“Terve magu terveks eluks”

Concept of Healthy Stomach.

Contemporary possibilities to investigate patients with gastric complaints with minimally invasive method: blood test panel with biomarkers

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Tallin 2015

Concept of healthy stomach

- **Is stomach mucosa healthy or is it sick?**
- **If sick - in which way is it ill?**
- ***H. Pylori* (Hp) infection? Eradication of Hp?**
- **Is atrophic gastritis present or not?**
- **Is stomach possibly hypochlorhydric or even acid-free – or might it be hyperacid?**
- **Might PPI be helpful – or malpractice?**
- **Cancer risk and ulcer risk? - does the patient need diagnostic endoscopy urgently?**

Clinical practice in Finland today

(age in mean 56 years; range 18-92 years)

- **Stomach mucosa is “sick”: 23%**
- **Stomach mucosa is “healthy”: 77%**
- **Severe atrophic corpus gastritis and acid free stomach occur in 3.5%**
- **PPI medication is prescribed to 13% of patients with acid free stomach - malpractice !?**
- **Reflux symptoms (GERD?) occur in 26% of patients with acid free stomach – risk of misdiagnosis !?**

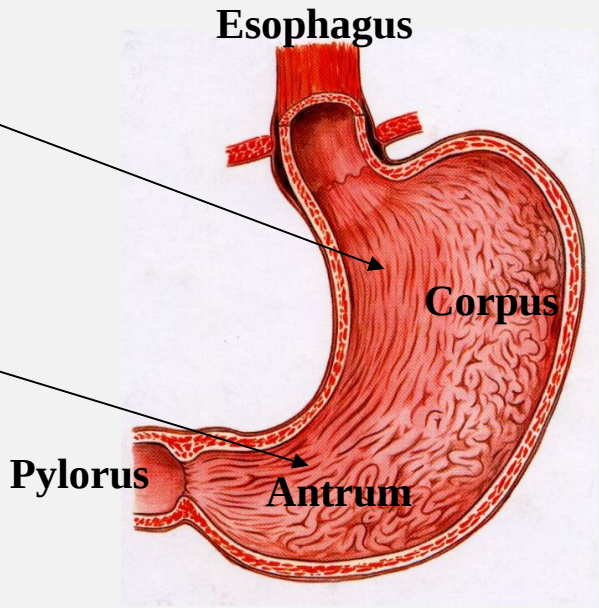
Telaranta-Keerie A et al. Scand J Gastroenterol 2010;45:1036-41

GastroPanel® biomarker test for stomach health – if biomarker levels in blood plasma are normal, stomach mucosa is healthy

Pepsinogen I or Pepsinogen I /II - biomarkers of corpus (oxyntic) mucosa

Amidated gastrin - 17 - biomarker of antrum (antral G cells)

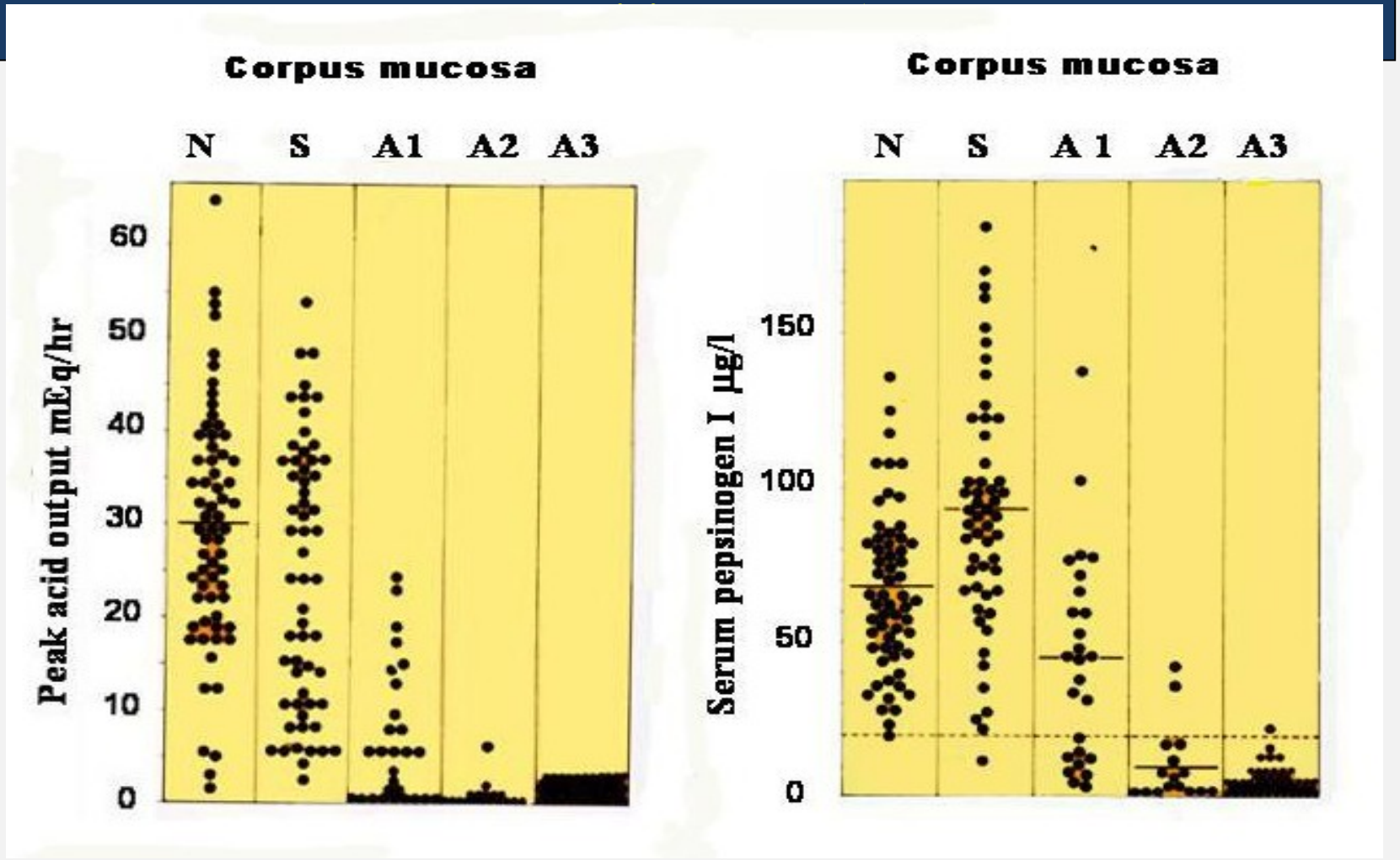
***H.pylori* antibodies - biomarker of gastritis (inflammation)**



Gastrin-17 is indicator of intragastric acidity. Plasma fasting gastrin-17 is high if the stomach is acid-free and low if hyperacid

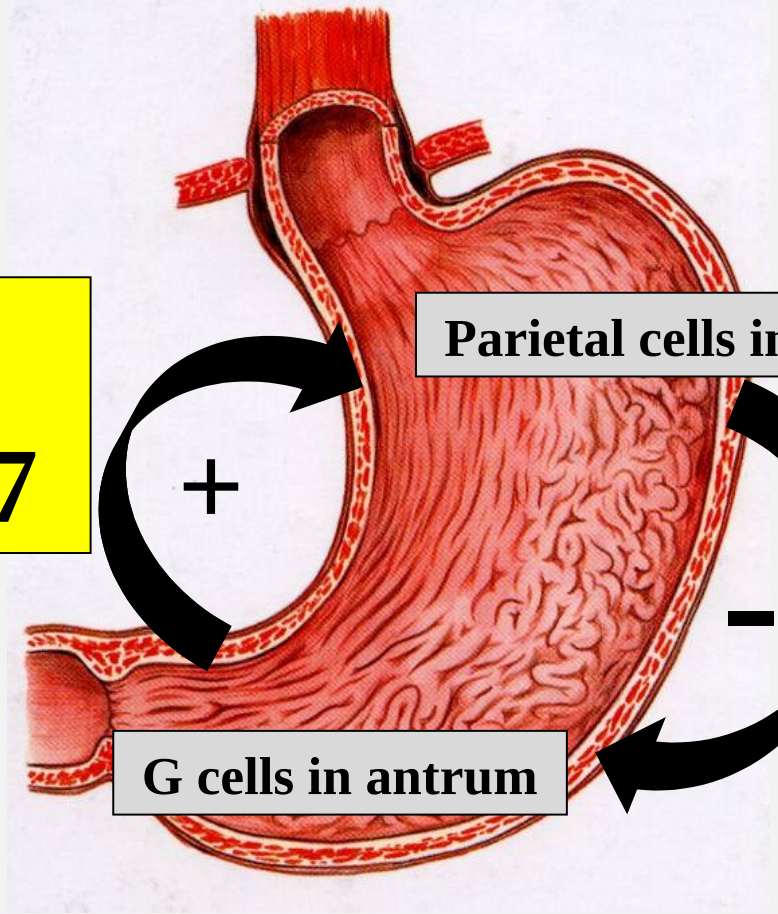
Acid output and plasma pepsinogen I

(Normal =N; *H.pylori* gastritis without atrophy =S; mild, moderate or severe atrophic corpus



Gastrin-17 and Control of Stomach Acid

Plasma gastrin-17



Acid; pH

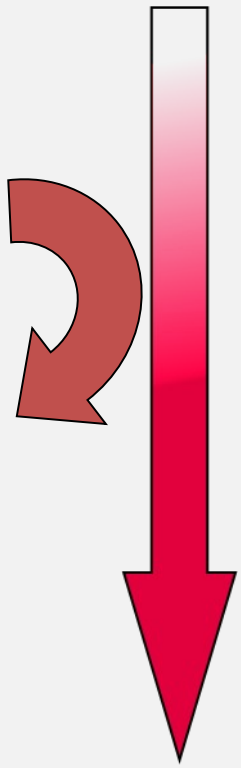
Normal fasting plasma level of G-17: 1-7 pmol/L

H. Pylori Infection and Chronic Gastritis "Correa Sequence"

- NaCl
- high pH
- microbe overgrowth
- N=O mutagens
- acetaldehyde

gene errors accumulate

epigenetic factors



H.pylori gastritis. → **ULCER**

- chronic atrophic gastritis and intestinal metaplasia
- acid-free stomach
- dysplasia (intraepithelial neoplasia)

→ **CANCER**

RELATIVE RISK OF PEPTIC ULCER OR GASTRIC CANCER IN GASTRITIS

ULCER RISK

antrum \ corpus	N	S	A1	A2	A3
N	1	0.5	0.1	0.1	0.1
S	10	10	2	1	0.5
A1	22	22	3	2	1
A2	26	26	3	2	1
A3	26	26	3	2	1

CANCER RISK

antrum \ corpus	N	S	A1	A2	A3
N	1	1	1	2	5
S	1	2	2	2	5
A1	2	2	2	3	5
A2	2	2	4	5	10
A3	18	18	36	36	90

N=normal; S="superficial", non-atrophic gastritis; A1-A3=mild, moderate or severe atrophic gastritis, respectively. Sipponen et al. Int J Cancer 1985

Three major clinical categories

- **Healthy (normal) stomach mucosa:**

  Biomarker levels in blood plasma are normal

- **Non-atrophic *H. pylori* (Hp+) gastritis:**

  Only H. pylori antibodies exist

- **Atrophic corpus gastritis (Hp+ or Hp-):**

  Pepsinogen I <30 µg/L and/or pepsinogen I/II ratio <3;
  if fasting G-17 is high (higher than 7 pmol/L): atrophic gastritis is in gastric corpus alone;
  if fasting G-17 is low (<7 pmol/L) : atrophic gastritis is in whole stomach

Three major clinical categories

- **Healthy (normal) stomach mucosa:**
  Minimal risk of gastric cancer or peptic ulcer
- **Non-atrophic *H. pylori* (Hp+) gastritis:**
  High ulcer risk, low cancer risk
- **Atrophic corpus gastritis (Hp+ or Hp-):**
  High cancer risk, no ulcer risk. Acid free stomach
  - *Approximately 50% of all gastric cancer s occur in this category*
  - *High risk of malabsorption of vitamin B_{12} and micronutrients (e.g. calcium, iron, magnesium and zinc)*
  - *Unexpected absorptions of pharmaceuticals. Stomach is colonized with bacteria and fungi . Risk of pulmonary and gi infections. Acetaldehyde accumulates*

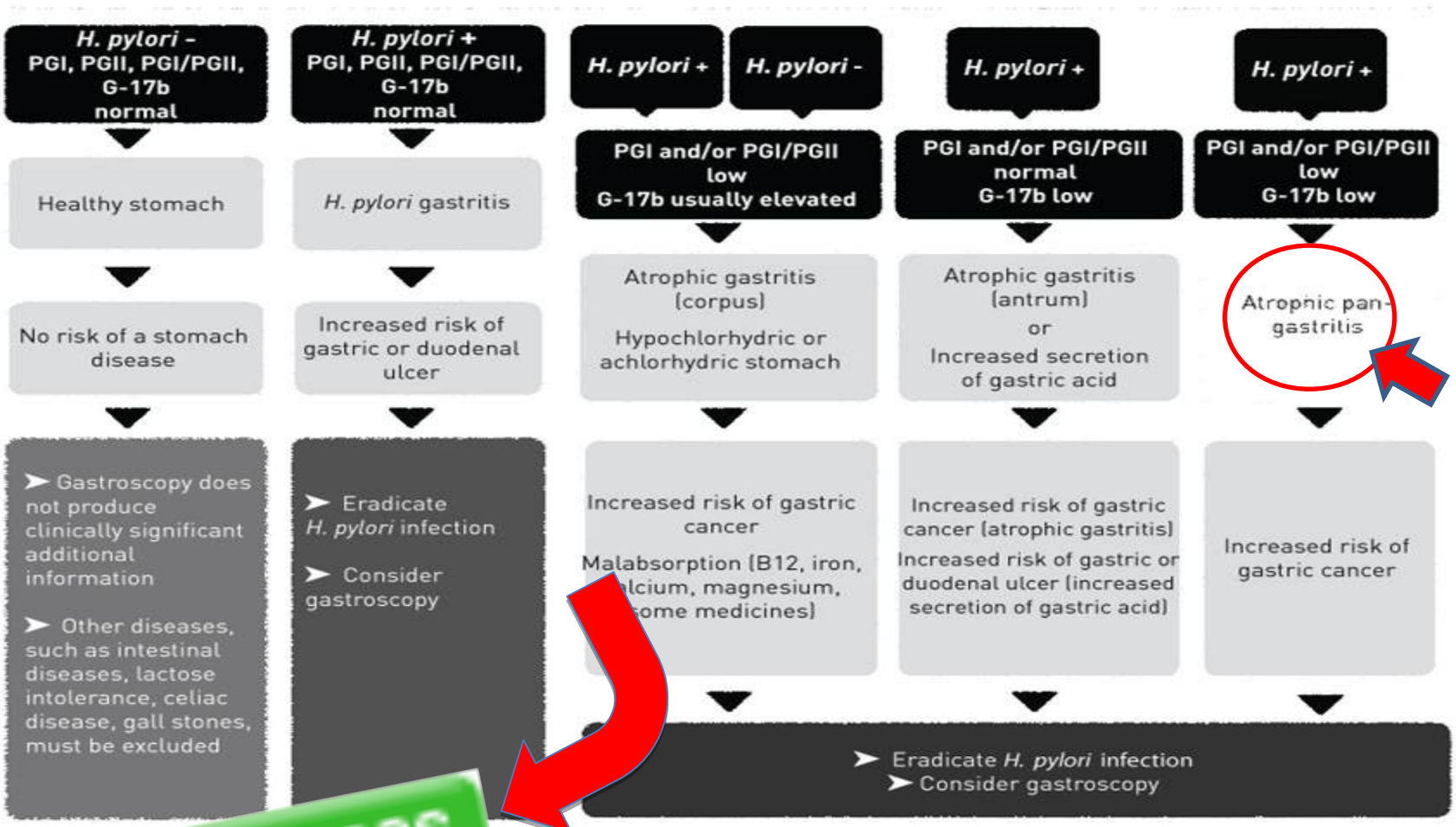
Three major clinical categories

- **Healthy (normal) stomach mucosa:**
  Instant gastroscopy is not mandatory except in cases with GERD (G-17 <2 pmol/L)

- **Non-atrophic *H.pylori* (Hp+) gastritis:**
  Eradication of H.pylori and gastroscopy thinkable

- **Atrophic corpus gastritis (Hp+ or Hp-):**
  Gastroscopy is mandatory because of the cancer risk.
  Eradication of H. pylori is recommended if Hp+.
  Acetium® is helpful in eradication of acetaldehyde

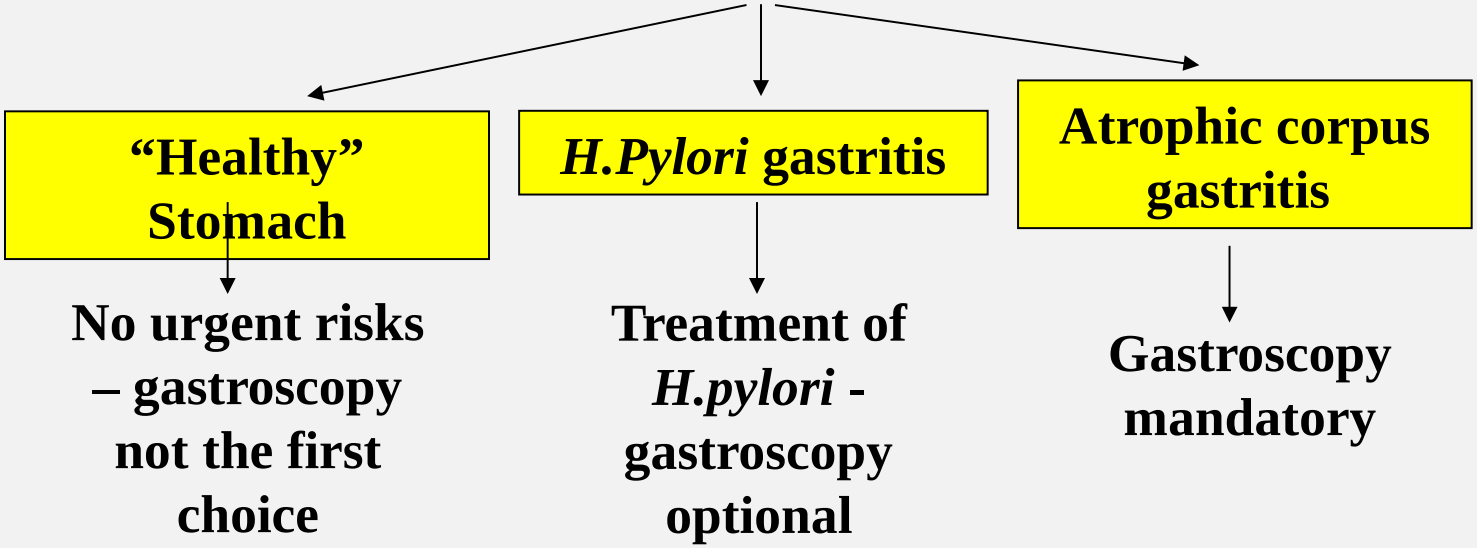
Agreement among experts



Open Access

Agréus, Kuipers, Kupcinskas, Malfertheiner, DiMario, Leja, Mahachai, Niv, van Oijen, Perez-Perez, Rugge, Ronkainen, Salaspuro, Sipponen, Sugano, Sung.: Rationale in diagnosis and screening of atrophic gastritis with stomach-specific plasma biomarkers Scand J Gastroenterol 2012;47: 136–147.

GastroPanel® - practice



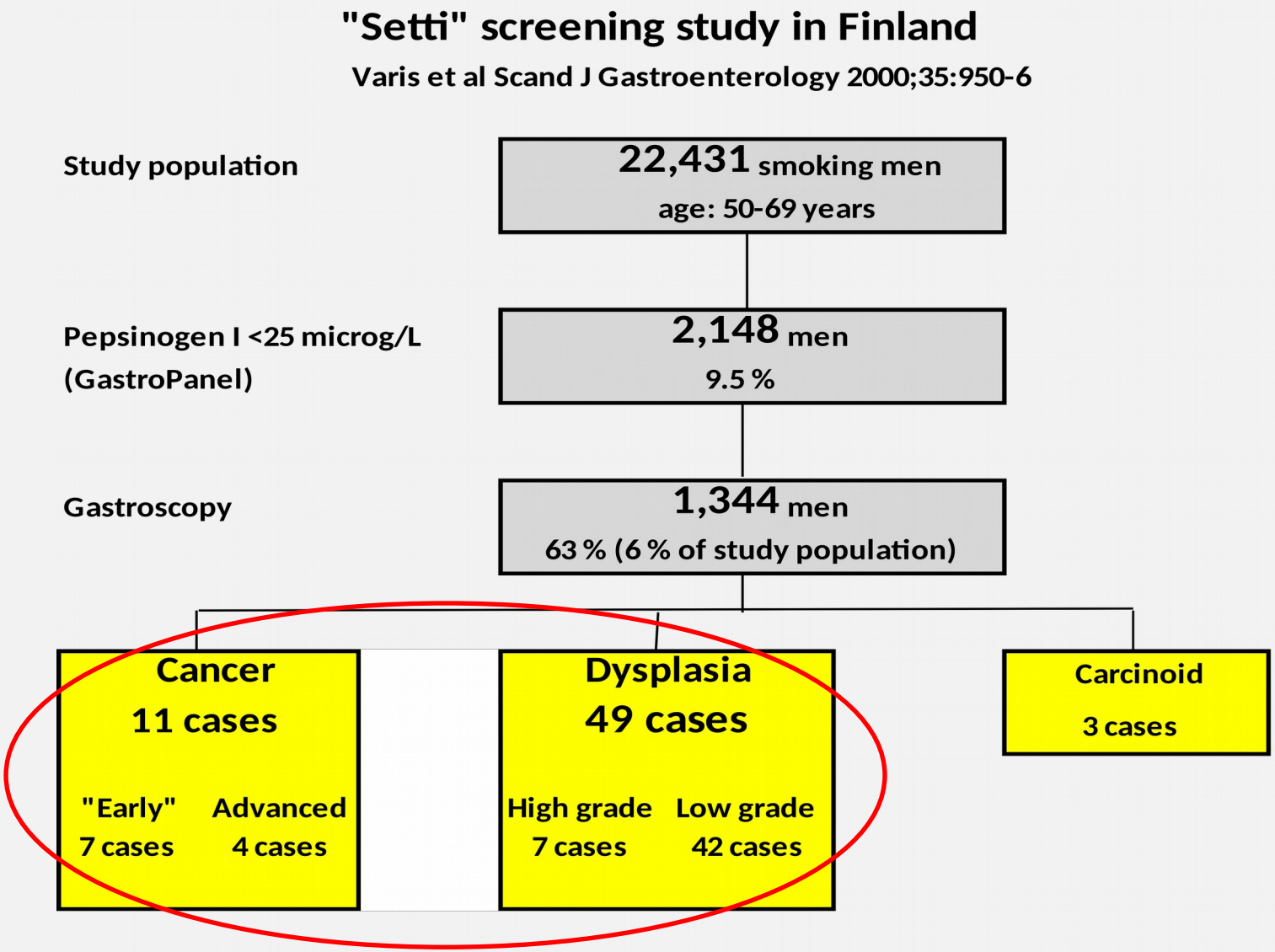
Developing populations (age 50 or more):

30% **50%** **20%**

Developed populations (age 50 or more):

70% **25%** **5%**

Biomarkers in cancer screening



”Kalixanda” population based study in Sweden. Accuracy of GastroPanel® 85%.

GastroPanel®	Endoscopy – biopsy histology			
	Normal	*H.pylori* gastritis	Atrophic corpus gastritis	Total
	Number of cases			
Normal	541	34	4	579
H.pylori gastritis	64	255	24	343
Atrophic gastritis	5	15	34	54
Total	610	304	62	976

Storskrubb et al. Scand J Gastroenterol. 2008;43:1448-55

GastroPanel® examination

"Healthy" versus diseased ("sick" stomach mucosa):

Tohoku – Japan: **Accuracy : 94%**
Sensitivity: 95%
Specificity: 93%

Atrophic gastritis versus non-atrophic gastritis

Kalixanda – Sweden: **Accuracy: 96%**
Sensitivity 71%
Specificity 98%

GastroPanel®

- Noninvasive and easy-to-use test
- Saves money
- Rationalizes diagnostics
- Enables screening of risk patients

- GastroPanel delineates reliably the patients with “healthy” stomach mucosa, i.e., those **without** significant risk of cancer or peptic ulcer!!

“Terve magu terveks eluks”

See in web: Healthy Stomach Initiative (HSI)Tallin 2015