

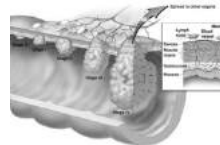
Cancer du côlon

Septin-9: un nouveau marqueur épigénétique pour le dépistage précoce

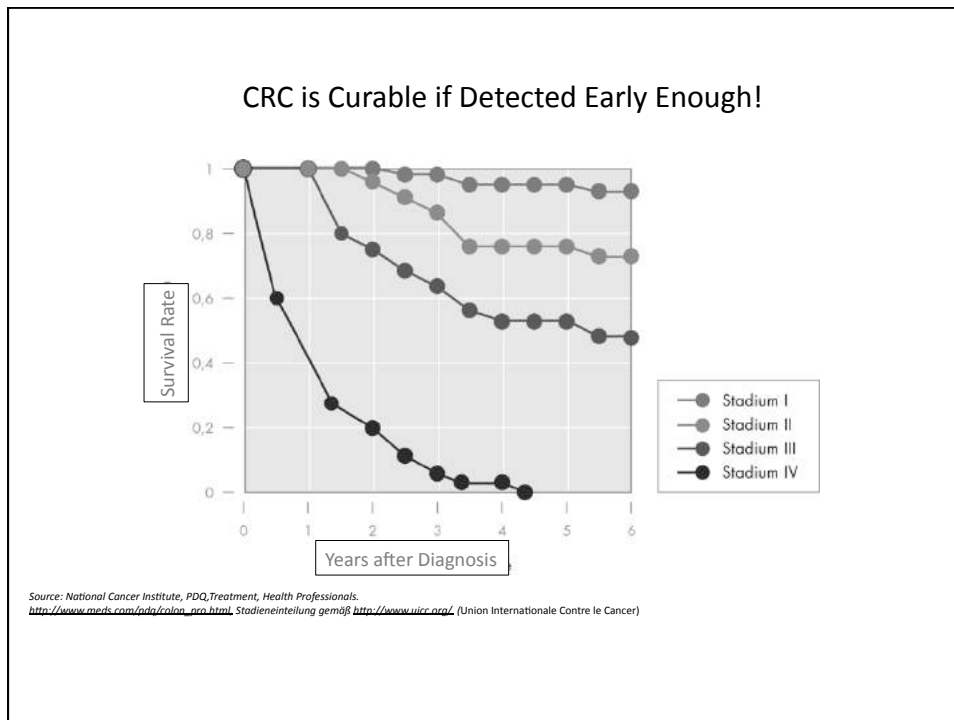


Colorectal Cancer (CRC) Screening Saves Lives....





- CRC is the second largest cancer killer – 450.000 new cases and 230.000 deaths each year in Europe
- Disease of the developed world: Highest prevalence in North America and Europe (15-20 deaths per 100.000 inhabitants¹)
- CRC is curable if detected early enough!
- 5-year survival for diagnosed and treated Stage I/II CRC: 90%
- **CRC screening has proven to reduce mortality**



¹) http://en.wikipedia.org/wiki/Colorectal_cancer ²) Survival rate for colorectal cancer by stage. Source: Globescan 2008, PDD, Treatment, Health Professionals www.merck.com/inf/inf/colon_ara.html



Depending on the country, there exist different CRC screening programs

COUNTRY	AGE	SCREENING PROGRAM
Germany 	50–55	FOBT every year
	55	Colonoscopy every 10 years or FOBT bi-annually
France 	50–74	FOBT every 2 years
UK 	50–75	FOBT every 2 years
U.S.A. 	50	Screening with FOBT annually, or sigmoidoscopy every 5 years, with FOBT every 3 years or colonoscopy every 10 years

Early detection of CRC seems to
be well-established....
So, what is the problem?

The Problem: the participation in CRC screening programs is very low... worldwide

- The accumulated participation rate for colonoscopy (age 55-74 in the years 2003-2008) is:
 - 17% women
 - 15% men
- The yearly participation rate in gFOBT testing (age 55-74 in the years 2003-2008) is:
 - 21% women
 - 13% men
- **NO participation NO compliance**
in any recommended examination
 - 62% women
 - 72% men



Source:

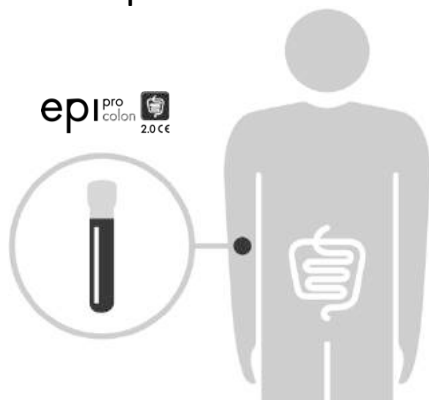


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At least 50 % of all eligible persons do not currently participate in CRC screening!

The Alternative: Septin9 test from blood

The blood-based Septin9 test for increased compliance to CRC screening



Why *patients* will want it:

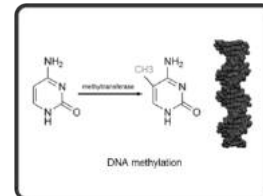
- non-invasive
- no dietary/medication restrictions
- quick and easy, done anytime
- affordable/reimbursable

Why *doctors* will use it:

- performance
- body of evidence
- easy to explain/perform
- helps with screening resistant patients
- encourages colonoscopy

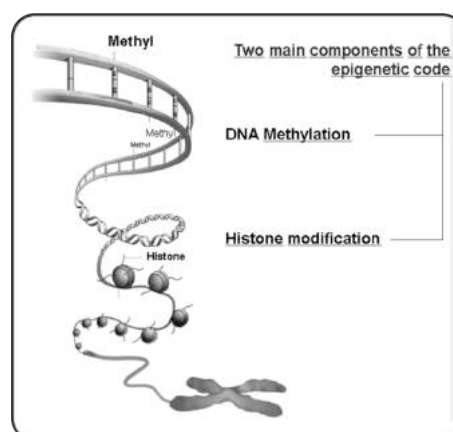
Est ce que le test Septin9 est un test génétique?

- Le test détecte des modifications épigénétiques



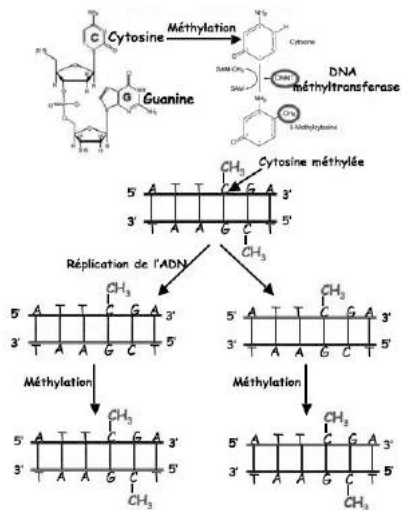
Le test Septin9 n'est pas un test génétique avec lequel une maladie génétique est détectée

Modifications épigénétiques

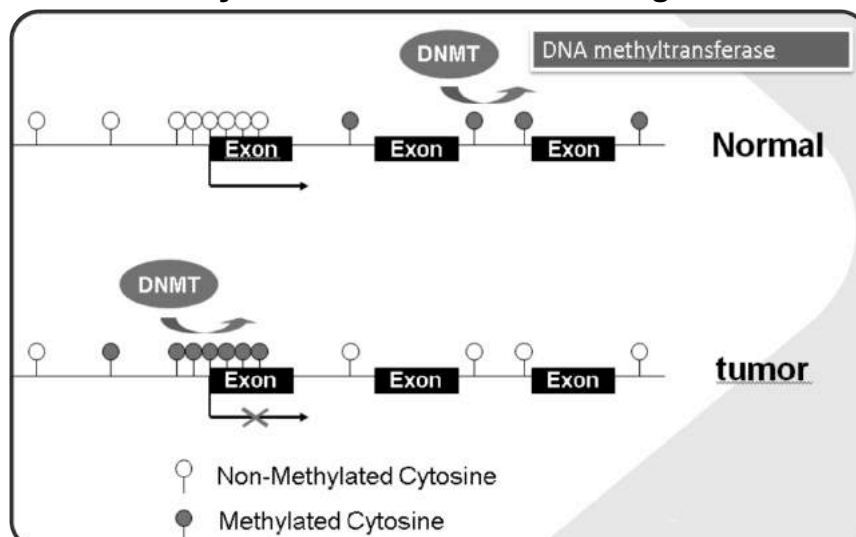


aus Qiu, Nature 2006; 441, 143-145

Méthylation de l'ADN



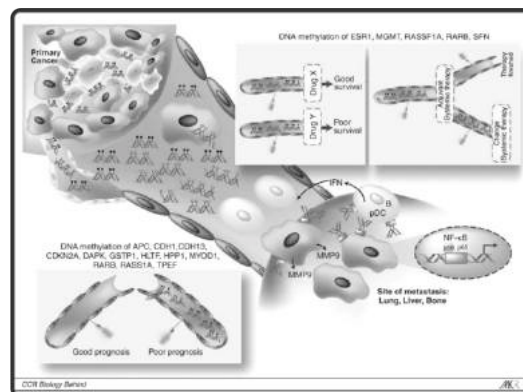
Méthylation de l'ADN et cancérogénèse



ADN tumoral sanguin

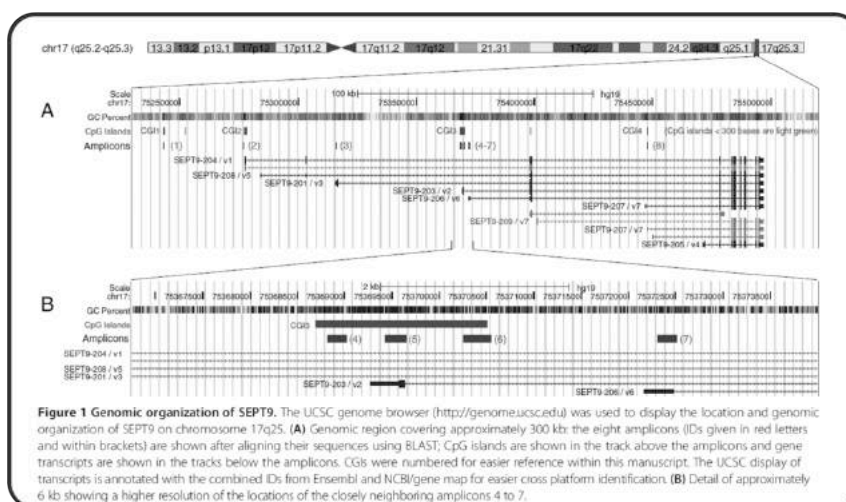
Le test doit être très sensible, capable de détecter 2 copies du génome

- L'ADN tumoral est **secrété** dans le sang à une concentration **<5pg/ml** (moins de 2 copies du génome)
- "ADN background" sain environ 10 ng / ml dans le sang



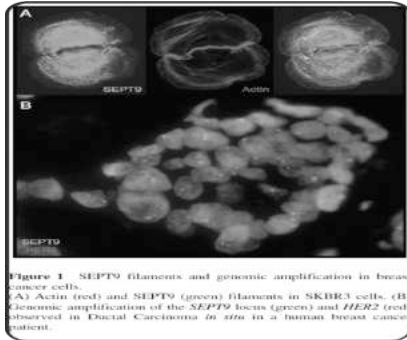
Widschwendter M, Clin Cancer Res 2006

Gène de la Septine 9



Wasserkort et al. BMC Cancer 2013, 13:398

Septines et cancer

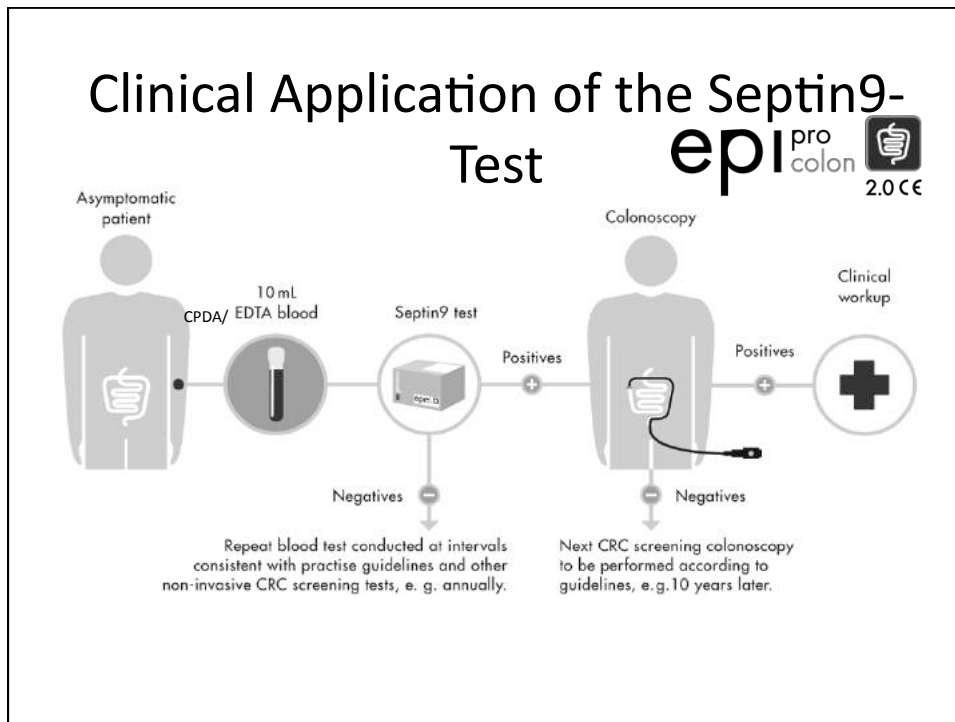


- Septines sont impliquées dans un processus appelé la **cytokinèse**.
- Septin-9 = **suppresseur tumoral**

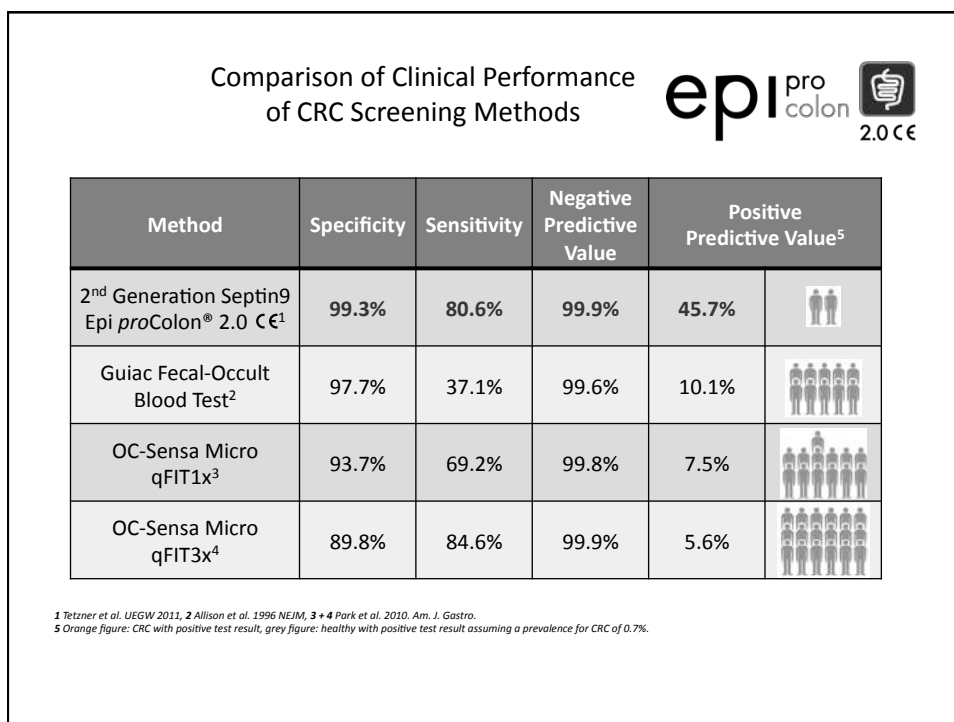
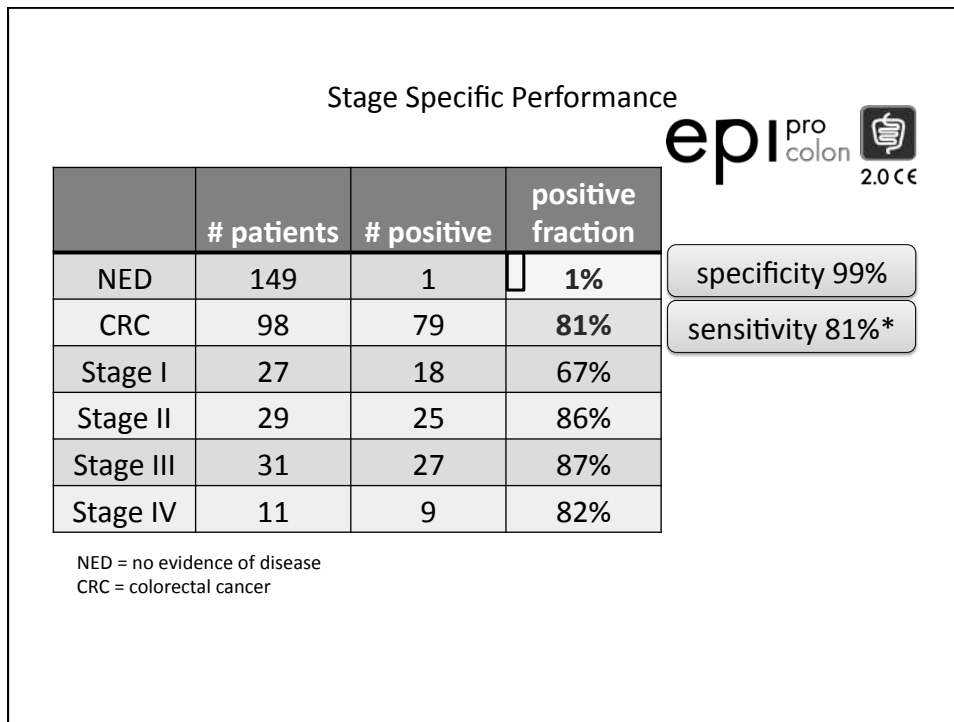
La méthylation inactive la septine-9

Conolly D. et al., Biol Chem (2011) 392 725-738

The Septin9-Test in the routine diagnostic



Study data



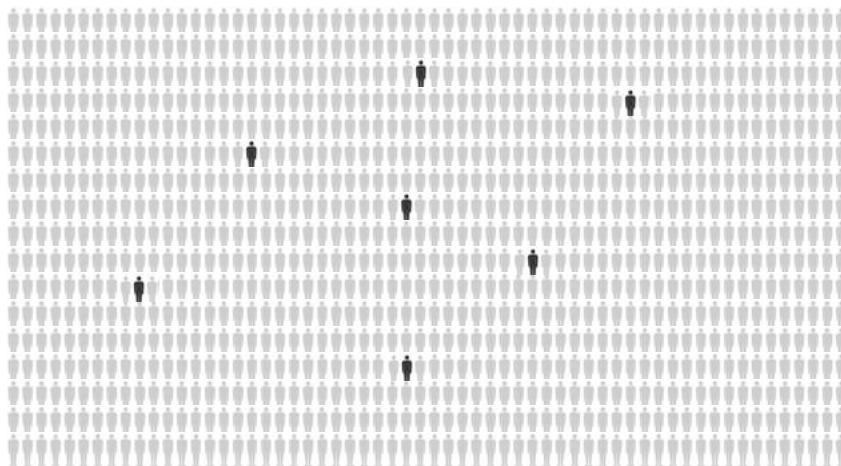
Septin9-test results

What does sensitivity and specificity mean for your patient?

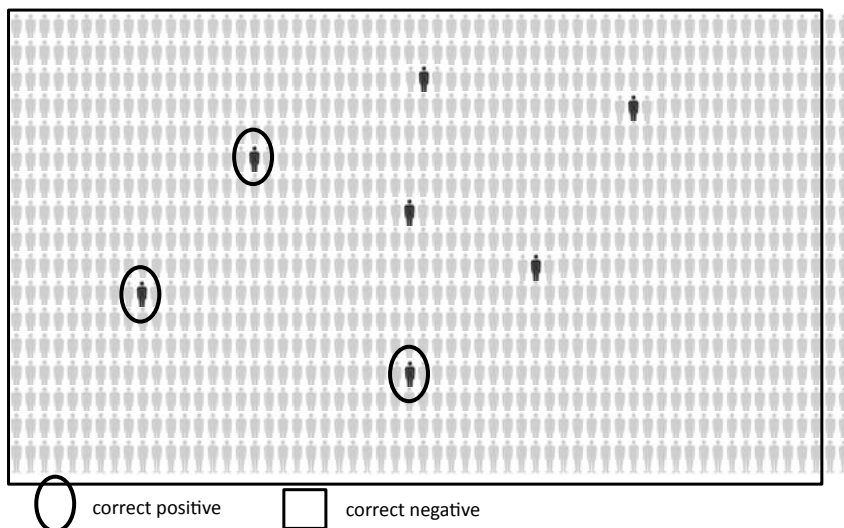
Definition of clinical performance

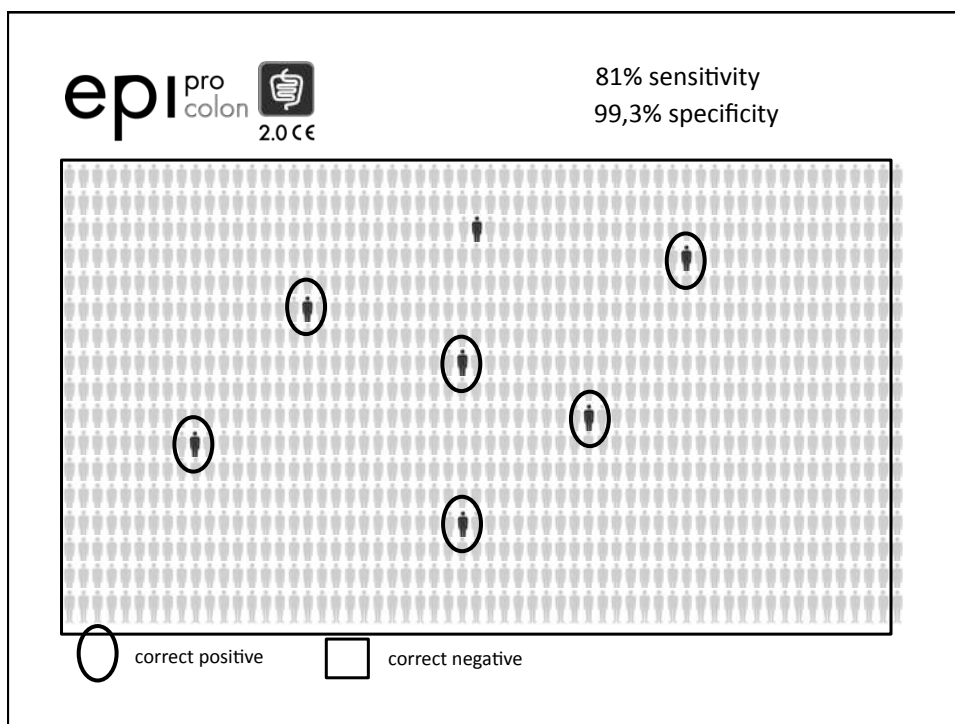
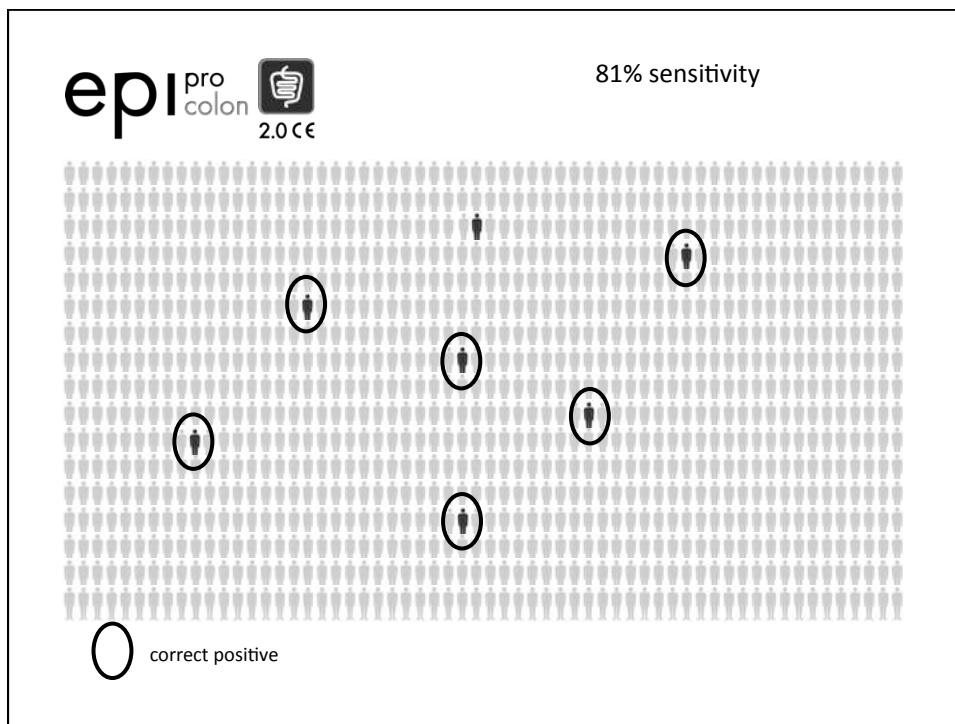
- Sensitivity
the efficiency to detect a CRC patient as really diseased: 81%
- Specificity
the efficiency to detect a healthy patient as really CRC free: 99%
- **Negative predictive value: 99.9%**
the likelihood of a negative result being really negative and CRC free
- **Positive predictive value: 45,7%**
the likelihood of a positive result being really CRC positive

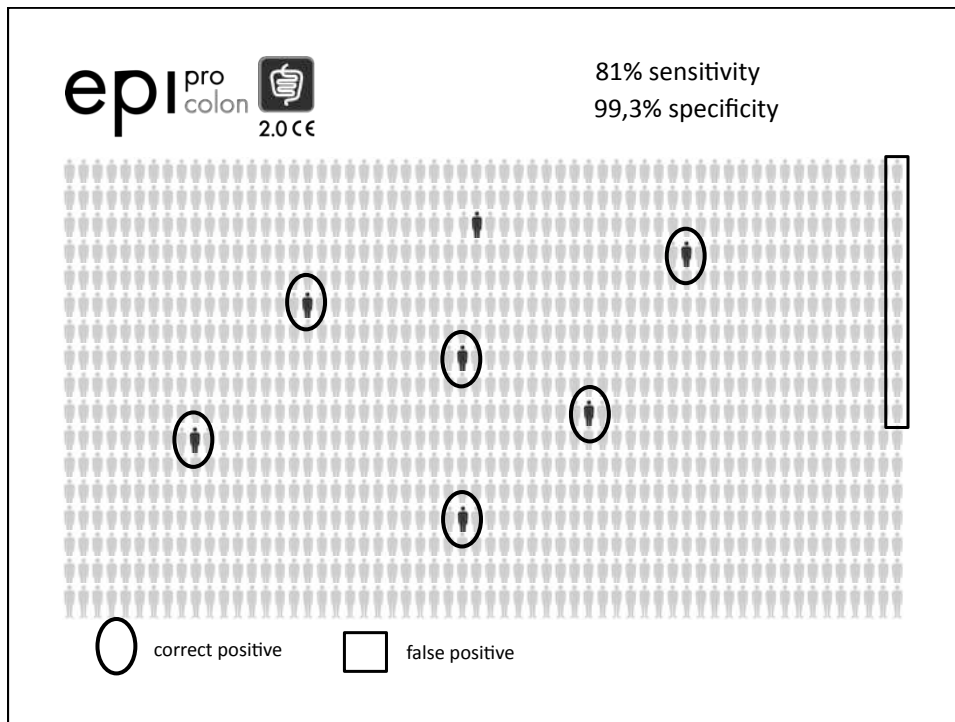
Prevalence of CRC is 0.7 %:
7 CRC cases in 1000 screening eligible individuals




Hemoccult®/gFOBT performance: <40 % sensitivity ~98 % specificity








Septin9 test result

- 

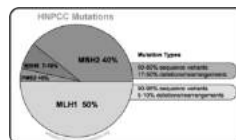
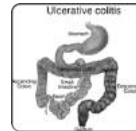
99,9 % of negative Epi pro Colon 2.0 CE tests are correctly classified (NPV 99,9%)
- 

Positive tested persons are indicated to undergo a colonoscopy for diagnosis and eventually undergo first curative steps. Approximately **one of every two** people who test positive for Epi proColon 2.0 CE will have CRC (PPV 45,7%)

Certains patients peuvent ils être exclus?

Septine 9 n'est pas approprié pour les patients:

- **Patients avec une maladie intestinale inflammatoire chronique**
 - Colite ulcéreuse
 - Maladie de Chron
- **Patients avec**
 - HNPCC
 - PAF
 - CRC déclaré



Conclusion

- The Septin9 test is positioned as an **additional choice** for CRC screening methods
- Septin9 testing is believed **to increase patient compliance** to CRC screening
- Septin9 testing is NOT intended to replace colonoscopy, but the opposite: it is believed that patients who refuse other screening options will agree to Septin9 testing and if tested positive, will be willing to undergo colonoscopy for definite diagnosis.
- Patients with a negative Septin9 test are asked for retesting on an annual basis, or biannual basis
- It is believed that wide acceptance of Septin9 testing will reduce mortality from CRC

Screen your patients Save lives !!!

Merci....