4th EUROPEAN COLORECTAL CANCER DAYS:
BRNO 2015 – PREVENTION AND SCREENING
29–30 May 2015, Brno, Czech Republic

COLORECTAL CANCER: A CHALLENGE FOR HEALTHY LIFE STYLE, SCREENING AND PROPER CARE

CT Colonography and CRC screening: an update

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SAPIENZA
UNIVERSITÀ DI ROMA

SCREENING

POPULATION ***OPPORTUNISTIC***

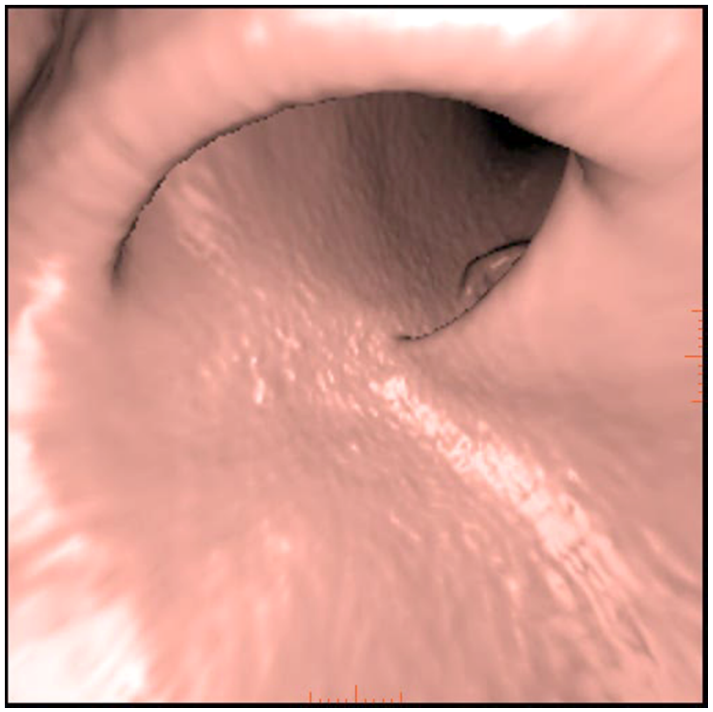
SCREENING

POPULATION

OPPORTUNISTIC

CTC in 2015

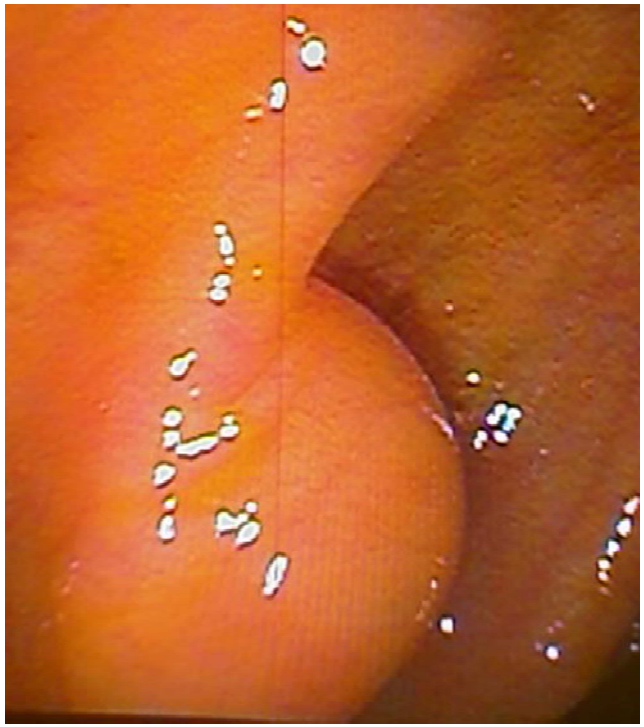
- The best radiological test for colon imaging
- Patient-friendly and safe
- Completely replacing BE
- Complimentary to CS



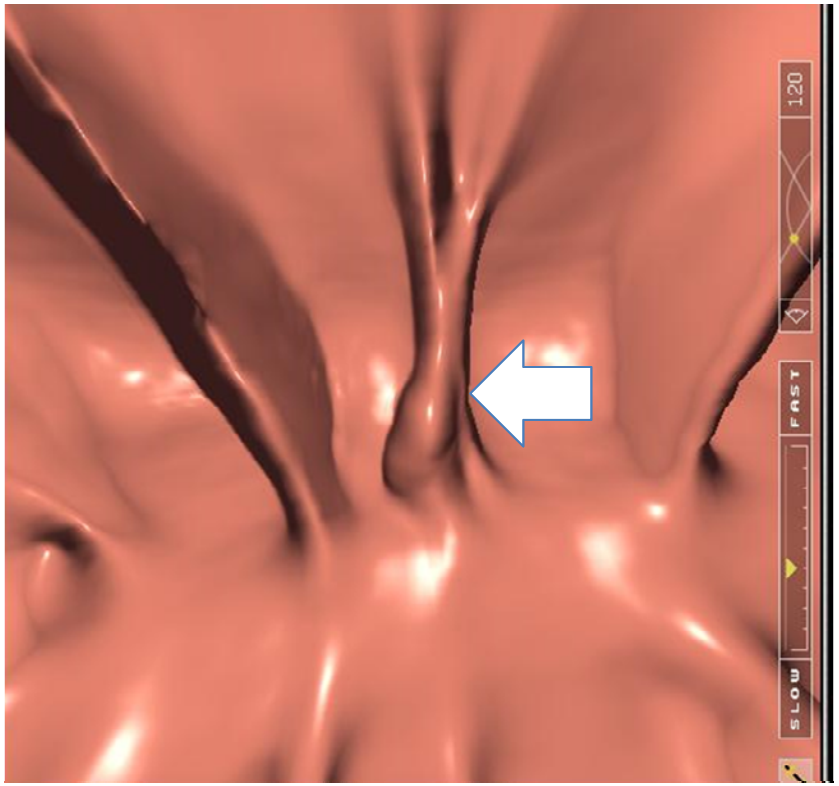
1994 - 2014

- 20th anniversary of CT Colonography
- Presented by DJ Vining at ARRS meeting in 1994
  (Am J Roentgenol 1994;62:Suppl:104)

1997: SINGLE-SLICE CTC



2014: MULTISLICE CTC



TECHNIQUE STANDARDIZATION

Eur Radiol (2007) 17: 575–579
DOI 10.1007/s00330-006-0407-y

NEWS FROM ESGAR

2007

Stuart A. Taylor
Andrea Laghi
Philippe Lefere
Steve Halligan
Jaap Stoker

European society of gastrointestinal and abdominal radiology (ESGAR): Consensus statement on CT colonography

Eur Radiol
DOI 10.1007/s00330-012-2632-x

GASTROINTESTINAL

2012

The second ESGAR consensus statement on CT colonography

Emanuele Neri · Steve Halligan · Mikael Hellström · Philippe Lefere · Thomas Mang · Daniele Regge · Jaap Stoker · Stuart Taylor · Andrea Laghi · ESGAR CT Colonography Working Group

TECHNIQUE

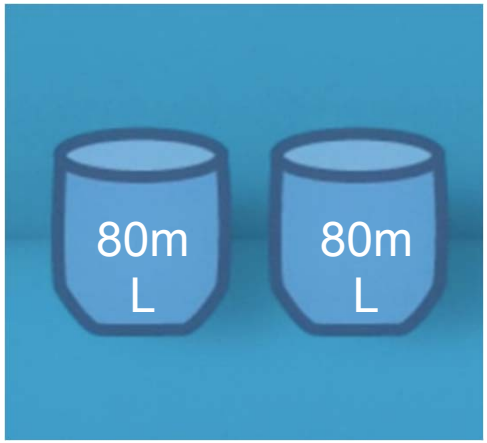
1. Bowel prep
2. Colon distention
3. CT scanning
4. Image reviewing

TECHNIQUE: BOWEL PREP

Low-fiber diet

Laxative-free

Iopamidol
Diatrizoate meglumine



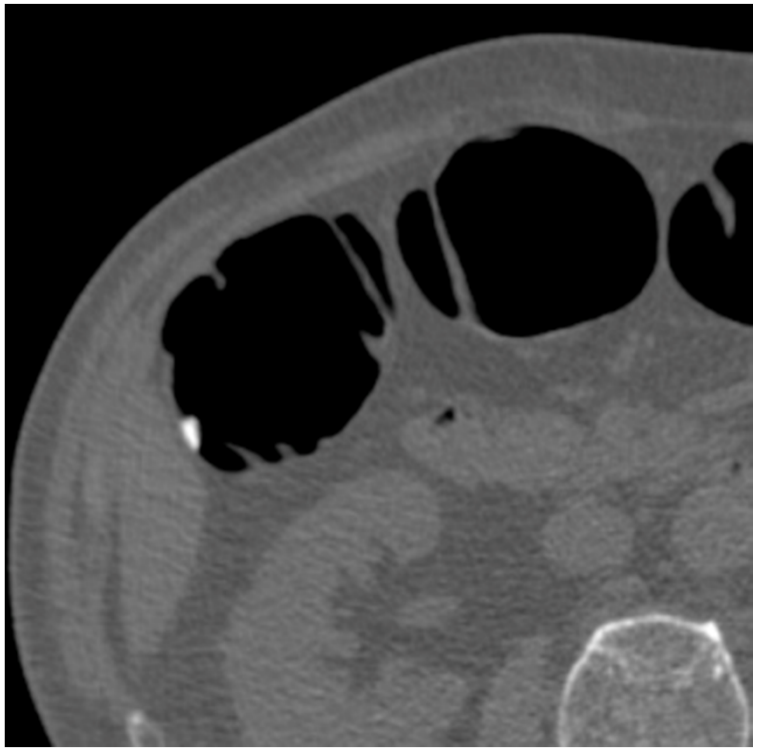
Reduced prep

1L PEG
4 tablets bysacodil

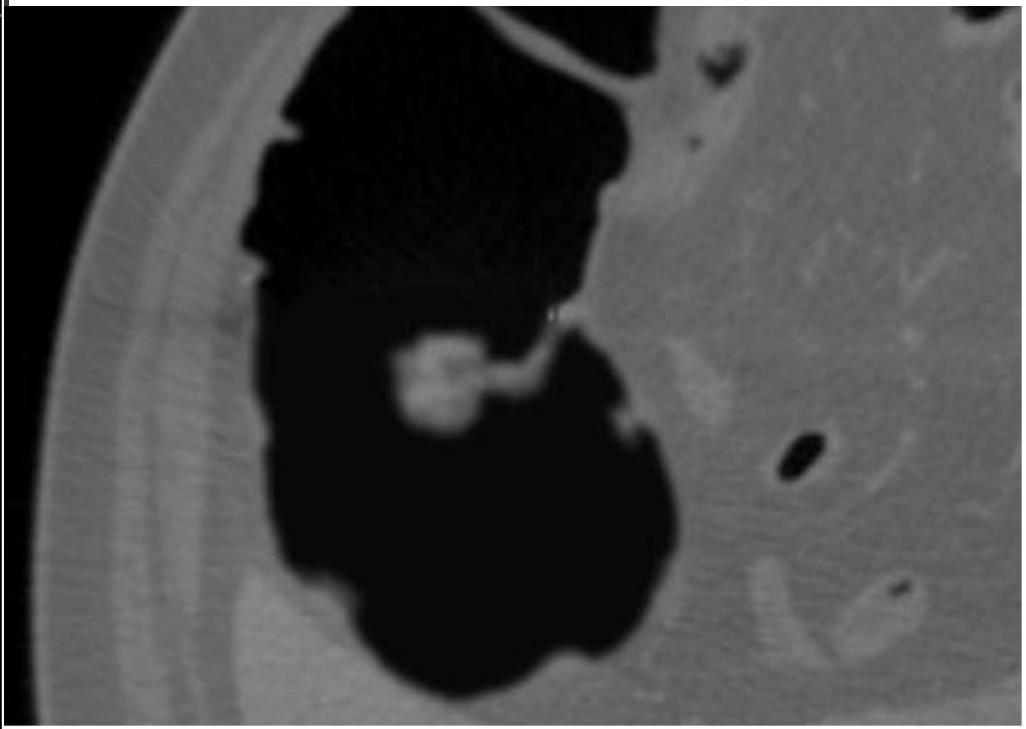
+

REDUCE PREP/LAXATIVE-FREE

- Partial cleansing (due to osmolarity)
- Iodine-tagged residual fluids and stools

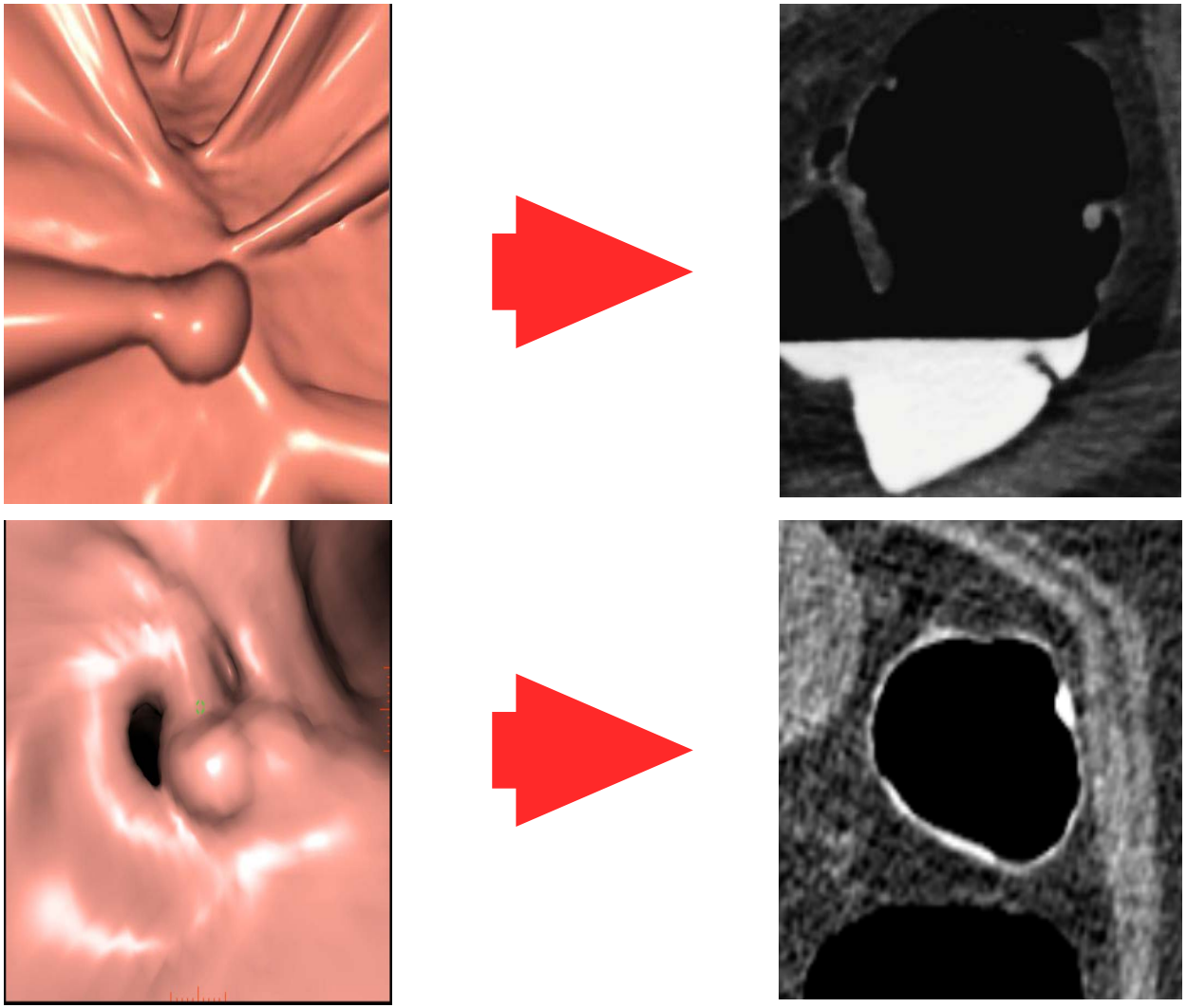


FLUID/FAECAL TAGGING



1) Identification of “submerged” lesions

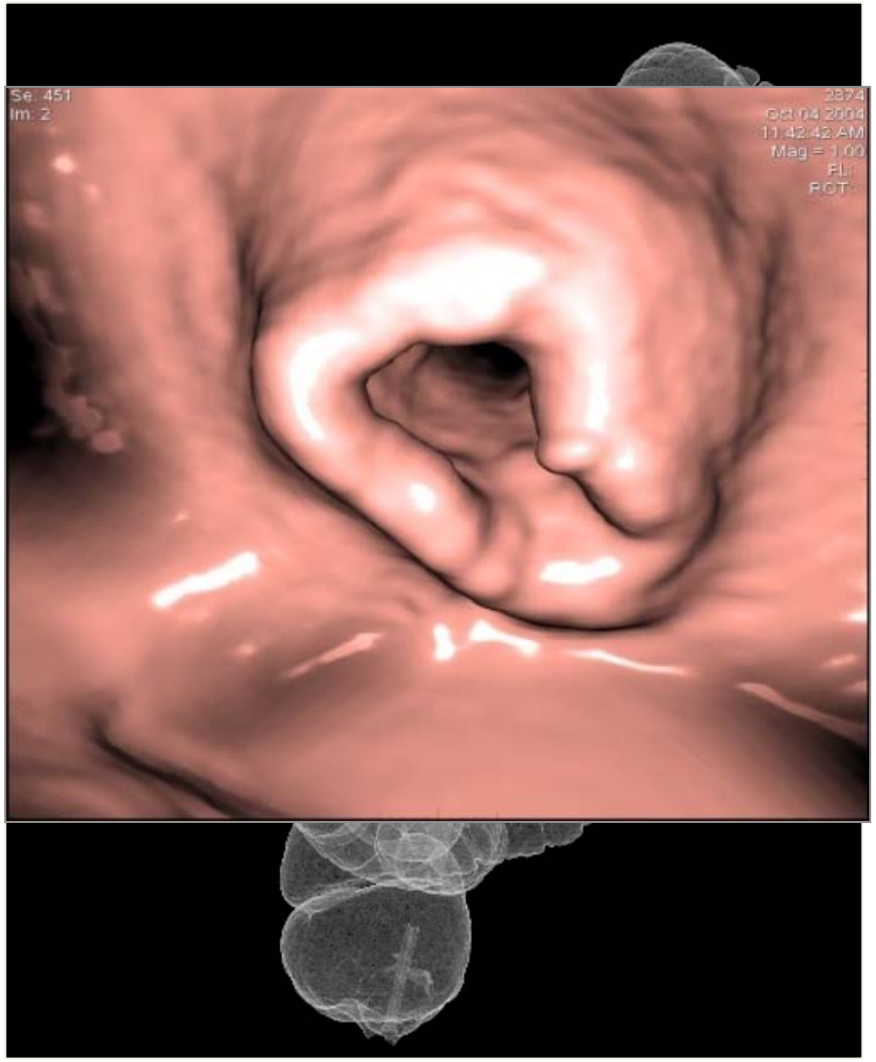
FLUID/FAECAL TAGGING



2) Characterization of tiny polyps

TECHNIQUE

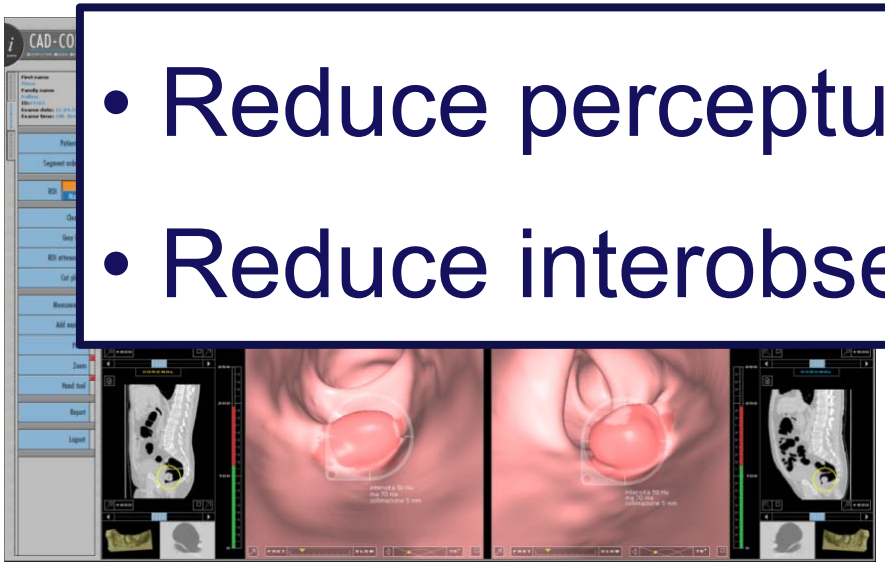
- No **SEDATION**
- Colon distention (room air/CO_2)
- Two 10s scans
- Overall time, 15 min



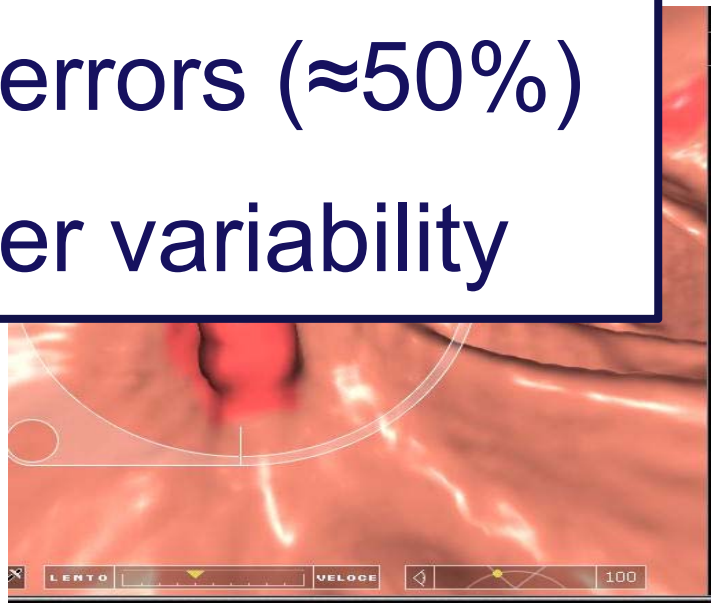
COMPUTED ASSISTED DIAGNOSIS

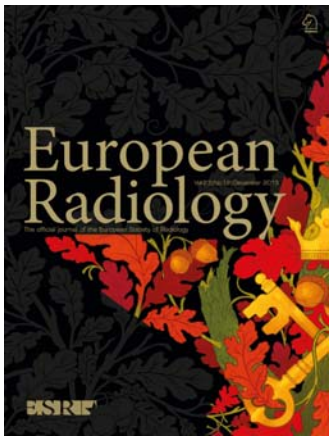
- Software for automatic detection of polyp candidates

2nd read CAD is recommended because it increases sensitivity for polyp detection without an unacceptable decrease in specificity.



- Reduce perceptual errors (≈50%)
- Reduce interobserver variability





Eur Radiol
DOI 10.1007/s00330-014-3435-z

GUIDELINE

Clinical indications for computed tomographic colonography: European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastrointestinal and Abdominal Radiology (ESGAR) Guideline

Cristiano Spada · Jaap Stoker · Onofre Alarcon · Federico Barbaro · Davide Bellini · Michael Bretthauer · Margriet C. De Haan · Jean-Marc Dumonceau · Monika Ferlitsch · Steve Halligan · Emma Helbren · Mikael Hellstrom · Ernst J. Kuipers · Philippe Lefere · Thomas Mang · Emanuele Neri · Lucio Petruzziello · Andrew Plumb · Daniele Regge · Stuart A. Taylor · Cesare Hassan · Andrea Laghi

Guideline

Clinical indications for computed tomographic colonography: European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastrointestinal and Abdominal Radiology (ESGAR) Guideline

Authors: Cristiano Spada[1], Jaap Stoker[2], Onofre Alarcon[3], Federico Barbaro[1], Davide Bellini[4], Michael Bretthauer[5], Margriet C. De Haan[2], Jean-Marc Dumonceau[6], Monika Ferlitsch[7], Steve Halligan[8], Emma Helbren[8], Mikael Hellstrom[9], Ernst J. Kuipers[10], Philippe Lefere[11], Thomas Mang[12], Emanuele Neri[13], Lucio Petruzziello[1], Andrew Plumb[8], Daniele Regge[14], Stuart A. Taylor[8], Cesare Hassan[1], Andrea Laghi[4]

Institutions: Institutions are listed at the end of article.

ESGE – ESGAR CTC GUIDELINES

ESGE/ESGAR **do not recommend CTC as a primary test for population screening** or in subjects with a first-degree positive family history (EL: Moderate ; RG: Weak)

CTC AND POPULATION CRC SCREENING

- EFFICACY
- ACCEPTABILITY
- SAFETY
- COST-EFFECTIVENESS
- LOGISTICS

CTC AND POPULATION CRC SCREENING

- **EFFICACY**
- **ACCEPTABILITY**
- **SAFETY**
- **COST-EFFECTIVENESS**
- **LOGISTICS**

CTC: THE EVIDENCES

RCT	Multi-center trials	Single center trials	Meta-analyses
COCOS SIGGAR	ACRIN IMPACT	Munich Pickhardt	Sosna, Chaparro Mulhall, Pickhardt Halligan, De Haan Rosman, Plumb

- **CTC = CS for CRC and >10 mm polyps**
- **CTC < CS for 6-9 mm polyps**
- **CTC << CS for <6 mm polyps**

CTC: THE EVIDENCES

RCT	Multi-center trials	Single center trials	Meta-analyses
COCOS SIGGAR	ACRIN IMPACT	Munich Pickhardt	Sosna, Chaparro Mulhall, Pickhardt Halligan, De Haan Rosman, Plumb

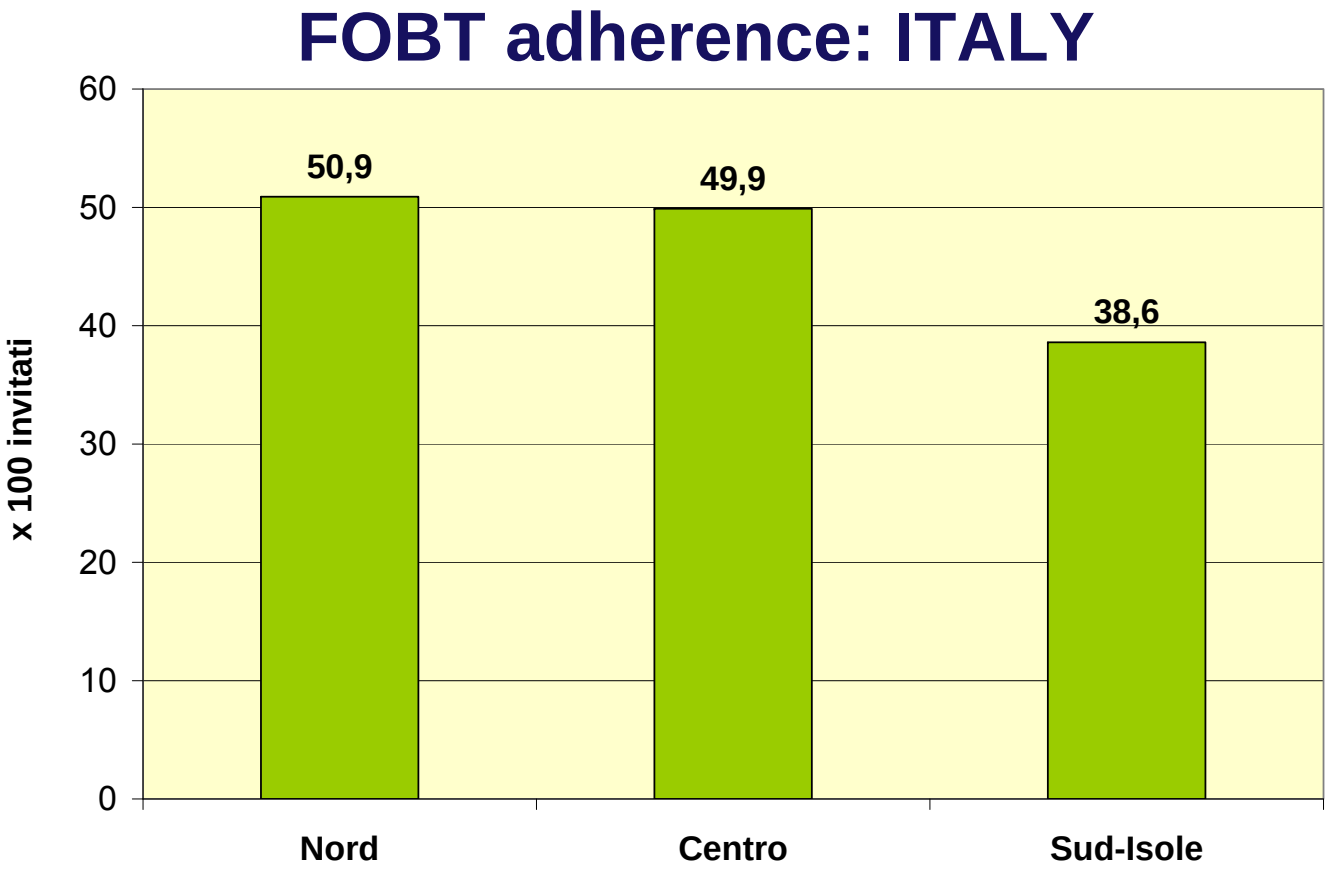
- **CTC > FS** (only left colon)
- **CTC >> FOBT** (cancer only)

CTC AND POPULATION CRC SCREENING

- EFFICACY
- **ACCEPTABILITY**
- SAFETY
- COST-EFFECTIVENESS
- LOGISTICS

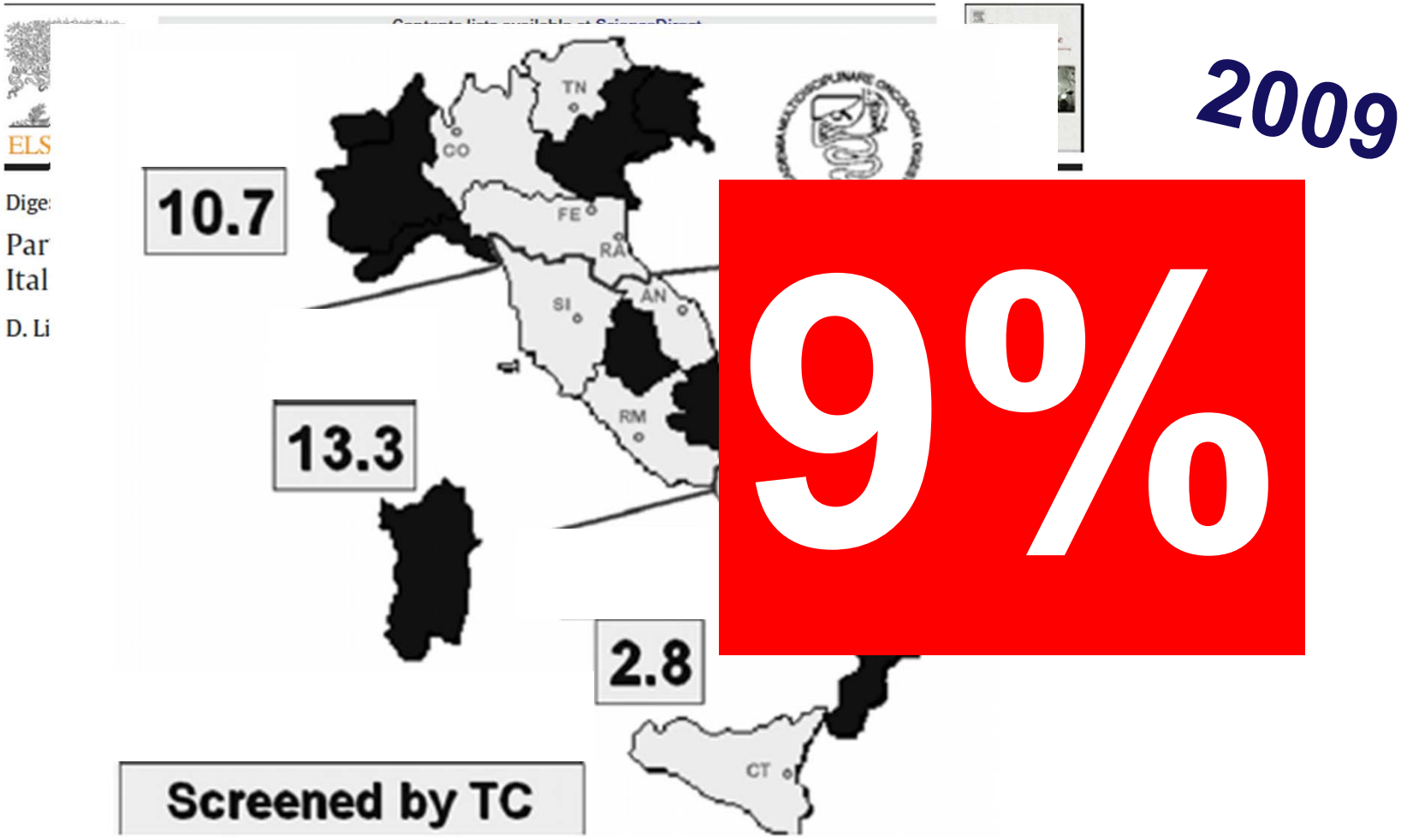
CTC AND POPULATION CRC SCREENING

- Exam **ACCEPTABILITY** influences subjects adherence to screening



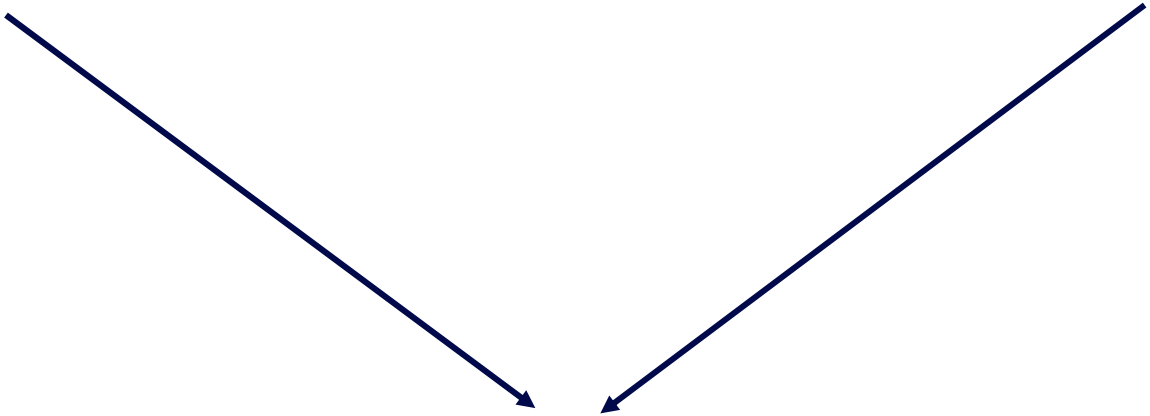
Data courtesy of dr Carlo Senore, CPO, Piedmont, Italy

CTC AND POPULATION CRC SCREENING



CTC AND POPULATION CRC SCREENING

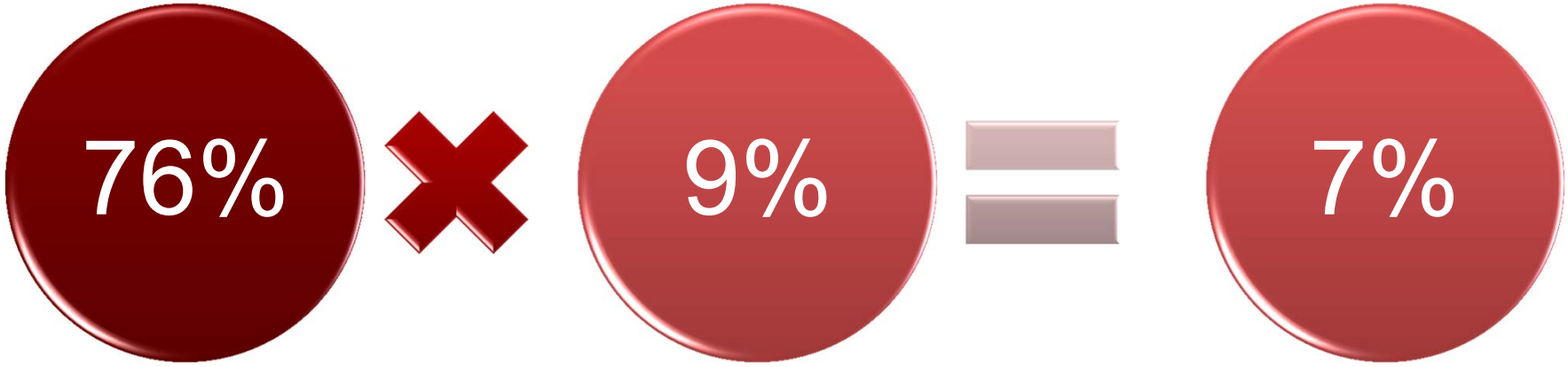
EFFICACY **ADHERENCE**



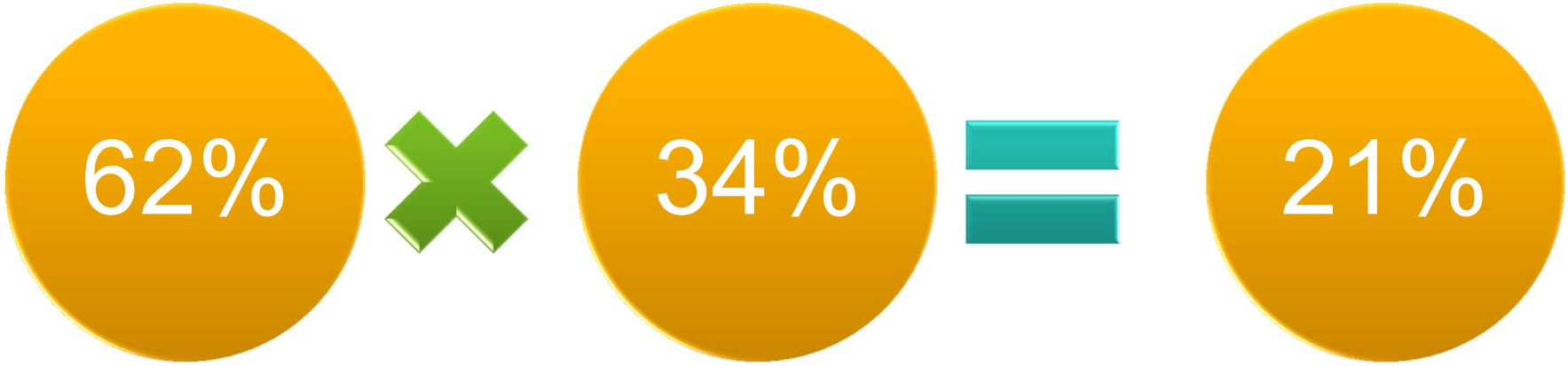
EFFICIENCY

(CRC prevention rate)

COLONOSCOPY



CT COLONOGRAPHY

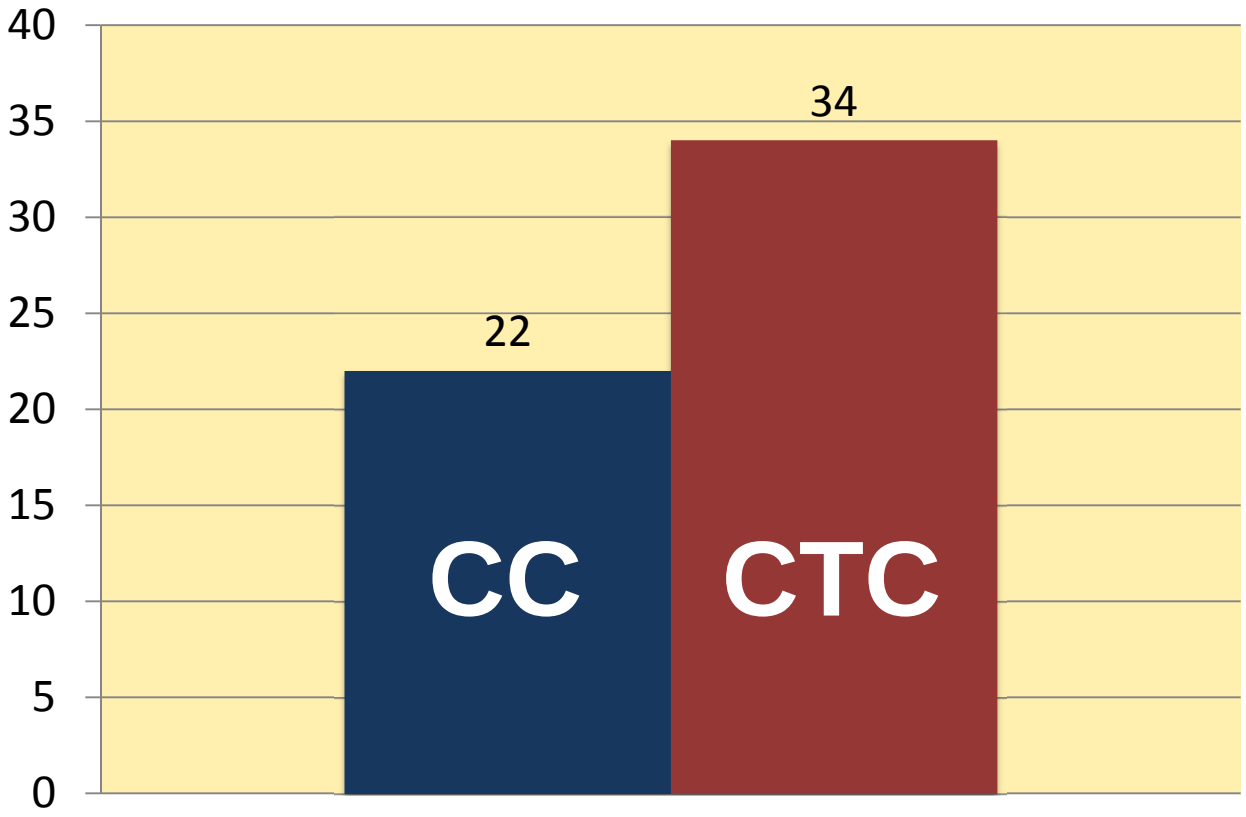


CTC adherence in screening

Participation and yield of colonoscopy versus non-cathartic CT colonography in population-based screening for colorectal cancer: a randomised controlled trial

Esther M Stoop, Margriet C de Haan*, Thomas R de Wijkerslooth, Patrick M Bossuyt, Marjolein van Ballegooijen, C Yung Nio, Marc J van de Vijver, Katharina Biermann, Maarten Thomeer, Monique E van Leerdam, Paul Fockens, Jaap Stoker, Ernst J Kuipers, Evelien Dekker*

www.thelancet.com/oncology **Published online November 15, 2011 DOI:10.1016/S1470-2045(11)70283-2**



CTC: ADHERENCE RATE

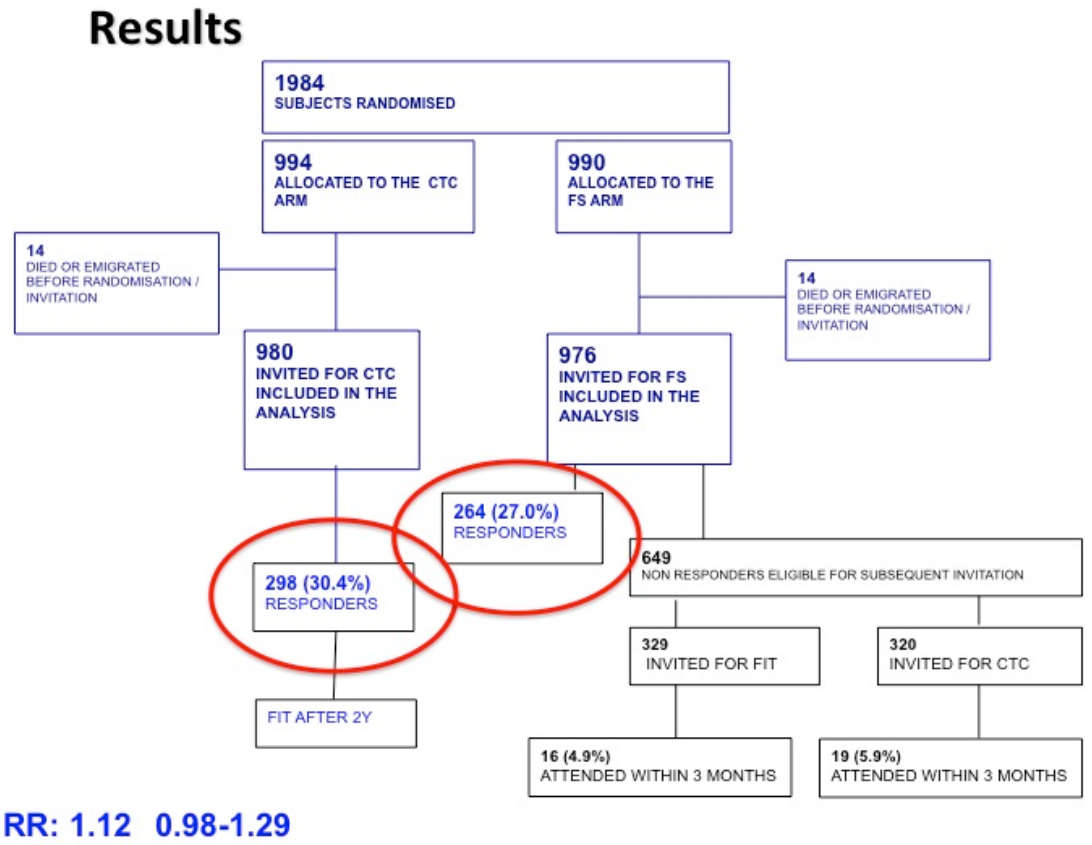
Protéus trial

RCT: FS vs CS

- CTC: **30.4%**
- FS: **27.0%**

p=ns

- Male uptake of CTC higher than FS (OR, 1.6; 95% CI: 1.1-2.3; P=0.01)



Regge D et al, data presented at ECR 2015

PROTEUS TRIAL: OPEN ISSUES

- "Unfair" comparison between a well-established test and a "new-comer" in a region where population-based CRC screening using FS works

Segnan N et al, SCORE trial, JNCI 2011

Regge D et al, data presented at ECR 2015

PROTEUS TRIAL: OPEN ISSUES

- Further “marketing” of CTC (PCP; public opinion)

- Among CTC invitees, the following key groups were more likely to uptake screening:
  - male (ORs, 2.4; 95% CI: 1.4-4.1)
  - retired (ORs, 2.10; 95% CI: 1.2-2.7)
  - those asking general practitioner for counseling (ORs, 2.6; 95% CI: 1.3-5.4)
  - those having friends/relatives with CRC (ORs, 4.1; 95% CI: 1.6-10.9)
  - those who have read information material (ORs, 7.3; 95% CI: 2.6-19.2)

Regge D et al, data presented at ECR 2015

PROTEUS TRIAL: OPEN ISSUES

- Unexplained higher adherence in males

- Participation rate in males is **HIGHER** (opposite to FS trial)
  - Why ?
  - Are males more scared of an endoscope ?
  - Or are they simply more interested in technological innovations?

Regge D et al, data presented at ECR 2015

PROTEUS TRIAL: OPEN ISSUES

- Bowel preparation and level of embarrassment in favor of FS

Regge D et al, data presented at ECR 2015

Patient's experience

		FS	CTC
Bowel preparation side effects	None/very mild	187	171
		80.3%	72.8%
	Mild	29	22
		12.4%	9.4%
	Moderate / severe	17	42
		7.3%**	17.9%**
Level of pain *	1	167	152
		71.7%	64.1%
	2		
	>2	36	40
		15.5%	18.2%
Level of anxiety *	1	192	180
		82.4%	75.9%
	2	28	40
		12.0%	16.9%
	>2	13	17
		5.6%	7.2%
Level of Embarassment *	1	193	175
		82.8%***	73.8%***
	2	22	35
		9.4%	14.8%
	>2	18	27
		7.7%	11.4%

19 vs 27%

*1=none, 5=very high

1. Preparation needs to be improved

** OR (TCT vs FS): 2.77; 95%CI:1.52-5.01

*** OR (TCT vs FS): 0.59; 95%CI:0.37-0..91

Patient's experience

		FS	CTC
Bowel preparation side effects	None/very mild	187	171
		80.3%	72.8%
	Mild	29	22
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	2		
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	2	22	35
		9.4%	14.8%
	>2	18	27
		7.7%	11.4%

19 vs 27%

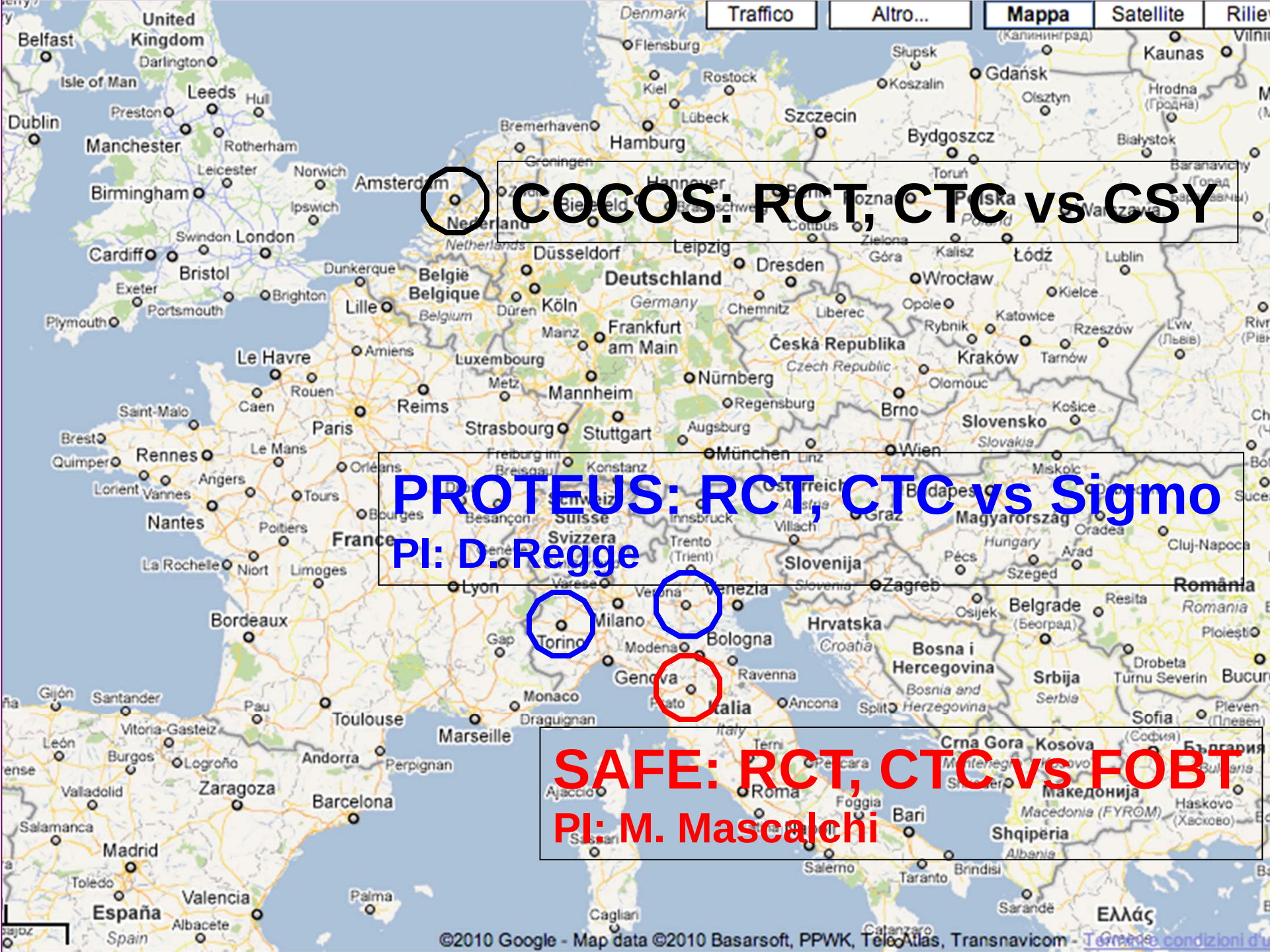
*1=none, 5=very high

1. Preparation needs to be improved

1I. CT room setup is probably not adequate for screening

16 vs 26%

** OR (TCT vs FS): 2.77; 95%CI:1.52-5.01
.59; 95%CI:0.37-0..91


COCOS: RCT, CTC vs CSY
PROTEUS: RCT, CTC vs Sigmo
PI: D.Regge
SAFE: RCT, CTC vs FOBT
PI: M. Mascalchi
Traffico
Altro...
Mappa
Satellite
©2010 Google - Map data ©2010 Basarsoft, PPWK, TeleAtlas, Transnavicom

CTC AND POPULATION CRC SCREENING

- EFFICACY
- ACCEPTABILITY
- **SAFETY**
- COST-EFFECTIVENESS
- LOGISTICS

CTC: SAFETY

SAFETY

- Radiation exposure
- Complications (perforations)

RADIATION EXPOSURE

- **Current recommendations**
  - Reasonably low-dose exam
  - Total effective dose: ≈ 5 mSv

2nd ESGAR Consensus Statement on CTC

  - Benefits clearly outweigh radiation risks

    Risk/benefit: **1:24 / 1:35**

Berrington de Gonzalez, AJR, 2010

RADIATION EXPOSURE

- New technology (**ITERATIVE** algorithm)
- Dose exposure lower than natural background

Annual radiation background	≈2.5-3.0 mSv
CTC (iterative recon)	≈1.5 mSv

RADIATION EXPOSURE

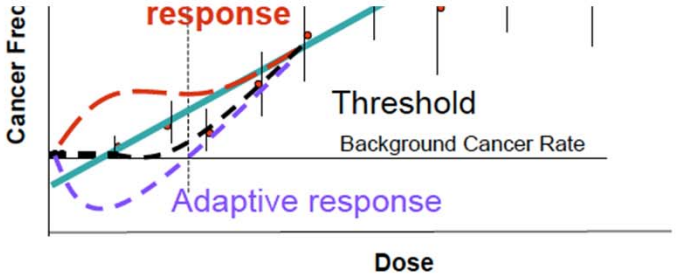
- Carcinogenic risk of low-dose radiation exposure **IS** neither **DEMONSTRATED** nor **SCIENTIFICALLY DEMONSTRABLE**
- Beyond LNT, other theories do exhist

Radiation Dose-Response Models

No data | Data and radiation-induced cancer

RADIATION RISK IN PERSPECTIVE

There is substantial and convincing scientific evidence for health risks following high-dose exposures. However, below 5–10 rem (which includes occupational and environmental exposures), risks of health effects are either too small to be observed or are nonexistent.



Health Physics Society
Telephone: 703-790-1745
Fax: 703-790-2672
Email: HPS@BurkInc.com
http://www.hps.org

RADIATION EXPOSURE

Some facts

American Journal of Epidemiology

Vol. 158, No. 1
Printed in U.S.A.
DOI: 10.1093/aje/kwg107

ORIGINAL CONTRIBUTIONS

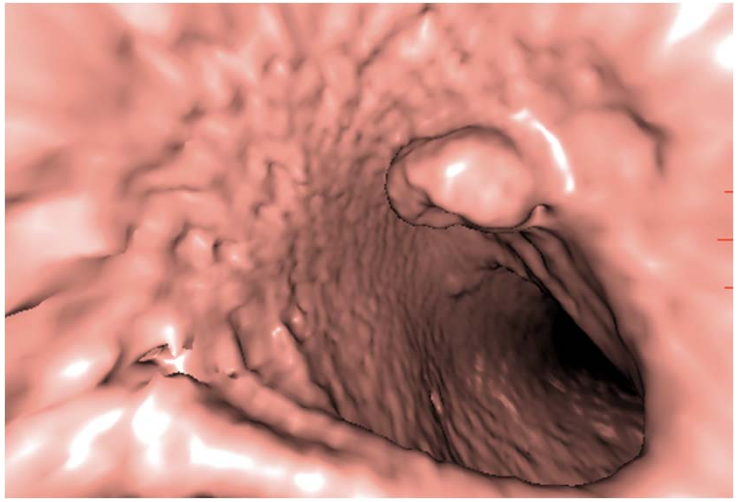
Mortality from Cancer and Other Causes among Airline Cabin Attendants in Europe: A Collaborative Cohort Study in Eight Countries

*Among airline cabin crew in Europe, there was **no increase in mortality that could be attributed to cosmic radiation** or other occupational exposures to any substantial extent*

Iterative Reconstruction: CTC

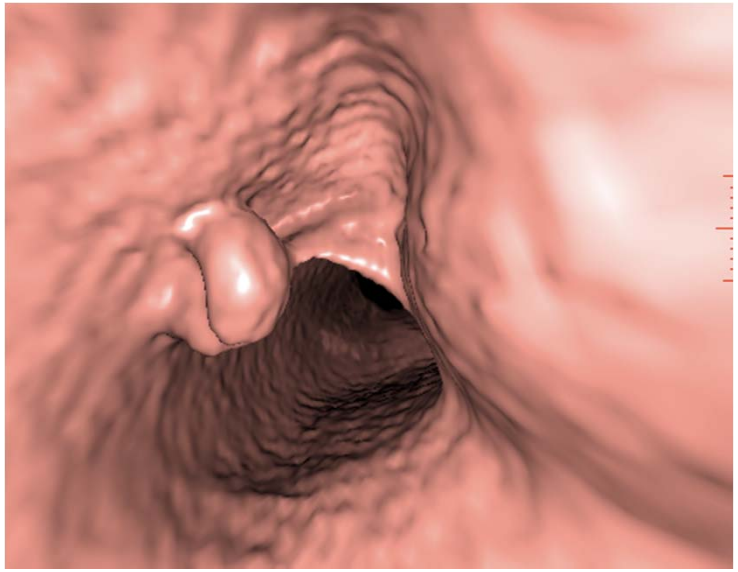
ASIR 50%

kV 100 + mAs 25 → mSv 0.75



FBP

kV 120 + mAs 50 → mSv 2.32



PERFORATION

Eur Radiol
DOI 10.1007/s00330-014-3190-1

GASTROINTESTINAL

Perforation rate in CT colonography: a systematic review of the literature and meta-analysis

Davide Bellini · Marco Rengo · Carlo Nicola De Cecco · Franco Iafrate · Cesare Hassan · Andrea Laghi

Meta-analysis

>100,000 patients

CTC, **0.02%** vs CS, **0.03%**

- CS data are underestimated
- Surgical rate: CTC, 0.008% (1:12,500)
  CS, 100%
- NO CTC-related deaths

B.A. M/65y, F/U

t0

t21d

CTC AND POPULATION CRC SCREENING

- EFFICACY
- ACCEPTABILITY
- SAFETY
- **COST-EFFECTIVENESS**
- LOGISTICS

COST/EFFECTIVENESS OF CTC

CTC	Follow-up Interval	Sensitivity for Cancer, Specificity	Test Costs[b]			
Hassan, 2007 (44)	10 years, all findings	95, 86	97	FSIG, COL	CS	Dominant vs. FSIG, ICER COL vs. CTC: 14,600
Ladabaum, 2004 (53)	10 years, all findings	95, 85	1,037	COL	36,300	Dominated by COL
Pickhardt, 2007 (19)	10 years, findings 6+ mm	95, 86	555	FSIG, COL	5,100	Dominant vs. FSIG, ICER COL vs. CTC: 74,200
Sonnenberg, 2000 (54)	10 years, all findings	80, 95	741	COL	17,800	Dominated by COL
Vijan, 2007 (23)	5 years, all findings	91, 91	707	gFOBT, COL, FSIG, FSIG + gFOBT	10,300–21,800	197,200
Zauber, 2009 (MISCAN) (22)	5 years, findings 6+ mm	84–92, 80–88	522	gFOBT, SENSA, COL, FSIG, FIT, FSIG + gFOBT	9,500–10,200	Dominated by COL, FSIG + gFOBT
Zauber, 2009 (SimCRC) (22)	5 years, findings 6+ mm	84–92, 80–88	522	gFOBT, SENSA, COL, FSIG, FIT, FSIG + gFOBT	3,600–4,200	Dominated by COL, FSIG + gFOBT
Zauber, 2009 (CRC-SPIN) (22)	5 years, findings 6+ mm	84–92, 80–88	522	gFOBT, SENSA, COL, FSIG, FIT, FSIG + gFOBT	1,900–2,100	Dominated by COL, FSIG + gFOBT

CTC dominated by CC, FSIG + gFOBT

COST/EFFECTIVENESS OF CTC

Eur Radiol (2013) 23:897–907
DOI 10.1007/s00330-012-2689-6

GASTROINTESTINAL

Unit costs in population-based colorectal cancer screening using CT colonography performed in university hospitals in The Netherlands

M. C. de Haan · M. Thomeer · J. Stoker · E. Dekker · E. J. Kuipers · M. van Ballegooijen

- Dutch costs of CT-screening were substantially lower than the cost assumptions that were used in published cost-effectiveness analyses on CTC screening
- Average costs per participant: €169.40

CTC AND POPULATION CRC SCREENING

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- SAFETY
- COST-EFFECTIVENESS
- **LOGISTICS**

Alimentary Pharmacology & Therapeutics

2008

Projected impact of colorectal cancer screening with computerized tomographic colonography on current radiological capacity in Europe

C. HASSAN*, A. LAGHI†, P. J. PICKHARDT‡,§, D. H. KIM‡, A. ZULLO*, F. IAFRATE† & S. MORINI*

28,760,130 European population
(30% compliance)

3,482 available CT units

START-UP PERIOD

6.6 CTC/CT unit/day

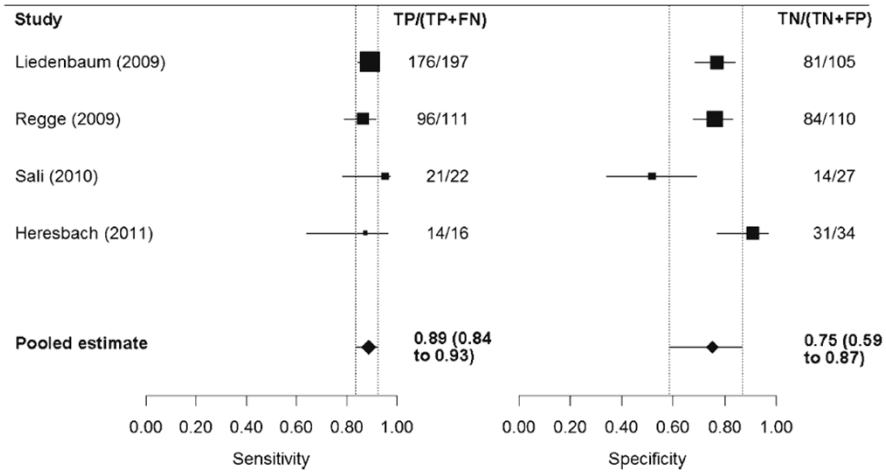
STEADY STATE

4.3 CTC/CT unit/day


That's all Folks!
?

ESGE – ESGAR CTC GUIDELINES

ESGE/ESGAR strongly recommend CTC in the case of **positive FOBT/FIT with incomplete or unfeasible CS** within organized population screening programs. (RG: Strong; EL: Low).



Se for >6 mm polyps is 89%

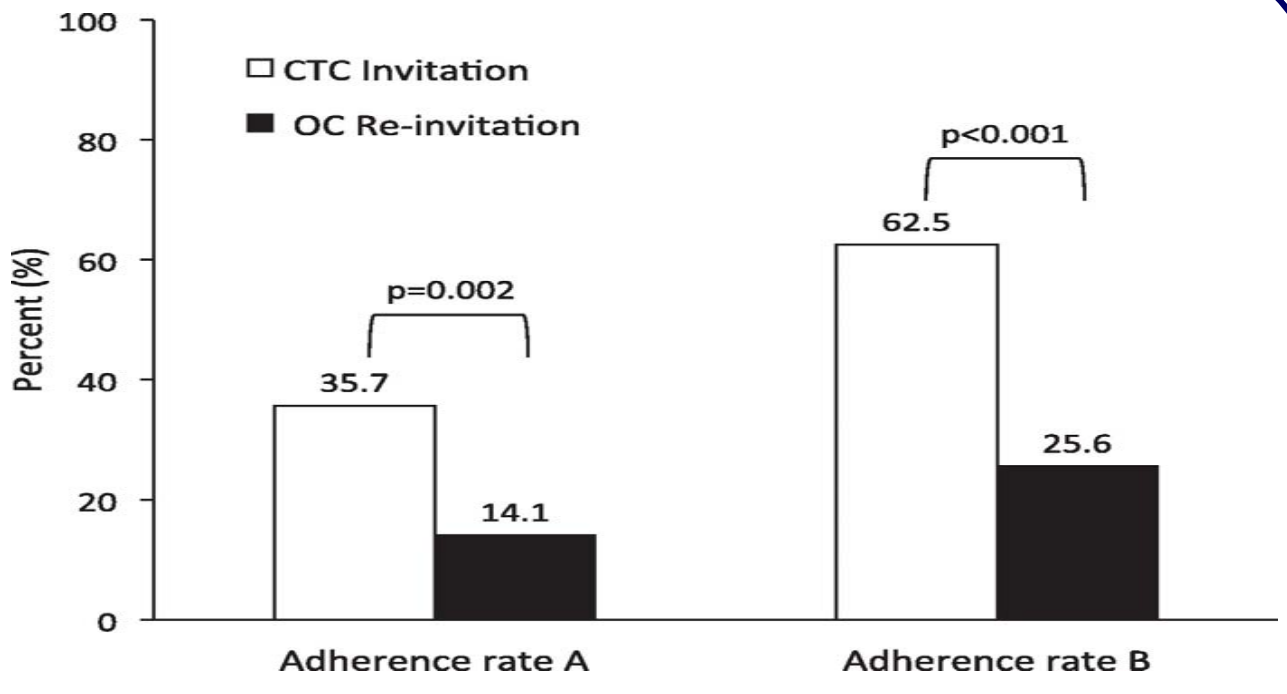
Sp is lower, 75%

"CTC is a good alternative if CS is undesirable"

Plumb AA et al. Eur Radiol 2014

CTC: integration into FOBT-based CRC screening programs

- **Patients with +FOBT/FIT refusing CS**



Sali L, et al. Dig Liv Dis 2013; 4:285-89

Data courtesy of dr Carlo Senore, CPO, Piedmont, Italy

SCREENING

POPULATION

OPPORTUNISTIC

- **EFFICACY**
- **SAFETY**

ESGE – ESGAR CTC GUIDELINES

ESGE/ESGAR …**suggest (CTC) as a CRC screening test on an individual basis** providing the screenes are adequately informed about test characteristics, benefits and risks. (EL: Moderate ; RG: Weak)

2008

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Special tests

Colon and rectal cancer

Beginning at age 50, both men and women at *average risk* for developing colorectal cancer should use one of the screening tests below. The tests that are designed to find both early cancer and polyps are preferred if these tests are available to you and you are willing to have one of these more invasive tests. Talk to your doctor about which test is best for you.

Tests that find polyps and cancer

- flexible sigmoidoscopy every 5 years*
- colonoscopy every 10 years
- double contrast barium enema every 5 years*
- CT colonography (virtual colonoscopy) every 5 years*

Tests that mainly find cancer

- fecal occult blood test (FOBT) every year*,**
- fecal immunochemical test (FIT) every year*
- stool DNA test (sDNA), interval uncertain*

2010

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President Obama Gets Virtual Colonoscopy (CT Colonography) Coverage to Seniors

PR Newswire 2010-03-02

Medicare Should Cover Screening CT Colonography for Older Americans Who Want It **WASHINGTON**, March /PRNewswire-USNewswire/ -- President Obama, in his first routine physical exam as commander in chief, received a CT colonography (CTC), commonly known as a virtual colonoscopy, to screen him for colorectal **cancer**. However, Obama Administration officials at the Centers for Medicare and Medicaid Services (CMS) previously denied coverage of the same exam for **seniors** enrolled in Medicare, cutting off access for many an exam proven to increase compliance with nationally accepted colon cancer...

CONCLUSIONS

- CTC **CANNOT** be proposed as a **population screening** test today
  - Recommendations from EU are for FOBT/FIT
  - Missing data on cost/effectiveness
  - Shortage of radiologists and equipments??
- CTC **CAN** be integrated in a **population screening** programme based on FOBT/FIT
  - To replace BE in pts with +FOBT/FIT and incomplete CC
  - To investigate pts with +FOBT/FIT who refuse CC

CONCLUSIONS

- CTC is effective, acceptable and safe as an **opportunistic** screening test
  - asymptomatic, average-risk subjects; starting @ age 50; time interval, 5 yrs