

# *HELICOBACTER PYLORI* INFECTION IN ARCTIC POPULATIONS

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# *H. PYLORI* INFECTION AND ARCTIC POPULATIONS

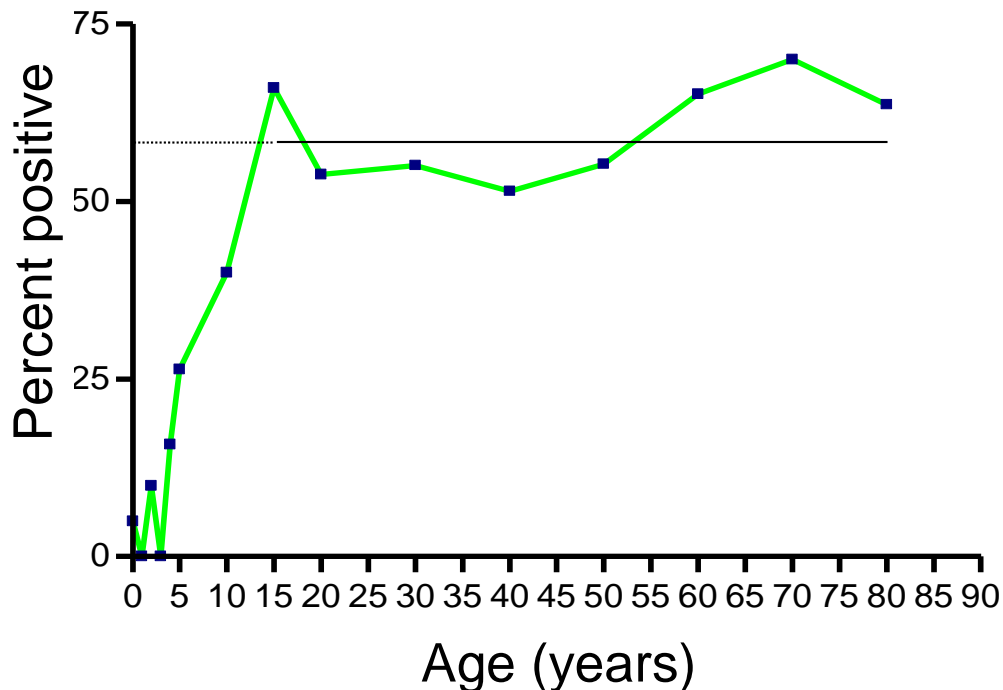


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- Gram negative rod shaped bacterium
  - Major cause of peptic ulcer disease
  - Associated with chronic gastritis, MALT lymphoma and gastric adenocarcinoma
  - Precise route of infection still unknown, but infection associated with human crowding and poor sanitation
  - World wide infection (overall 50% of population infected)
  - In western countries infection rate is 20% at age 20; 50% at age 50
  - In developing countries very early infection occurs 80% infected at age of 5 years
  
  - Incidence rate of gastric carcinoma in Greenland increasing in contrast to most other countries in the world
  
  - Role of *H. pylori*?

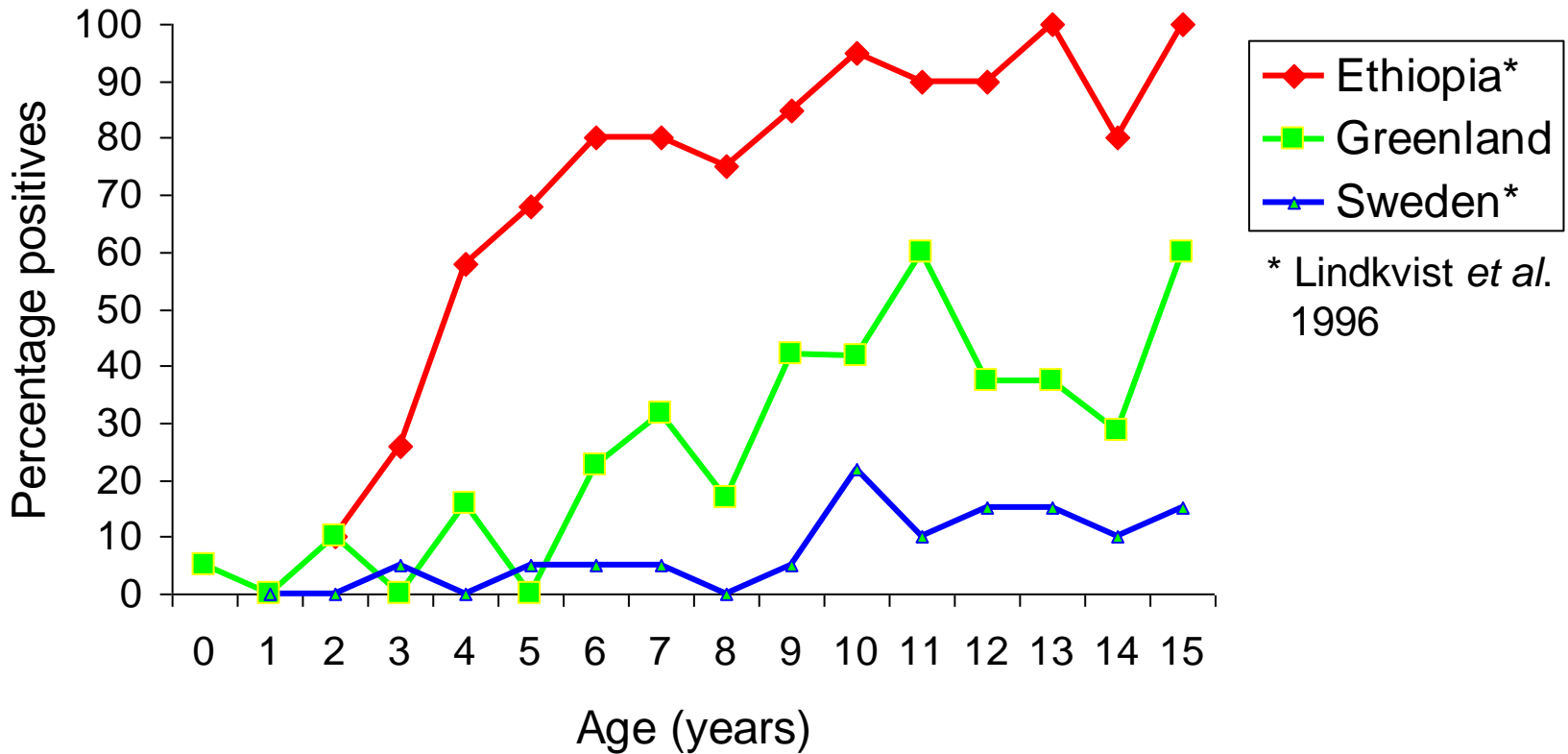
# AGE SPECIFIC PREVALENCE SISIMIUT WEST GREENLAND, 1998



- Population screening
- 5,300 inhabitants, 685 tested
- IgG antibodies
- Average seropositivity 15-85 years: 58%
- Canadian Inuit 15-74 years (McKeown *et al.* 1999): 53%



# COMPARISON WITH OTHER COUNTRIES (0-15 YEARS)



# RISK FACTORS FOR *H. PYLORI* INFECTION, CHILDREN 5-14 years



- Sex & age
- Birth order, sibship size
- Housing conditions
- Crowding
- Socioeconomic status
- Ethnicity (parent's place of birth)
- Smoking (passive and active)
- Institutional care
- Breast feeding

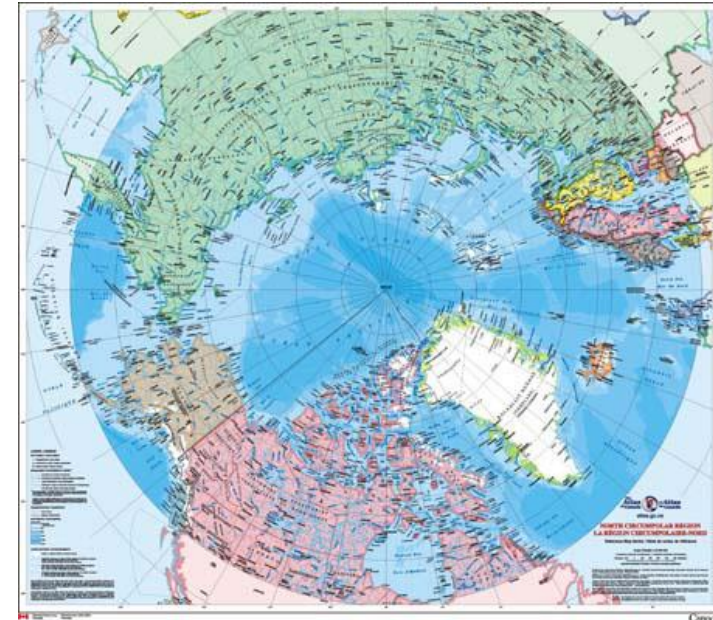
Risk factor	aOR	95% CI	p-value
Siblings at 5 years age			
0	0.39	(0.07-2.05)	
1	1		
2	1.15	(0.37-3.57)	
3+	4.86	(1.40-16.8)	0.015
Crowding (persons/room)			
<1	1		
1= $\leq$ <1.5	2.75	(0.83-9.13)	
1.5= $\leq$ <2	6.83	(1.62-28.1)	
2+	3.54	(0.74-17.0)	0.057

# OTHER ARCTIC AREAS

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- Alaska: 63 – 75% seroprevalence aboriginal populations; 24% in Caucasian Alaskans
- Canada: 21 – 95% seroprevalence; >50% exclusively in aboriginal populations
  - HP found in water from water trucks
- Siberia: 77% seroprevalence
- *Greenland: 47-77% (58%)*



# ANTIMICROBIAL TREATMENT AND RESISTANCE



- 2 or 3 antimicrobials
  - Amoxicillin, clarithromycine, metronidazole, levofloxacin, tinidazole, tetracycline, furazolidone & rifabutine
- PPI, H2-blocker or bismuth
- Worldwide, increasing resistance to clarithromycine, metronidazole, levofloxacin
- Antimicrobial resistance in HP isolates from Alaskan natives
  - Clarithromycine 30%
  - Metronidazole 42-66%
  - Levofloxacin 8-19%

# REINFECTION RATES

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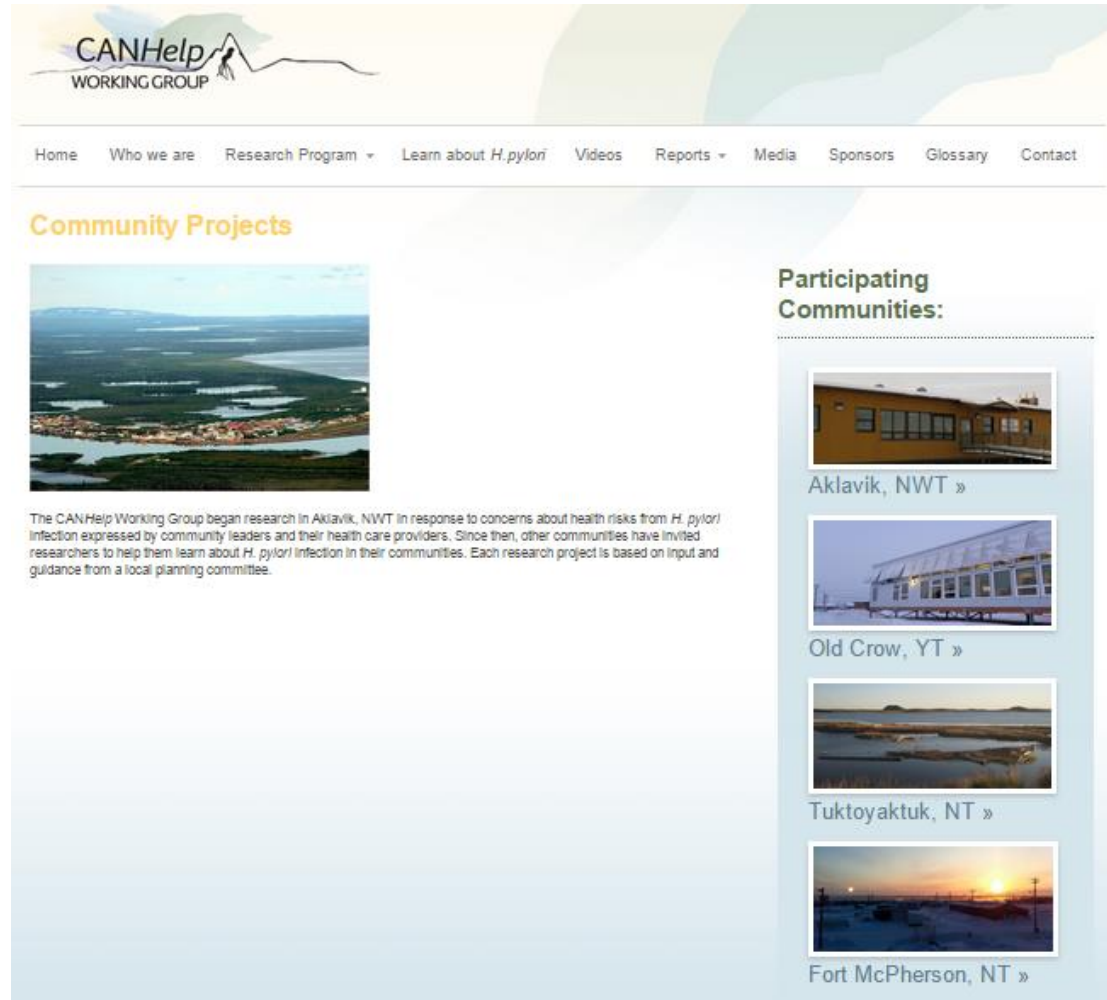
- Developed world <3% per year
- Developing countries 10-50% 1-2 years after treatment
- Alaskan natives (patients) 2006 two years after treatment:
  - 22.1% rural Alaskan natives
  - 14.5% urban Alaskan natives
  - 12% urban non-natives
  - 5% US general
- Canadian North (HP screening) 2007-2012:
  - Aboriginal population 2.4% reinfection rate/year
  - Caucasians 0%



# COMMUNITY CONCERNS CANADA



*The CANHelp Working Group began research in Aklavik, NWT in response to concerns about health risks from H. pylori infection expressed by community leaders and their health care providers. Since then, other communities have invited researchers to help them learn about H. pylori infection in their communities. Each research project is based on input and guidance from a local planning committee.*



The screenshot shows the website for the CANHelp Working Group. At the top is the logo, which includes the text "CANHelp WORKING GROUP" and a stylized mountain range. Below the logo is a navigation menu with links for Home, Who we are, Research Program, Learn about H. pylori, Videos, Reports, Media, Sponsors, Glossary, and Contact. The main content area is titled "Community Projects" and features a large photograph of a coastal town with a bay. Below this photo is a paragraph of text: "The CANHelp Working Group began research in Aklavik, NWT in response to concerns about health risks from H. pylori infection expressed by community leaders and their health care providers. Since then, other communities have invited researchers to help them learn about H. pylori infection in their communities. Each research project is based on input and guidance from a local planning committee." To the right of the main content is a section titled "Participating Communities:" which lists four communities with small thumbnail images and right-pointing arrows: Aklavik, NWT; Old Crow, YT; Tuktoyaktuk, NT; and Fort McPherson, NT.

# RECOMMENDATIONS FOR ARCTIC AREAS WITH HIGH HP PREVALENCE



- US and European guidelines recommend 'test and treat' strategy in adults with dyspepsia (not in children)
- However, in populations where >60% are seropositive, HP treatment of HP positive persons is overkill
- Arctic expert group 2015:
  - No HP screening or testing as part of routine evaluation of dyspepsia
  - Endoscopy in case of worrisome symptoms (weight loss, faecal blood)
  - HP treatment: duodenal or gastric ulcers, MALT lymphoma\*
  - Antimicrobials according to local resistance pattern\*
  - Test of cure two months after end of therapy\*

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## REVIEW ARTICLE

### The diagnosis and treatment of *Helicobacter pylori* infection in Arctic regions with a high prevalence of infection: Expert Commentary

B. J. McMAHON<sup>1,2</sup>, M. G. BRUCE<sup>2\*</sup>, A. KOCH<sup>3</sup>, K. J. GOODMAN<sup>4</sup>,  
V. TSUKANOV<sup>5</sup>, G. MULVAD<sup>6</sup>, M. L. BORRESEN<sup>3</sup>, F. SACCO<sup>1</sup>, D. BARRETT<sup>1</sup>,  
S. WESTBY<sup>1</sup> AND A. J. PARKINSON<sup>2</sup>

\*Similar to Recommendations of the European Society of Pediatric Gastroenterology and Nutrition (ESPGHAN) and the North American Society of Pediatric Gastroenterology and Nutrition (NASPGHAN)

# CONCLUSIONS

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- HP age-specific infection pattern in Arctic populations intermediate between developing and developed countries
- >50% adults seropositive
- Risk factors crowding and sibship size – poor hygiene?
- High rates of antimicrobial resistance and reinfection in Alaskan natives – Greenlanders unknown
- Recommendations for HP testing and treatment in Arctic and other high prevalence populations discouraging ‘test and treat’ strategy

# THANK YOU FOR YOUR ATTENTION

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"Oh, hey! I love these things!....Crunchy on the outside and chewy center!"

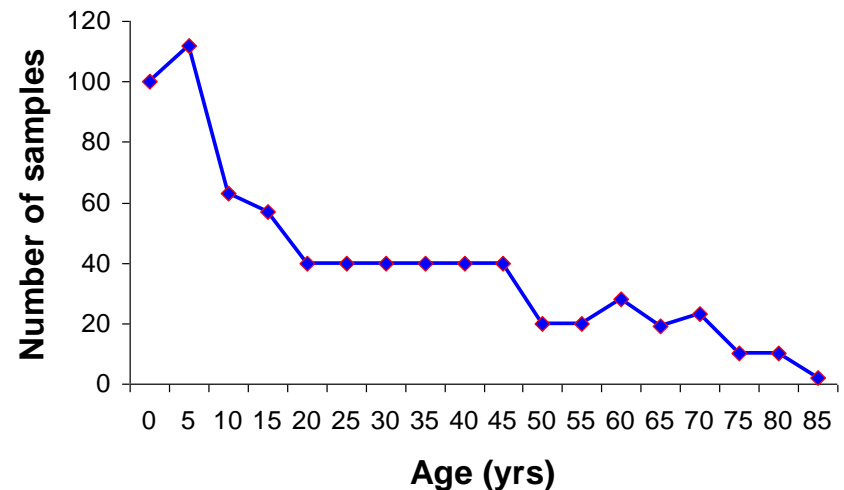


# STUDY POPULATION



- Sisimiut
  - 5,300 inhabitants, second largest town in Greenland
- Children 0-4 years
  - Cohort study on respiratory tract infections (Aug. 1996 - Dec. 1998)
- Schoolchildren and adults, 5-87 years
  - Cross sectional study, part of HIV-screening (nov.1998)

- 685 blood samples
- All persons born in Greenland
- Age (0-87 yrs)
- 322 men (47%)
- 363 women (53%)



# RISK FACTOR ANALYSES

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- Data
  - Two sets of questionnaires
    - School children 5-14
    - Adults 15-87
  - Register information
    - Greenlandic Birth Order Study Database, birth and family information for persons living in Greenland and alive by 1973 or later
- Logistic regression analysis
  - Sex- and age adjusted
  - Significant risk factors ( $p < 0.1$ ) entered in multivariate model, stepwise removal of insignificant factors

# RISK FACTOR ITEMS

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- Children (5-14)

- Sex
- Age
- Birth order and sibship size
- Housing conditions
- Crowding
- Socioeconomic status (parent's education and profession)
- Ethnicity (parent's place of birth)
- Smoking (passive and active)
- Institutional care
- Breast feeding

- Adults (15<=)

- Sex
- Age
- Birth order and sibship size
- Housing conditions
- Crowding (present and in childhood)
- Socioeconomic status (education and profession)
- Ethnicity
- Smoking and alcohol



# SEX AND *H. PYLORI* INFECTION, AGE ADJUSTED



Age group		N	OR	95% CI	p-value
Total (0-87)	Females	338	1		
	Males	301	1.62	(1.14–2.30)	0.006
0-4	Females	49	1		
	Males	50	2,04	(0.36-11.7)	0.41
5-14	Females	71	1		
	Males	80	2,03	(1.04–3.96)	0.03
15-87	Females	218	1		
	Males	171	1,54	(0.99–2.39)	0.05

# ADULTS RISK FACTORS



Risk factor	p-value	Risk factor	p-value
Place of birth (town/settlement)	0.76	No. of rooms in household	0.15
Mother's age at birth	0.90	No. of persons in household	0.60
Birth order	0.57	Domestic crowding	0.35
No. of siblings at 5 years age	0.88	Living in town/settlement	0.84
School education	0.19	Use of alcohol	0.88
Professional education	0.25	Current smoking	0.01
Social status	0.99	Yes, daily	1
		Not daily	0.65
		No	1.77

# CHILDREN BIRTH ORDER PARAMETERS



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Risk factor	N	OR	95% CI	p-value
Birth order				
1	71	1		
2	55	0.64	(0.27-1.52)	
3	42	1.62	(0.65-4.03)	
4+	25	5.34	(1.71-16.67)	0.003
Siblings at 5 years age				
0	21	0.43	(0.12-1.54)	
1	72	1		
2	58	0.82	(0.36-1.89)	
3+	42	3.05	(1.23-7.55)	0.006

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# CHILDREN CROWDING PARAMETERS



Risk factor	N	OR	95% CI	p-value
Rooms in household				
1-2	32	1		
3	52	0.65	(0.23-1.84)	
4	62	0.73	(0.27-2.00)	
5+	37	0.70	(0.22-2.25)	0.87
Persons in household				
1-2	26	1		
3	21	0.66	(0.15-2.83)	
4	43	0.62	(0.18-2.14)	
5	39	0.75	(0.22-2.58)	
6+	49	2.99	(0.92-9.75)	0.014
Crowding (persons/room)				
<1	56	1		
1= $\leq$ <1.5	69	3.4	(1.23-9.38)	
1.5= $\leq$ <2	29	7.7	(2.33-25.2)	
2+	29	6.5	(1.82-23.1)	0.002

# INSTITUTIONAL CARE & SOCIAL PARAMETERS



Risk factor	N	OR	95% CI	p-value
Institutional care before 6 years of age				
5-6 years	81	1		
3-4 years	46	0.70	(0.29-1.71)	
0-2 years	16	0.45	(0.11-1.86)	
Not having attended	23	2.40	(0.82-7.04)	0.06
Highest education in family				
Baccalaurate/ higher education	11	1		
Skilled worker	54	2.39	(0.76-7.51)	
9 <sup>th</sup> -12 <sup>th</sup> grade	52	1.92	(0.58-6.36)	
8 <sup>th</sup> grade/unskilled worker	49	4.20	(1.15-15.3)	0.15
Ethnicity (parent's place of birth)				
Greenland/Greenland	179	3.48	(0.69-1.7)	
Greenland/Denmark	14	1		0.096

# HP- STATUS AND DISEASE ASSOCIATION - ADULTS



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Risk factor	N	OR	95% CI	p-value
Self-perceived health				
Very good/good	249	1		
Average	106	1.14	(0.67-1.94)	
Bad/very bad	12	0.31	(0.08-1.16)	0.15
GI symptom (any) within last 30 days				
No	138	1		
Yes	170	1.06	(0.65-1.73)	0.81
Previous GI disease				
No	233	1		
Yes	56	1.87	(0.94-3.72)	0.07
Anemia				
No	232	1		
Yes	46	1.03	(0.51-2.06)	0.94

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# HELICOBACTER PYLORI IN ARCTIC POPULATIONS



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- High rates of HP seropositivity among adults
    - Greenlandic Inuit: 58%
    - Canadian Inuit: 53%
    - Canadian Indians: 95%
    - Alaskan natives: 78%
  - Early age at infection
    - Greenlandic Inuit: 5-15 years; Canadian Indians: 67% by age 2 years
    - Intermediate infection pattern (between western and developing countries)
  - Risk factors
    - Indians, Canada: Overcrowding, primitive toileting, infected siblings
    - *Inuits, Canada: HP in community water samples*
    - General: Childhood, poor socio-economic conditions in childhood, crowding
    - Other arctic populations ?

# CONCLUSIONS

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- Male sex and increasing age are the most predominant risk factors for *H. pylori* infection
- Among children domestic crowding and increasing sibship size are risk factors, social factors unknown
- No association between HP seropositivity and GI symptoms or diseases in adults



# HOUSING PARAMETERS, CHILDREN



Risk factor	N	OR	95% CI	p-value
Type of household				
Single family house	59	1		
Terrace/cluster house	22	3.57	(1.16-11.0)	
Apartment	95	1.15	(0.53-2.50)	
Institution	10	5.49	(0.8-37.84)	0.04
Institution vs. other types				
Other types	176	1		
Institution	10	4.24	(0.66-27.39)	0.11
Rooms in household (except for children living in institutions)				
1-2	32	1		
3	52	0.65	(0.23-1.84)	
4	62	0.73	(0.27-2.00)	
5+	37	0.70	(0.22-2.25)	0.87

# ETHNICITY AND MOTHER'S AGE, CHILDREN



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Risk factor	N	OR	95% CI	p-value
Ethnicity (parent's place of birth)				
Greenland/Greenland	179	3.48	(0.69-1.7)	
Greenland/Denmark	14	1		0.096
Mother's age at child's birth				
<20	40	1		
20-24	68	1.25	(0.50-3.13)	
25-29	52	1.38	(0.52-3.61)	
30<=	33	1.76	(0.60-5.19)	0.78

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# BACKGROUND

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- Curved gram negative bacterium isolated in 1984
- Causes gastritis, gastric and duodenal ulcers
- Correlation to gastric cancer (MALT-lymphoma)
- Chronic infection
- Route of infection still unknown
- World wide infection (overall 50% of population infected)
- In western countries infection rate is 20% at age 20; 50% at age 50
- In developing countries very early infection occurs 80% infected at age of 5 yrs

# OBJECTIVES

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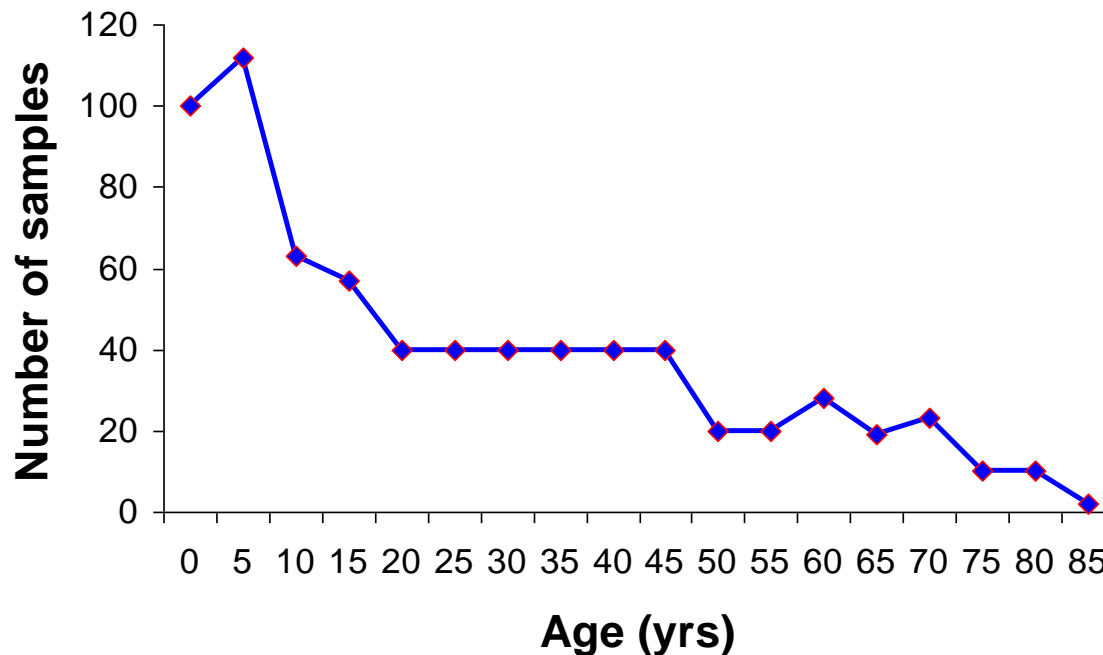


- To determine
  - *The age specific prevalence of H. pylori antibodies among Greenlanders*
  - Whether this prevalence follows a western pattern or a pattern observed in developing countries
  - Gastrointestinal symptoms and diseases associated with *H. pylori* seropositivity
  - Risk factors for *H. pylori* seropositivity

# H. PYLORI STUDY POPULATION



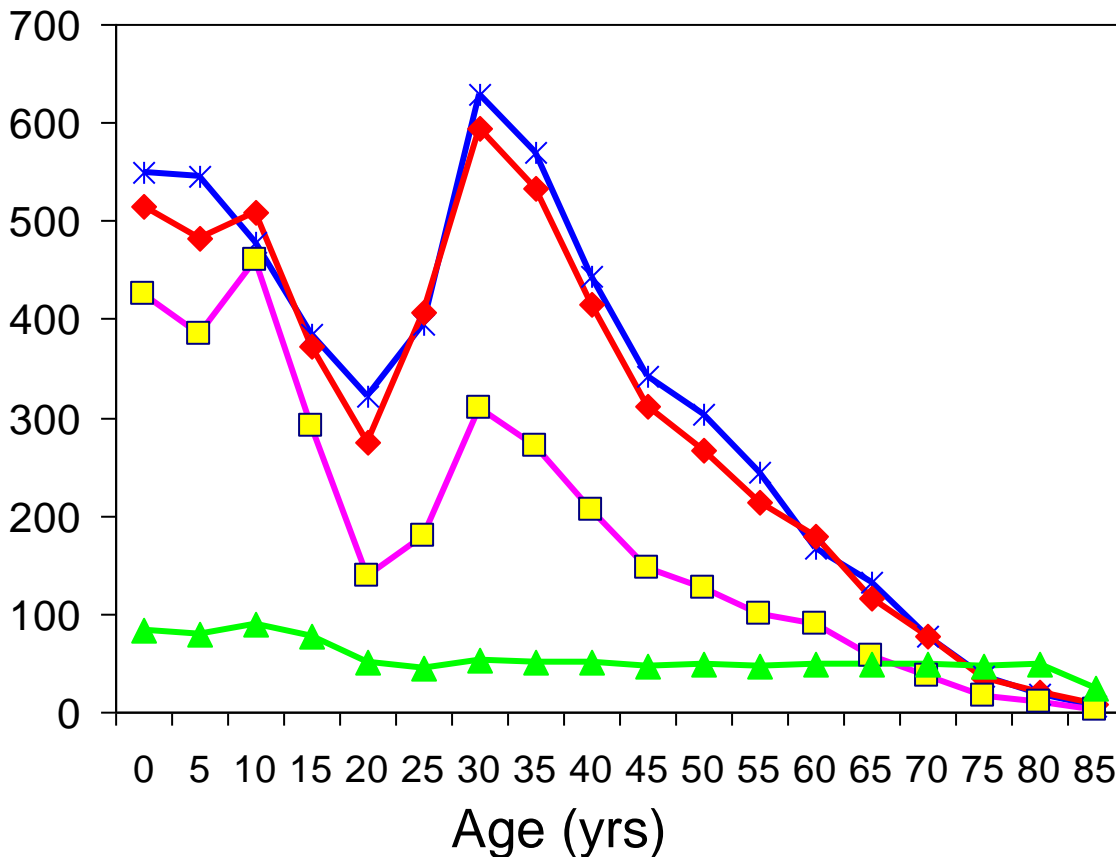
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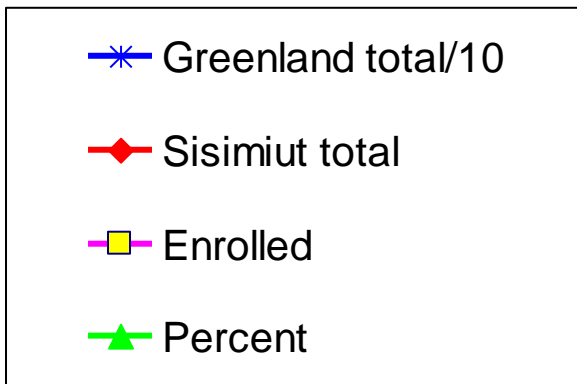
# AGE DISTRIBUTION OF STUDY POPULATION



## Inhabitants



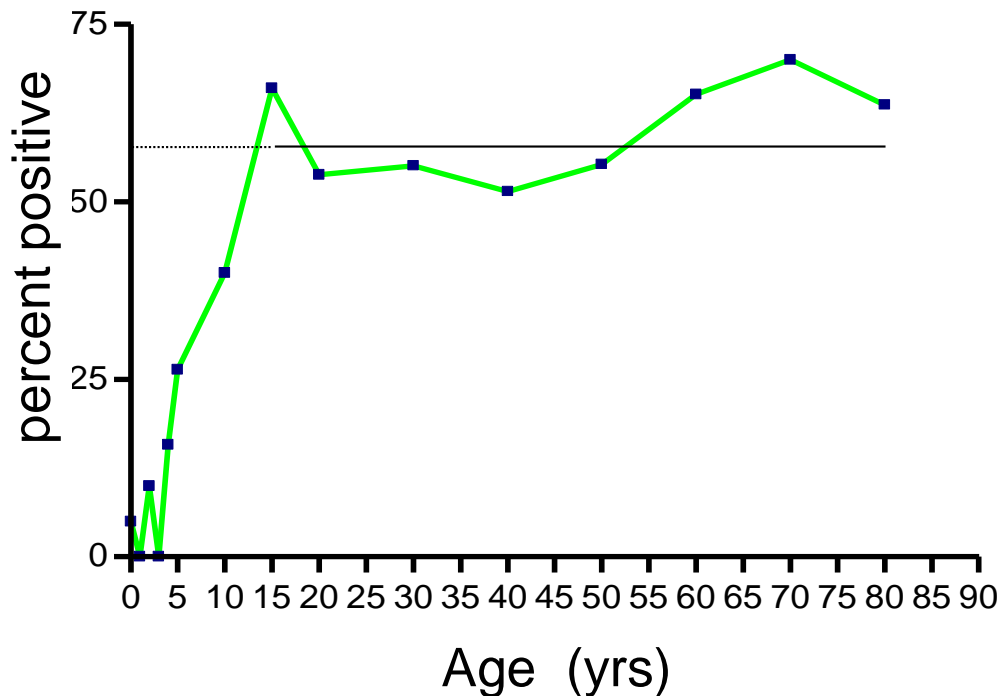
5.334 inhabitants,  
3.283 enrolled  $\Rightarrow$   
62% of total population  
49% , 51% 



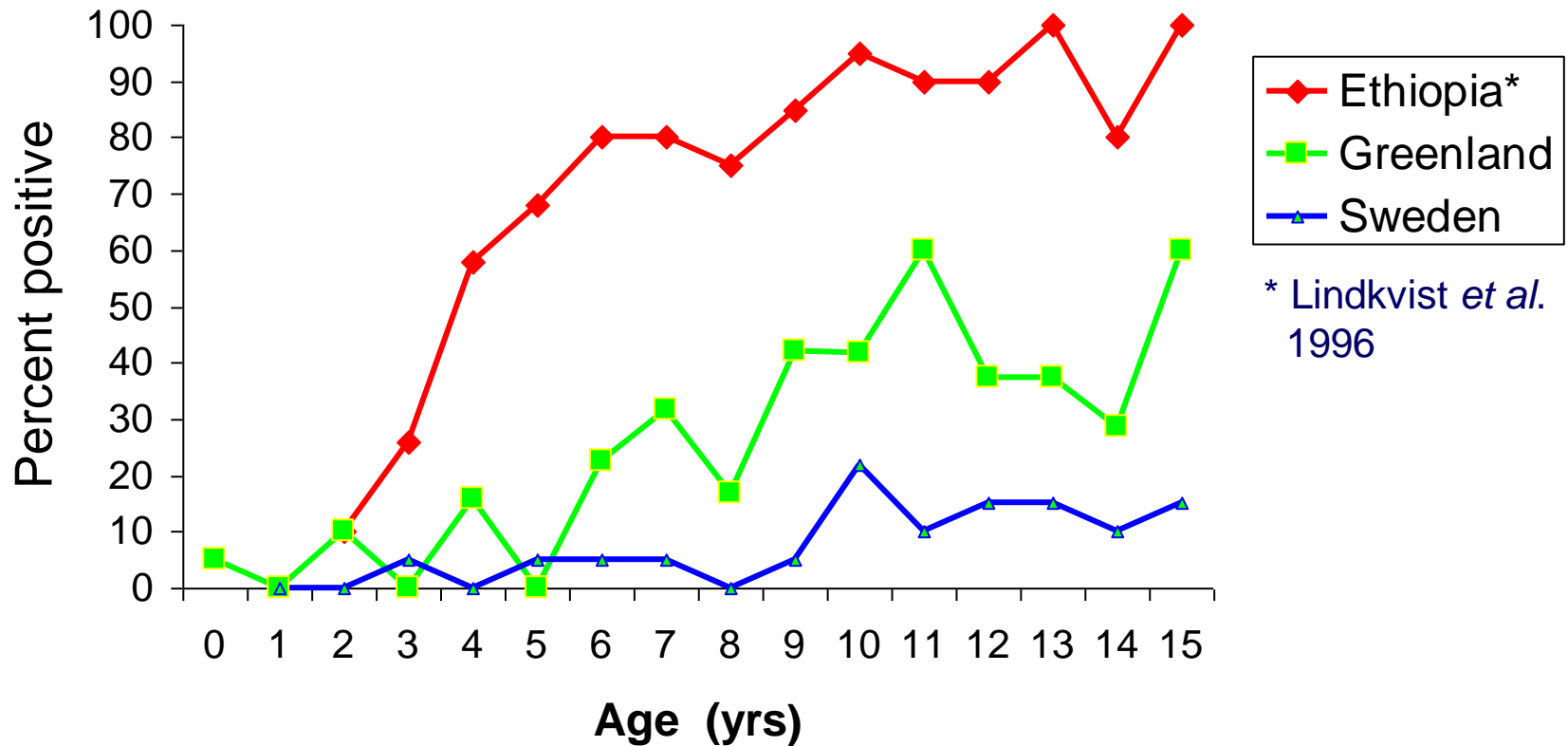
# RESULTS, IgG TESTING



- 280 (41%) positive
- 359 (52%) negative
- 46 (7%) inconclusive
- Average seropositivity (15-85 years): 58%
- Canadian Inuit (15-74 years) (McKeown *et al.* 1999): 53%



# COMPARISON WITH OTHER COUNTRIES (0-15 YEARS)





# SMOKING, ADULTS



Risk factor	N	OR	95% CI	p-value
Current smoking				
Daily	185	1		
Not daily	47	0.65	(0.32-1.32)	
No smoking	145	1.77	(1.08-2.89)	0.01
Ever smoked				
Yes	316	1		
No	66	1.11	(0.61-2.01)	0.74
No. of cigarettes daily, daily smokers only				
1-5	89	1		
6-10	74	2.40	(1.05-5.48)	
11-15	34	1.72	(0.64-4.62)	
16+	31	2.39	(0.85-6.71)	0.17