

Helicobacter pylori Infection and Markers of Gastric Cancer Risk in Alaska Native People

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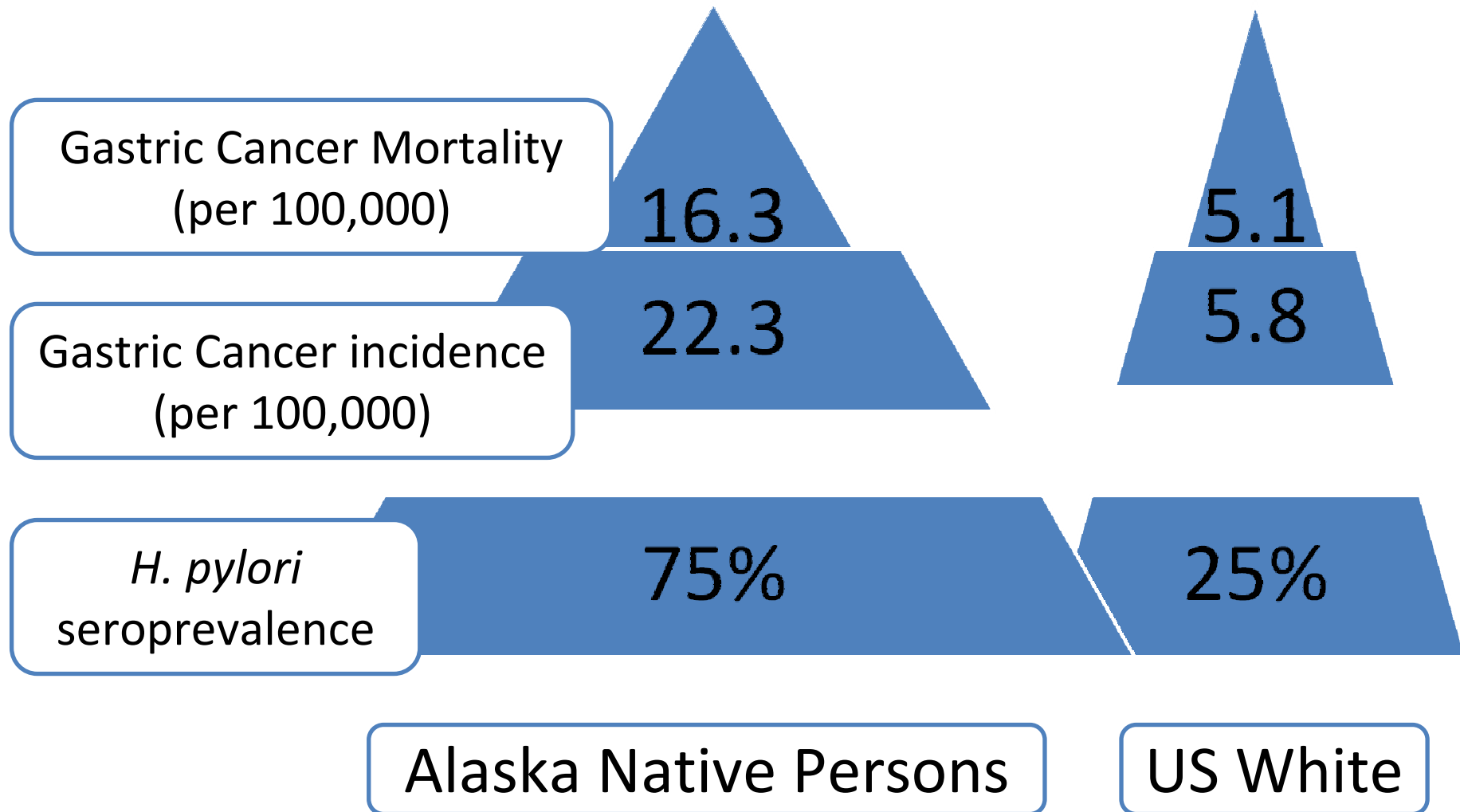
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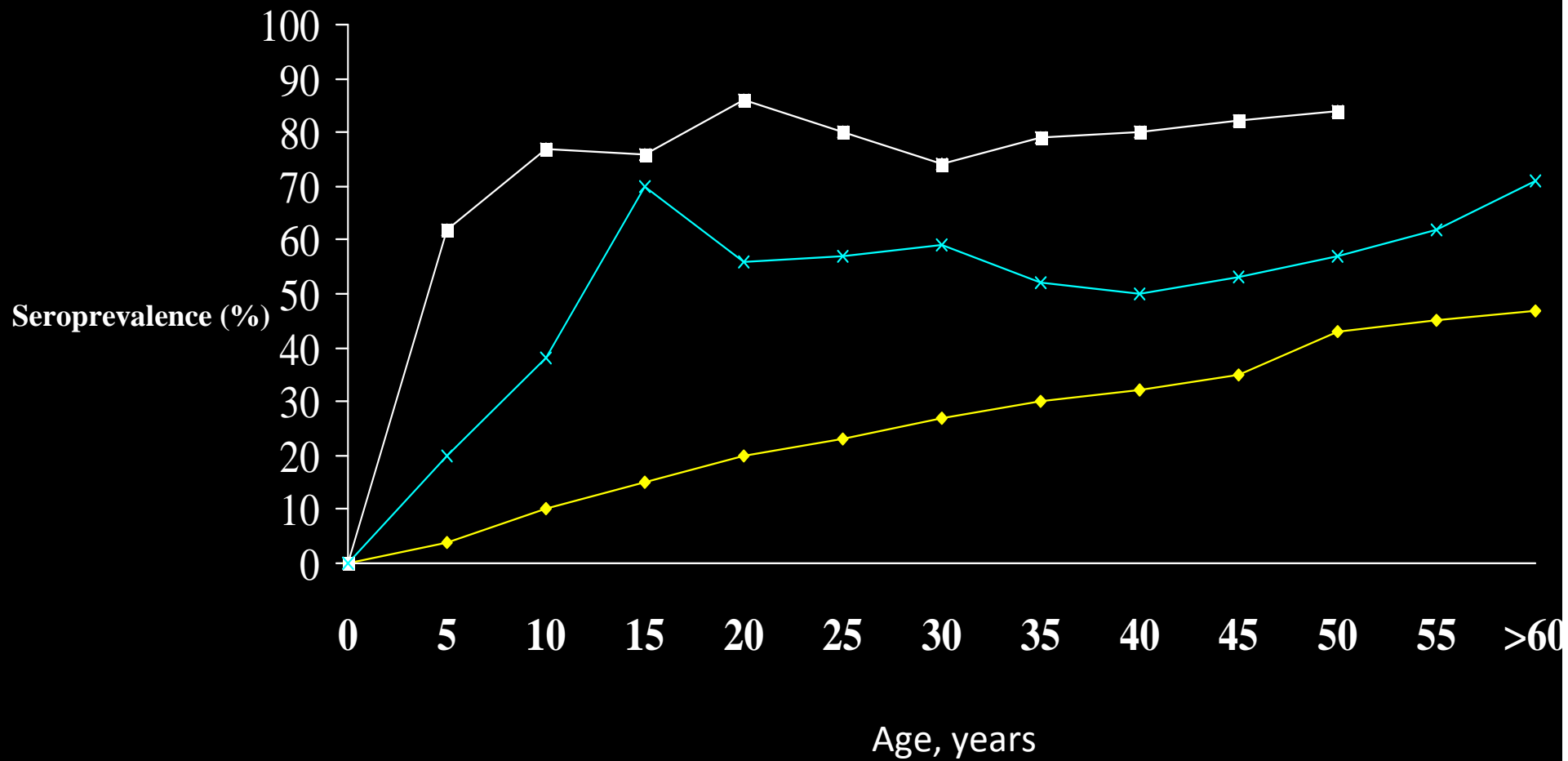
Gastric Cancer Background

- Cancer is the leading cause of death for Alaska Native people (AN)
- Gastric cancer is the 5th most frequently diagnosed cancer in Alaska Native people
 - Incidence 4 times that of white US population
- Mortality rate 3 times higher than U.S. population

Gastric Cancer & *H. pylori* in AN



—◆— U.S. —■— Alaska Natives —×— Greenland



Study Objectives

- Determine association between gastric cancer & *H. pylori* infection (IgG antibodies) among Alaska Native persons
- Determine if prevalence of antibody to cytotoxin-associated gene A, presence of pepsinogen I & II, or blood group are risk factors for gastric cancer among AN/AI
- Describe gastric cancers in Alaska Native persons

Study Participants

- Identified using the Alaska Area Specimen Bank and the Alaska Tumor Registry
- Cases:
 - Alaska Native adults ≥ 18 years of age residing in Alaska
 - Diagnosed with gastric adenocarcinoma between 1969 and 2008
 - At least 1 serum specimen drawn prior to cancer diagnosis in the Alaska Area Specimen Bank
- Controls:
 - Alaska Native adults ≥ 18 years of age residing in Alaska
 - Without gastric adenocarcinoma
 - At least 1 serum specimen in the Alaska Area Specimen Bank collected during the time period 1969-2008

Design

- 3 controls matched to each case by:
 - Region of residence in Alaska
 - Age group
 - Sex
 - Date of serum specimen collection

Study Design

- Type: Retrospective case-control study
- Time period: 1969-2008
- Five rural Alaska regions participated

Laboratory Testing

- Anti-*H. pylori* antibody (*Helicobacter pylori* IgG ELISA; Biohit)
- Anti-CagA antibody (*Helicobacter pylori* p120 (CagA) ELISA; ravo Diagnostika)
- Pepsinogen I & II (ELISA, Biohit)
- Blood grouping (Affirmagen pooled reagent red blood cells)

- We used the manufacturer's cut offs for normal versus abnormal levels of pepsinogen I (25 µg/L) and the pepsinogen I/II ratio (2.5).

Results

Descriptive Epidemiology

	Case (N=122) N (%)	Control (N=346) N (%)
Male	89 (73%)	252 (72.8%)
Region of Residence		
Northwest	28 (23%)	78 (22.5%)
Southeast	8 (6.6%)	20 (5.8%)
Southwest	59 (48.4%)	172 (49.7%)
West	27 (22.1%)	76 (22.0%)
Mean age at specimen collection, years	45 (16%)	41 (17%)
Mean specimen collection time prior to diagnosis, years	13	NA
Mean age at gastric cancer diagnosis, years	59	NA

Results: Univariate Analysis

	<u>Case (N=122)</u>		<u>Control (N=346)</u>		OR	p
	N	Percent	N	Percent		
<i>H. pylori</i> IgG +	112	91.8	285	82.4	2.59	0.01
CagA +	116	95.1	322	93.1	1.40	0.47
<i>H. pylori</i> or Caga +	122	100.0	342	98.8		
Pepsinogen I <25 ug/L	5	4.1	7	2.1	1.97	0.27
Pepsinogen I/II < 2.5	6	5.0	10	2.9	1.72	0.33
Blood Group						
A (referent)	51	41.8	136	39.3		
AB	8	6.6	34	9.8	0.64	0.29
B	12	9.8	42	12.1	0.79	0.53
O	51	41.8	134	38.7	1.01	0.98

Results: Non-Cardia Gastric Cancer Cases (N = 94)

Univariate analysis	OR	p
<i>H Pylori</i> IgG +	3.49	0.01
CagA +	1.10	0.84
Pepsinogen I low	3.48	0.11
Pepsinogen I/II low	2.30	0.25
Blood group (A referent)		
AB	0.69	0.45
B	0.72	0.43
O	0.96	0.88
Multivariate analysis		
<i>H Pylori</i> IgG +	4.1	.003
Pepsinogen I low	6.1	.04

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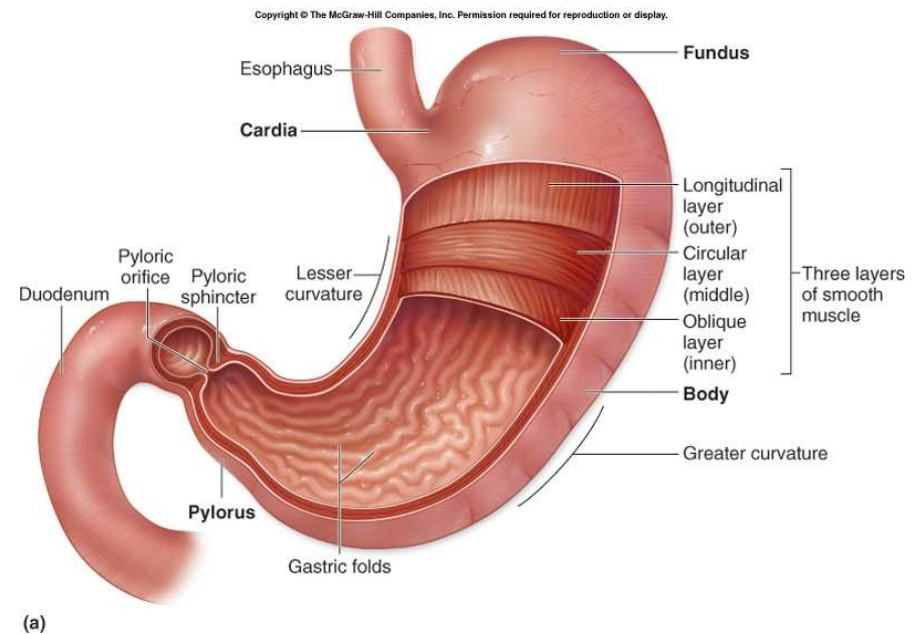
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Descriptive Analysis of Gastric Cancers

	N = 122	%
Histology		
Adenocarcinoma, NOS	81	66.4
Linitis plastica	4	3.3
Adenocarcinoma, intestinal type	8	6.6
Adenocarcinoma, diffuse type	3	2.5
Tubular adenocarcinoma	1	0.8
Papillary adenocarcinoma	2	1.6
Mucinous adenocarcinoma	3	2.5
Mucin-producing adenocarcinoma	1	0.8
Signet ring cell adenocarcinoma	19	15.6
Histologic grade		
	N = 98	
Well Differentiated	6	6.1
Moderately Differentiated	35	35.7
Poorly Differentiated	55	56.1
Undifferentiated	2	2.0

Gastric Cancer Location

Cancer site	N = 122	%
Cardia, NOS	28	23.0
Fundus	7	5.7
Antrum	19	15.6
Pylorus	6	4.9
Lesser curvature	30	24.6
Greater Curvature	13	10.7
Overlapping	4	3.3
Stomach, NOS	15	12.3



Conclusions

- Exposure to *H. pylori* in our study population was very high
- Previous *H. pylori* infection associated with gastric cancer in AN
- For non-cardia cases, low pepsinogen I also a risk factor
- Exposure to CagA virulence gene not associated with gastric cancer in our study

Goals / Challenges

- Lay ground work for a larger scale prospective study that includes tissue collection looking at gastric cancer and *H. pylori* infection in Alaska Native people
 - Bacterial virulence factors
 - Host genetic predisposition
 - Environmental co-factors

Acknowledgements

- Staff at the Arctic Investigations Program

