

# Changing trends in the prevalence of *H. pylori* infection in Japan (1908-2003): a systematic review and meta-regression analysis of 170,572 individuals

Chaochen Wang<sup>1</sup>, Takeshi Nishiyama<sup>1</sup>, Shogo Kikuchi<sup>1</sup>, Manami Inoue<sup>2</sup>, Norie Sawada<sup>2</sup>, Shoichiro Tsugane<sup>2</sup>, Yingsong Lin<sup>1</sup>

1. Department of Public Health, Aichi Medical University, Nagakute, Aichi, Japan;
2. Division of Cohort Consortium Research, Center for Public Health Sciences, National Cancer Center, Tokyo, Japan

## BACKGROUND

- ▶ Gastric cancer burden remains high in Japan, with approximately 50,000 deaths/year (2nd leading cause of cancer deaths).
- ▶ Evidence supports a central role for *H. pylori* in the development of upper-gastrointestinal diseases, including peptic ulcer and noncardia gastric cancer.
- ▶ Studies have suggested that the prevalence of *H. pylori* infection increases with age; however, this phenomenon is presumably due to a birth-cohort effect.
- ▶ We systematically reviewed the existing literature that presented estimates of the prevalence of *H. pylori* infection in the Japanese population.
- ▶ The ojectives are:

1. to derive a robust prevalence estimate of *H. pylori* infection by birth year;
2. to clarify whether *H. pylori* infection exhibits a birth-cohort pattern.

## DATA SOURCES AND SEARCH STRATEGY

- ▶ The PRISMA statement for preferred reporting of systematic reviews and meta-analyses was used as a guide to conduct this study. (Fig 1. Flowchart of Study Selection)
- ▶ **PubMed:** (“*Helicobacter*”[Mesh] OR “*Helicobacter pylori*”[title/abstract]) AND (“Prevalence”[Mesh] OR “prevalence”[title/abstract] OR “infection rate”) AND (“Japan”[Mesh] OR “Japan”[title/abstract] OR “Japanese”[title/abstract])
- ▶ **EMBASE:** (“prevalence”/exp OR prevalence:ab, ti OR “infection rate”/exp OR “infection rate”: ab, ti) AND (“Japan”/exp OR “Japan: ab, ti” OR “Japanese: ab, ti”) AND (“*helicobacter*”/exp OR “*helicobacter pylori*”: ab, ti) AND (humans)/lim.
- ▶ We also scrutinised the reference lists, and searched for unpublished data by contacting the head of ongoing projects.
- ▶ The risk-of-bias assessment was independently performed by two authors (Y.L. and C.W.) using the **Joanna Briggs Institute Prevalence Critical Appraisal Tool**<sup>a</sup>.

<sup>a</sup>[http://joannabriggs.org/assets/docs/critical-appraisal-tools/JBI\\_Critical\\_Appraisal-Checklist\\_for\\_Prevalence\\_Studies.pdf](http://joannabriggs.org/assets/docs/critical-appraisal-tools/JBI_Critical_Appraisal-Checklist_for_Prevalence_Studies.pdf)

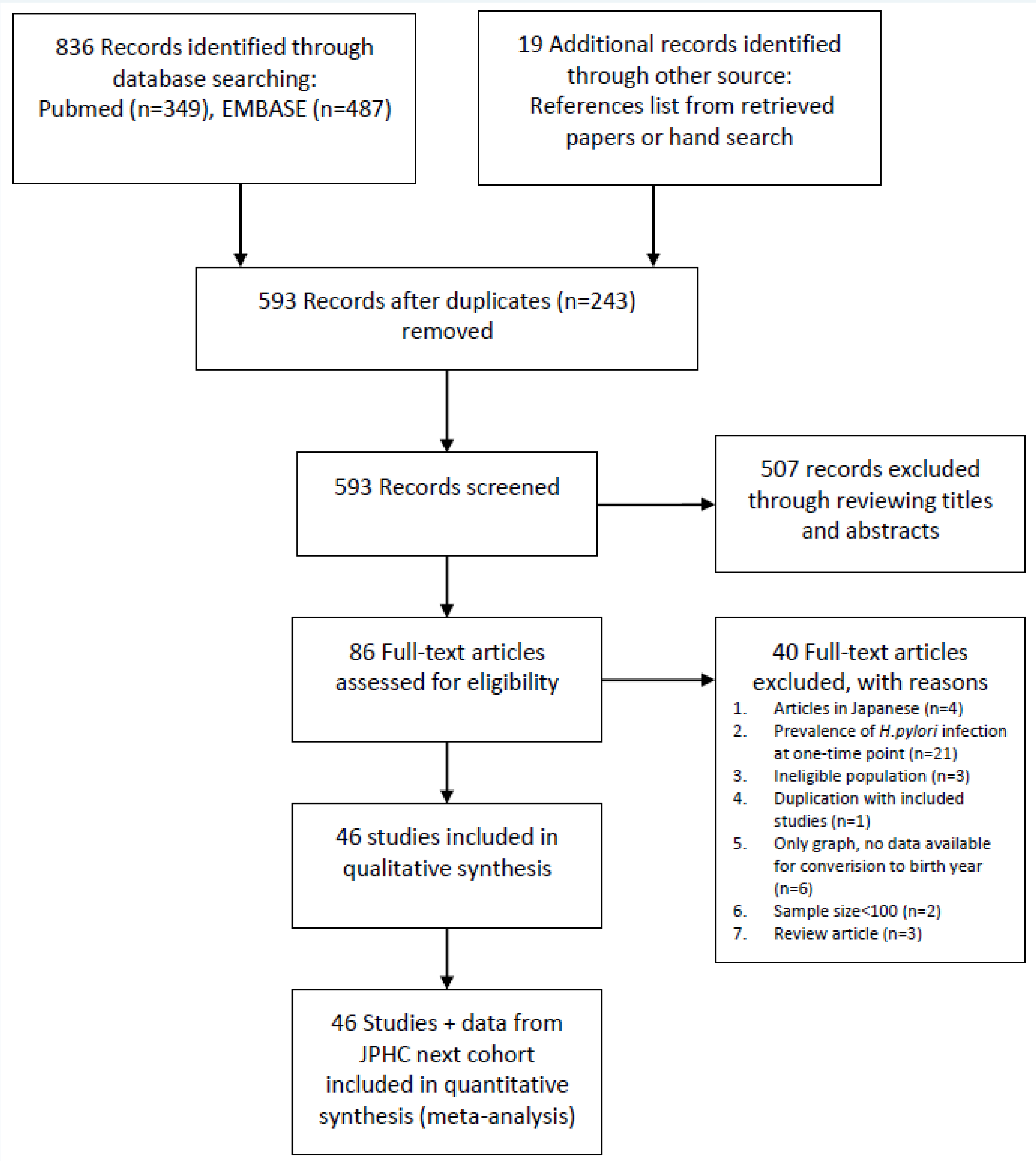


Figure 1. PRISMA Flowchart of Study Selection

## STATISTICAL ANALYSIS (1)

- ▶ More details on how to estimate prevalence of *H. pylori* by birth year can be found **here**<sup>a</sup>.
- ▶ Prevalence by birth year was extracted from 47 studies (300 data points).
- ▶ Observations were weighted by the inverse of the sum of the within-study variance and the residual between-study variance using the meta package.

<sup>a</sup>[https://winterwang.github.io/For\\_Inoue\\_pylori/](https://winterwang.github.io/For_Inoue_pylori/)

## STATISTICAL ANALYSIS (2)

- ▶ Penalized cubic spline was used to model the prevalence as a function of birth year in the framework of generalized additive mixed model (GAMM) implemented in the mgcv package in R.
- ▶ Pre-specified explanatory variables included in the meta-regression were as follows:  
Study ID, birth year, population source (community-based or clinical-based), diagnostic testing (serological test, or others; others: urinary assays, salivary assays, stool antigen tests, <sup>13</sup>C-urea breath test, and gastric biopsy), types of ELISA kits for measuring *H. pylori* positivity (antigen derived from domestic or foreign strains), and data collection period (prior to the year 2000, or later than 2000), with **study ID as a random effect** and **other variables as fixed effects**.

## RESULTS

- ▶ Details/characteristics of the studies included in the current meta-regression analysis are available **online**<sup>a</sup>.
- ▶ Summary of the results of risk of bias diagnosis is available **here**<sup>b</sup>.

<sup>a</sup><http://rpubs.com/winterwang/288338>

<sup>b</sup><http://rpubs.com/winterwang/riskofbias>

Figure 2: Multivariable adjusted prevalence of *H. pylori* by birth year

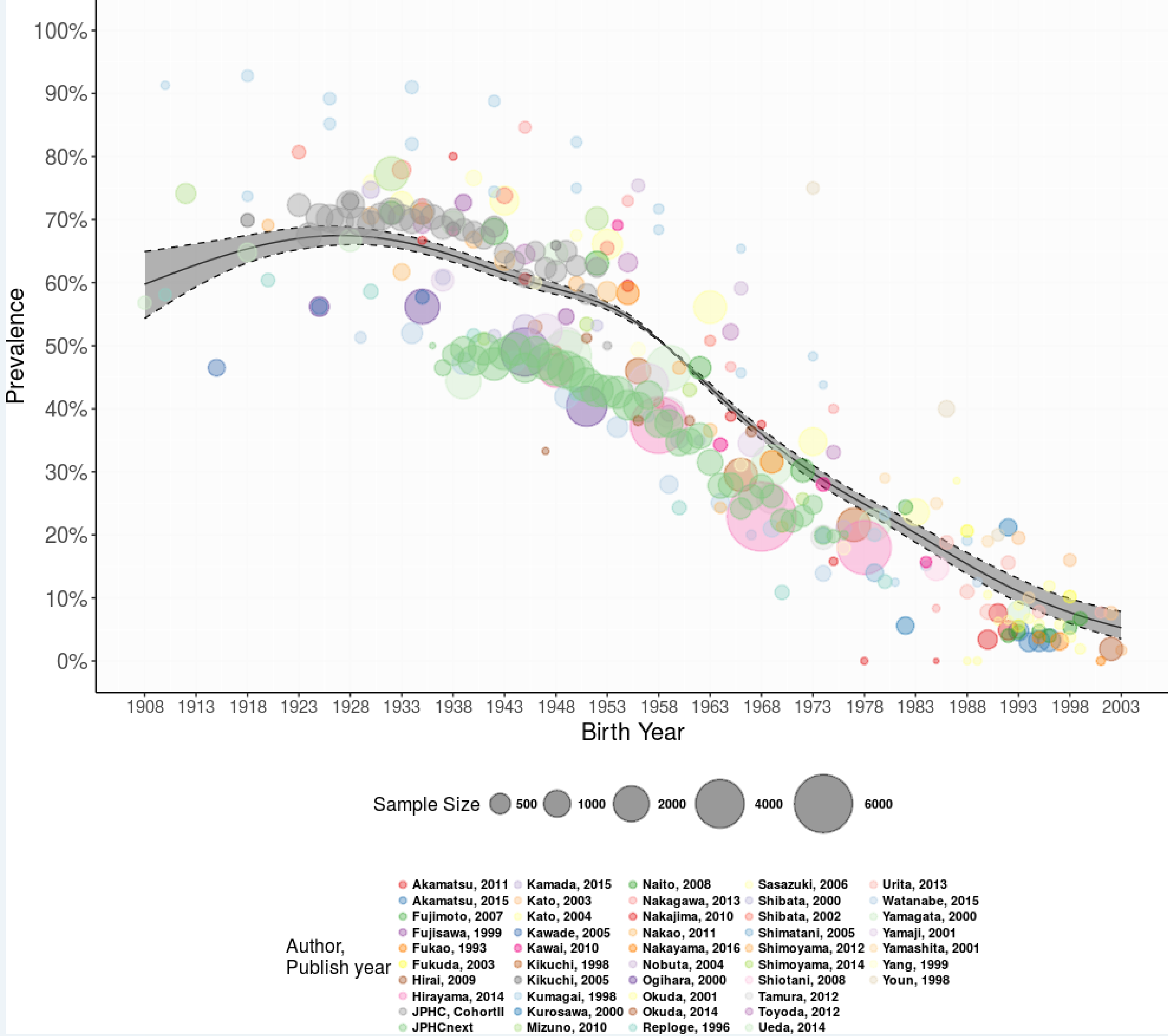


Table 1. Estimated prevalence of *H. pylori* infection by birth year

Birth year	Prevalence	95% Low	95% High
1908	0.597	0.543	0.649
1909	0.603	0.553	0.651
1910	0.609	0.563	0.654
...	...	...	...
1925	0.674	0.657	0.690
1926	0.675	0.659	0.690
1927	0.675	0.660	0.690
1928	0.675	0.660	0.688
...	...	...	...
1950	0.582	0.574	0.590
...	...	...	...
1990	0.138	0.121	0.157
...	...	...	...
1996	0.087	0.070	0.108
1997	0.081	0.064	0.102
1998	0.076	0.058	0.098
...	...	...	...
2002	0.057	0.039	0.082
2003	0.053	0.035	0.078

## CONCLUSION

- ▶ Prevalence of *H. pylori* infection exhibits a **birth cohort effect** in Japan, with prevalence decreasing steadily in individuals born in successive years, **from 58.2% in 1950 to 13.8% in 1990**.
- ▶ Given the fact that the birth-cohort pattern of *H. pylori* shapes the trends of gastric cancer over time, our findings help to inform screening efforts aimed at prevention and early detection of gastric cancer in Japan.

## COI Declaration:

The authors have no conflict of interest with any corporate organizations relating to this presentation.