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

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BACKGROUND

- Gastric cancer burden remains high in Japan, approximately 50,000 deaths/year in Japan (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, while the whole picture remains obscure.
- We systematically reviewed the existing literature that presented estimates of the prevalence of *H. pylori* infection in the Japanese population.
- The obejectives 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- We also scrutinised the reference lists, and searched for unpublished data by contacting the head of ongoing projects.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**[a].

[a] http://joannabriggs.org/assets/docs/critical-appraisal-tools/JBI_Critical_Appraisal-Checklist_for_Prevalence_Studies.pdf

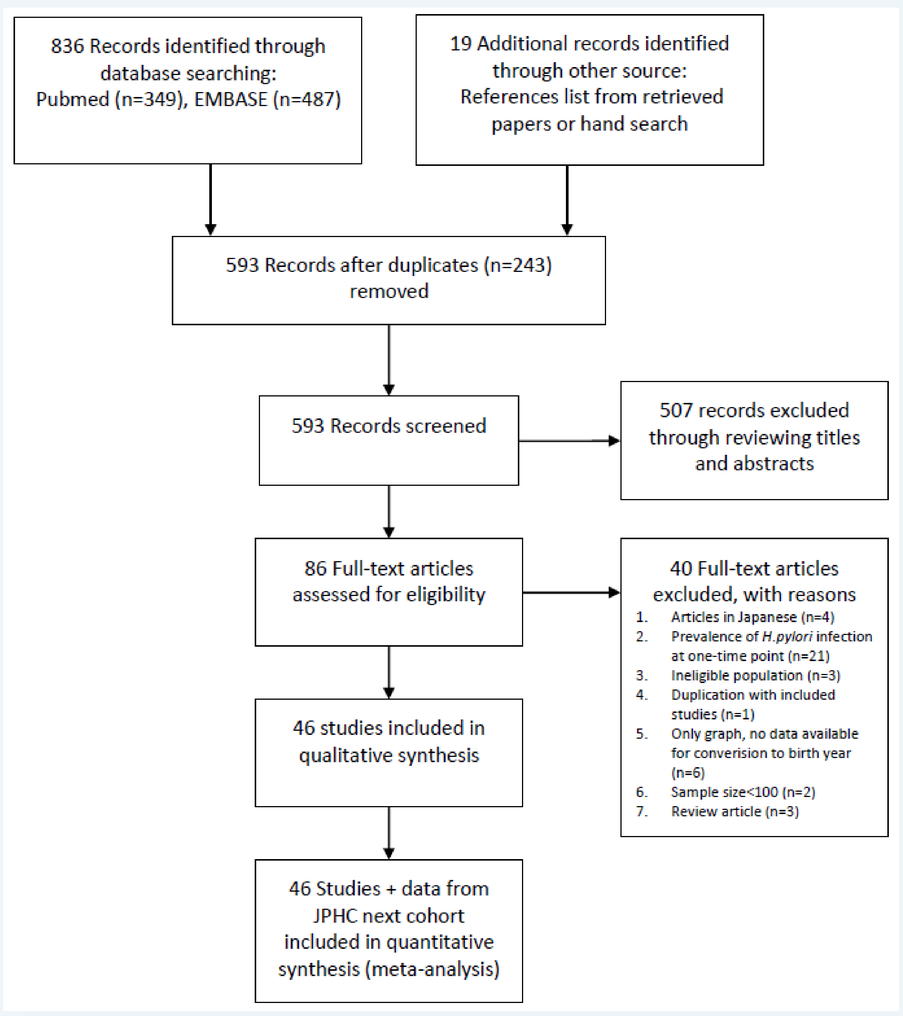

Figure 1: PRISMA Flowchart of Study Selection

STATISTICAL ANALYSIS (1)

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

[a] 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, 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**[a]
- Summary of the results of risk of bias diagnosis is available **here**[b]

[a] http://rpubs.com/winterwang/288338
[b] http://rpubs.com/winterwang/riskofbias

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

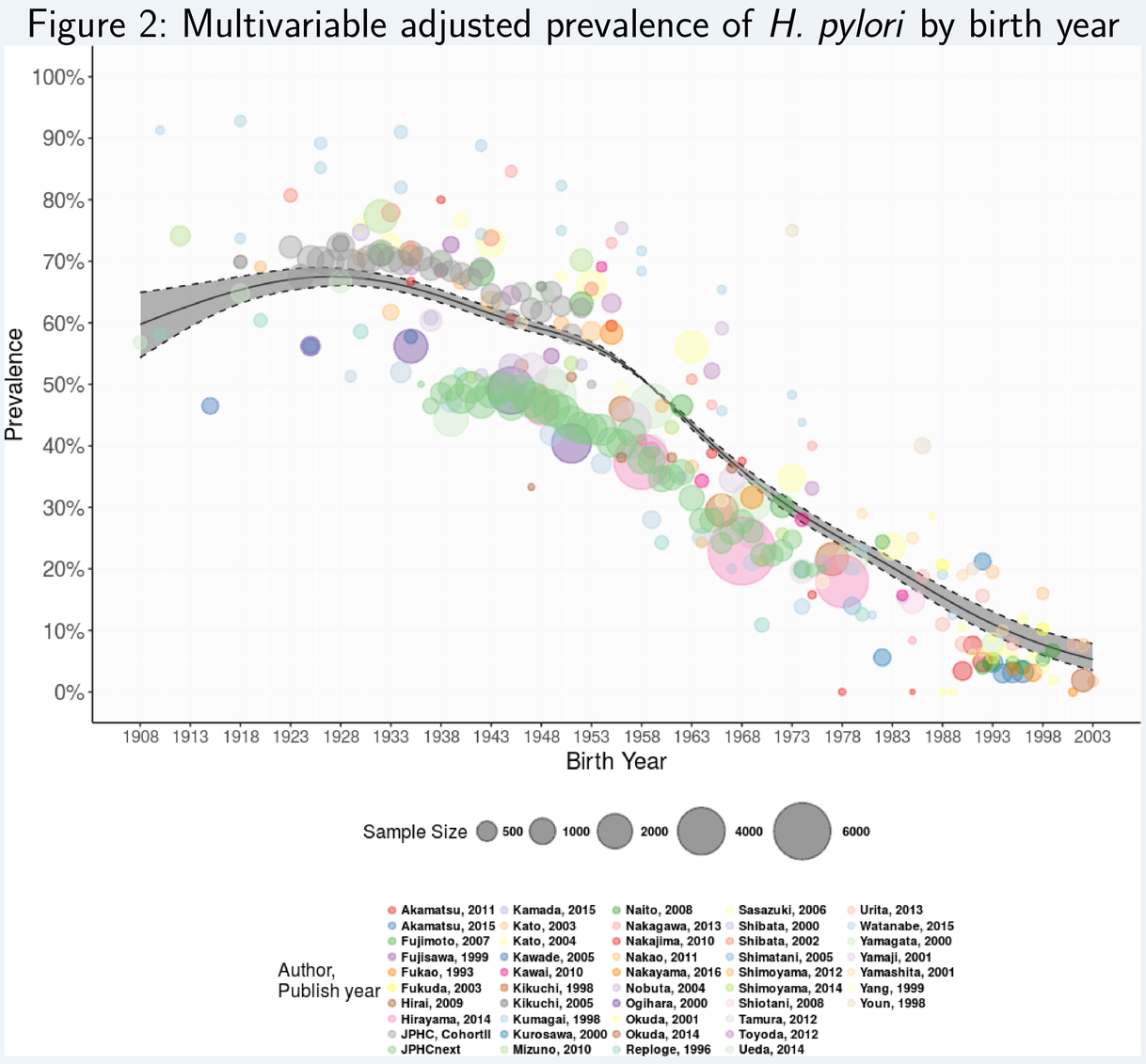

Table 1. Estimated prevalence of *H. pylori* infection by birth year

Birth Year	Prevalence	95% CI low	95% CI high
1908	0.574	0.520	0.626
1909	0.580	0.530	0.628
1910	0.586	0.540	0.631
1911	0.592	0.549	0.633
1912	0.597	0.559	0.635
...	...	...	...
1925	0.650	0.634	0.667
1926	0.651	0.635	0.667
1927	0.652	0.636	0.666
1928	0.651	0.637	0.665
1929	0.651	0.637	0.664
...	...	...	...
1996	0.080	0.064	0.100
1997	0.075	0.059	0.095
1998	0.070	0.054	0.091
...	...	...	...
2002	0.053	0.036	0.076
2003	0.049	0.032	0.074

CONCLUSION

- Prevalence of *H. pylori* infection exhibits **a birth cohort effect** in Japan, with prevalence decreasing steadily in individuals born in successive years, **from 55.6% in 1950 to 12.8% in 1990**.