# Screening for Gastric and Colorectal Cancers



### Mārcis Leja

Faculty of Medicine, University of Latvia

Riga, February 9, 2017



# Screening

Screening is identification of groups of individuals from general population in whom the likelyhood of asymptomatic or oligosymptomatic disease is increased by using simple diagnostic tests

The <u>objective</u> of screening is to decrease the <u>mortality</u> caused by the target disease



# WHO criteria for screening

- 1. The condition sought should be an <u>important health problem</u> for the individual and community.
- 2. There should be an <u>accepted treatment</u> or useful intervention for patients with the disease.
- 3. <u>Facilities for diagnosis and treatment should be available.</u>
- 4. There should be a recognizable latent or early symptomatic stage.
- 5. There should be a <u>suitable screening test</u> or examination.
- 6. The test should be <u>acceptable</u> for the population.
- 7. The <u>natural history</u> of the disease should be <u>adequately und</u>erstood.
- 8. There should be an <u>agreed policy for referring</u> for further examination and whom to treat as patients.
- 9. The <u>cost</u> should be economically balanced in relation to possible expenditure on medical care as a whole.
- 10. Case finding should be a <u>continuing process</u> and not a once only project.

### **Screening recommended by European Commission**

- Breast cancer (mammography)
- Cervical cancer (PAP-smear)
- Colorectal cancer (occult blood in the stool)

# **Current Europen activities**

# Second Report on Cancer Screening in the European Union

### International Agency for Research on Cancer



# EU Joint Action





# **European Guide** on Quality Improvement in Comprehensive Cancer Control

Tit Albreht, Régine Kiasuwa & Marc Van den Bulcke



Co-funded by the Health Programme of the European Union

### 5. Running a full-scale program

Long-term evaluation of performance and outcome Continuous communication Continuous training and quality improvement Prospective evaluation of new methods Stopping if no more effective

### 1. Pre-planning

Acquirement and synthesis of evidence Assessment of baseline conditions Prioritization Setting policy objectives and targets Creating communication strategy

### 4. National implementation

Enlargement of organization Early evaluation of performance and outcome Communication Training Reducing barriers and social inequalities Modification or stopping if indicated

### 2. Planning

Establishing governance structure and legislation Establishing coordination & QA teams Developing IT and information systems Contracting local and regional teams Training staff and reference centers Establishing quality assurance protocols

### 3. Piloting

erna

ca

(Randomized) evaluation of performance, logistics and outcome Training Reducing barriers and social inequalities Rollout, modification or stopping if indicated

#### Chapter 4

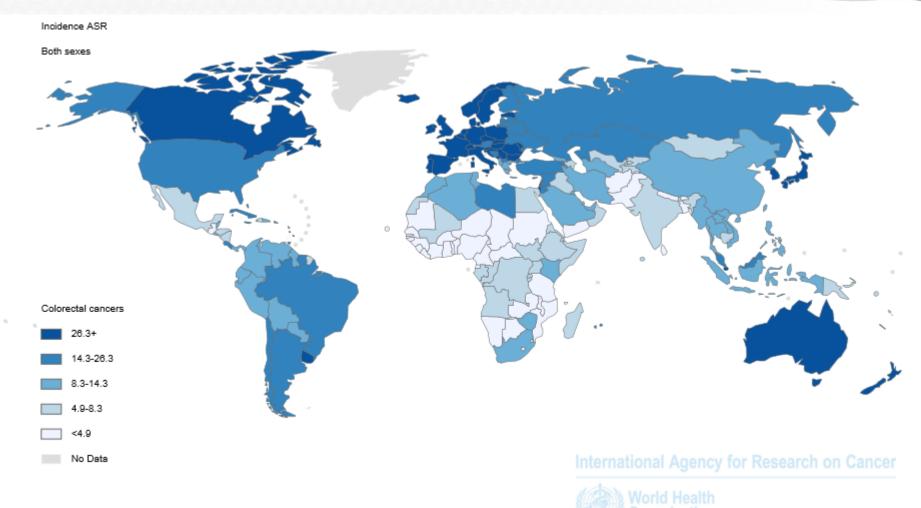
# Cancer screening: policy recommendations on governance, organization and evaluation of cancer screening

Stefan Lönnberg, Mario Šekerija, Nea Malila, Tytti Sarkeala, Marcis Leja, Ondřej Májek, Marco Zappa, Eveline Heijnsdijk, Sirpa Heinävaara, Harry de Koning and Ahti Anttila

### Main messages

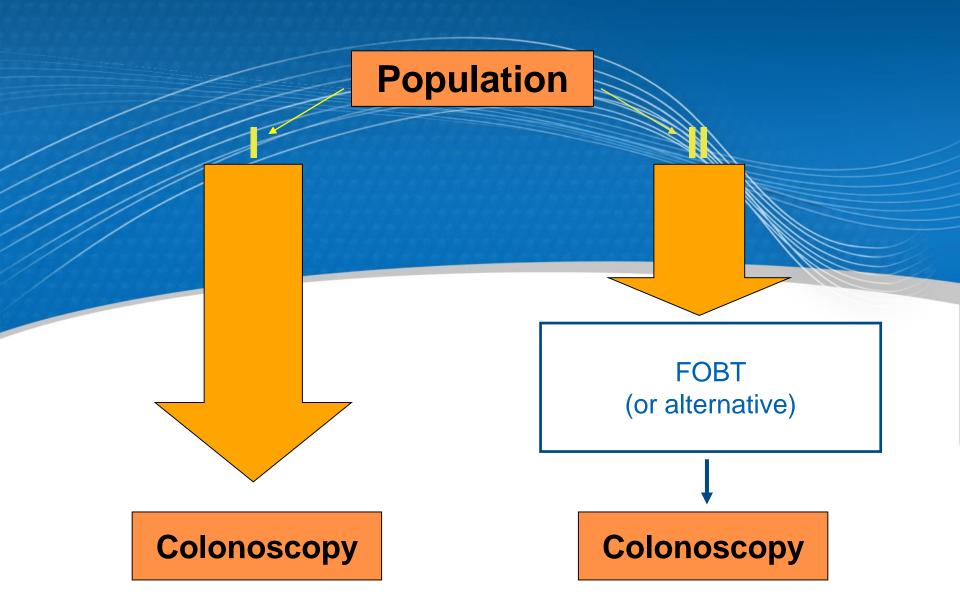
- 1 National structures for governance of screening are here identified as important requirements for evidence-based decision-making and for establishing adequate legal, financial and organizational frameworks for effective cancer screening programmes with integrated quality assurance. We recommend transparent, structured and publicly documented decisionmaking, informed political commitment and broad stakeholder involvement in order to build strong professional support for the aims and means of the screening programme. Governance structures recommended here are currently lacking in many European settings, which may contribute substantially to inequalities in cancer prevention outcomes observed both between and within countries.
- 2 Organization for the practical implementation and the continual gradual improvement of population-based cancer screening programmes further requires careful coordination of this multistep process with feedback and corrective modification at each step, plus revolution of the quality circle. Information systems that permit registration and monitoring of process and outcome are crucial for maintaining current levels of quality, and for guiding further improvement.

# Colorectal Cancer global incidence, ASR, both genders

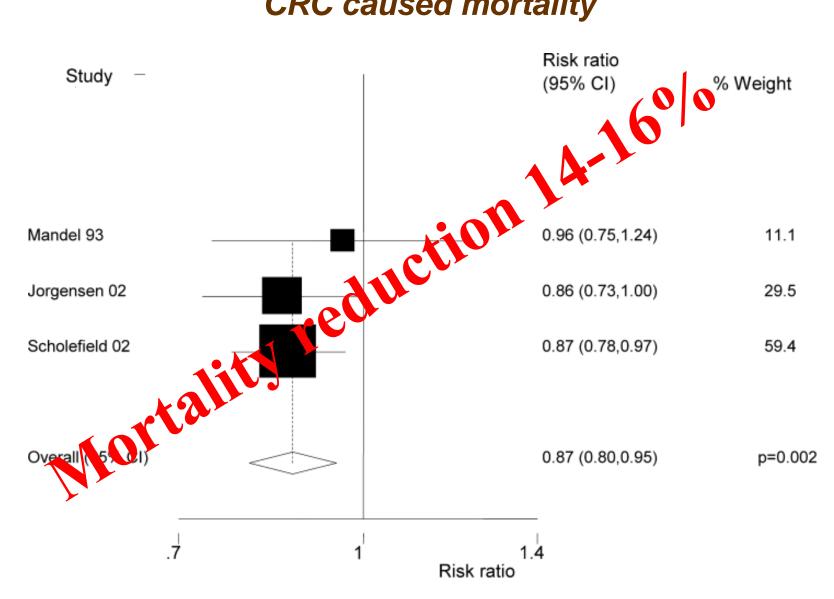


Source: GLOBOCAN 2012 (IARC)

# **Colorectal cancer screening strategies**

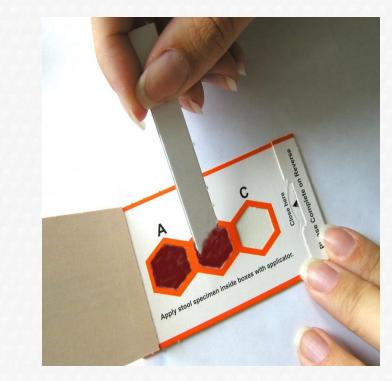


### FOBT comparison to no screening in respect to the CRC caused mortality



Moayyedi P et al. Am J Gastroenterol. 2006

### **Patient's part**



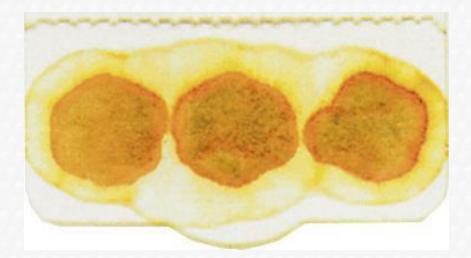
**x** 3



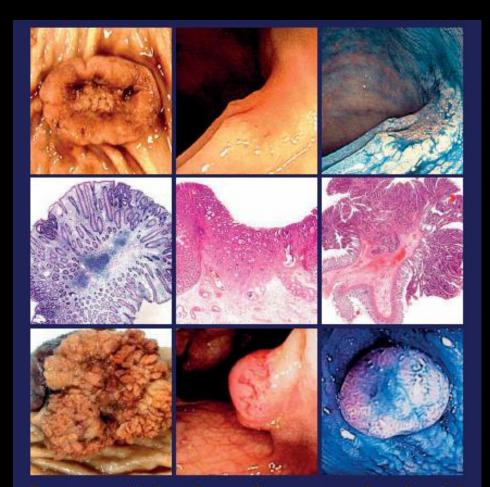
# "Laboratory" part



# Result







# European guidelines for quality assurance in colorectal cancer screening and diagnosis First Edition



**European Commission** 

### **DAZ.**online

Das Internetportal der Deutschen Apotheker Zeitung

#### <u>Pharmazie</u> | <u>Politik</u> | Wirtschaft | Recht | Spektrum | Apothekertag

Sie sind hier: Tagesnews-Politik > News

Politik



Patienten sollen künftig zur Krebsvorsorge eingeladen werden. (Foto: Bilderbox)

#### KREBSBEKÄMPFUNG

Kabinett beschließt Gesetz zum Kampf gegen Krebs

Berlin - Das Bundeskabinett hat in seiner heutigen Sitzung das "Gesetz zur Weiterentwicklung der Krebsfrüherkennung und zur Qualitätssicherung durch klinische Krebsregister" (Krebsfrüherkennungs- und registergesetz) beschlossen. Es sei eine "richtungweisende strukturelle Maßnahme zur Verbesserung der Krebsfrüherkennung", erklärte Bundesgesundheitsminister Daniel Bahr (FDP).

Der demographische Wandel führe zu neuen Herausforderungen im Kampf gegen die Krankheit.

Ausgangspunkt für den Gesetzentwurf ist der "Nationale Krebsplan", der 2008 vom Bundesministerium für Gesundheit, der Deutschen Krebsgesellschaft, der Deutschen Krebshilfe und der Arbeitsgemeinschaft Deutscher Tumorzentren initiiert wurde. Ziel des Plans ist es, die Krebsfrüherkennung, die onkologischen Versorgungsstrukturen und die Qualitätssicherung und Patientenorientierung weiter voranzutreiben. Der heute vom Kabinett beschlossene Gesetzentwurf greift dabei zwei zentrale Punkte aus dem Nationalen Krebsplan auf: Die Optimierung der Krebsfrüherkennung und die Einführung flächendeckender klinischer Krebsregister.

So sollen Patienten künftig stärker erreicht werden, indem sie besser über ihre Ansprüche auf Vorsorgeuntersuchungen informiert werden und persönlich zur Krebsfrüherkennung eingeladen werden. Außerdem werden die Länder im neuen Gesetz dazu verpflichtet, klinische Krebsregister mit einem festgelegten Aufgabenprofil einzurichten. Zu deren Aufgaben gehören insbesondere die Erfassung und Auswertung der Daten über das Auftreten, die Behandlung und den Verlauf von Krebserkrankungen in der ambulanten und stationären Versorgung.

Die Krebsregister sollen dabei überwiegend aus Mitteln der gesetzlichen Krankenversicherung finanziert werden. Die konkrete Gestaltung und vor allem die Finanzierung derselben ist bei den Kassen allerdings noch umstritten. Doris Pfeiffer, Vorstandsvorsitzende des GKV-Spitzenverbandes, erklärte, "Verantwortung, Finanzierung und Nutzen" stehen bei den geplanten klinischen Registern "in keinem angemessenen Verhältnis". Während der Nationale Krebsplan noch von einer geteilten Verantwortung von Bund, Ländern und Selbstverwaltung spreche, finde sich davon in dem jetzt diskutierten Entwurf nur noch wenig.

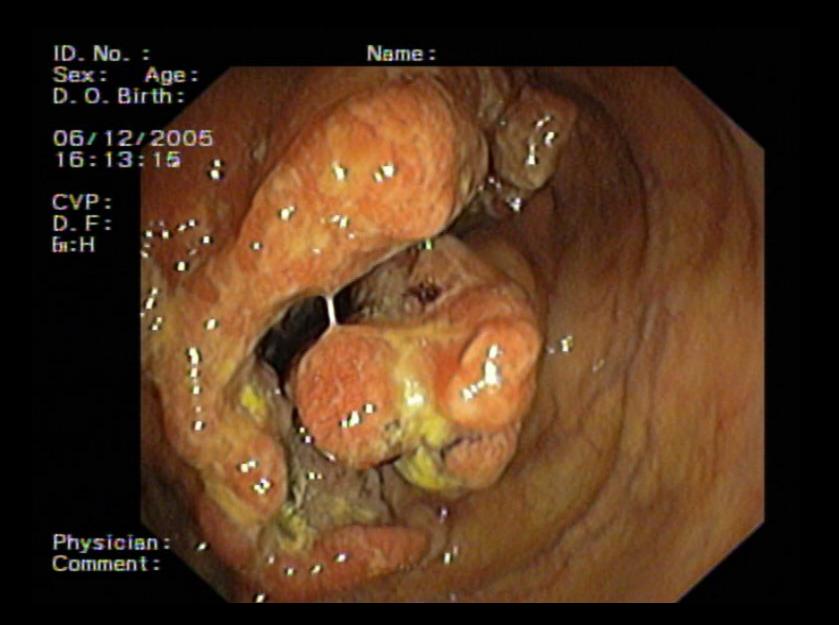
# Change in the test-type



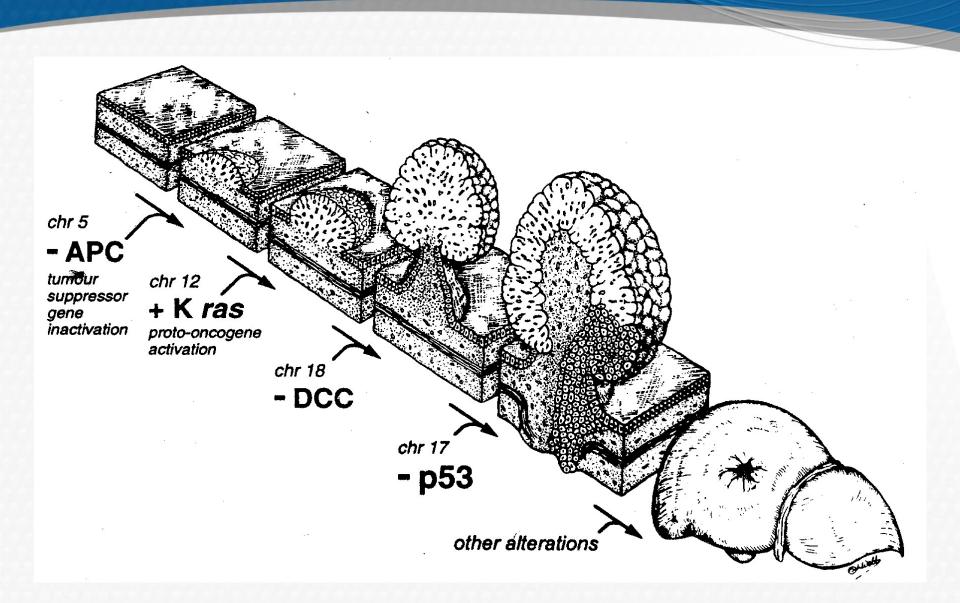


**x** 1





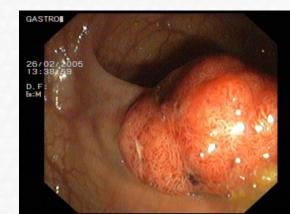
# The development of colorectal cancer

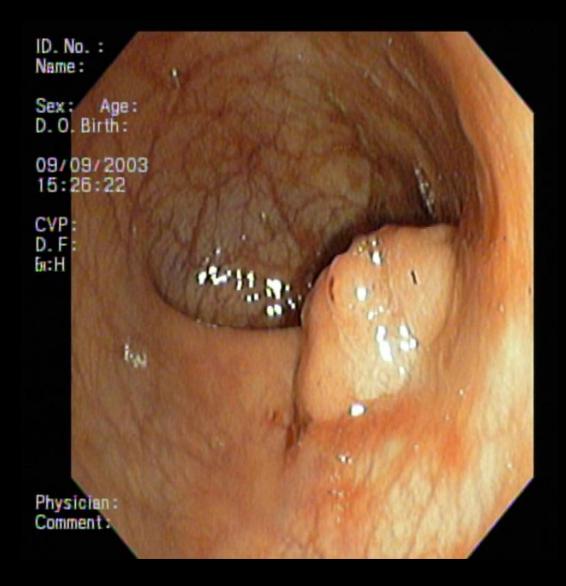


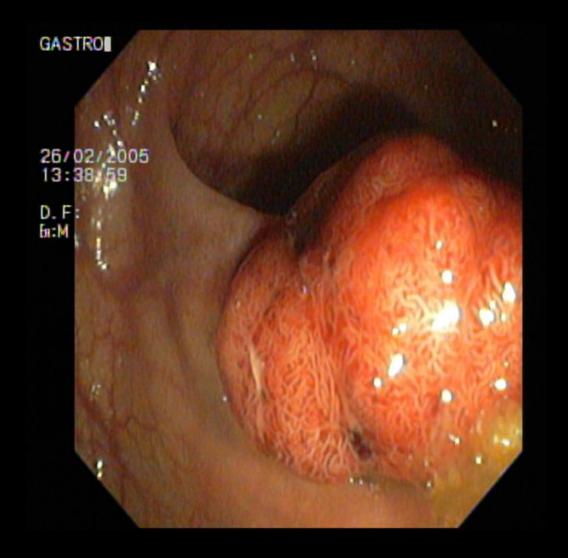
# Effect of colonoscopic polypectomy on incidence of colorectal cancer

	↓ Incidence
*U.S. National Polyp Study	76-90%
+Italian Multicenter Study Group	66%

Winawer, Zauber et al NEJM 1993 +Citarda et al GUT 2001



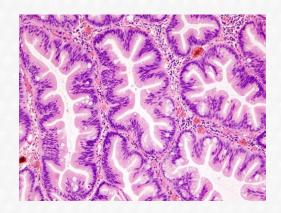




With courtesy from GASTRO archive

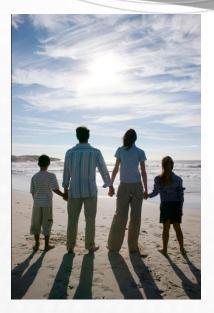
# High-risk adenomas of the colon

- Adenomatous polyps > 1 cm
- Adenomatous polyps with villous component
- Adenomatous polyps with high-grade dysplasia
- Adenomatous polyps with invasive cancer



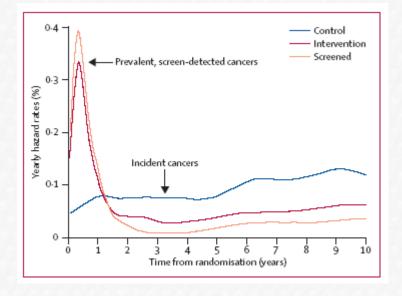
# CRC in the first degree relatives

- Increase in risk
  - > double
  - Lifetime risk 10-12%
- Diagnostic method of choice
  - colonoscopy
- Age for initial diagnostics
  - 40 years or 10 years before the earliest case
  - 5-year control interval recommended



# Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

Wendy S Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andrew R Hart, John M A Northover, D Max Parkin, Jane Wardle, Stephen W Duffy, Jack Cuzick, UK Flexible Sigmoidoscopy Trial Investigators



Sigmoidoscopy with polypectomy significantly decrease the mortality from colorectal cancer

# **Effective colonoscopy**

- Good bowel-prep
- Intubation of caecum gets registered
- Registered number of detected adenomas
- Polypectomy being performed during the initial colonoscopy
- Effective polypectomy technique
- Surveillance of pts with high-risk polyps and other risk groups
- Recommendations for the follow-up investigation



Modified from Rex, AGA, 2010



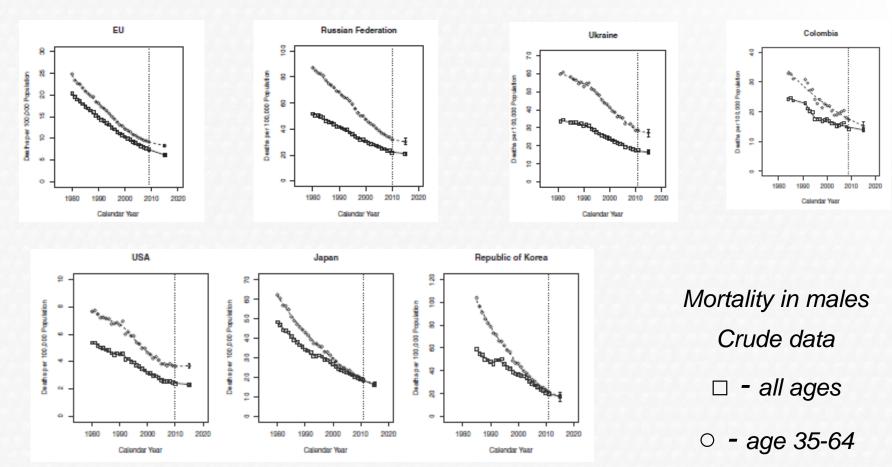


- IARC/WHO *H.pylori* Class I carcinogen
  - 1994 IARC Working Group on the Evaluation of Carcinogenic Risks to Humans
  - Reinforced by WHO, 2011
- The proportion of infection-related cancers
  - H.pylori is the cause of at least 90% of non-cardia gastric cancer
- Subtyping of *H.pylori* strain virulence
  - Not recommended by the current guidelines

IARC Monogr Eval Carcinog Risks Hum . 1994 IARC. A Review of Carcinogen—Part B: Biological Agents . 2011 Dr Martel et al. The Lancet Oncology. 2012. Worldwide trends in gastric cancer mortality (1980–2011), with predictions to 2015, and incidence by subtype

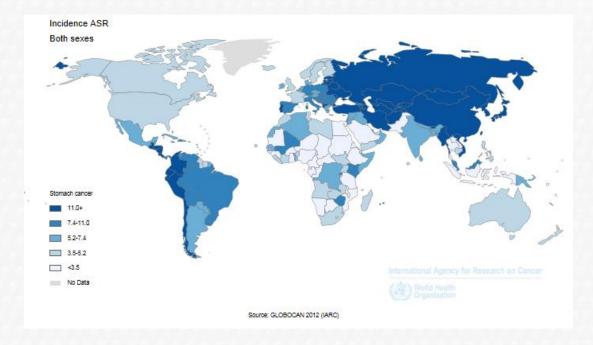
Ana Ferro<sup>a</sup>, Bárbara Peleteiro<sup>a,b</sup>, Matteo Malvezzi<sup>c</sup>, Cristina Bosetti<sup>c</sup>, Paola Bertuccio<sup>c</sup>, Fabio Levi<sup>d</sup>, Eva Negri<sup>c</sup>, Carlo La Vecchia<sup>c,e</sup>, Nuno Lunet<sup>a,b,\*</sup>

### Eur J Cancer, 2014



## **Neglected disease**

- ~ 1 M new cases annually
- ~ 1 M new cases in forseeable future (30 years)



Forman & Sierra. IARC Working Group Reports, No. 8 2014

## **Changing emphasis**

#### VIEWPOINT

### Prevention of Gastric Cancer

Rolando Herrero, MD, PhD Section of Early Detection and Prevention, International Agency for Research on Cancer, Lyon, France. This year, it is estimated that more than 700 000 people will die of gastric cancer, making this disease the third most common cause of cancer death globally.<sup>1</sup> Although gastric cancer rates have been declining by approximately 2% per year, the numbers of cases and deaths are expected to increase in coming years, reflecting increasing numbers of older (and thus, higher-risk)

Population-based *Hpylori* treatment could select for antibiotic-resistant pathogens in the community, although in many countries, such an effect might be overshadowed by indiscriminate use of antibiotics for other human and veterinary purposes. Treating *Hpylori* will alter the overall composition of the intestinal flora; the health consequences are unknown.

JAMA September 24, 2014 Volume 312, Number 12

# Changing attitude of IARC

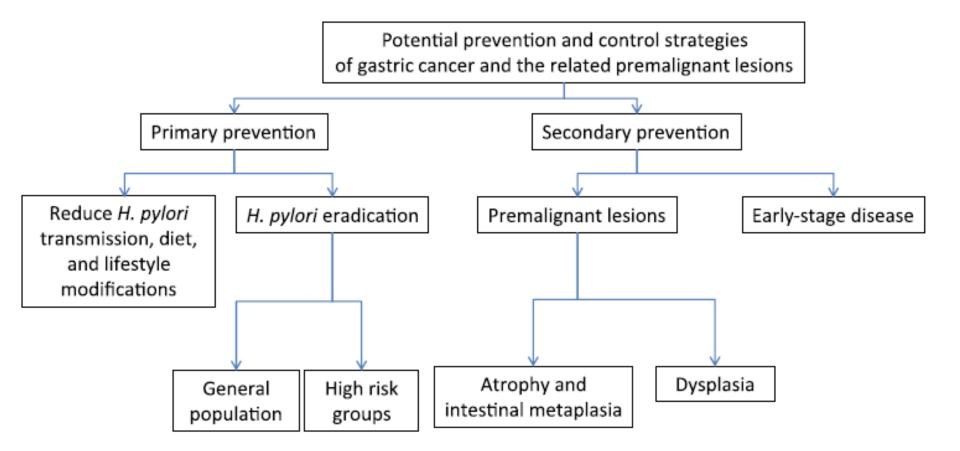
Expert workshop, Dec., 2013

# IARC Position in gastric cancer prevention Lyon, December 4-6, 2013



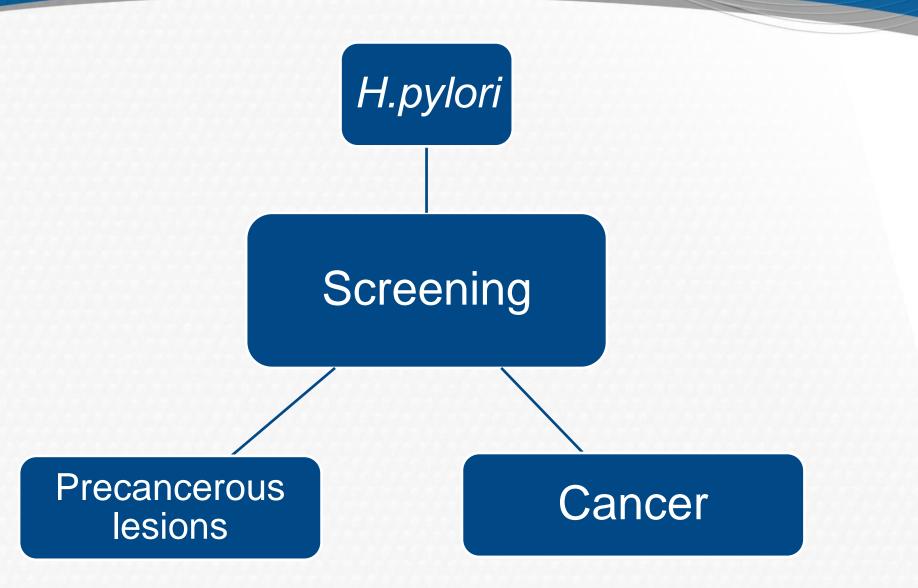
- GC likely to remain condition of high global health importance for the foreseeable future unless effective control measures are implemented
- The importance has been ignored in many parts of the world
- H.pylori eradication middle-aged population is to decrease the risk reduction of 35-40%, and is costeffective
- Implementation of wide eradication by meand of rigorous clinical trials should be considered

# **Prevention strategies**



Leja et at. Best Pract Res Clin Gastroenterol. 2014

Screening options to decrease gastric cancer-cause mortality



# Organized, nationwide cancer screening programs

Country	Japan	S.Korea
Initiation	1983	1999
Target population	≥40 y, both genders	≥40 y, both genders
Method	X-ray	1) Endoscopy
	(endoscopy from 2016)	2) X-ray
Frequency	Annual	Biennial
Coverage	~ 4 M /year	~6.1 M in 2011
Participation	9-20%	44.5% in 2011

Leja et al Best Pract & Res Clinical Gastroenterol 2014

Country	China	Costa Rica	Kazakhstan
Initiation	2008	1996	2013
Target population	40-69 y, both genders	50-74 y, both genders	50-60 y, both genders
Method	Endoscopy	X-ray	Endoscopy
Frequency	Annual	Single-time	Biennial
Coverage (total)	400,000	43,255	306,480 (until June, 2014)
Participation	60-80%	~20%	ND

# Screen-and-treat for H.pylori

- Three recent meta-analysis suggesting the costefficacy of this approach
  - Areia M et al., Helicobacter, 2013
  - Lansdorp-Vogelaar I, et al. Best Pract Res Clin Gastroenterol. 2013
  - Moayyeddi P. IARC Working Group Reports, No. 8 2014
- Concerns
  - Adverse events
  - Resistance

No country has implemented the strategy

Region / Country	Lunqu /China	Matsu / Taiwan	Changhua / Taiwan
Initiation	2011	2004	2012
Target population	24-58 y, both genders	≥ 30 y, both genders	50-69 y, both genders
Method	UBT	UBT	Faecal HpAg
Frequency	Single-time	Single-time	Single-time
Coverage (total)	~200,000	~5,000	~12,000
Participation	55%	~80%	~30%

Leja et al Best Pract & Res Clinical Gastroenterol 2014

# Mass eradication of *H.pylori* in Matzu

The benefit of mass eradication of *Helicobacter pylori* infection: a community-based study of gastric cancer prevention

Yi-Chia Lee,<sup>1,2</sup> Tony Hsiu-Hsi Chen,<sup>1</sup> Han-Mo Chiu,<sup>2</sup> Chia-Tung Shun,<sup>3</sup> Hung Chiang,<sup>4</sup> Tzeng-Ying Liu,<sup>5</sup> Ming-Shiang Wu,<sup>2,6</sup> Jaw-Town Lin<sup>2</sup>

Gut, 2013

- 25% reduction of gastric cancer incidence
- 78.7% reduction of *H.pylori* infection
- 77.2% reduction of atrophy
- No change in IM
- BUT: observational interventional study

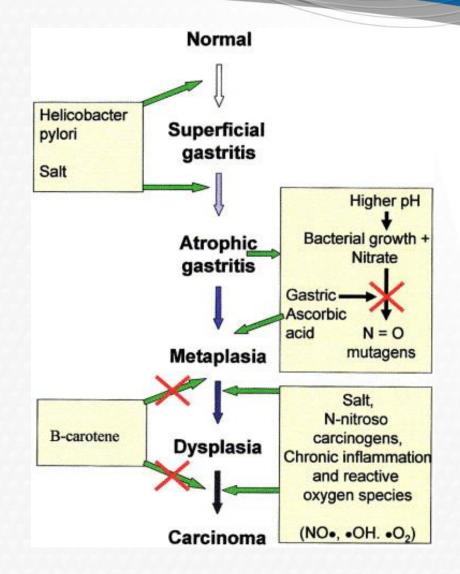
#### **Multistep Model for the Progression of Gastric Cancer**



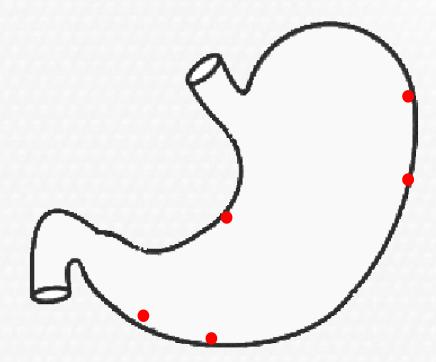
Dec. 4, 2013

#### Correa P et al. Lancet, 1975

Fox JG, Wang TC. N Engl J Med 2001. Houghton J, Wang TC. Gastroenterology 2005



# **Biopsy sampling (updated Sydney classification)**



1/5	.Materiāls	:

5

#### biopsija

2 gab. no antrum mazās kurvatūras, 2) 1 gab. no leņķa rajona, 3) 2 gab. no korpusa mazās kurvatūras.

#### Makroskopija

- 1. 2 biopsijas gabaliņi, vidēji 2 mm ∅, (A1-2)
- 2. 1 biopsijas gabaliņš, vidēji 2 mm 🖉, (B1)
- 3. 2 biopsijas gabaliņi, vidēji 2 mm 🖉, (C1-2)

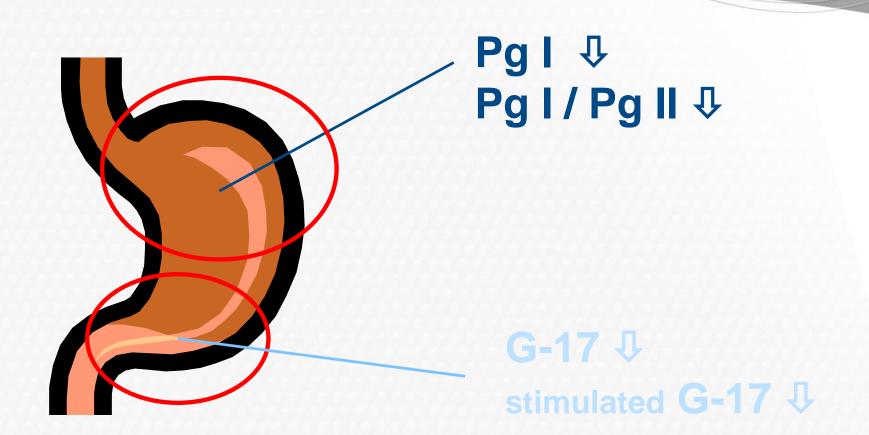
#### Mikroskopija

Lokalizācija	H.pylori kolonizācija	Neitrofilie leikociti	Mononukle- ārās šūnas	Atrofija	Intestinālā metaplāzija
Korpuss	+	++	+++	++	1.12
Leņķis	+	++	++	+	10-0
Antrums	+	++	++	6 <del>4</del>	020

#### <sup>Slēdziens</sup> Izteikts aktīvs hronisks atrofisks korpus un antrum gastrīts. H.pylori (+).

 Manipulācijas kods: 54009
Arhīvs: Makro [-] Bloki [5] Stikli [10] Krāsojums [Giemsa,H&E,] Testēšanas pārskata beigas.

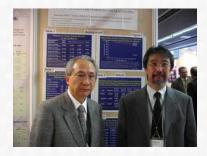
# Biomarkers for atrophy (pepsinogens, *GastroPanel*)



*GastroPanel:* Pg I, Pg II, G17 IgG antibodies to *H.pylori* 

Agreus et al. Scand J Gastroenterol. 2012

# **Pepsinogens for screening**







#### REVIEW

Meta-analysis on the validity of pepsinogen test for gastric carcinoma, dysplasia or chronic atrophic gastritis screening

M Dinis-Ribeiro,<sup>1,2,3</sup> G Yamaki,<sup>1</sup> K Miki,<sup>4</sup> A Costa-Pereira,<sup>3</sup> M Matsukawa<sup>1</sup> and M Kurihara<sup>1</sup>

J Med Screen 2004;11:141-147

Scandinavian Journal of Gastroenterology, 2007; 42: 2-10

informa healthcare

CURRENT OPINION

Importance of atrophic gastritis in diagnostics and prevention of gastric cancer: Application of plasma biomarkers

#### PENTTI SIPPONEN<sup>1,2</sup> & DAVID Y. GRAHAM<sup>3</sup>

<sup>1</sup>Dimision of Pathology, HUSLAB, Helsinki University Central Hospital (HUCH), Finland, <sup>2</sup>Deparament of Pathology, Jorvi Hospital, Espoo, Finland, and <sup>3</sup>Deparament of Medicine, Veterans Affairs Medical Center, and Baylor College of Medicine, Hoston, Texas, USA



#### Available online at www.sciencedirect.com

Digestive and Liver Disease

Digestive and Liver Disease 40 (2008) 523-530

Mini-Symposium

Non-invasive tests in gastric diseases

#### F. di Mario\*, L.G. Cavallaro

Section of Gastroenterology, Department of Clinical Sciences, University of Parma, Italy Reserved 31 January 2008; accepted 18 February 2008 Available online 24 April 2008

#### Pepsinogen testing in current guidelines

#### Asia-Pacific – useful marker to identify populations at high risk for GC

Asia–Pacific consensus guidelines on gastric cancer prevention

Kwong Ming Fock,\* Nick Talley,<sup>†</sup> Paul Moayyedi,<sup>‡</sup> Richard Hunt,<sup>‡</sup> Takeshi Azuma,<sup>§</sup> Kentaro Sugano,<sup>¶</sup> Shu Dong Xiao,<sup>\*\*</sup> Shiu Kum Lam,<sup>††</sup> Khean Lee Goh,<sup>‡‡</sup> Tsutomu Chiba,<sup>55</sup> Naomi Uemura,<sup>¶</sup> Jae G Kim,<sup>\*\*\*</sup> Nayoung Kim,<sup>†††</sup> Tiing Leong Ang,\* Varocha Mahachai,<sup>‡†‡</sup> Hazel Mitchell,<sup>555</sup> Abdul Aziz Rani,<sup>¶¶</sup> Jyh Ming Liou,<sup>\*\*\*\*</sup> Ratha-korn Vilaichone<sup>††††</sup> and Jose Sollano<sup>‡†††</sup>

Fock et al. J Gastroenterol Hepatol 2008.

Maastricht IV-V – pepsinogens as tool for risk stratification

Malfertheiner et al. Gut. 2012, 2017.

#### MAPS – pepsinogens can predict extensive atrophic gastritis

Guidelines for the Management of Precancerous Conditions and Lesions in the Stomach (MAPS)

An European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHSG), European Society of Pathology (ESP) and Sociedade Portuguesa de Endoscopia Digestiva (SPED) Guideline

Dinis-Ribeiro M<sup>1,5</sup>, Areia M<sup>2,5</sup>, de Vries A<sup>3</sup>, Marcos-Pinto R<sup>4,6</sup>, Monteiro-Soares M<sup>5</sup>, O'Connor A<sup>7</sup>, Pereira C<sup>8</sup>, Pimentel-Nunes P<sup>1</sup>, Correia R<sup>5</sup>, Ensari A<sup>9</sup>, Dumonceau JM<sup>10</sup>, Machado JC<sup>11</sup>, Macedo G<sup>12</sup>, Malfertheiner P<sup>13</sup>, Matysiak-Budnik T<sup>14</sup>, Megraud F<sup>15</sup>, Miki K<sup>16</sup>, O'Morain C<sup>7</sup>, Peek RM<sup>17</sup>, Ponchon T<sup>18</sup>, Ristimaki A<sup>19,20</sup>, Rembacken B<sup>21</sup>, Carneiro F<sup>12,22</sup>, Kuipers EJ<sup>3</sup> Dinis-Riberiro et al. Endoscopy & Virchows Archiv .2012.

# Increased risk of gastric cancer in individuals with decreased pepsinogens

- Hisayama study (2446 individuals >40y; follow-up 14 years)
  - HR 4.56 (95% CI: 2.42-8.60) in men
  - HR 5.84 (95% CI: 2.0-17.11) in women
- Wakayama City Study (5209 men; follow-up 10 years)
  - HR 3.60 (95% CI: 2.17-5.96) overall
  - HR 4.47 (95% CI: 2.37-8.42) for intestinal
  - HR 2.41 (95% CI: 1.02-5.71) for diffuse type
- Watabe et al. (9293 individuals; follow-up 4.7 years)
  - HR 6.0 (95% CI: 2.4-14.5) in Group C
  - HR 8.2 (95% CI: 3.2-21.5) in Group D
- Kyoto Prefecture Study (2,859)
  - HR 11.23 (95% CI: 2.71-46.51) in Group C
  - HR 14.81(95% CI: 2.47-88.80) in Group D

Yanaoka et al. Cancer epidemiology, biomarkers & prevention 2008

Watabe et al. Gut 2005

Mizuno et al. Dig Dis Sci 2010

Oishi et al. Am J Epidemiol 2006

# Population-based study in Russia (Siberia)

- Case-control study based on study population of 9360 individuals
- Recruited during HAPIEE program in 2003-2005; followed 2012
- Age 45-69 years
- 60 GC cases revealed, 54 included to the analysis

Group	Indicators of AG and HP infection (%)					
	PGI <30 µg/l	PGII <3 $\mu$ g/l	PGI/PGII <3	G-17 <1 pmol/l	H. pylori IgG (>30 EIU)	
Gastric cancer Control p-Value OR (95% CI)	34.6 15.4 0.006 2.9 (1.3-6.4)	15.7 2.0 0.001 9.0 (1.8-44.3)	39.2 16.2 0.002 3.3 (1.5-7.3)	19.6 11.5 0.179 1.8 (0.7-4.8)	80.0 90.1 0.134 0.4 (0.1-1.3)	



#### RESEARCH ARTICLE

Significance of Serum Pepsinogens as a Biomarker for Gastric Cancer and Atrophic Gastritis Screening: A Systematic Review and Meta-Analysis

Ya-kai Huang, Jian-chun Yu\*, Wei-ming Kang, Zhi-qiang Ma, Xin Ye, Shu-bo Tian, Chao Yan

- PGs for GC: Sensitivity: 69%; Specificity: 73%
- PGs for AG: Sensitivity: 69%; Specificity: 88%

#### **Kyoto conference**

- *H. pylori* gastritis should be defined as an infectious disease
- *H. pylori* infected individuals **should be offered eradication therapy**, unless there are competing considerations
- The **maximum benefit** of *H. pylori* eradication is obtained if it is done while the mucosal damage is still non-atrophic
- Eradication regimens should be based on the best locally effective regimen, ideally using individual susceptibility testing or community antibiotic susceptibility, or antibiotic consumption data and clinical outcome data. The choice of agents available differs in different regions and in part dictates what regimens are possible

### H.pylori & gastric cancer – in Maastricht V

- H.pylori is the most consistent risk factor for gastric cancer
- The influence of environmental factors is subordinate to the effect of *H.pylori* infection
- H.pylori eradication reduces the risk of gastric cancer development
- 'Screen and treat' strategy is recommended in communities with high risk for gastric cancer
- 'Screen and treat' strategy should be considered in communities with intermediate to low risk for gastric cancer
- *H. pylori* eradication for gastric cancer prevention is costeffective in communities with a high risk for gastric cancer

International Agency for Research on Cancer



Helicobacter pylori Eradication as a Strategy for Preventing Gastric Cancer IARC Working Group Report Volume 8

**IARC 2014** 

http://www.iarc.fr/en/publications/pdfs-online/wrk/wrk8/index.php

# Criteria for implementing a NEW cancer screening

- Key criteria for decision whether to implement
  - STEP 1. Effectiveness
    - RCTs with mortality as the endpoint
  - STEP 2. Benefits versus harms
  - STEP 3. Economic evaluation
- Implementation research in each country
  - Feasibility for fulfilling national requirements
- Evaluation, affordability, sustainability

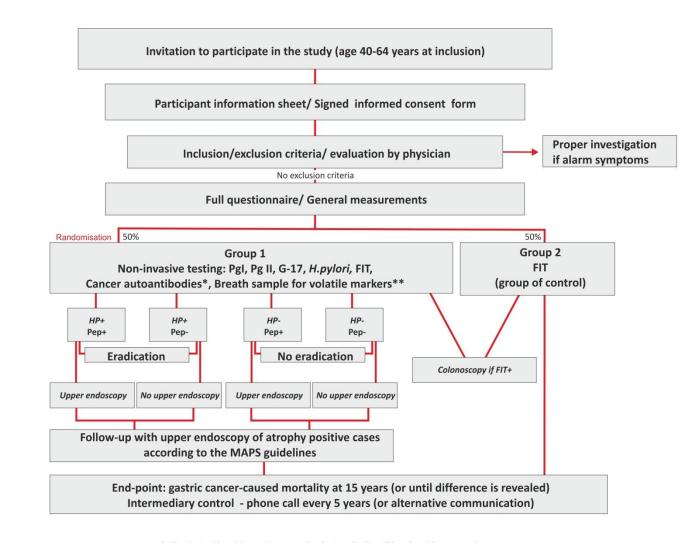


### **Gastric cancer screening**

- Insufficient RCTs
- Long-term adverse effects not sufficiently addressed
  - Potential increase in antibiotic-resistant microorganisms in the community
- Choice of the appropriate target age groups
- Choice of medication



#### **GISTAR** study design



\* All patients with positive gastric cancer-related autoantibodies will be referred for upper endoscopy \*\* Based on volatile marker test results referral for upper endoscopy will be done only if specific panel characteristic for gastric cancer will be revealed

# Conclusions

- 1. The possibilities to reduce digestive cancer mortality are far underutilized
- Mortality from preventable digestive cancers can be further decreased by identification and surveillance of pre-cancerous lesions (adequate biopsy work-up, noninvasive tests)
- 3. CRC screening has to be implemented in organized screening program settings
- 4. There is not enough evidence to implement an organized GC screening
- 5. Studies like GISTAR is the way to go in implementing GC prevention strategies
- 6. There is still space to improve the existing screening tests

# Thank you!