric cancer and its mortality during the chemoprevention period can be extrapolated by using the Poisson regression models and the effectiveness of intervention can be calculated in a similar manner.

**Appendix Table 2: Histological severity scores obtained before (2004) and after (2008) *Helicobacter pylori* treatment of the study participants (*n* = 841), based on the updated Sydney classification.**

| Parameter | Before chemoprevention | After chemoprevention | *P* |
|---|---|---|---|
| Antrum | | | |
| Acute inflammation | | | |
| Median (range) | 2 (0–3) | 0 (0–3) | <.0001 |
| Mean ± SD | 1.57 ± 0.83 | 0.14 ± 0.42 | |
| Chronic inflammation | | | |
| Median (range) | 2 (0–3) | 1 (0–3) | <.0001 |
| Mean ± SD | 2.09 ± 0.46 | 1.24 ± 0.66 | |
| Gastric atrophy | | | |
| Median (range) | 1 (0–3) | 0 (0–3) | <.0001 |
| Mean ± SD | 1.27 ± 0.67 | 0.29 ± 0.49 | |
| Intestinal metaplasia | | | |
| Median (range) | 0 (0–3) | 0 (0–3) | .91 |
| Mean ± SD | 0.61 ± 1.04 | 0.61 ± 0.89 | |
| MALT | | | |
| Median (range) | 1 (0–3) | 0 (0–3) | <.0001 |
| Mean ± SD | 1.17 ± 1.09 | 0.16 ± 0.54 | |
| Corpus | | | |
| Acute inflammation | | | |
| Median (range) | 1 (0–3) | 0 (0–3) | <.0001 |
| Mean ± SD | 0.92 ± 0.88 | 0.08 ± 0.3 | |
| Chronic inflammation | | | |
| Median (range) | 2 (0–3) | 1 (0–3) | <.0001 |
| Mean ± SD | 1·73 ± 0·62 | 0·79 ± 0·67 | |
| Gastric atrophy | | | |
| Median (range) | 1 (0–3) | 0 (0–2) | <.0001 |
| Mean ± SD | 0.67 ± 0.71 | 0.15 ± 0.39 | |
| Intestinal metaplasia | | | |
| Median (range) | 0 (0–3) | 0 (0–3) | .60 |
| Mean ± SD | 0.13 ± 0.54 | 0.12 ± 0.47 | |
| MALT | | | |
| Median (range) | 0 (0–3) | 0 (0–3) | <.0001 |
| Mean ± SD | 0.36 ± 0.76 | 0.11 ± 0.4 | |

Abbreviation: SD, standard deviation; MALT, mucosa-associated lymphoid tissue.

## Appendix Table 3: Individual factors associated with changes in histological severity scores before and after chemoprevention.

| Individual factor | Unadjusted regression coefficient | *P* | Adjusted regression coefficient | *P* |
|---|---|---|---|---|
| Successful eradication of *H. pylori* | 0.567 (0.112) | <.001* | 1.387 (0.023) | .023* |
| Age | -0.017 (0.004) | <.001* | -0.003 (0.011) | .820 |
| Male sex | -0.095 (0.072) | .188 | – | – |
| Smoking | 0.035 (0.089) | .694 | – | – |
| Alcohol consumption | 0.037 (0.074) | .615 | – | – |
| Diabetes mellitus | -0.071 (0.159) | .656 | – | – |
| First-degree relatives with gastric cancer | 0.066 (0.129) | .611 | – | – |
| Treatment-age interaction | – | – | -0.016 (0.012) | .174 |

Intragastric histology was parameterized using an increasing ordinal scale adopted from Mera *et al* (ref. 4), which was modified using the updated Sydney classification: 1 = normal, 2 = non-atrophic gastritis, 3 = gastric atrophy, and 4 = intestinal metaplasia. For the subdivisions of gastric atrophy and intestinal metaplasia, each tertile was given a value: 0 = mild, 0.33 = moderate, and 0.67 = severe, respectively. A continuous histological score was thus formulated and the outcome variable was defined as the histological score in 2004 minus that in 2008. Data are presented as regression coefficients (standard errors) in the univariate and multivariate linear regression models.

Univariate analyses showed that successful eradication of *H. pylori* was associated with a significant decrease in histological scores; however, this effect was modified by the individual's age after we refitted the model by adding the interaction term. Histological regression after the eradication of *H. pylori* infection was more prominent in young adults. Accordingly, the mean ages of subjects with normal/superficial gastritis, gastric atrophy, and intestinal metaplasia in this population were 48.8, 50.9, and 55.1 years, respectively. *$P < .05$.

**Appendix Table 4: Number of subjects at risk, number of incident cases, incidence rates of gastric cancer per 100,000 subjects, and standardized incidence ratios in the reference population in Taiwan per year of the study period.**

| Year | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| No. of subjects | 5,711 | 5,959 | 7,240 | 7,536 | 6,560 | 6,733 | 8,851 | 8,763 | 8,806 | 9,359 | 10,345 | 9,786 | 9,965 | 9,961 |
| No. of gastric cancers | 4 | 5 | 5 | 4 | 4 | 2 | 6 | 1 | 3 | 9 | 1 | 2 | 2 | 1 |
| Incidence rate | 70.040 | 83.914 | 69.061 | 53.079 | 60.976 | 29.704 | 67.789 | 11.412 | 34.068 | 96.164 | 9.667 | 20.437 | 20.070 | 10.039 |
| SIR | 5.034 | 5.154 | 3.799 | 3.378 | 3.395 | 1.707 | 4.055 | 0.650 | 2.030 | 5.564 | 0.599 | 1.184 | 1.187 | 0.619 |

Abbreviation: SIR, standardized incidence ratio

Note that the number of subjects at risk also included those who were less than 30 years of age.

## Appendix Figure 1: Location of Matsu Island.

Matsu Island is an archipelago of five major islands (Nangan, Beigan, Eastern Jiunguang, Western Jiunguang, and Dungyin) in the Taiwan Strait, located about 100 miles from the shore of Taiwan near the northern coast of Fujian Province in mainland China. The prevalence of *Helicobacter pylori* infection on each island is specified.