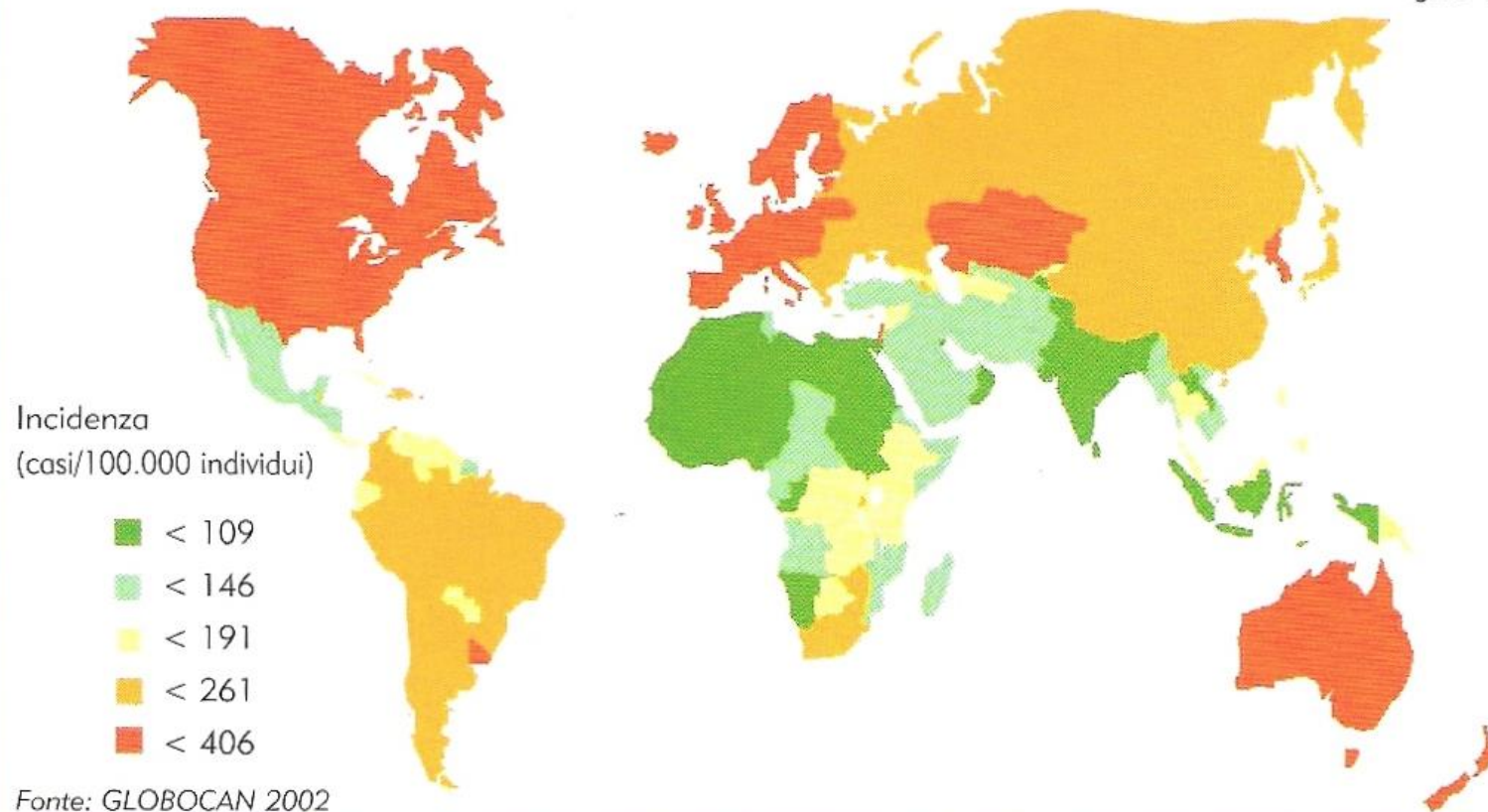
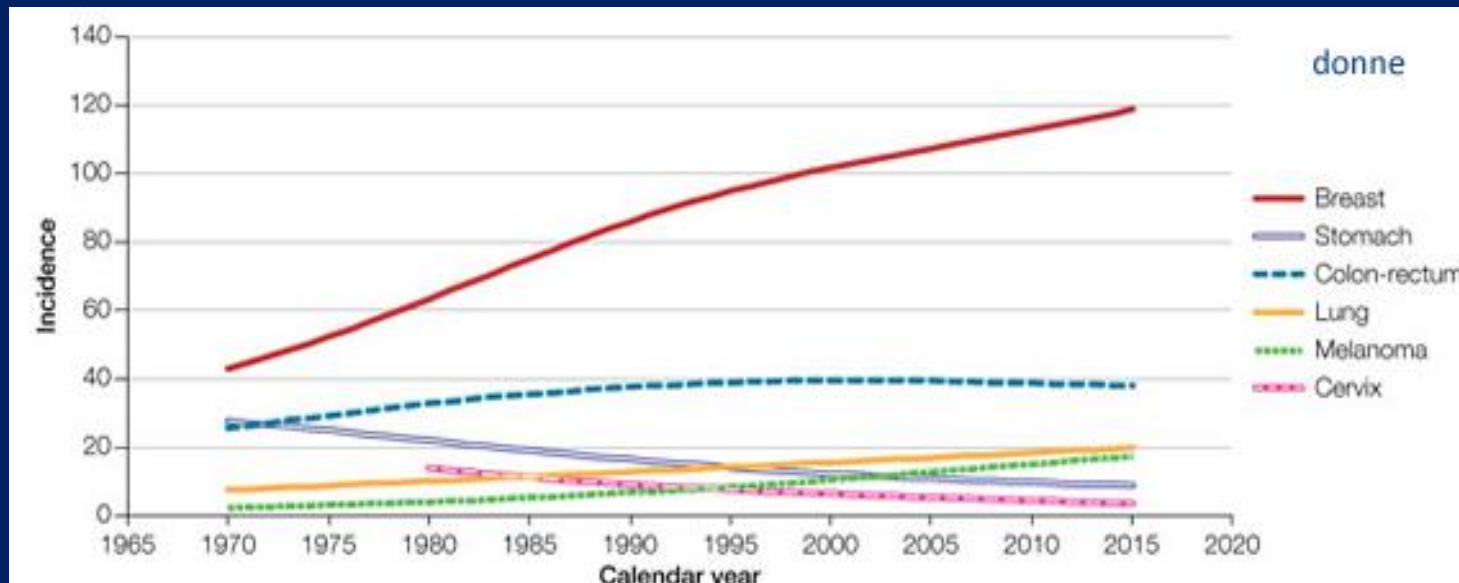
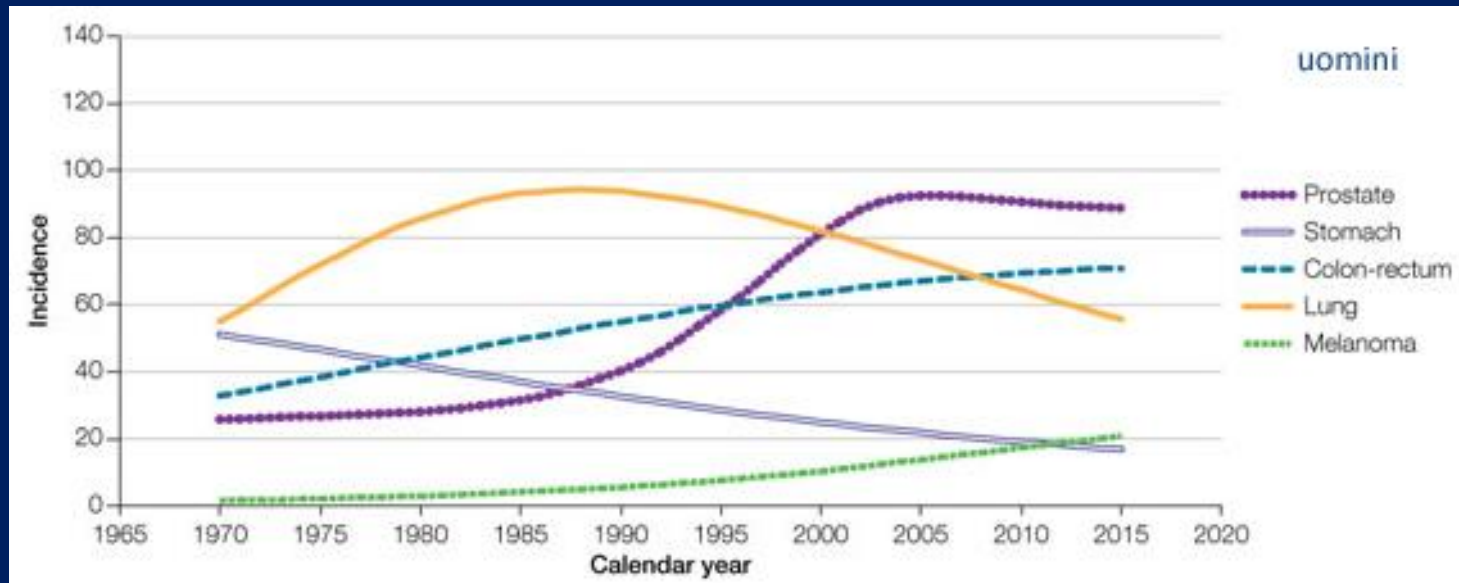
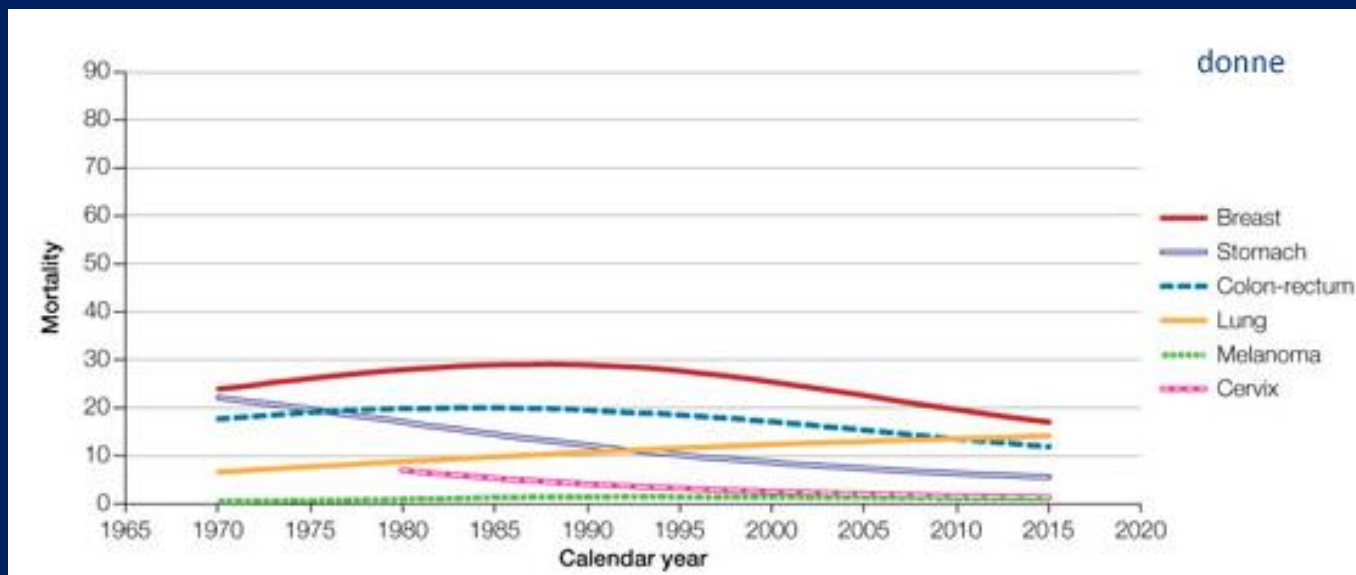
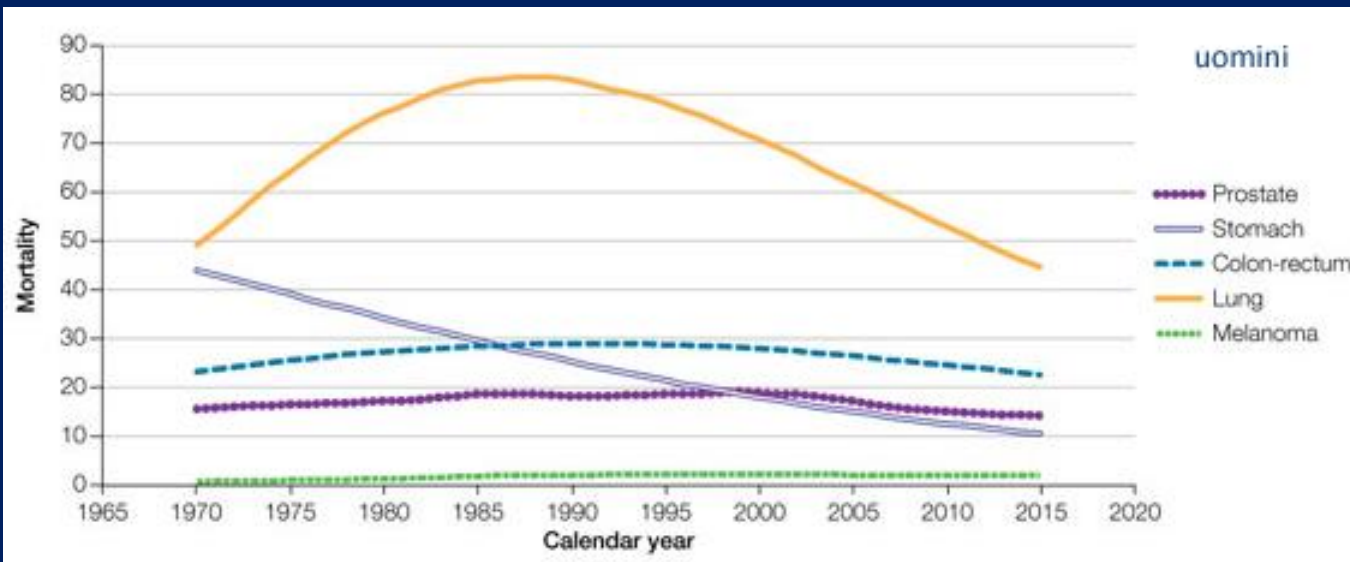


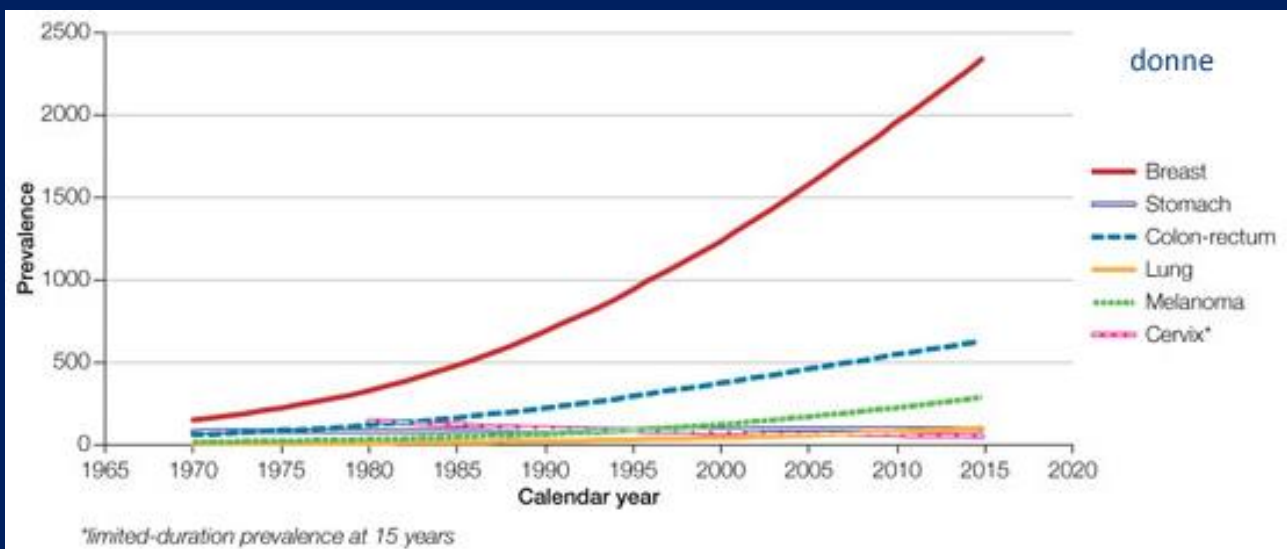
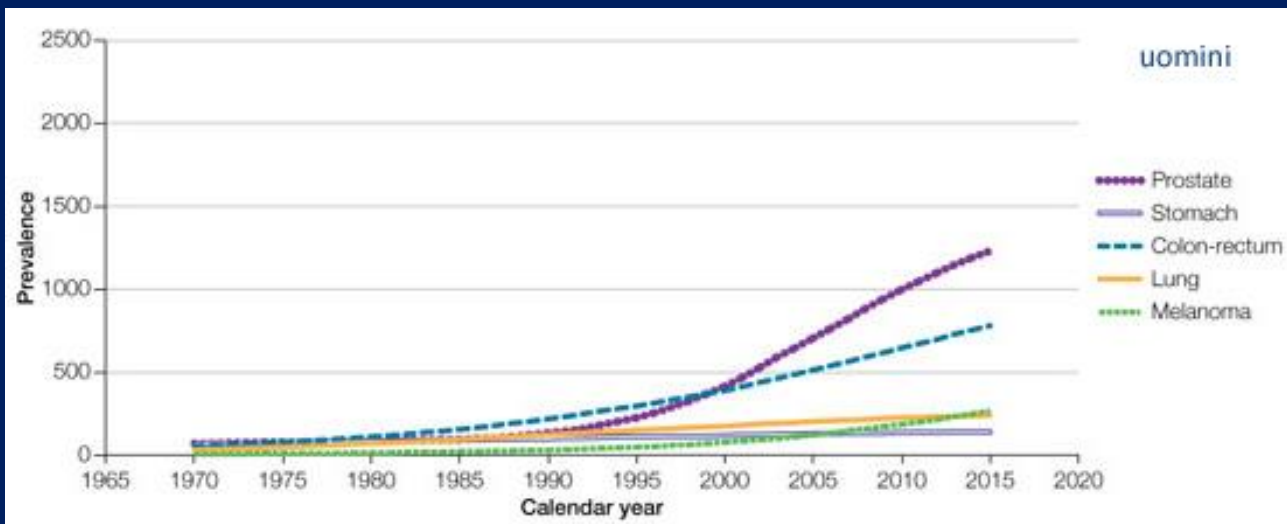
DISTRIBUZIONE MONDIALE DELL'INCIDENZA DEL CANCRO

Figura 3









Secondary Causes of Constipation

Mechanical Obstruction

Anal stenosis

Colorectal cancer

Extrinsic compression

Rectocele or sigmoidocele

Stricture

Medications

Antacids

Anticholinergic agents (antiparkinsonian, antipsychotics, antispasmodics, tricyclic antidepressants)

Anticonvulsants (carbamazepine, phenobarbital)

Antineoplastic agents (vinca derivatives)

Calcium channel blockers (verapamil)

Diuretics (furosemide)

5-HT₃ antagonists (e.g., alosetron)

Iron supplements

Nonsteroidal anti-inflammatory drugs

Mu-opioid agonists (loperamide, morphine)

Metabolic and Endocrinologic Disorders

Diabetes mellitus

Heavy metal poisoning (e.g., arsenic, lead, mercury)

Hypercalcemia

Hyperthyroidism

Hypokalemia

Hypothyroidism

Panhypopituitarism

Pheochromocytoma

Porphyria

Pregnancy

Neurologic and Myopathic Disorders

Amyloidosis

Autonomic neuropathy

Chagas' disease

Dermatomyositis

Intestinal pseudo-obstruction

Multiple sclerosis

Parkinsonism

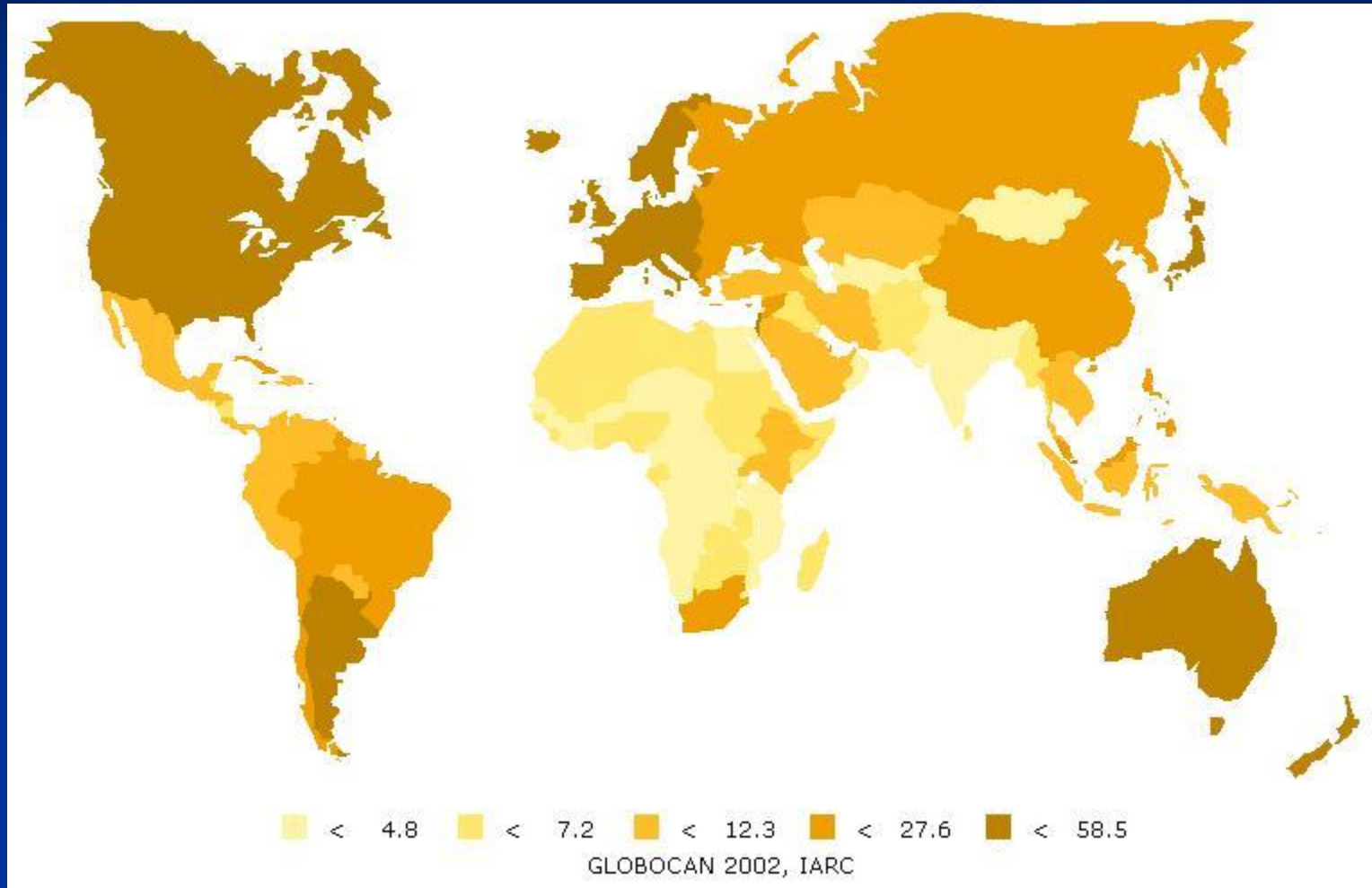
Progressive systemic sclerosis

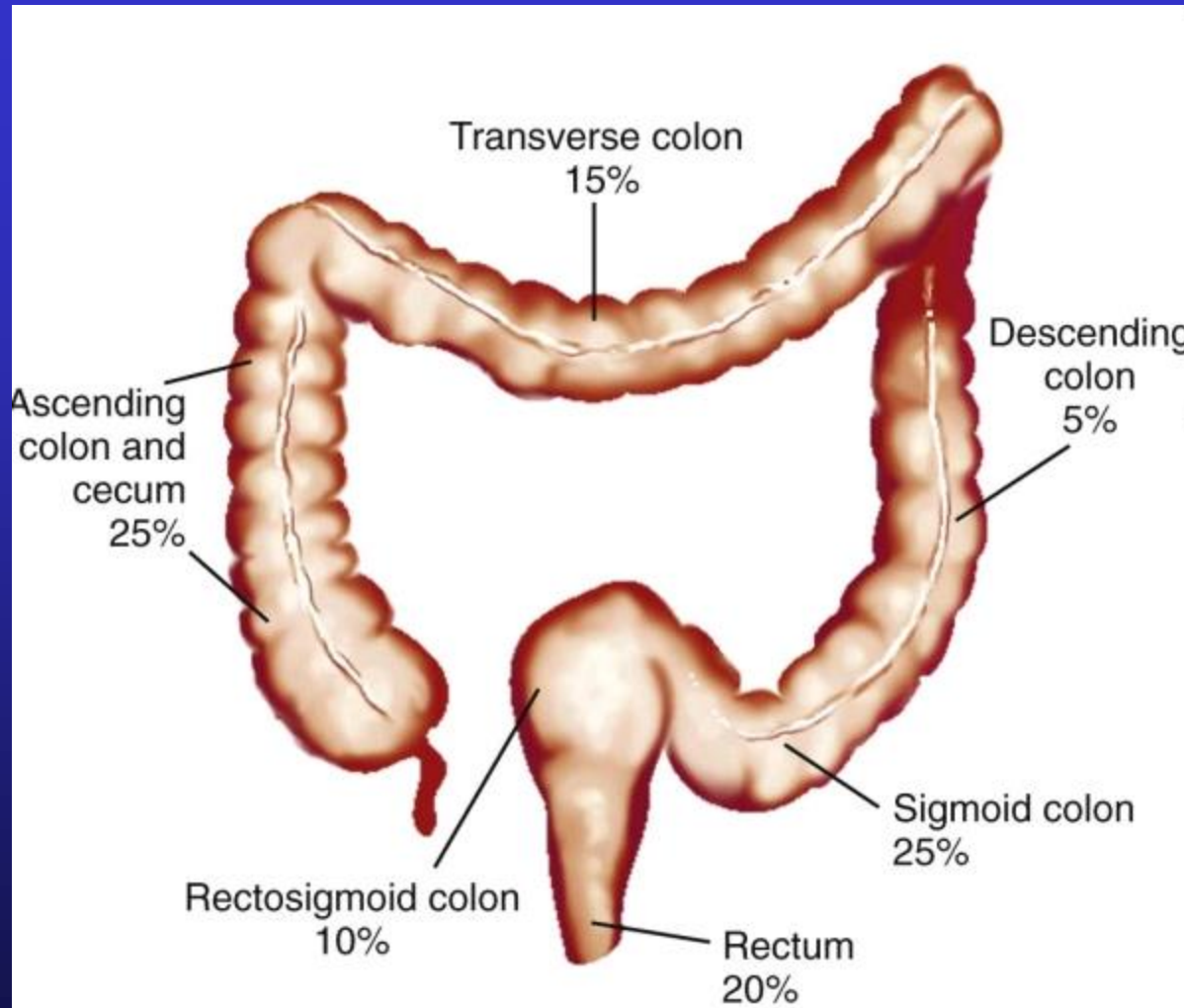
Shy-Drager syndrome

Spinal cord injury

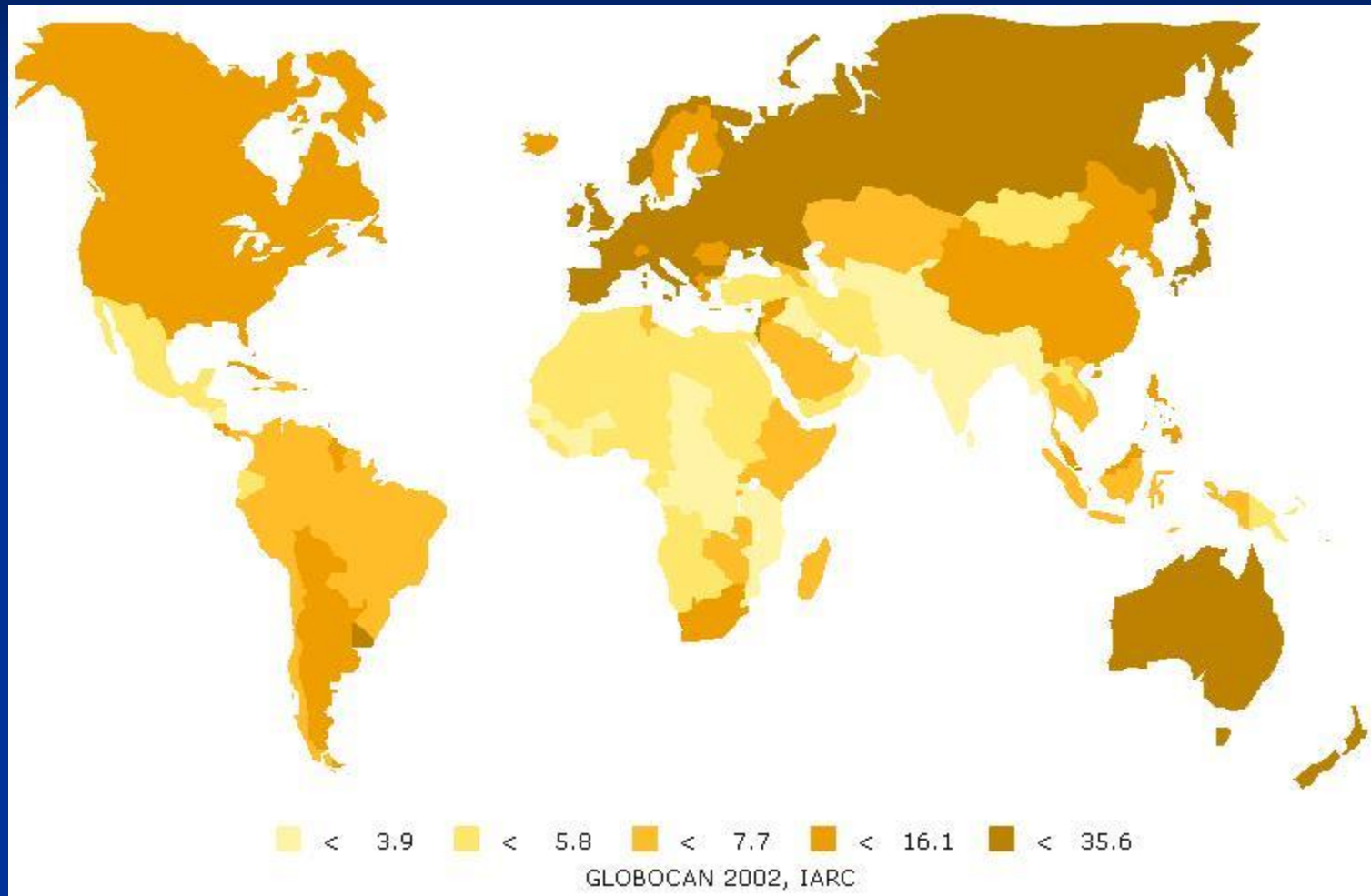
Stroke

INCIDENZA DEL CCR NEL MONDO





MORTALITÀ DEL CCR NEL MONDO



■ IL CCR NEL MONDO

Incidenza: 3° posto

~1'000'000 nuovi casi/anno

Mortalità: 2° posto

~500'000 morti/anno

■ IL CCR IN EUROPA

Incidenza¹ : 2° posto

~ 400'000 nuovi casi/anno

Mortalità¹ : 2° posto

~ 200'000 morti/anno

Sopravvivenza² : 53,5% (a 5 anni)

1 - ESMO (European Society for Medical Oncology): Cancer epidemiology, 2007.

2 - The EURO CARE-4 study. The Lancet Oncology, 2007.

■ IL CCR IN ITALIA

Incidenza: **2° posto (11,9%)**¹

~ **48'000**(F 30%) **nuovi casi/anno**²

Mortalità: **2° posto (11,3%)**¹

~ **15'000**(F 40%) **morti/anno**²

Sopravvivenza: **57,5%** (a 5 anni)³

1 - AIRTUM (Associazione Italiana Registri Tumori) : I nuovi dati di incidenza e mortalità (2003-2005). 2009

2 - Stime del CNESPS (Centro Nazionale Epidemiologia Sorveglianza Promozione Salute). 2009

3 - The EURO CARE-4 study. The Lancet Oncology. 2007

■ IL CCR IN EMILIA-ROMAGNA

Incidenza: ~ **4'000** nuovi casi/anno (13,9%)

Mortalità: ~ **1'500** morti/anno (11%)

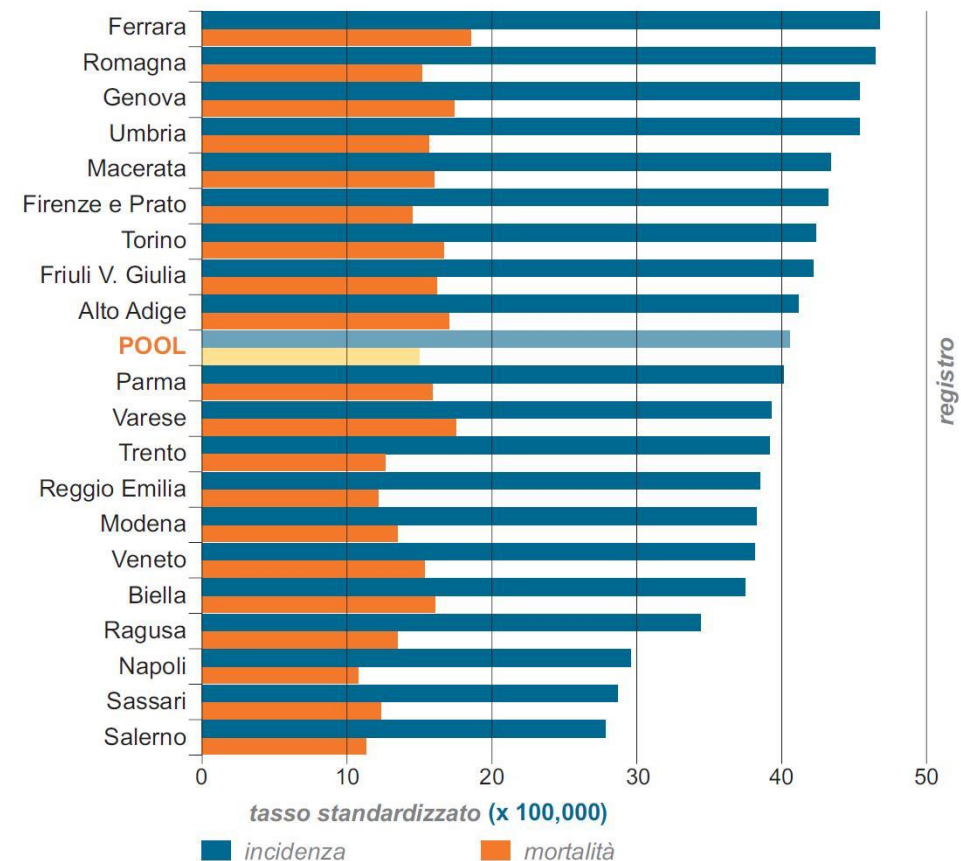
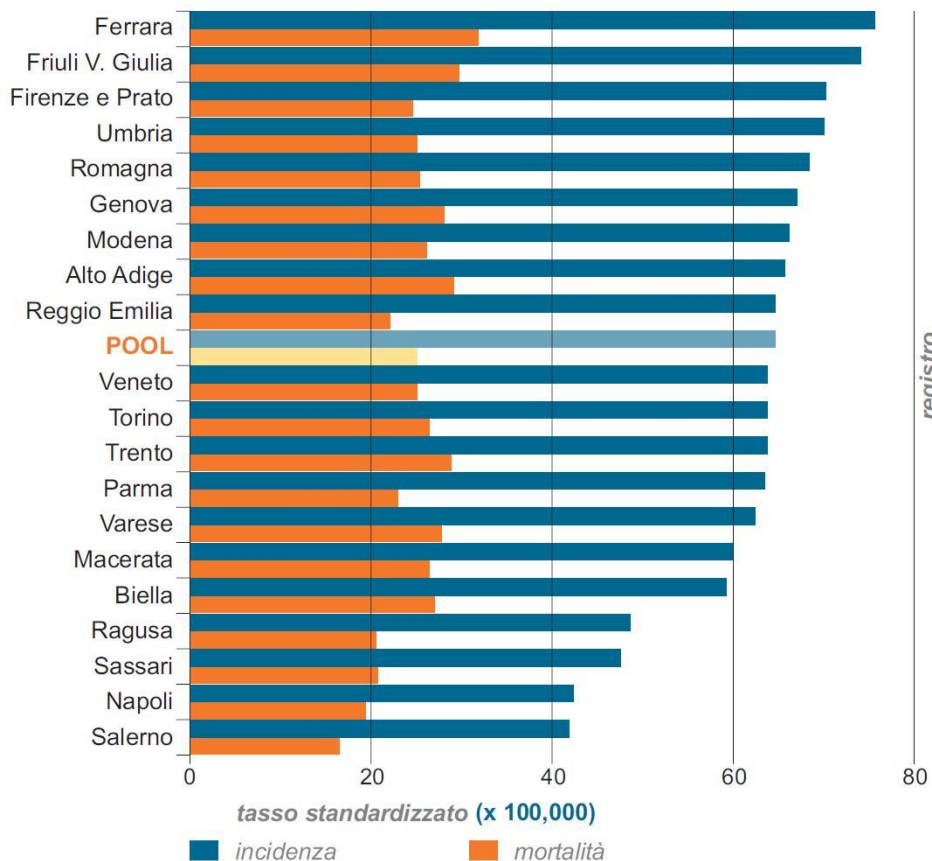
Sopravvivenza: ~ **60%** (a 5 anni)

■ IL CCR A FERRARA

Incidenza e mortalità (1999-2002)

♂ Maschi

♀ Femmine



(Fonte AIRTUM)

Numero di casi di cancro colorettaale per AUSL per il periodo 2003-2009

Popolazione residente

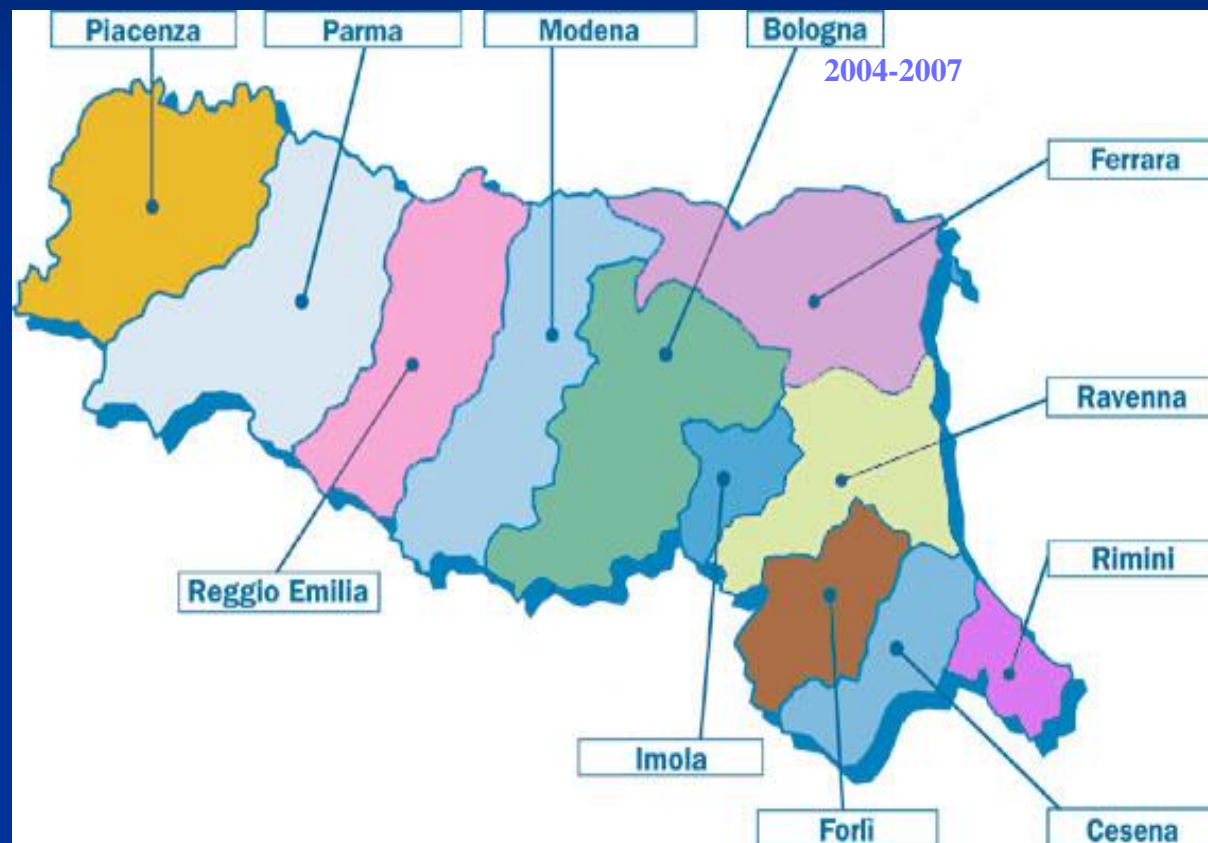
in Regione Emilia-

Romagna

al 01/01/2010:

4.395.606

Centro	Totale casi	% di casi per centro	Numero medio annuo di casi
Piacenza	1,635	6.4	273
Parma	2,818	11.0	403
Reggio E.	2,392	9.3	399
Modena	3,978	15.5	663
Bologna	3,499	13.6	875
Imola	904	3.5	129
Ferrara	2,451	9.6	490
Ravenna	3,110	12.1	444
Forlì	1,374	5.4	196
Cesena	1,392	5.4	199
Rimini	2,096	8.2	299
Totale RER	25,649	100.0	4370



Increasing incidence of colorectal cancer in Asia: implications for screening

Joseph J Sung, James YW Lau, KL Goh, WK Leung, for the Asia Pacific Working Group on Colorectal Cancer*

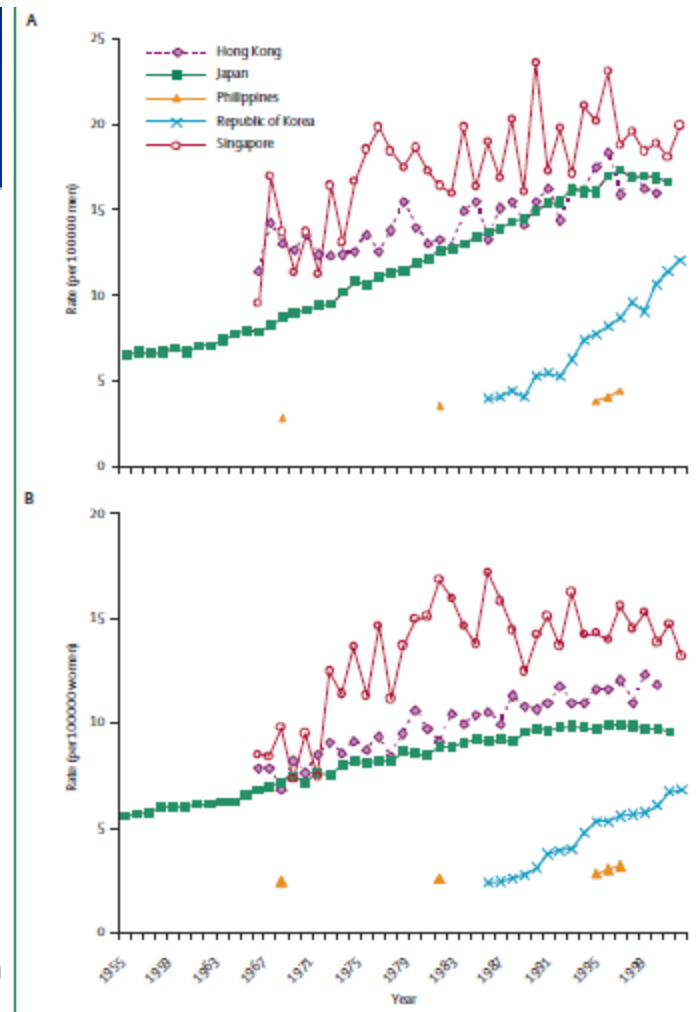
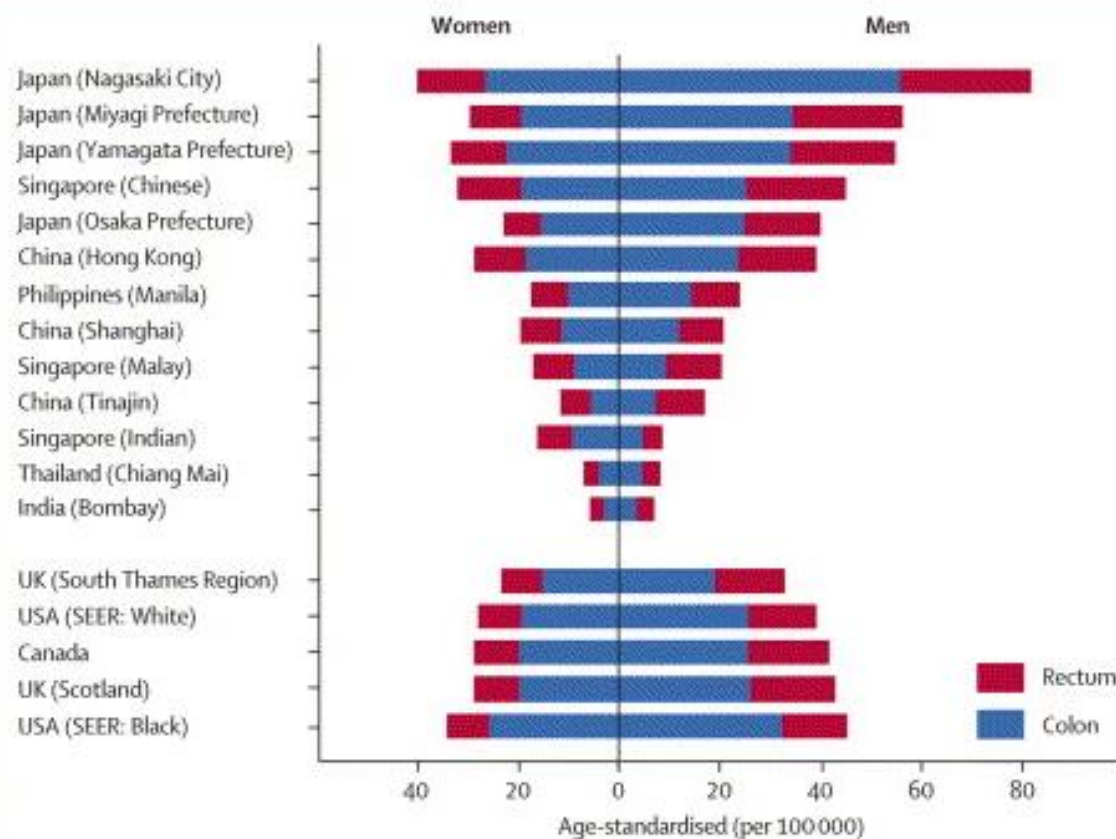


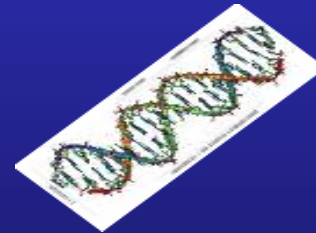
Figure 3: Mortality rates of colorectal cancer in five Asian countries in (A) men and (B) women, 1955-99*

Fattori di rischio

- Stile di vita



- Fattori ereditari



- Et : l'incidenza aumenta 10 volte dalla IV alla VI decade

- Malattie dell'intestino



Fattori di rischio individuali

- **Età \geq 50 aa**
 - 90% CCR si sviluppa da 50 aa. In poi
 - Da 50 a 80 aa il rischio di CCR = x 2.5
- **Polipi adenomatosi non FAP**
 - +frequente dopo 50 aa
 - La trasformazione da adenoma a carcinoma varia da 3 a 37% in base alla dimensione e al grado di atipia
- **Storia familiare di CCR**
 - La presenza nei genitori: comporta un rischio x2, x3
- **Storia familiare di polipi adenomatosi**
- **Poliposi familiare nel colon (adenomatose e amartomatose)**
- **Hereditary non-polyposis colorectal cancer (HNPCC)**
- **Malattie infiammatorie intestinali (Colite ulcerosa e M. di Crohn)**
 - Stretta correlazione con la durata della malattia e l'andamento clinico (+recidive = + rischio)

Fattori di rischio ambientali

■ Fattori favorenti l'insorgenza



- Carcinogeni e mutageni ambientali
- Amine eterocicliche
- Prodotti del metabolismo batterico
- Consumo di alcol
- Fumo
- Sovrappeso, vita sedentaria

Fattori protettivi



**Dieta ricca di fibre vegetali
Cruciferi (cavoli, rape, etc..)**

**Vitamine antiossidanti (vitamina
C ed E)**

Assunzione di folati

**Consumo di aspirina e inibitori
della COX-2**

Table 123-1 Factors That May Influence Carcinogenesis in the Colon and Rectum

Probably Causative

High-fat and low-fiber diet (adjusted for energy intake)*

Red meat consumption

Possibly Causative

Beer and ale consumption (especially for rectal cancer)

Cigarette smoking

Diabetes mellitus

Environmental carcinogens and mutagens

Heterocyclic amines (from charbroiled and fried meat and fish)

Low dietary selenium

Probably Protective

Aspirin, NSAIDs, and cyclooxygenase-2 inhibitors

Calcium

Hormone replacement therapy (estrogen)

Low body mass

Physical activity

Possibly Protective[†]

Carotene-rich foods

High-fiber diet

Vitamins C and E

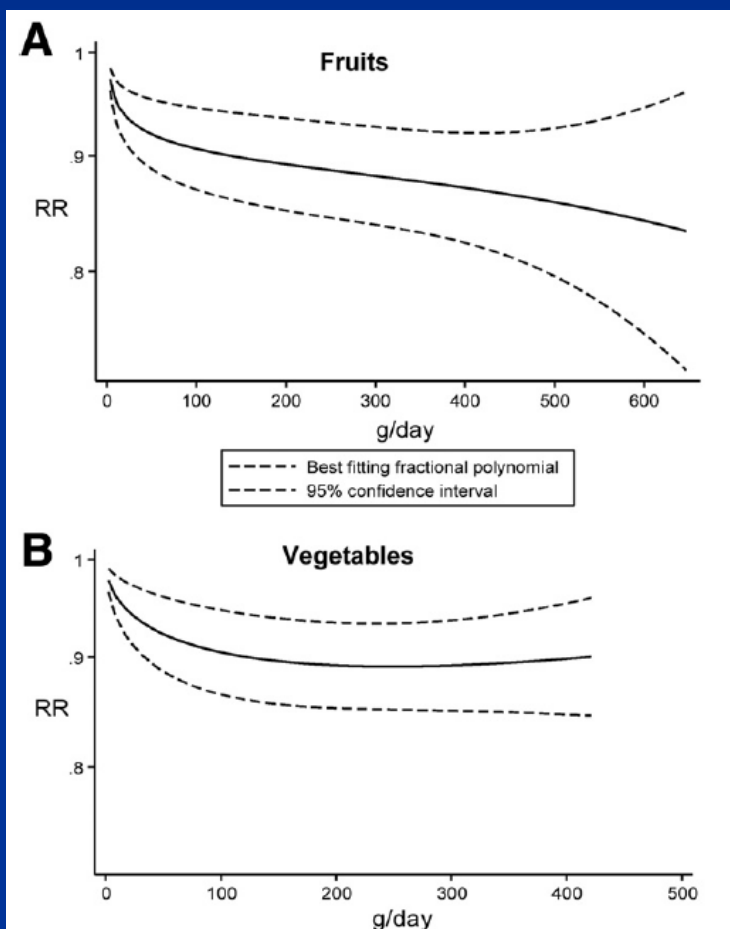
Vitamin D

Yellow-green cruciferous vegetables

Nonlinear Reduction in Risk for Colorectal Cancer by Fruit and Vegetable Intake Based on Meta-analysis of Prospective Studies

DAGFINN AUNE,* ROSA LAU,* DORIS S. M. CHAN,* RUI VIEIRA,* DARREN C. GREENWOOD,† ELLEN KAMPMAN,§ and TERESA NORAT*

*Department of Epidemiology and Biostatistics, School of Public Health, Imperial College, London, UK; †Biostatistics Unit, Centre for Epidemiology and Biostatistics, University of Leeds, Leeds, UK; §Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands



To our knowledge this is also the first meta-analysis to explore the potential nonlinear association of fruit and vegetable intake with colorectal cancer risk. Although some caution is needed in interpreting the exact quantities and size of the risk estimates because of the measurement errors associated with use of the dietary assessment methods, *our results indicate that there is a low threshold level of between 100 and 200 g/d that can reduce risk about 10%. Above that level there seems to be no additional benefit of increasing vegetable intake in terms of colorectal cancer risk, and for fruit a slight further reduction with higher intakes is observed (an approximate 15% reduction for an intake of 600 g/d).*

Nonlinear Reduction in Risk for Colorectal Cancer by Fruit and Vegetable Intake Based on Meta-analysis of Prospective Studies

DAGFINN AUNE,* ROSA LAU,* DORIS S. M. CHAN,* RUI VIEIRA,* DARREN C. GREENWOOD,[‡] ELLEN KAMPMAN,[§] and TERESA NORAT*

**Department of Epidemiology and Biostatistics, School of Public Health, Imperial College, London, UK; [‡]Biostatistics Unit, Centre for Epidemiology and Biostatistics, University of Leeds, Leeds, UK; [§]Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands*

Fruit and vegetables are also good sources of folate, which has been associated with decreased risk of colorectal cancer in a number of studies, but not all studies.

Folate plays an important role in DNA methylation and is necessary for synthesis of thymine.

Folate deficiency can lead to misincorporation of uracil instead of thymine into DNA and increase the number of chromosomal breaks.

In addition, fruit and vegetables are good sources of various antioxidants, vitamins, minerals, and other bioactive compounds, which might prevent cancer

PREVENZIONE PRIMARIA

- **Norme dietetiche**
- **Controllo di alcune abitudini voluttuarie**
- **Mantenimento del peso ideale**
- **Utilizzo di farmaci**

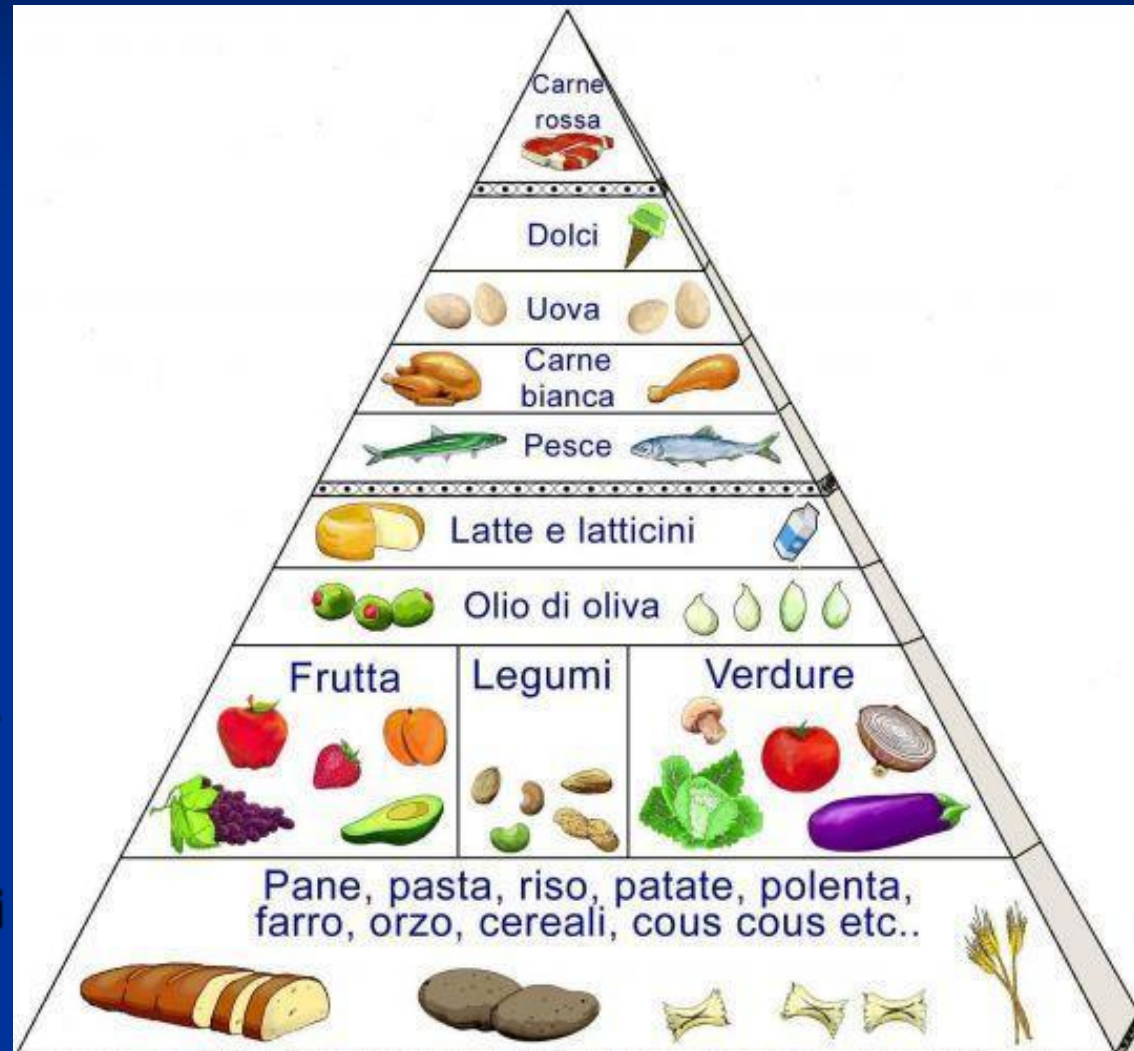
■ NORME DIETETICHE

👉 CARNI ROSSE

👉 PESCE e POLLAME

👉 VERDURA, FRUTTA
CEREALI, LEGUMI:

⇒ fibre, antiossidanti, folati



Effetto della Fibra sul

transito intestinale



LA FIBRA SOLUBILE

(pectine, gomme, mucillaggini, Galattomannani)

fermentabile, ha proprietà chelanti, ovvero tende a formare un composto gelatinoso all'interno del lume intestinale; questo gel che si viene a formare aumenta la viscosità del contenuto con conseguente rallentamento dello svuotamento intestinale. Tuttavia le sue proprietà chelanti fanno sì che essa interferisca con l'assorbimento di alcuni macronutrienti (glucidi e lipidi) riducendo i livelli di colesterolo nel sangue e diminuendo il rischio di malattie cardiovascolari.



LA FIBRA INSOLUBILE,
cellulosa, emicellulosa, lignina

non fermentabile, assorbe rilevanti quantità acqua aumentando il volume delle feci, che si fanno abbondanti, poltacee e più morbide. Questo permette di stimolare la velocità di transito nel lume intestinale, di conseguenza, diminuire l'assorbimento dei nutrienti. Questo spiega perché la *fibra solubile* abbia, al contrario di quella insolubile, più azione *costipante* che lassativa (a meno che non venga assunta insieme a grosse quantità di liquidi).

■ CONTROLLO DI ALCUNE ABITUDINI VOLUTTUARIE

 FUMO

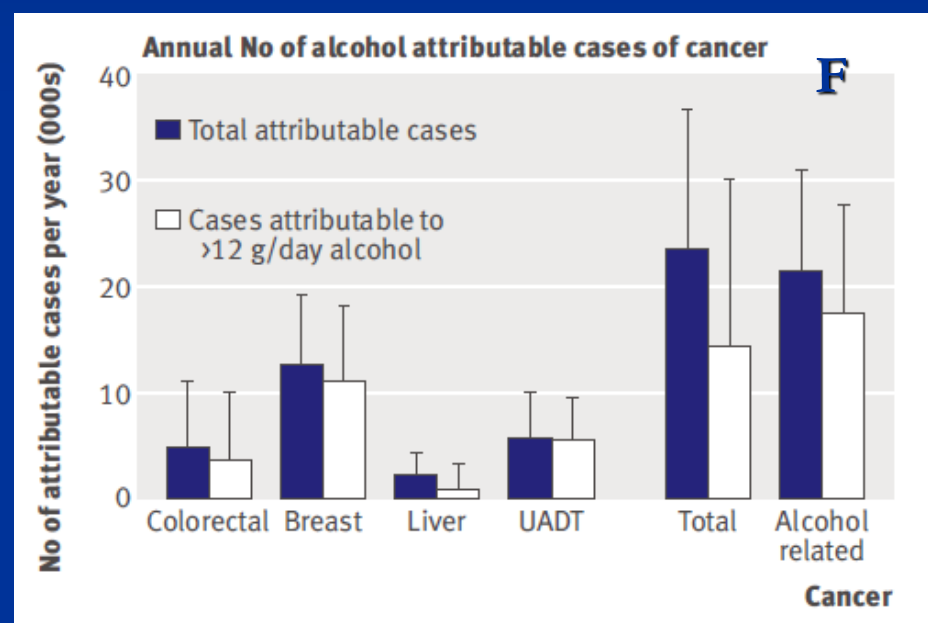
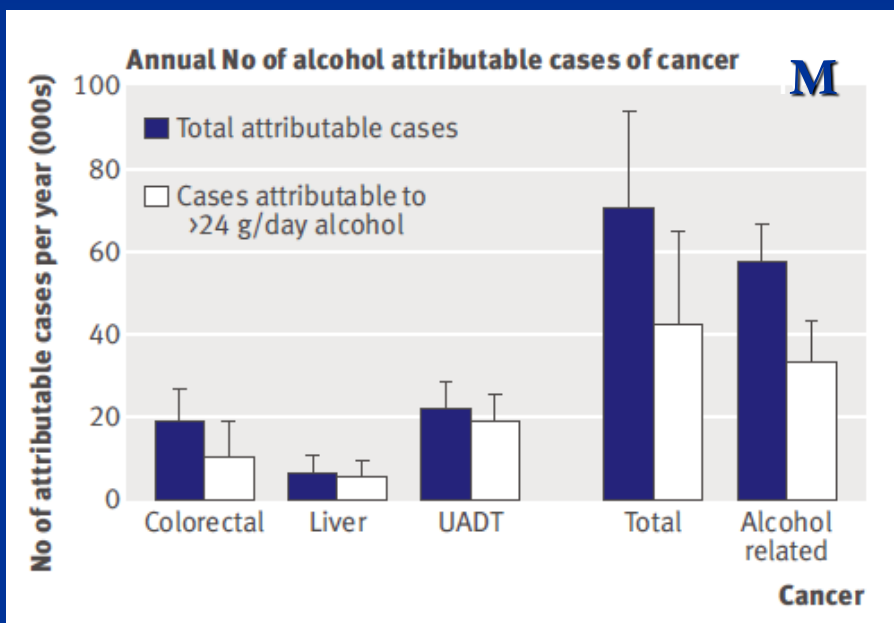
 ALCOOL

■ MANTENIMENTO DEL PESO IDEALE

 ATTIVITÀ FISICA

 OBESITÀ

Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study



Metabolic Factors and the Risk of Colorectal Cancer in 580,000 Men and Women in the Metabolic Syndrome and Cancer Project (Me-Can), Stocks, Cancer 2011

Original Article

Table 2. The Relative Risk of Incident Colorectal Cancer in Men and Women by Quintiles of Metabolic Factors^a

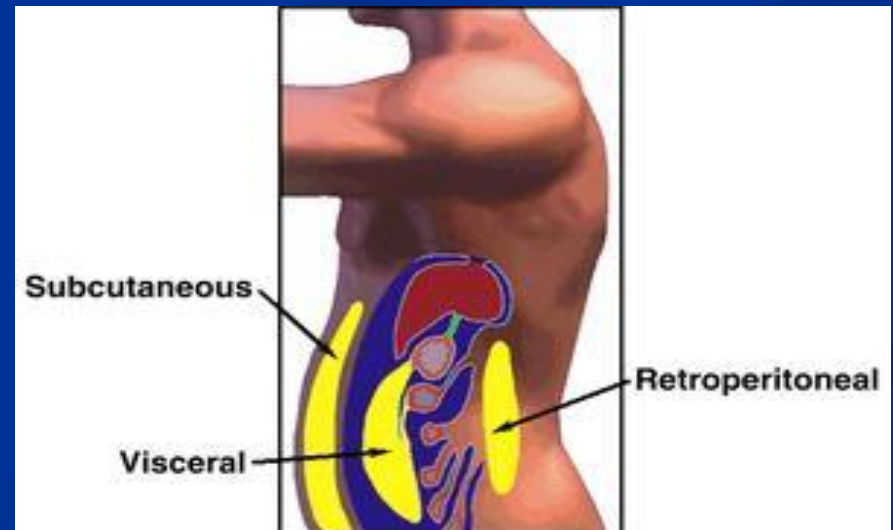
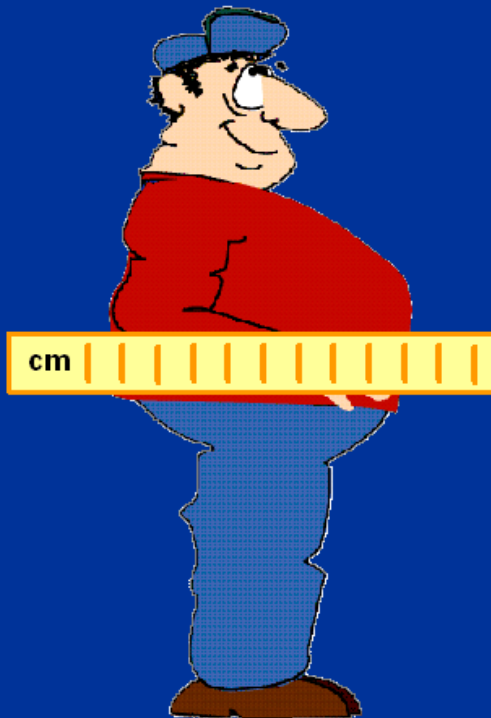
Exposure	Q	Mean±SD	Men		Women		RR (95% CI)
			No. of Cases	RR (95% CI)	No. of Cases	RR (95% CI)	
BMI, kg/m ²	1	21.5±1.3	399	1.00 (Referent)	20.0±1.2	233	1.00 (Referent)
	2	23.8±0.8	484	1.08 (0.93-1.26)	22.3±0.8	297	1.04 (0.87-1.27)
	3	25.4±0.8	588	1.22 (1.06-1.41)	24.1±0.8	372	1.10 (0.92-1.33)
	4	27.1±0.9	642	1.27 (1.10-1.46)	26.4±1.0	439	1.12 (0.93-1.35)
	5	30.8±2.8	721	1.51 (1.32-1.73)	31.7±3.6	520	1.29 (1.09-1.55)

In line with findings from previous studies, in our study, high BMI was related more strongly to colon cancer than to rectal cancer, and the association was stronger in men than in women.²⁴⁻²⁶ However, the use of BMI as a measure of obesity is hampered by the finding that **BMI is not a specific measure of abdominal fat mass**, which is linked to metabolic aberrations, such as insulin resistance. High abdominal obesity, assessed as the **waist circumference or as the waist-to-hip ratio**, have been associated with an increased risk of colorectal cancer risk in men; whereas, in women, waist measures, but not BMI, have been associated positively with risk.

La circonferenza vita è un indicatore del tessuto adiposo viscerale

Uomini >102 cm = Rischio aumentato

Donne >88 cm = Rischio aumentato



Risk factors for colonic and rectal cancer mortality: evidence from 40 years' follow-up in the Whitehall I study

David S Morrison,¹ George David Batty,² Mika Kivimaki,³ George Davey Smith,⁴ Michael Marmot,³ Martin Shipley³

.....*A significant effect of current smoking on rectal cancer mortality was only apparent after events in the first 10 years of follow-up were excluded. No convincing evidence was found that body mass index, diabetes mellitus, blood pressure or physical activity were associated with colorectal cancer mortality.*

Conclusion Smoking significantly increases mortality from colorectal cancer and its decreasing prevalence in the UK may partly explain falling mortality from the disease.

PREVENZIONE SECONDARIA



SCREENING

Test di screening:

- ✓ Test ricerca sangue occulto fecale (SOF)
- ✓ Rettosigmoidoscopia
- ✓ Combinazione SOF + rettosigmoidoscopia
- ✓ Pancolonscopia

Test complementare:

- ✓ Colografia-TC

SOF immunologico

- ✓ **sensibile:**

sensibilità 78%

- ✓ **specifico:**

specificità 93%, > specificità per sanguinamenti colici

- ✓ **riproducibile:**

metodo quantitativo (\Rightarrow cut off a 100ng/ml = concentrazione di emoglobina nel campione), lettura automatizzata, laboratorio unico per tutta la Provincia

- ✓ **esente da complicazioni:**

non invasivo, innocuo



- ✓ **accettabile dalla popolazione target:**

facile esecuzione, campione singolo, non richiede restrizioni dietetiche

- ✓ **conveniente:**

miglior rapporto costo-beneficio

PANCOLONSCOPIA

- ✓ Gold standard delle metodiche di screening
- ✓ Sensibilità ~ 90%
- ✓ Specificità ~ 100%
- ✓ possibilità di diagnosi e di trattamento terapeutico
- ✓ **POLIPECTOMIA**
 - riduce l'incidenza di CCR del 75%
 - riduce la mortalità del 69%
- ✓ **indicatori di qualità** per la pancolonscopia
 - tasso di intubazione ciecale (> 90% diagnostica e >95% screening)
 - tempo di retrazione dell'endoscopio (> 6 minuti)
 - tasso di identificazione degli adenomi ( > 25%,  >15%)

Biennio 2005-2007 Ferrara

Persone invitate ad eseguire FOBT-test

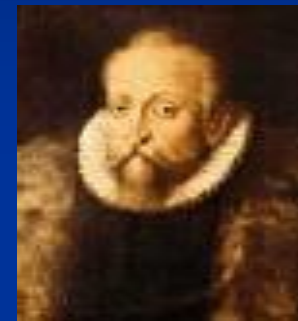


26156

Donne



49749



23593

Uomini

Il FOBT test è stato eseguito da 21432
persone (43.4%)

1281 FOBT positivi

(5.9%)

20149 FOBT negativi

(94.1%)

1155 (91%) hanno accettato la
colonscopia



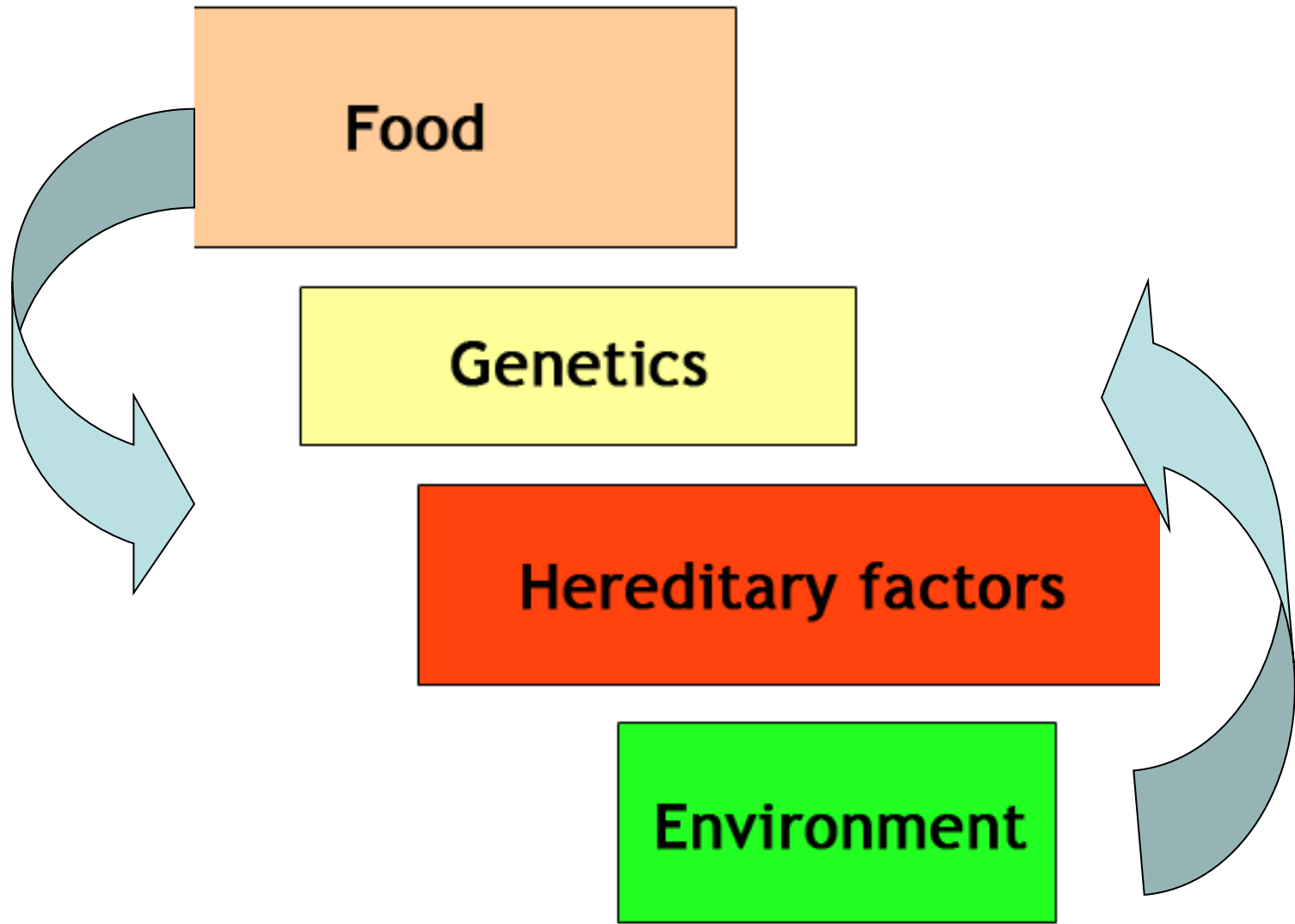
Colorectal cancer molecular biology moves into clinical practice

Colin C Pritchard,¹ William M Grady^{2,3}

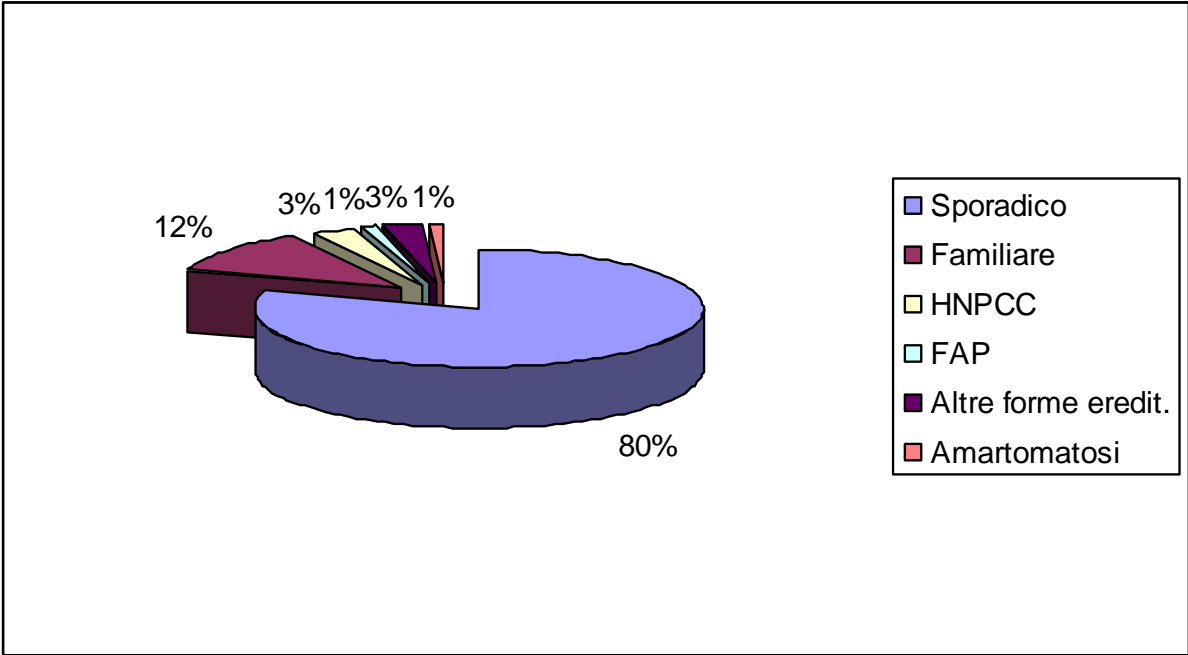
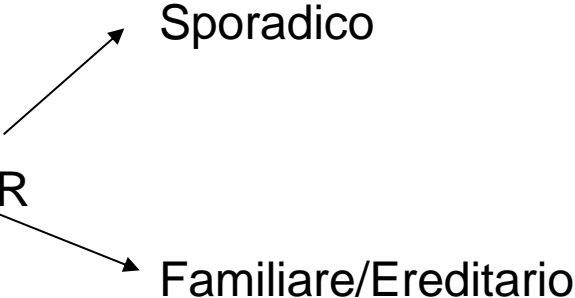
MOLECULAR MECHANISMS OF COLORECTAL CARCINOGENESIS

The adenoma/carcinoma progression sequence

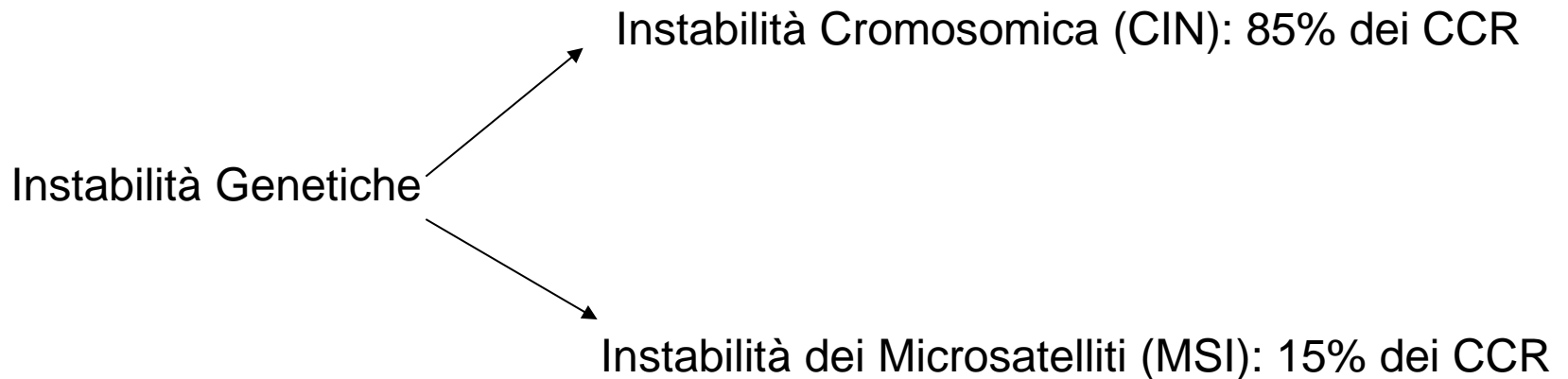
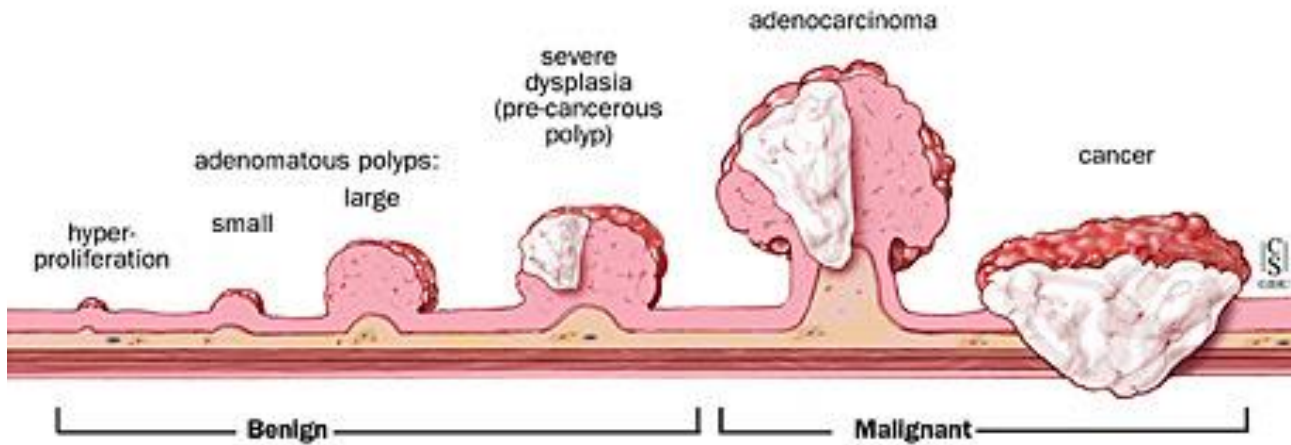
Colorectal cancer arises as the result of the accumulation of acquired genetic and epigenetic changes that transform normal glandular epithelial cells into invasive adenocarcinomas. Steps that



Suddivisione Percentuale delle forme di CCR



La maggior parte dei CCR insorge da una lesione sporadica che inizia con una iperplasia, e segue..... Adenoma, Adenoma cancerizzato, Adenocarcinoma.

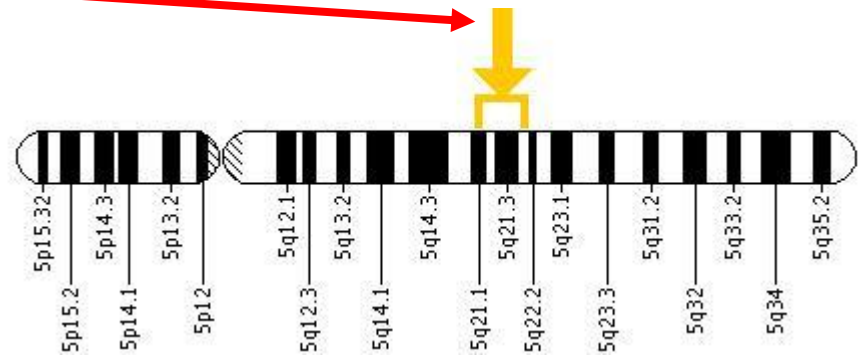
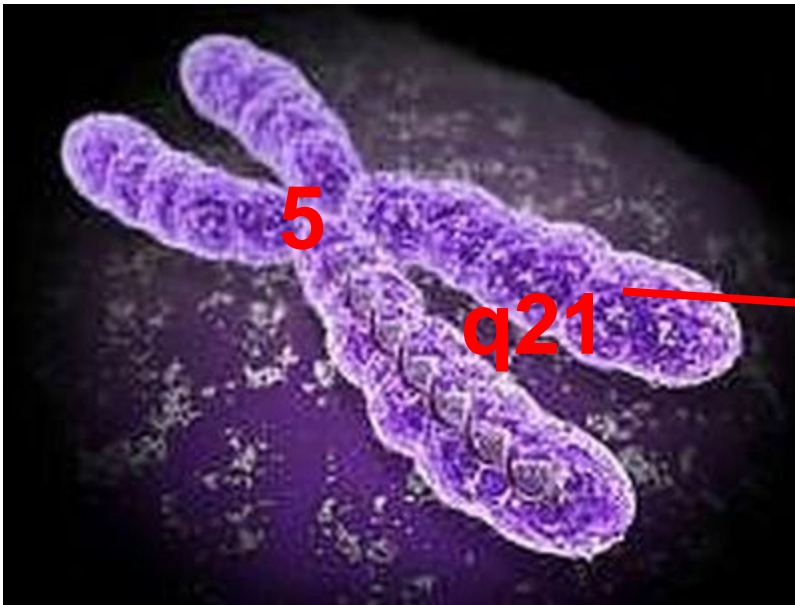


Delezione o mutazione “non senso”
del gene APC (Adenomatous Polyposis)

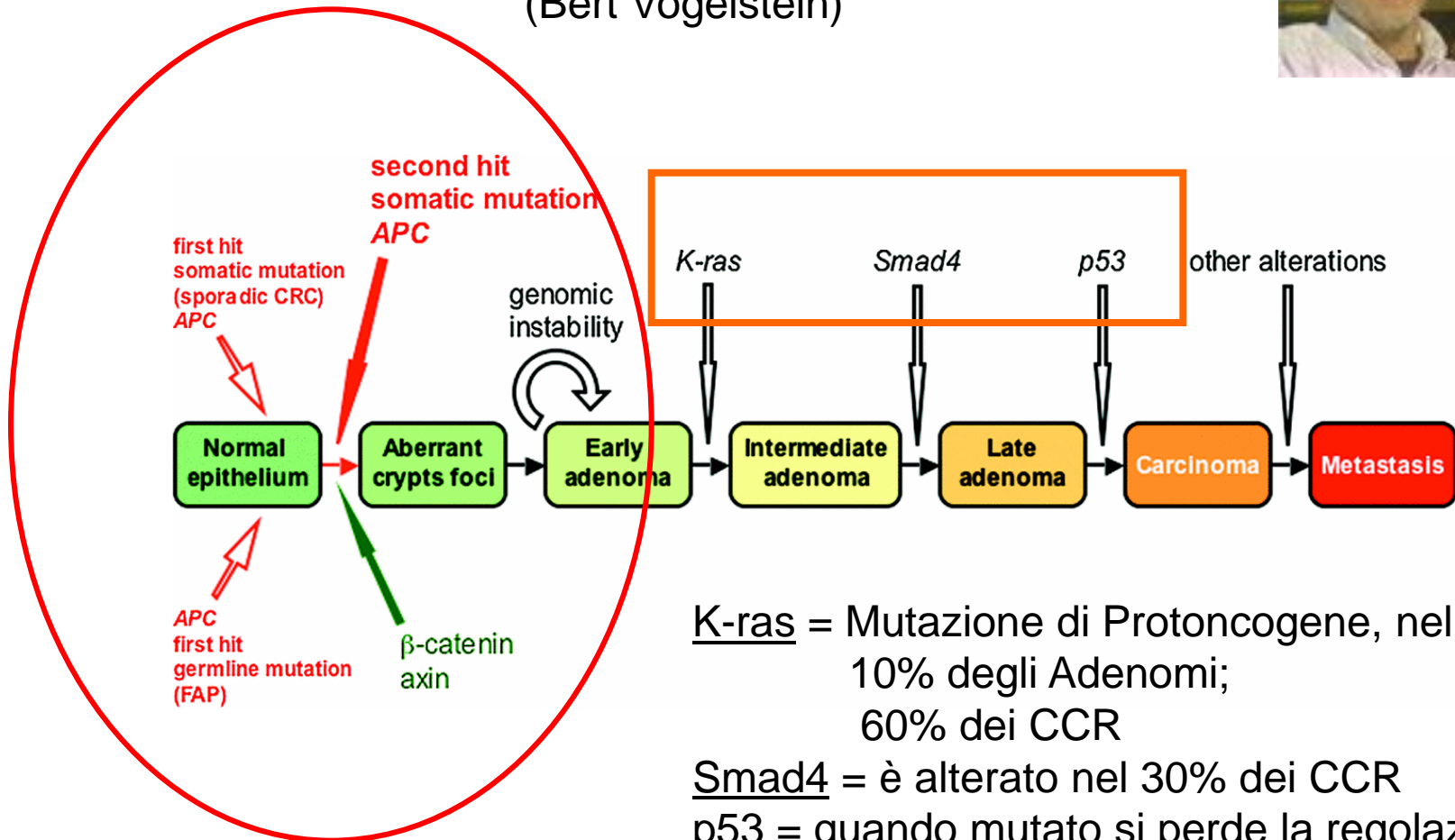
Sporadica

Familiare (FAP: ereditato l'allele
Mutato del gene APC)

Instabilità Cromosomica (CIN)



La sequenza Adenoma-Carcinoma (Bert Vogelstein)



K-ras = Mutazione di Protooncogene, nel 10% degli Adenomi; 60% dei CCR

Smad4 = è alterato nel 30% dei CCR

p53 = quando mutato si perde la regolazione del ciclo cellulare ed è mutato nel 70% dei CCR