



QUALITY IN ENDOSCOPY

ESGE / ESDO SYMPOSIUM

COLONOSCOPY &
COLONIC NEOPLASMS

Prague, Czech Republic April 17-18, 2015

Biomarkers & multi-target stool DNA?: *Alternative for screening*

Session No.: 5

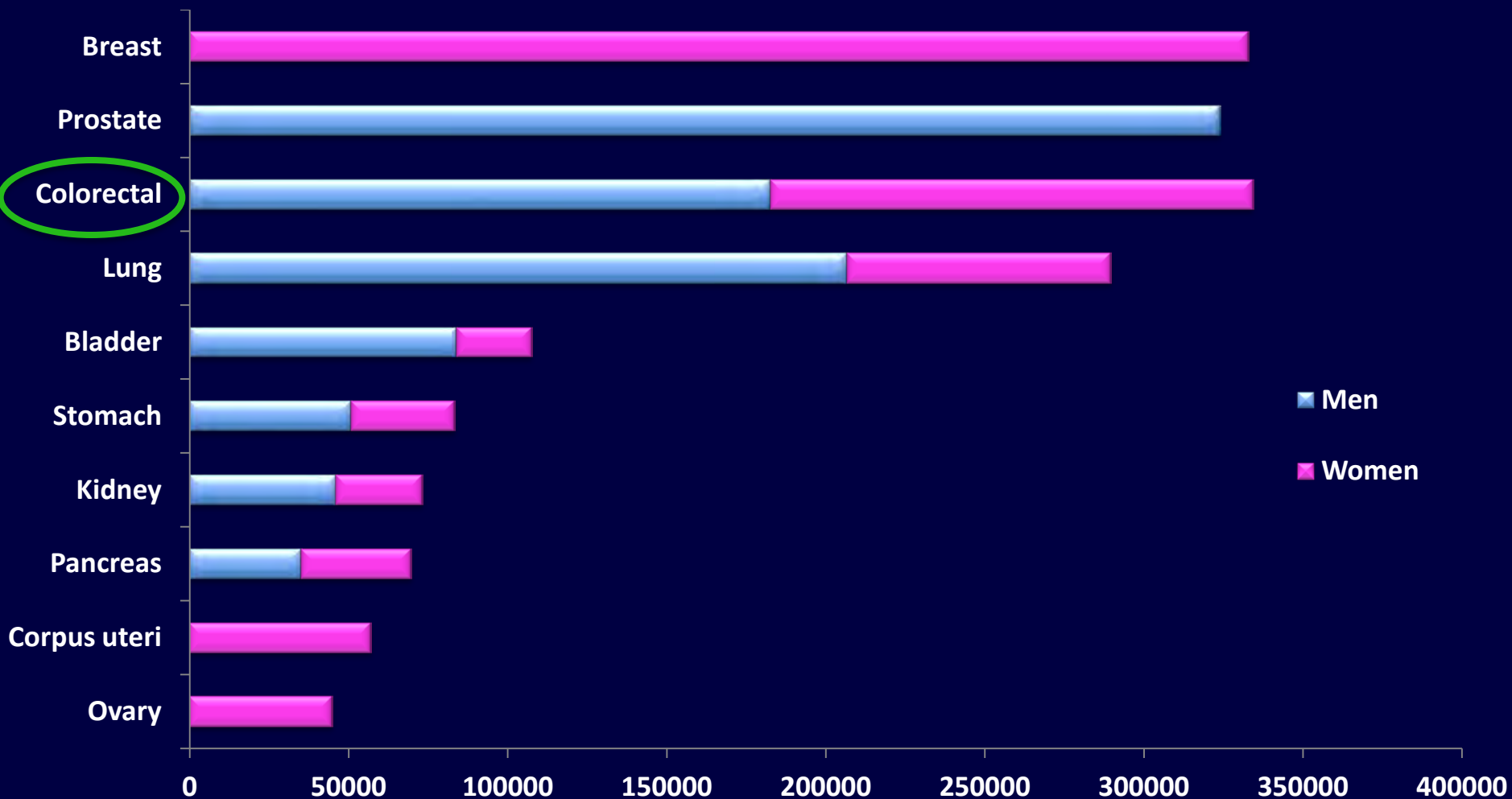
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Institution: CHU Dijon

Country: France



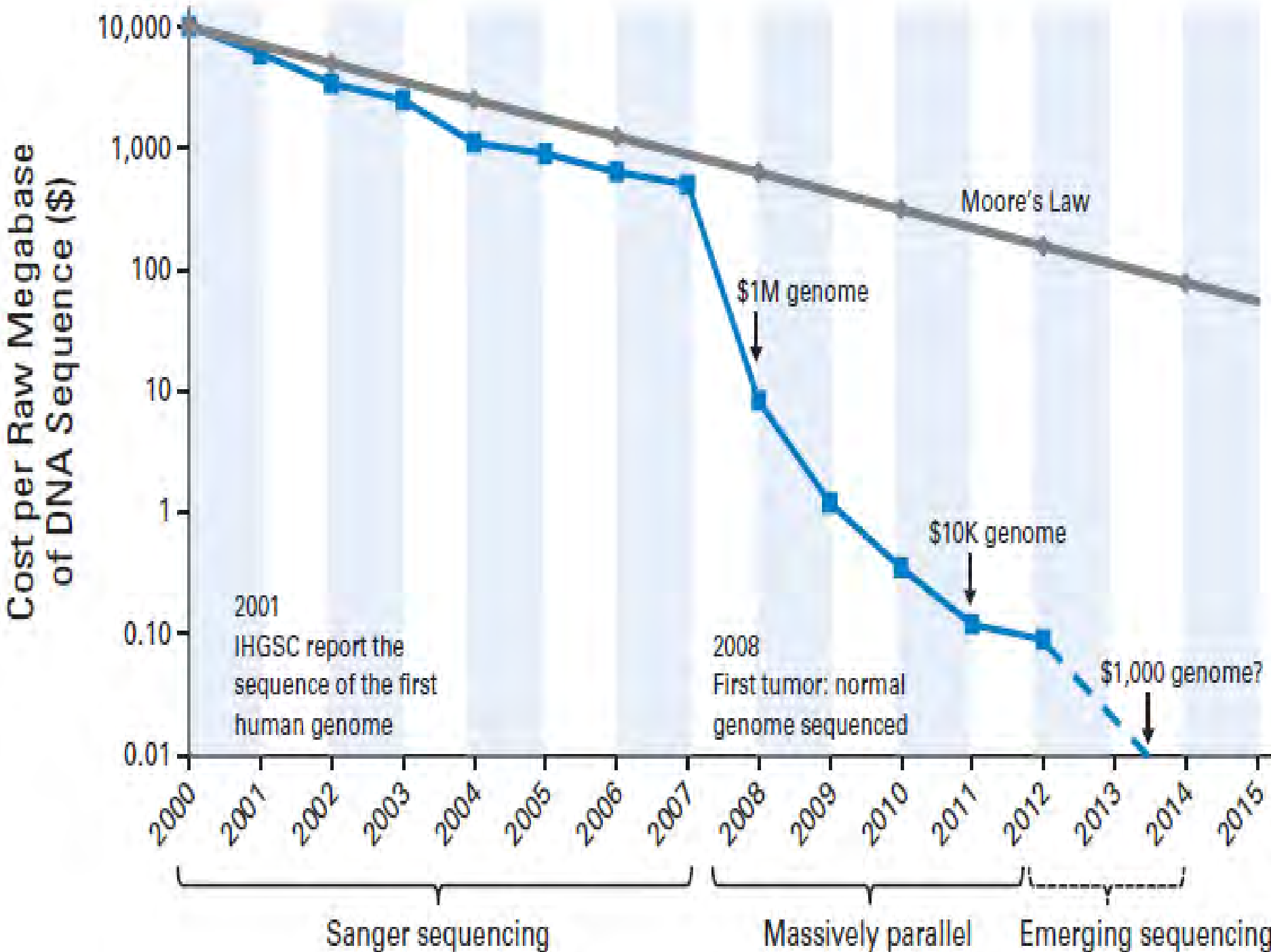
Incidence of the 10 most frequent cancers in Europe (27) 2012



Cancer results from multiple Cells alterations



Alterations are multiple and they can be found using molecular biology



Stool DNA Test for CRC screening : what is it ?

- **Principle :**
 - Detecting alterations of DNA in exfoliated cells
- **Multiple molecular markers (gene cell physiology):**
 - gene mutations (APC, Kras, P53)
 - DNA methylation abnormalities (Vimentin, Septin, Wif1, ...)
 - Hb level

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- **Conflicting results in initial studies**

*Imperiale TF NEJM 2004
Ahlquist DA Ann Int Med 2008
Itzkowitz Am J Gastroenterol 2008*

- **Ongoing studies :**
 - Colohybridotest ® (France)

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- **Lastest results : Cologuard ®**

Multitarget Stool DNA Test Vs. FIT

12,776 participants

1,760 not evaluable

1,168 did not undergo colonoscopy
128 did not undergo stool test

9,989 Cologuard® + FIT + Colonoscopy

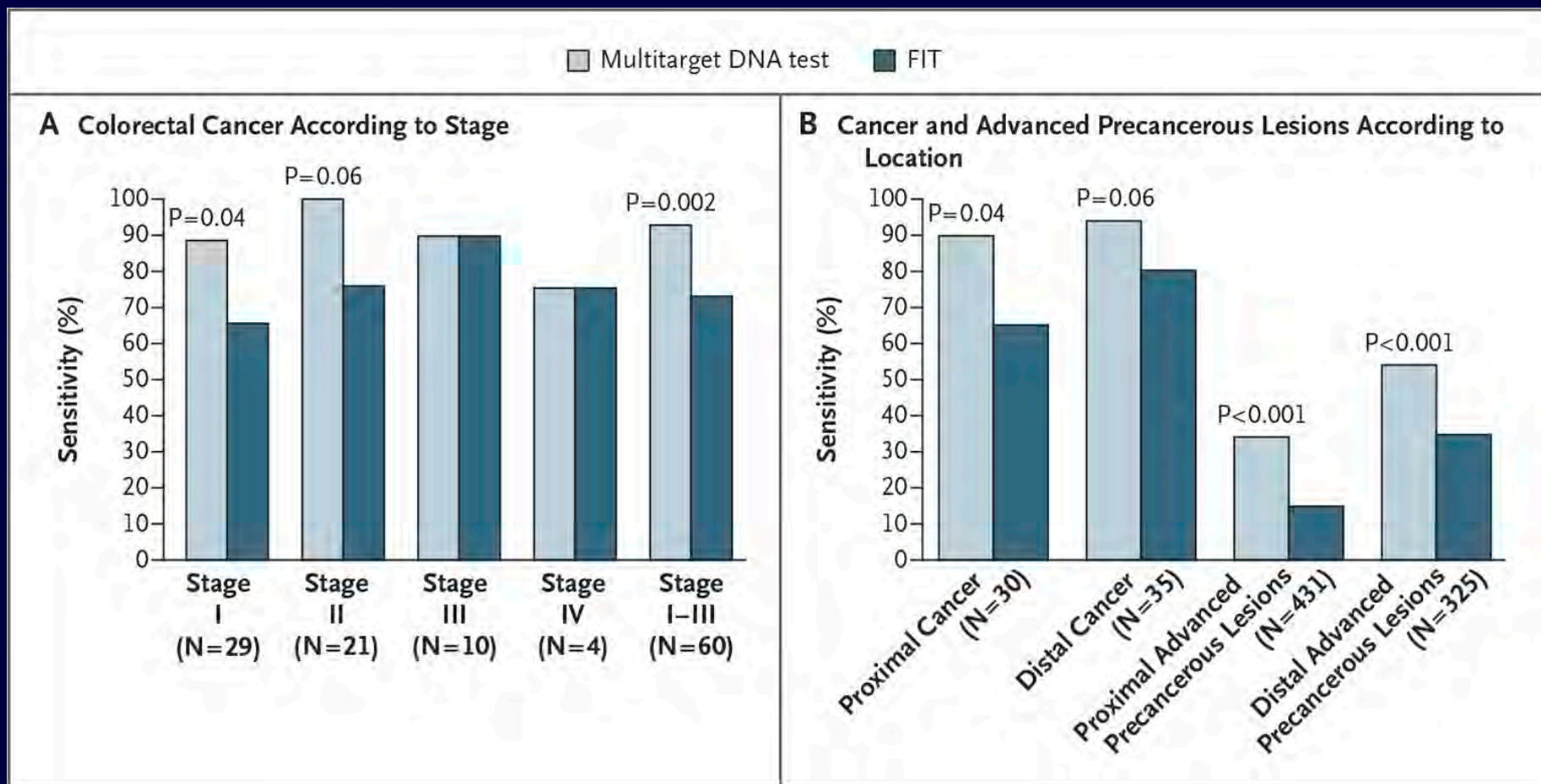
65 CRC

757 large adenomas

2,893 small adenomas

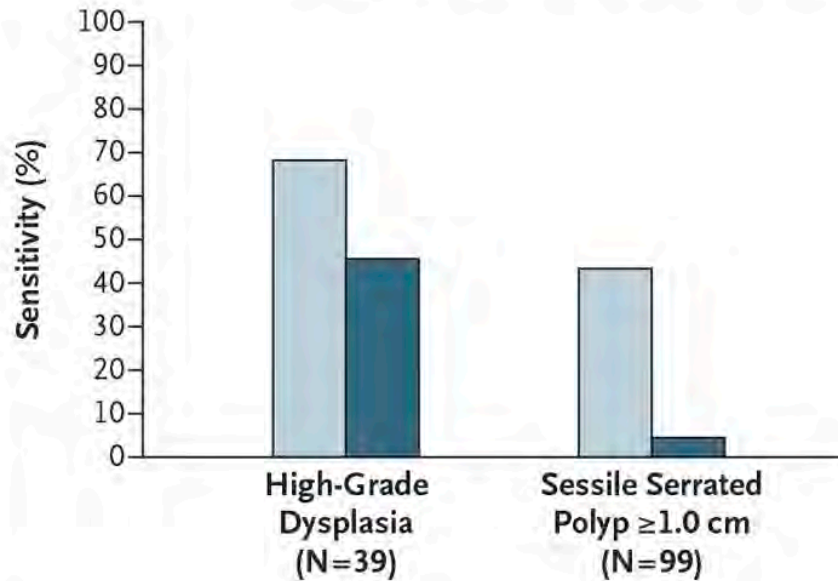
6,274 negative results

Sensitivity of the Multitarget Stool DNA Test and FIT, by Subgroups

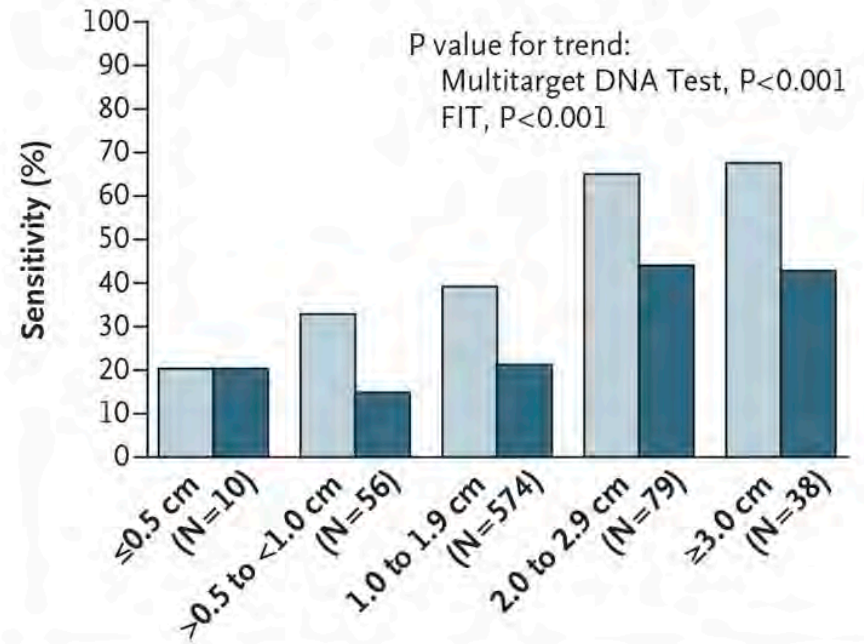


Sensitivity of the Multitarget Stool DNA Test and FIT, by Subgroups

C Higher-Risk Types among Advanced Precancerous Lesions



D Advanced Precancerous Lesions According to Size of Largest Lesion



CRC Screening using DNA vs FIT

	Cologuard*	FIT**
N	9 989	9 989
Sensitivity		
Cancer	92%	74%
Large Adenomas	42%	24%
Hight grade Dysplasia	69%	46%

**mutations KRAS, NDRG4 & 8MP3, B actin, Hb level*

***100ng/mL buffer*

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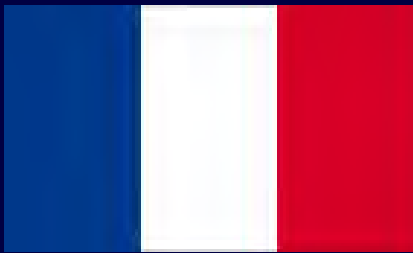
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Extrapolation of Findings to an Expanded Population of 10,000 Persons at Average Risk for CRC Undergoing Screening with Colonoscopy, Cologuard®, and FIT.

Colonoscopy finding	N	Cologuard		FIT	
		+	-	+	-
Cancer	65	60	5	48	17
Advanced adenomas	758	321	437	180	578
Small Adenomas	2896	498	2398	220	2676
Negative results	6281	732	5549	248	6033
Total	10,000	1611	8389	696	9304

Limits

- **Sophisticated technology:**
 - Dissemination
 - implementation could be difficult
- **Cost : 599 US \$ per test → 533 €**
- **Screening interval still to determine**
- **Positive rate more than twice higher (16.1% vs. 7.0%)**



France :

2009: National screening program (Hemocult II®)

2015: now implemented with FIT (OC Sensor®)

Cost: 1€/test

The Future

NEXT EXIT



Serum test

- Detection of the extra-cellular free tumoral DNA in the blood
- DNA Marker : **SEPTIN 9**
 - Hypermethylation of the Septin 9 gene (ch17q25)
 - Tumour tissue had relative quantities of mSEPT9 above the highest relative quantities found in normal colon mucosal tissue.

Lofton-Day C, Clin Chem 2008
 - retrospective study (4300 subjects)
 - prospective study (n=8000) First generation
 - Second generation: Cost 150 €

CRC Screening using Septin 9 test

	Sensitivity	Specificity
Cancer	48%	92%
Stade I	35%	
Stade II	63%	
Stade III	46%	
Stade IV	77%	
Advanced adenomas	11%	

Conclusion

- **Molecular biology is booming**
- **In asymptomatic persons at average risk for colorectal cancer, multitarget stool DNA testing detected significantly more cancers than did FIT but had more false positive results**
- **This has an implication in term of cost and colonoscopy resources**
- **However, this technic is now validated by FDA**
- **The development of serum tests could dramatically change CRC screening in future but this technic is not ready**
- **For these reasons the FIT is the best alternative for CRC screening for the moment**

Screening utility

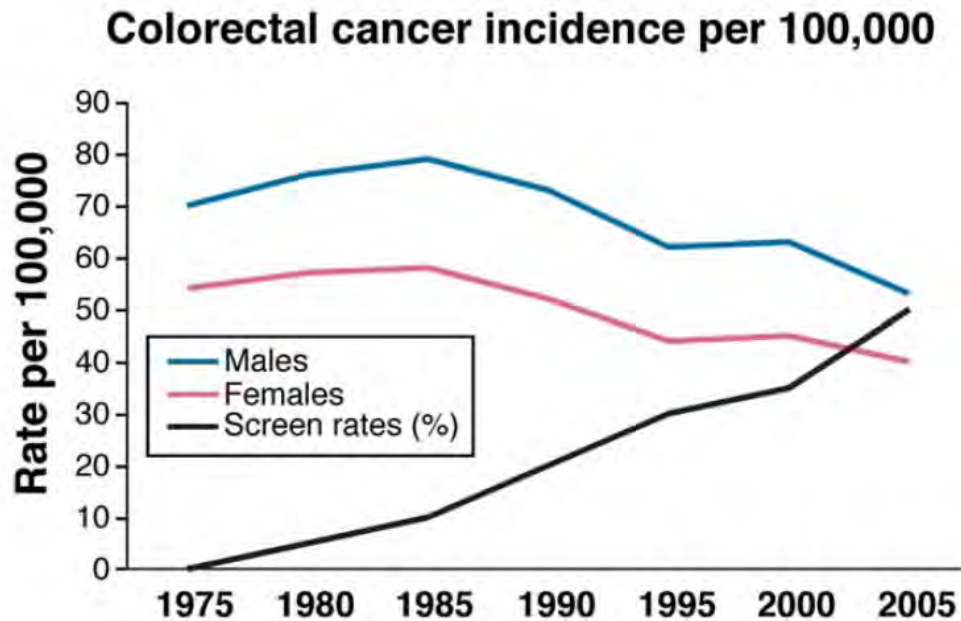


Figure 2. CRC incidence rates per 100,000 and rates of CRC screening in individuals older than age 50.¹

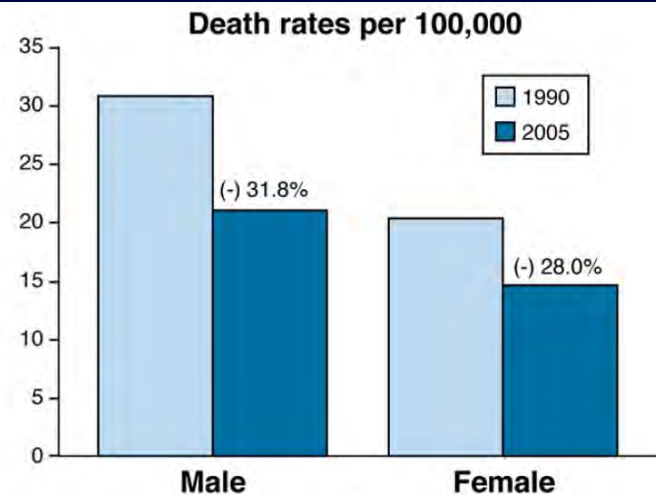


Figure 1. Death rates from CRC per 100,000 population.¹