



Update from IARC

David Forman
Head, Section of Cancer Information
IARC, Lyon, France

Helicobacter Circumpolar meeting
Copenhagen
21 Sep 2011

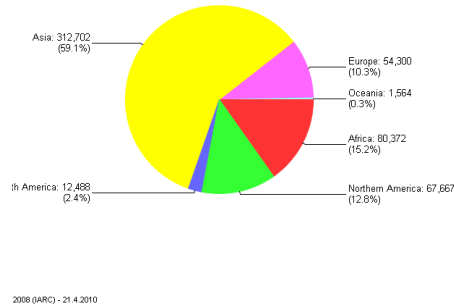
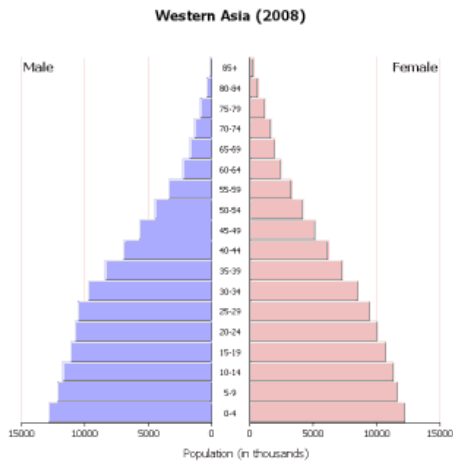
Update from IARC

- Mapping global burden of cancer
- Descriptive epidemiology of cancer in indigenous communities
- Monograph 100B – infectious agents
- Intervention studies consortium

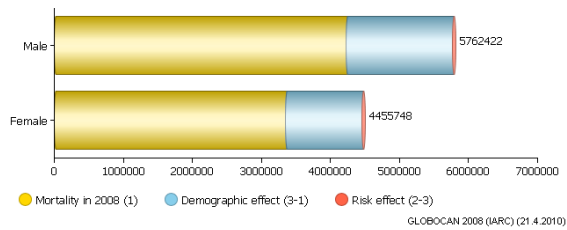
GLOBOCAN 2008

Cancer Incidence and Mortality Worldwide

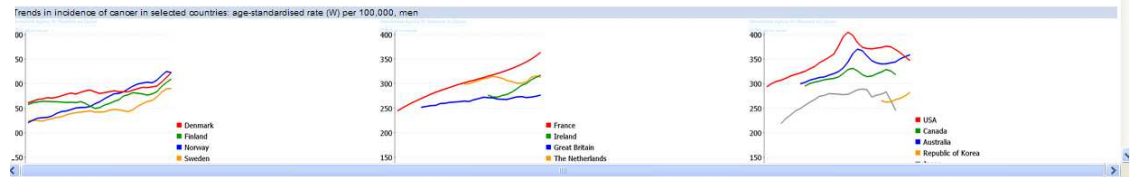
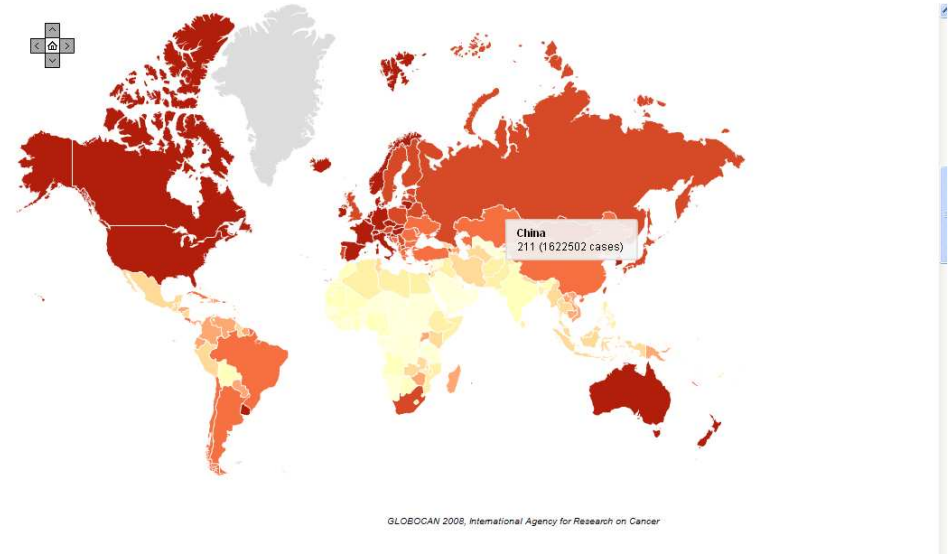
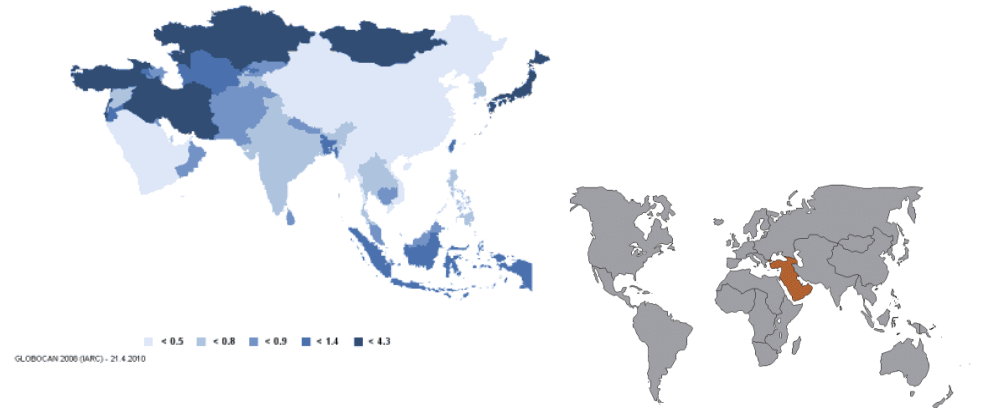
cancer
Number of cancer cases, all ages



World
All cancers but non-melanoma skin cancer
Number of cancer deaths in 2020 (all ages)



Estimated age-standardised incidence rate per 100,000
Testis (C62), all ages



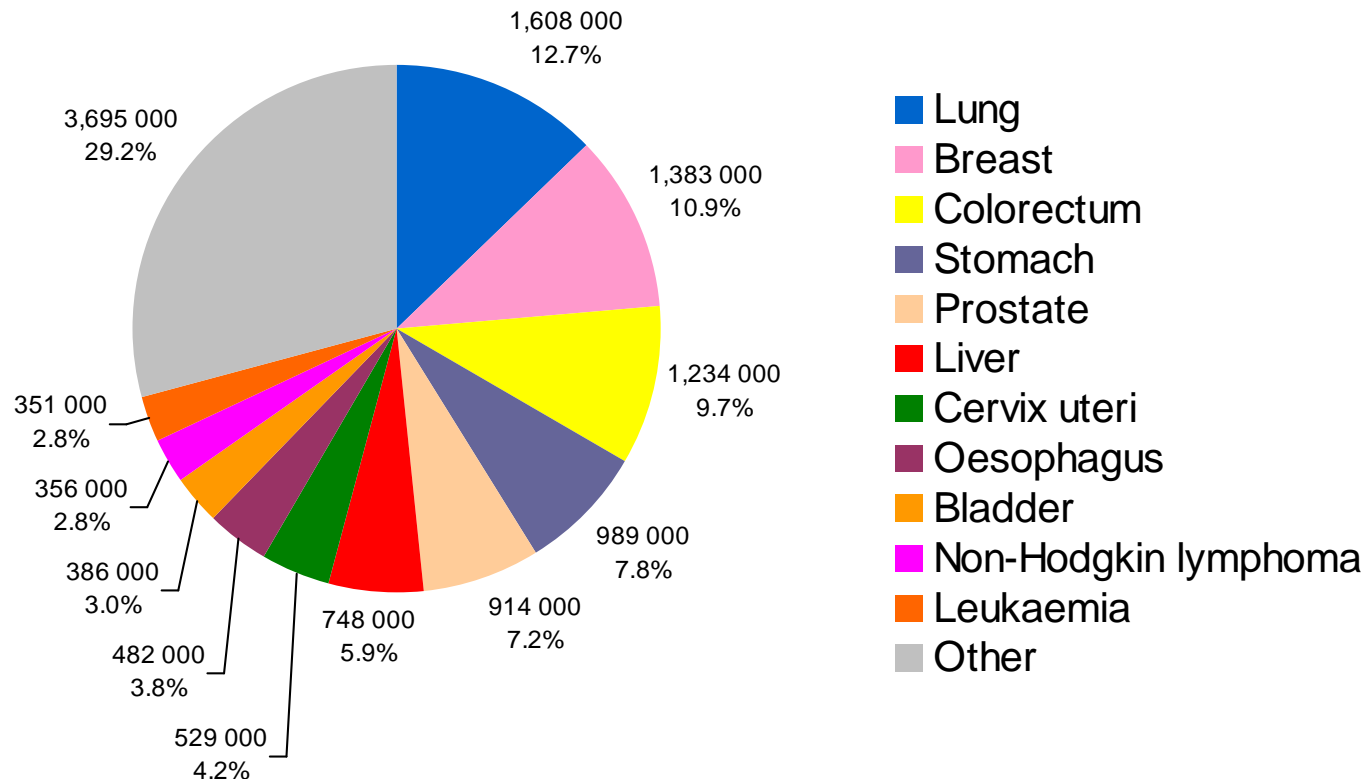
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GLOBOCAN 2008 online <http://globocan.iarc.fr>

Global Burden of Cancer (2008)

Incidence: 12.7 million new cases worldwide (both sexes)
(5.6 in more developed regions, 7.1 in less developed regions)



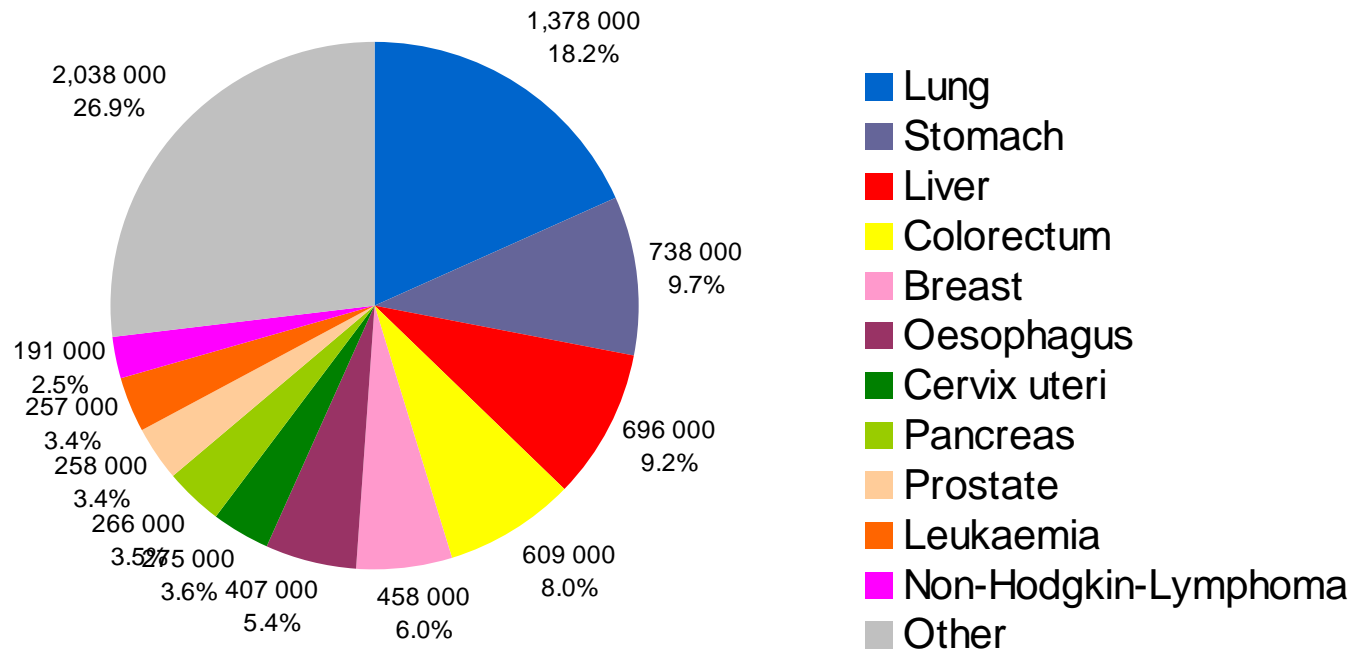
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IARC, GLOBOCAN 2008

Global Burden of Cancer (2008)

Mortality: 7.6 million deaths worldwide (both sexes)
(2.8 in more developed regions, 4.8 in less developed regions)

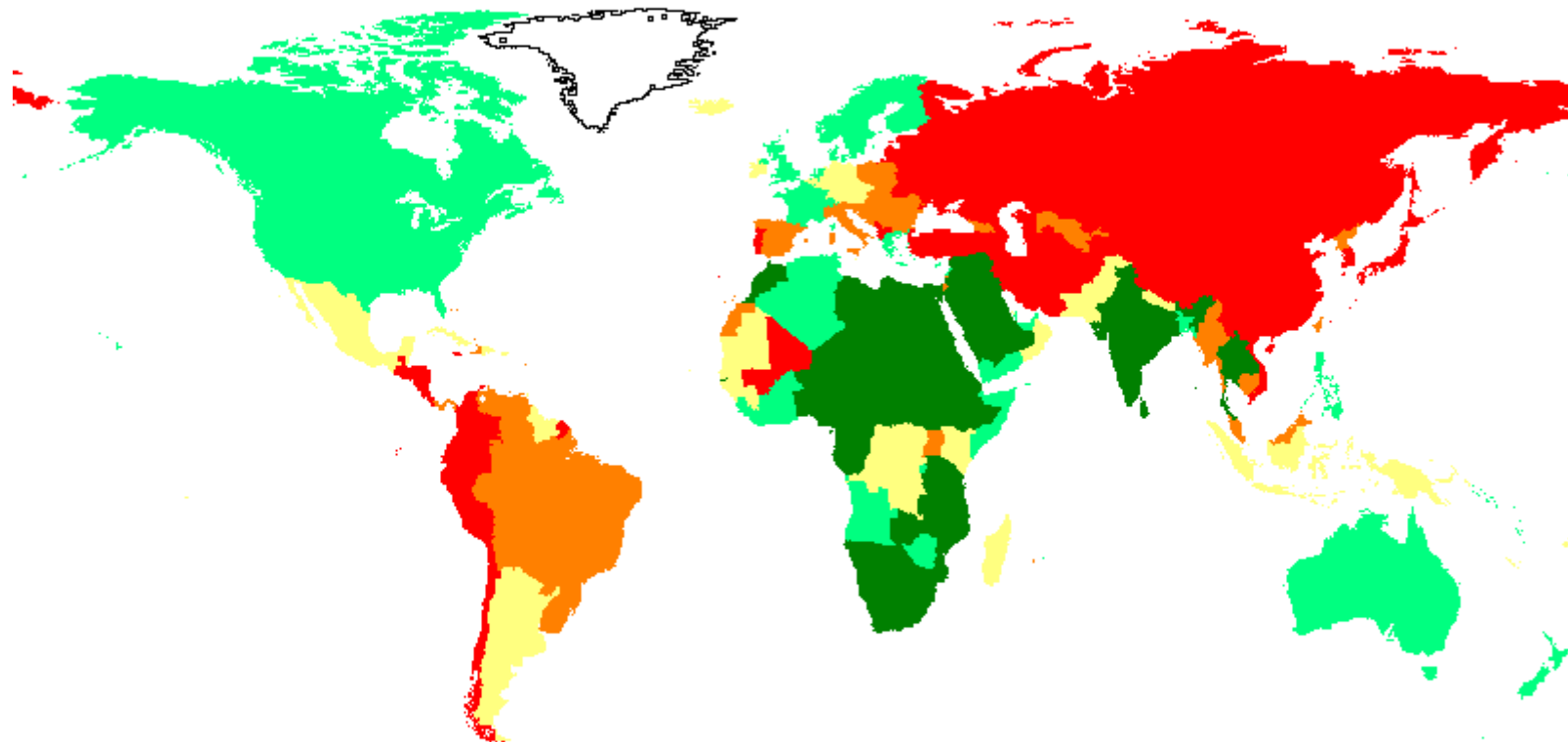


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IARC, GLOBOCAN 2008

Estimated age-standardised incidence rate per 100,000
Stomach: both sexes, all ages

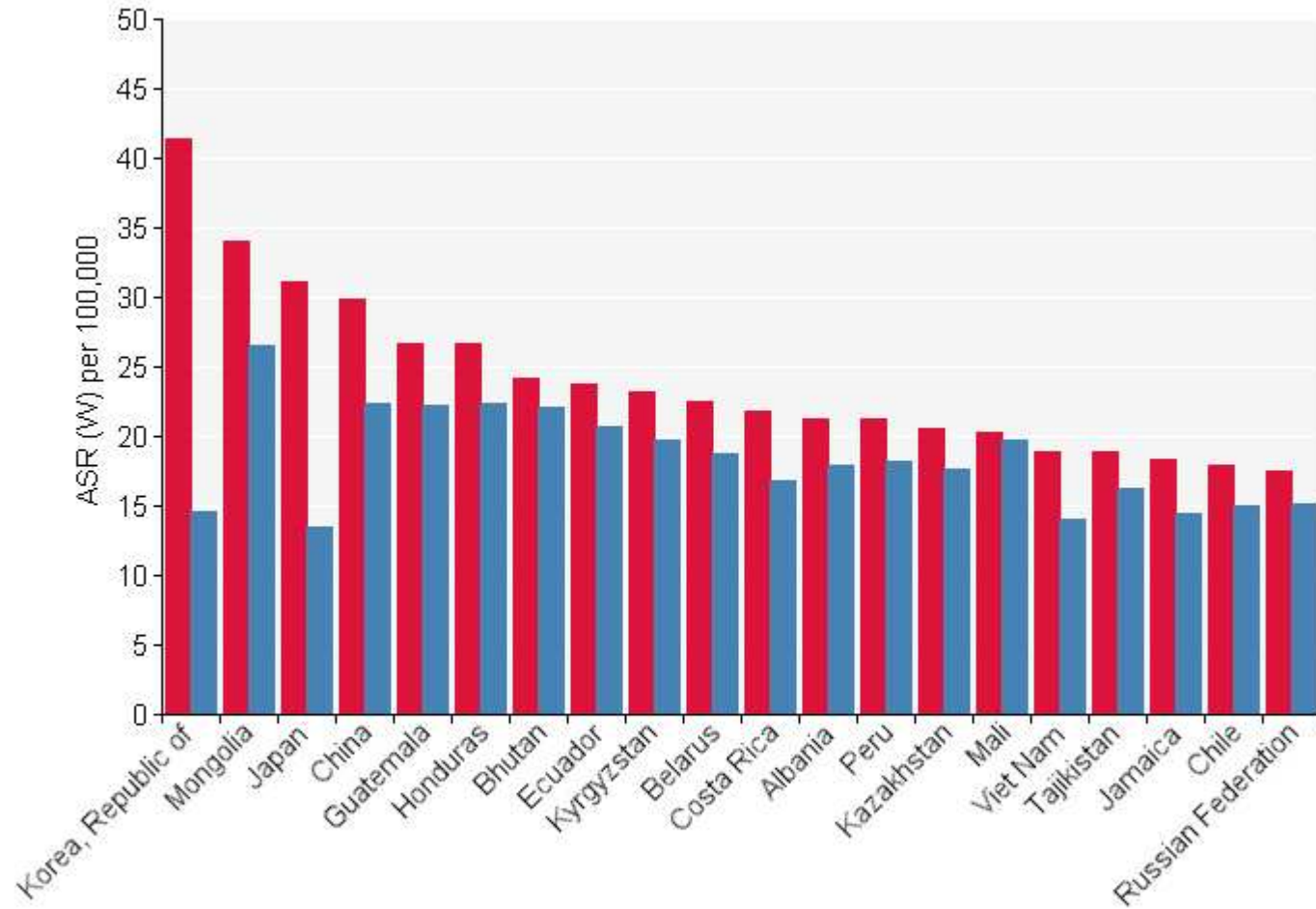


■ < 4.0 ■ < 6.0 ■ < 8.3 ■ < 13.4 ■ < 41.4

Internati

GLOBOCAN 2008 (IARC) - 2.8.2010

Stomach: both sexes, all ages



■ Incidence
■ Mortality

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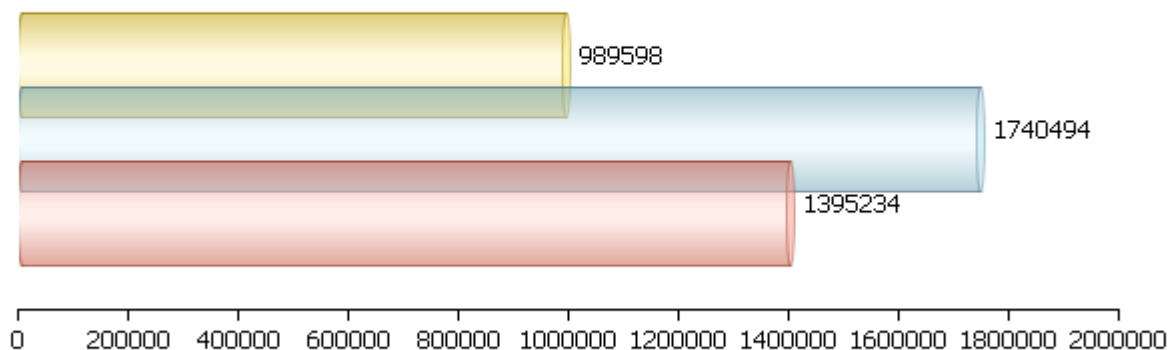


World Health Organization

GLOBOCAN 2008 (IARC) (17.10.2010)

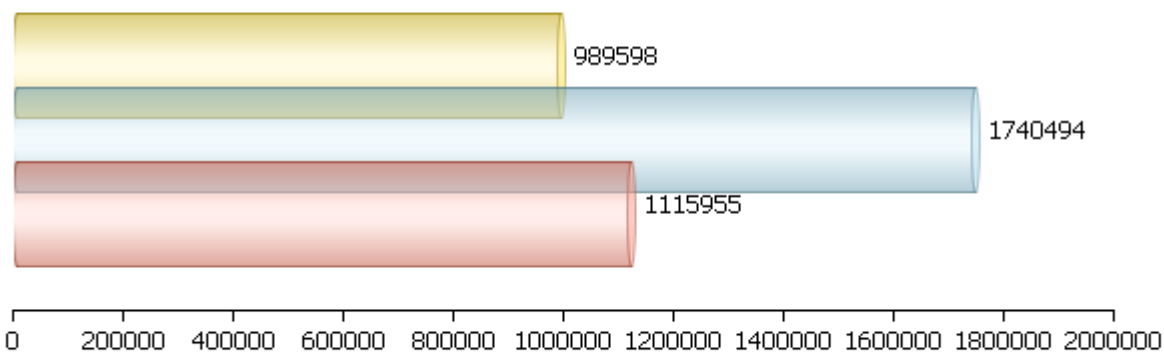
World
Stomach
Number of new cancers in 2030 (all ages) - Both sexes

1% p.a.
decline



World
Stomach
Number of new cancers in 2030 (all ages) - Both sexes

2% p.a.
decline



Internat



● Incidence in 2008 ● Demographic ● Demographic and risk

Descriptive epidemiology of cancer in indigenous communities

- Absence of systematic, global information regarding burden of disease in indigenous communities
- Such communities frequently experience substantively higher incidence, mortality and survival rates than overall population
- High risk communities overlooked in national vital statistics of disease and international comparisons

Descriptive epidemiology of cancer in indigenous communities

- Lung cancer incidence and mortality rates often elevated and increasing in indigenous communities when overall population rates maybe low and declining;
- Cervical cancer survival rates often poorer in indigenous communities when overall population rates maybe improved and increasingly benefiting from screening.

Descriptive epidemiology of cancer in indigenous communities

- Focus – Australia, New Zealand, Pacific Islands, USA & circumpolar countries
- All major cancers
- Incidence, mortality and survival
- Literature review – peer reviewed and “grey” reports
- Work with existing registry (CI5-X submissions) and mortality data sources to identify population stratifications
- Establish collaborative links to identify new (ad-hoc?) stratified sources of information
- Supplement with risk factor and screening data e.g. tobacco consumption, cervical cytology
- Report on barriers to assessment – advocacy
- Suzanne Moore (NHMRC-Aus IARC Fellow)

IARC Monograph 100B

Evidence scope for *H. pylori*

- Update of all agents previously evaluated as class I – definite Human carcinogens (*H. pylori* evaluated in 1994 – vol 61);
- Evaluated 500+ original peer reviewed papers
- Did not formally review evidence from earlier Monograph
- Made use of systematic reviews and meta-analyses where available
- All sources fully documented
- Many detailed tabulations
- Only considered cancer endpoints
- Full monograph now available online: www.iarc.fr

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IARC Monograph 100B

Summary evaluation on *H. pylori*

Overall evaluation

Infection with *Helicobacter pylori* is carcinogenic to humans (Group 1).

- There is *sufficient evidence* in humans for the carcinogenicity of infection with *Helicobacter pylori*.
- Infection with *Helicobacter pylori* causes non-cardia gastric carcinoma and low-grade B-cell MALT gastric lymphoma.
- There is *sufficient evidence* in experimental animals for the carcinogenicity of infection with *Helicobacter pylori*.
- Infection with *Helicobacter pylori* causes gastric adenocarcinoma and MALT gastric lymphoma in mice and gastric adenocarcinoma in gerbils.
- There is *evidence suggesting lack of carcinogenicity* of infection with *H. pylori* for oesophageal adenocarcinoma in humans.

Bouvard *et al* (2009) Lancet Oncology **10**:321-2

[International Agency for Research on Cancer](http://www.iarc.fr/)



IARC Monograph 100B

Epidemiological evidence re: gastric cancer

- Evaluated 17 prospective studies, 6 intervention trials and 3 meta-analyses
- Did not consider retrospective (case-control) studies except a small number using western blot to assess infection
- Distinction between non-cardia and cardia GC
- Reviewed impact of CagA status



IARC Monograph 100B

Epidemiological evidence re: gastric cancer

Non-cardia

- The Working Group noted that, since the 1994 Monograph, a substantial number of prospective observational studies, both nested case-control and cohort, had provided results supportive of an association between *H. pylori* infection and non-cardia GC.
- The magnitude of the risk is increased when more sensitive assay procedures are used and there appears to be a stronger association with CagA positive strains of *H. pylori*.
- There is sufficient evidence of carcinogenicity in humans for non-cardia GC.
- Results from randomized studies have not had sufficient power to evaluate the effect of the impact of *H. pylori* eradication on GC risk.



IARC Monograph 100B

Epidemiological evidence re: gastric cancer

Cardia

- The Working Group noted that, although many studies have reported a lack of association between *H. pylori* infection and the risk of cardia GC, there are substantial difficulties in the reliability of classification of cardia GC that may lead to variability between studies.
- Some studies maybe more inclusive of distal non-cardia GC while other studies maybe more inclusive of lower oesophageal adenocarcinoma cases.



IARC Monograph 100B

Epidemiological evidence re: Oesophageal adenocarcinoma

- Evaluated 2 prospective studies, 15 retrospective studies and 3 meta-analyses
- The observational epidemiological studies are all consistent in showing a lack of association between *H. pylori* infection and an increased risk of oesophageal adenocarcinoma.
- Several of these studies and meta-analyses show a statistically significant *reduced* risk of oesophageal cancer but it is not clear that this represents a causal relationship.
- There is sufficient evidence for a lack of carcinogenicity in humans for oesophageal adenocarcinoma.

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IARC Monograph 100B

Other cancers considered

(inadequate evidence of carcinogenicity in humans)

- Oesophageal squamous cell cancer
 - 2 prospective, 5 retrospective studies
- Hepatocellular carcinoma
 - 17 retrospective studies including pcr analyses of Helicobacter sp.
- Cholangiocarcinoma
 - pcr analyses of Helicobacter sp.
- Colorectal cancer
 - 2 prospective, 12 retrospective studies
- Pancreatic cancer
 - 3 prospective, 1 retrospective studies
- Lung cancer
 - 4 retrospective studies
- Head and neck cancers
 - 4 retrospective studies
- Childhood leukaemia
 - 1 prospective study

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IARC Monograph 100B

Mechanistic evidence

Established mechanistic events

- inflammation
- oxidative stress
- altered cellular turn-over
- gene expression
- methylation
- mutation



Intervention studies for prevention of gastric cancer

- Gastric cancer 2nd cause of cancer death; 10% of total
- Disease burden will increase in low-income economies
- Prognosis remains poor
- *H. pylori* a proven risk factor for distal gastric cancer with strong epidemiological, mechanistic and pathological evidence
- Offers additional protection against peptic ulcer and (small proportion of) dyspepsia
- Economic modelling studies show cost-effective (or even cost neutral)
- Magnitude of risk greater than appreciated

Gastric cancer and *H. pylori* infection: case-control comparisons with improved assay procedures

Population	Cases (% Hp pos)	Controls (% Hp pos)	OR (95% C.I.)	Ref
Sweden	298 (91)	244 (56)	21.0 (8.3-53.4)	Ekstrom Gastro (2001)
Germany	68 (97)	360 (67)	18.3 (2.4-136.7)	Brenner AJE (2004)
Japan	511 (99)	511 (90)	10.2 (4.0-25.9)	Sasazuki CEBP (2006)
Australia	44 (95)	174 (62)	15.9 (3.6-69.6)	Mitchell APT (2008)

Intervention studies for prevention of gastric cancer

Concerns about risks:

- Does infection protect against other diseases?
 - Oesophageal adenocarcinoma
 - Gastro-oesophageal reflux
 - Asthma and atopy
- Impact of large population-based antibiotic therapy
 - Microbial resistance
 - Rare adverse events
 - Susceptibility to other infections
- Psychological impact of identifying infection and uncertainty of treatment

H. pylori eradication trials with gastric cancer as an endpoint

Location	No (age)	Follow-up	Erad. rate	GC in int. grp	GC in cont. grp	p	
China	1630 35-65yrs	7.5 yrs	85%	7(0.86%)	11(1.3%)	0.33	Wong JAMA 2004
China	2258 35-64yrs	10 yrs	73%	19(1.7%)	27(2.4%)	0.19	You JNCI 2006
Japan EMR-GC patients	544 20-79yrs	3yrs	75%	9 (3.3%) 2 nd metachr.c ancers	24(8.8%) 2 nd metachr. cancers	0.009	Fukase Lancet 2008

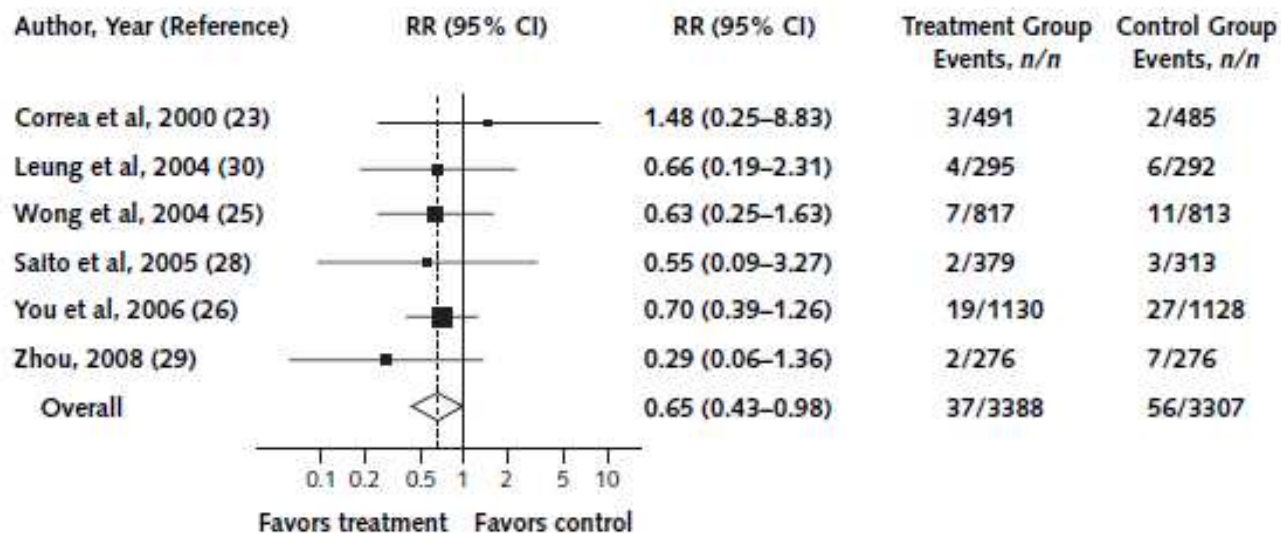
H. pylori eradication trials with gastric cancer as an endpoint

Location	No (age)	Follow-up	Erad. rate	GC in int. grp	GC in cont. grp	p	
China	552 35-75yrs	10 yrs	89%	2 (0.7%)	7 (2.5%)	n.s.	Zhou Gastro 2008
Japan	692 20-59yrs	4 yrs	85%	2 (0.5%)	3 (1.0%)	n.s.	Saito Gastro 2005
Colombia	976 29-69yrs	6 yrs	74%	3 (0.6%)	2 (0.4%)	n.s.	Correa JNCI 2000

Meta-analysis: Can *Helicobacter pylori* Eradication Treatment Reduce the Risk for Gastric Cancer?

Lorenzo Fuccio, MD; Rocco Maurizio Zagarl, MD; Leonardo Henry Eusebi, MD; Liborla Laterza, MD; Vincenzo Cennamo, MD; Liza Ceroni, MD; Diego Grilli, PhD; and Franco Bazzoli, MD

Figure 2. Forest plot of 6 studies reporting gastric cancer in treated and nontreated groups.



Intervention studies for prevention of gastric cancer

- Current evidence base suggestive of effect with borderline statistical significance
- Too few trials and generally underpowered for cancer endpoints
- No trials have investigated adverse events
- Relevance to populations (e.g. in Europe) where susceptible to potential adverse events
- None are trials of screening process *per se*.

Intervention studies for prevention of gastric cancer

- Gastric cancer is, and will remain, a major global cancer challenge;
- Therapeutic prospects for gastric cancer remain dismal;
- *H. pylori* is a major cause of gastric cancer;
- Eradication of *H. pylori* at an early stage of pathogenesis prevent the cancer;
- Public health and regulatory authorities will not be convinced by current evidence base to implement screening;
- More randomised studies of screening strategies are needed to quantify magnitude of benefit and risk;
- Many populations remain with a high burden of gastric cancer and appropriate for future studies.

Intervention studies for prevention of gastric cancer

- International Consortium
- Coordinate (and pool?) ongoing studies in China, Latin America, UK + (?) elsewhere
- Existing studies inconclusive for public health action
- Act as a stimulus for further studies and positive funding decisions
- Rolando Herrero



We welcome collaborations:

cin@iarc.fr

formand@iarc.fr

Use our software:

Cancer *mondial* <http://www-dep.iarc.fr/>

GLOBOCAN2008 <http://globocan.iarc.fr/>

CI5 <http://ci5.iarc.fr/>

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