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Confronto delle performance del FIT nei programmi di screening: una meta-analisi

Relative performance comparison
of immunochemical fecal occult blood tests
in organised population-based
colorectal cancer screening programmes:
a systematic review and meta-analysis
from experimental studies

*Deandrea S, Rubeca T, Anghinoni E, Rapi
S, Randi G, Bencivenni S, Corradini R,
Passamonti U, Sassatelli R, Senore C*



OBIETTIVI DELLO STUDIO

- Condurre una revisione sistematica della letteratura mirata agli studi sperimentali effettuati in programmi di popolazione
- Tracciare un profilo della performance dei vari test combinando i parametri di accuratezza diagnostica raccolti dai vari studi, al netto dei fattori confondenti (struttura per età e sesso, incidenza di base, etc.)
- Fornire evidenze ai programmi di screening e alle società scientifiche per la selezione del test più adatto

METODI

1. Stesura protocollo e definizione criteri di inclusione
2. Identificazione degli studi in letteratura
3. Estrazione dei dati e ricalcolo degli indicatori
4. Analisi dei fattori associati alla performance del test OC Sensor (analisi *WITHIN TEST*)
5. Normalizzazione di tutti i cut-off in $\mu\text{g/g}$ feci
6. Confronto tra test a cut-off normalizzati (analisi *BETWEEN TESTS*)

#1 PROTOCOLLO

UNIVERSITY *of York*
Centre for Reviews and Dissemination

PROSPERO International prospective register of systematic reviews

**Relative performance comparison of immunochemical fecal occult
blood tests in organised population-based colorectal cancer
screening programmes: a systematic review and a meta-analysis
from experimental studies**

Silvia Deandrea, Tiziana Rubeca, Emanuela Anghinoni, Carlo Senore, Giorgia Randi

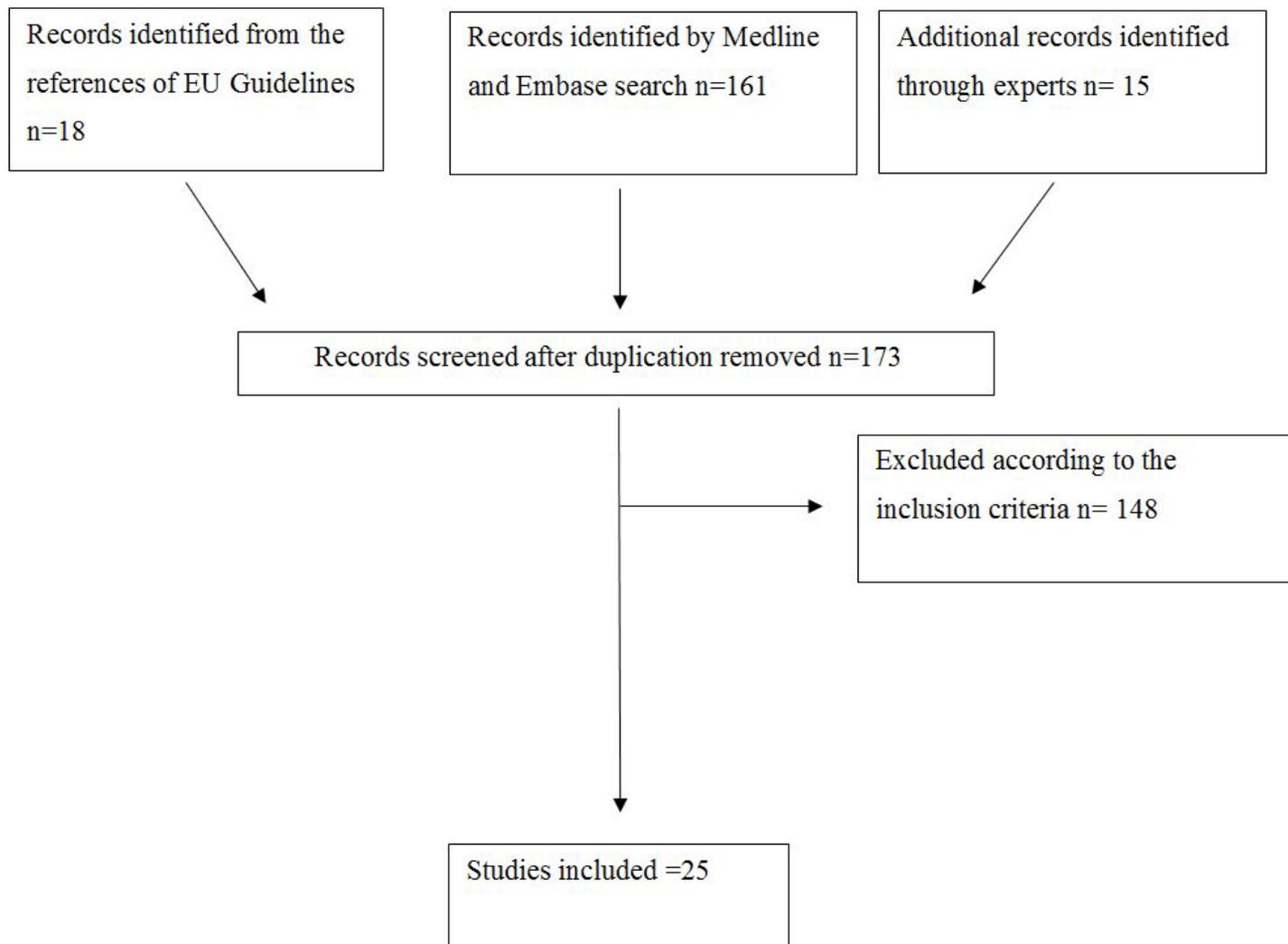
Citation

Silvia Deandrea, Tiziana Rubeca, Emanuela Anghinoni, Carlo Senore, Giorgia Randi. Relative performance comparison of immunochemical fecal occult blood tests in organised population-based colorectal cancer screening programmes: a systematic review and a meta-analysis from experimental studies. PROSPERO 2015:CRD42015017128 Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015017128

#1 CRITERI DI INCLUSIONE

- Test immunochimico per la ricerca del sangue occulto fecale (FIT) confrontato con guaiaco (FOBT) – con altro FIT – con stesso FIT a cut off diversi
- Disegno sperimentale (randomizzato o paired)
- Programma di popolazione (anche pilota)
- Soggetti non ad alto rischio in fascia 50-74 aa

#2 IDENTIFICAZIONE STUDI



#2 CARATTERISTICHE DELLE COORTI INCLUSE (n=20)

Characteristics	N	%
Country		
Australia	2	10.0
France	5	25.0
Israel	1	5.0
Italy	4	20.0
Netherlands	3	15.0
Spain	2	10.0
USA	3	15.0
Publication Year		
≤2000	2	10.0
2001-2005	1	5.0
2006-2010	9	45.0
2011 onward	8	40.0
Sample Size (FIT only)		
≤1000	2	10.0
1000-5000	6	30.0
5001-9999	5	25.0
10000+	7	35.0

Characteristics	N	%
Screening round		
First	13	65.0
Subsequent	5	25.0
Unclear	2	10.0
Study design		
Paired Study	12	60.0
Randomized cohorts	7	35.0
Other	1	5.0

#2 CARATTERISTICHE DEI FIT

Test name	Producer	Type of test	Detection Method	Study N
OC Light	Eiken Chemical	qualitative	immunocromatography	1
Hemeselect	Smith Kline Diagnostics	qualitative	RPHA	2
Instant-view	Alpha Scientifics Designs, Inc.	qualitative	immunocromatography	1
FlexSure OBT	Beckman Coulter/Smith Kline Diagn.	qualitative	colorimetric reaction	1
InSure	Quest Diagnostics (Enterix)	qualitative	immunocromatography	2
OC SensoMicro (OC-Hemodia)	Eiken Chemical	quantitative	latex immunoturbidimetry	7
OC Sensor Diana	Eiken Chemical	quantitative	latex immunoturbidimetry	1
Magstream 1000	Fujirebio	quantitative	magnetic particles	4
FOB Gold	Sentinel Diagnostics	quantitative	latex immunoturbidimetry	4
NS-Plus	Alphresa Pharma Corp	quantitative	colloidal-gold immunoturbidimetry	0
HM-JACKarc	Kyowa MedexCo Ltd	quantitative	latex immunoturbidimetry	1

#3 ESTRAZIONE DATI – IL DATABASE

MetanFIT2014_1Aug2015_updated.xls [Compatibility Mode] - Microsoft Excel

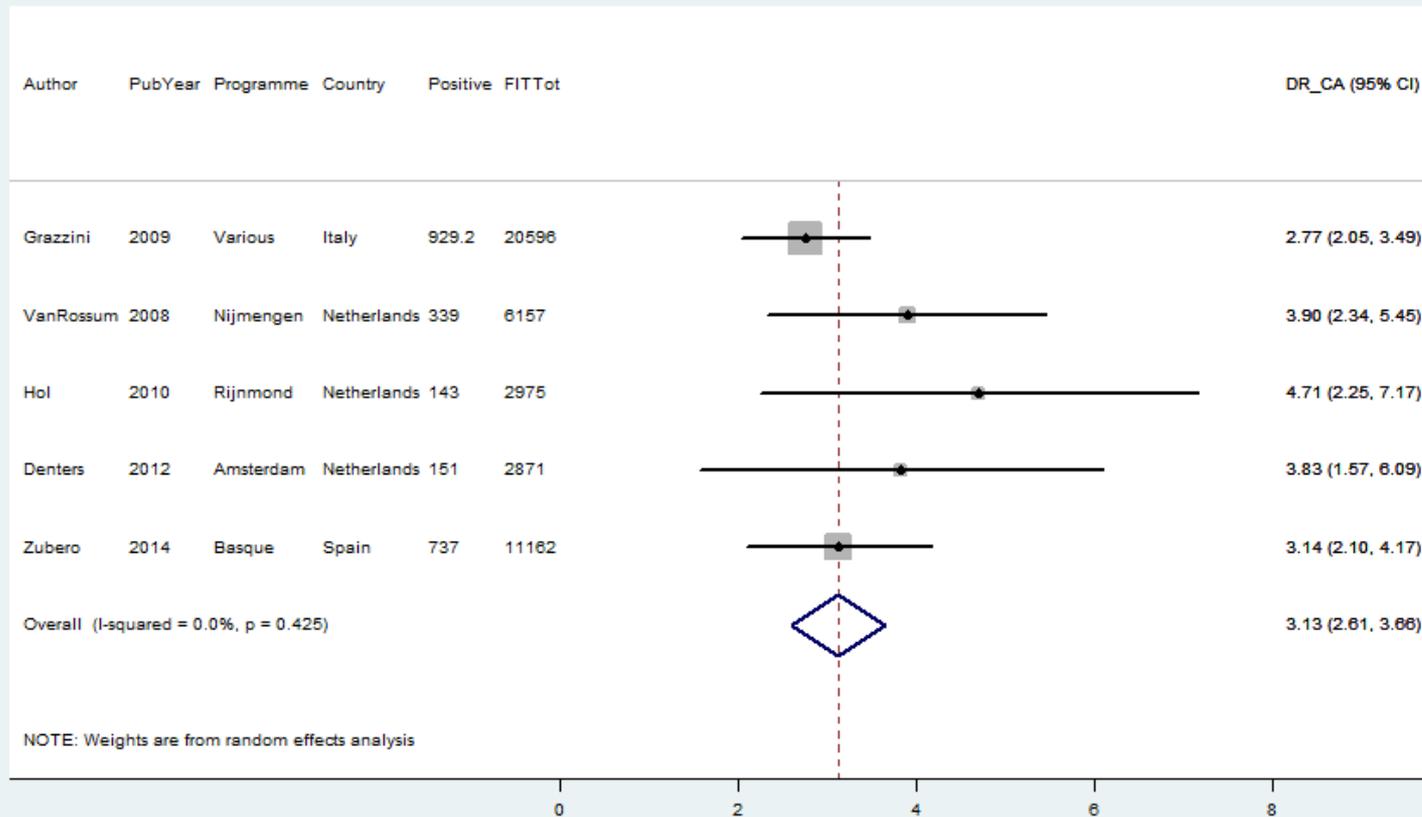
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	S	T	U	V	W	X	Y	Z	AA	AB
1	RecordId	StudyId	StudyCode	Author	PubYear	StudyYear	Country	Programme	Round	RoundDef	AgeRange	MeanAge	AgeSup	Male	Test	TestCode	TestCodeDe	SizeTot	SizeFIT	SizeFOBT	FITTot	Positive	Colonsc	CRC	HA	tudyDesig	dydDes
2	1	1	A	Allison	1996	1990	USA	serPermane	1	1	5	58.8	31.1	40.7	Hemeselect	1	1	8104	7493	8065	7493	440.0	355	22	68	Paired	A
3	2	2	B	Castiglione	1996	1993	Italy	Florence	1	1	2	54.2	0	47.1	Hemeselect	1	1	5165	5165	5165	5165	181.0	150	15	33	Paired	A
4	3	2	B	Castiglione	1996	1993	Italy	Florence	1	1	2	54.2	0	47.1	Hemeselect	1	1	5165	5165	5165	5165	479.0	401	19	49	Paired	A
5	4	3	C	Hugues	2005	2001	Australia	Queensland	1	1	3	.	11.7	42.9	Inform	2	2	1218	935	284	935	89.0	89	2	29	andomise	B
6	5	4	D	Rubeca	2006	2004	Italy	Florence	5	2	4	60	0	48.8	OC-Sensor	3	3	4133	4133	4133	4133	140.0	126	7	37	Paired	A
7	6	4	D	Rubeca	2006	2004	Italy	Florence	5	2	4	60	0	48.8	FOB - Gold	4	4	4133	4133	4133	4133	131.0	122	5	32	Paired	A
8	7	5	E	Smith	2006	2002	Australia	Adelaide	1	1	3	64	28.5	47.8	Insure	6	2	2351	2351	2351	2351	131.0	131	14	20	Paired	A
9	8	6	F	Allison	2007	1998	USA	serPermane	1	1	5	58.8	10.9	47.5	FlexsureOBT	7	6	5932	5799	5356	5356	173.0	173	9	31	Paired	A
10	9	7	G1	Guittet	2007	2004	France	Calvados	1	1	3	62.1	17	42.4	Magstream	5	5	10673	10673	10673	10673	733.0	530	21	139	Paired	A
11	10	7	G1	Guittet	2007	2004	France	Calvados	1	1	3	62.1	17	42.4	Magstream	5	5	10673	10673	10673	10673	352.0	246	19	91	Paired	A
12	11	7	G1	Guittet	2007	2004	France	Calvados	1	1	3	62.1	17	42.4	Magstream	5	5	10673	10673	10673	10673	256.0	183	16	74	Paired	A
13	12	8	G2	Guittet	2009	2005	France	Calvados	1	1	3	63.4	18.8	41.3	Magstream	5	5	20512	20512	20512	20512	851.0	676	35	191	Paired	A
14	13	8	G2	Guittet	2009	2005	France	Calvados	1	1	3	63.4	18.8	41.3	Magstream	5	5	20512	20512	20512	20512	596.0	469	31	154	Paired	A
15	14	8	G2	Guittet	2009	2005	France	Calvados	1	1	3	63.4	18.8	41.3	Magstream	5	5	20512	20512	20512	20512	510.0	395	28	137	Paired	A
16	15	8	G2	Guittet	2009	2005	France	Calvados	1	1	3	63.4	18.8	41.3	Magstream	5	5	20512	20512	20512	20512	1304.0	1028	41	250	Paired	A
17	16	8	G2	Guittet	2009	2005	France	Calvados	1	1	3	63.4	18.8	41.3	Magstream	5	5	20512	20512	20512	20512	615.0	479	33	154	Paired	A
18	17	8	G2	Guittet	2009	2005	France	Calvados	1	1	3	63.4	18.8	41.3	Magstream	5	5	20512	20512	20512	20512	504.0	391	17	135	Paired	A
19	18	9	G3	Guittet	2012	2005	France	Calvados	1	1	3	63.4	18.7	41.6	Magstream	5	5	32225	32225	32225	32225	1225.0	995	60	288	Paired	A
20	19	9	G3	Guittet	2012	2005	France	Calvados	1	1	3	63.4	18.7	41.6	Magstream	5	5	32225	32225	32225	32225	902.0	743	51	240	Paired	A
21	20	9	G3	Guittet	2012	2005	France	Calvados	1	1	3	63.4	18.7	41.6	Magstream	5	5	32225	32225	32225	32225	773.0	630	48	215	Paired	A
22	21	9	G3	Guittet	2012	2005	France	Calvados	1	1	3	63.4	18.7	41.6	Magstream	5	5	32225	32225	32225	32225	1225.0	987	68	302	Paired	A
23	22	9	G3	Guittet	2012	2005	France	Calvados	1	1	3	63.4	18.7	41.6	Magstream	5	5	32225	32225	32225	32225	902.0	737	60	235	Paired	A
24	23	9	G3	Guittet	2012	2005	France	Calvados	1	1	3	63.4	18.7	41.6	Magstream	5	5	32225	32225	32225	32225	773.0	634	52	263	Paired	A
25	24	10	H	VanRossum	2008	2007	Netherlands	Nijmegen	1	1	3	60.7	12.6	47.8	OC-Sensor	3	3	10993	6157	4836	6157	526.0	428	28	161	andomise	B
26	25	10	H	VanRossum	2008	2007	Netherlands	Nijmegen	1	1	3	60.7	12.6	47.8	OC-Sensor	3	3	10993	6157	4836	6157	409.8	336	27	136	andomise	B
27	26	10	H	VanRossum	2008	2007	Netherlands	Nijmegen	1	1	3	60.7	12.6	47.8	OC-Sensor	3	3	10993	6157	4836	6157	339.0	280	24	121	andomise	B
28	27	10	H	VanRossum	2008	2007	Netherlands	Nijmegen	1	1	3	60.7	12.6	47.8	OC-Sensor	3	3	10993	6157	4836	6157	.	248	24	112	andomise	B
29	28	10	H	VanRossum	2008	2007	Netherlands	Nijmegen	1	1	3	60.7	12.6	47.8	OC-Sensor	3	3	10993	6157	4836	6157	.	234	24	107	andomise	B
30	29	10	H	VanRossum	2008	2007	Netherlands	Nijmegen	1	1	3	60.7	12.6	47.8	OC-Sensor	3	3	10993	6157	4836	6157	.	215	24	97	andomise	B
31	30	10	H	VanRossum	2008	2007	Netherlands	Nijmegen	1	1	3	60.7	12.6	47.8	OC-Sensor	3	3	10993	6157	4836	6157	.	198	24	89	andomise	B
32	31	10	H	VanRossum	2008	2007	Netherlands	Nijmegen	1	1	3	60.7	12.6	47.8	OC-Sensor	3	3	10993	6157	4836	6157	.	187	23	86	andomise	B
33	32	11	I	Grazzini	2009	2006	Italy	Various	1	1	4	59.9	0	46.2	OC-Hemodia	8	3	20596	20596	0	20596	1124.7	1001	59	368	Cohort	C
34	33	11	I	Grazzini	2009	2006	Italy	Various	1	1	4	59.9	0	46.2	OC-Hemodia	8	3	20596	20596	0	20596	929.2	827	57	322	Cohort	C
35	34	11	I	Grazzini	2009	2006	Italy	Various	1	1	4	59.9	0	46.2	OC-Hemodia	8	3	20596	20596	0	20596	828.1	737	56	301	Cohort	C
36	35	11	I	Grazzini	2009	2006	Italy	Various	1	1	4	59.9	0	46.2	OC-Hemodia	8	3	20596	20596	0	20596	1648.0	1465	69	465	Cohort	C
37	36	11	I	Grazzini	2009	2006	Italy	Various	1	1	4	59.9	0	46.2	OC-Hemodia	8	3	20596	20596	0	20596	1380.0	1221	69	406	Cohort	C
38	37	11	I	Grazzini	2009	2006	Italy	Various	1	1	4	59.9	0	46.2	OC-Hemodia	8	3	20596	20596	0	20596	1215.0	1082	67	380	Cohort	C

#4 ANALISI *WITHIN* TEST

- Solo studi con OC Sensor – 1 campione in un unico giorno
- Modello ad effetti random
- Meta-regressione per individuare fattori associati alla performance dell'OC Sensor nei diversi studi

#4 ANALISI WITHIN TEST – FOREST PLOT

OC Sensor 100 - Pooled detection rate, cancer - First Round



#4 ANALISI *WITHIN* TEST – METAREG SU OC-SENSOR

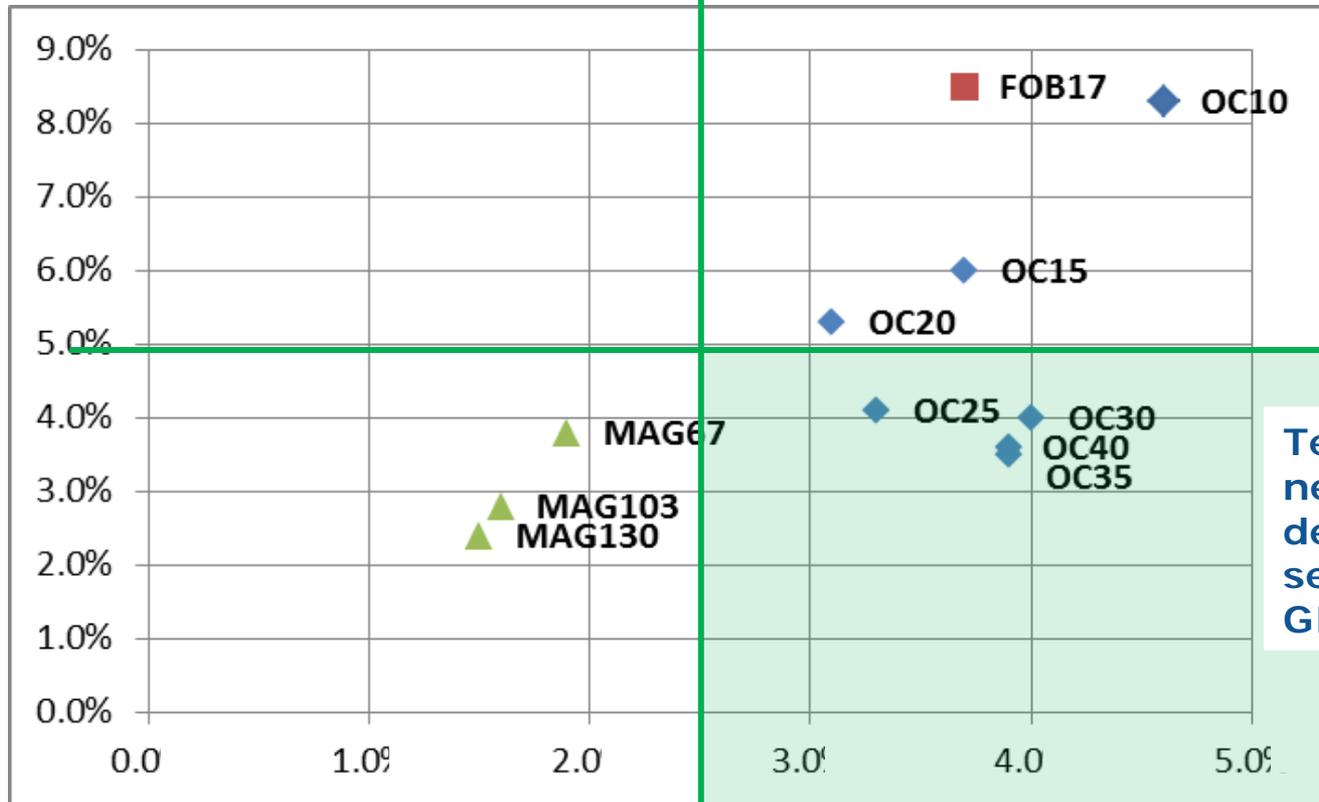
- Aumento di DR per CRC associato significativamente a:
 - area geografica e incidenza (Francia e Olanda)
 - età media della popolazione
 - percentuale di maschi nella popolazione
- L'effetto dell'area geografica (ma non dell'incidenza) è associato significativamente anche a DR per adenomi avanzati e a PPV sia per CRC sia per adenomi avanzati

#5 ANALISI *BETWEEN TESTS*

- Solo studi con 1 campione in un unico giorno
- Solo test con un numero sufficiente di record: OC-Sensor, FOB-Gold, Magstream, HM Jack
- Cut-off normalizzati in $\mu\text{g/g}$ feci \rightarrow test confrontabili
- Le differenze tra i test esplorate con ANOVA appaiono significative nella maggior parte dei casi

TASSO DI POSITIVITA' VS DETECTION RATE PER CRC – PRIMI ESAMI

Positivity Rate %

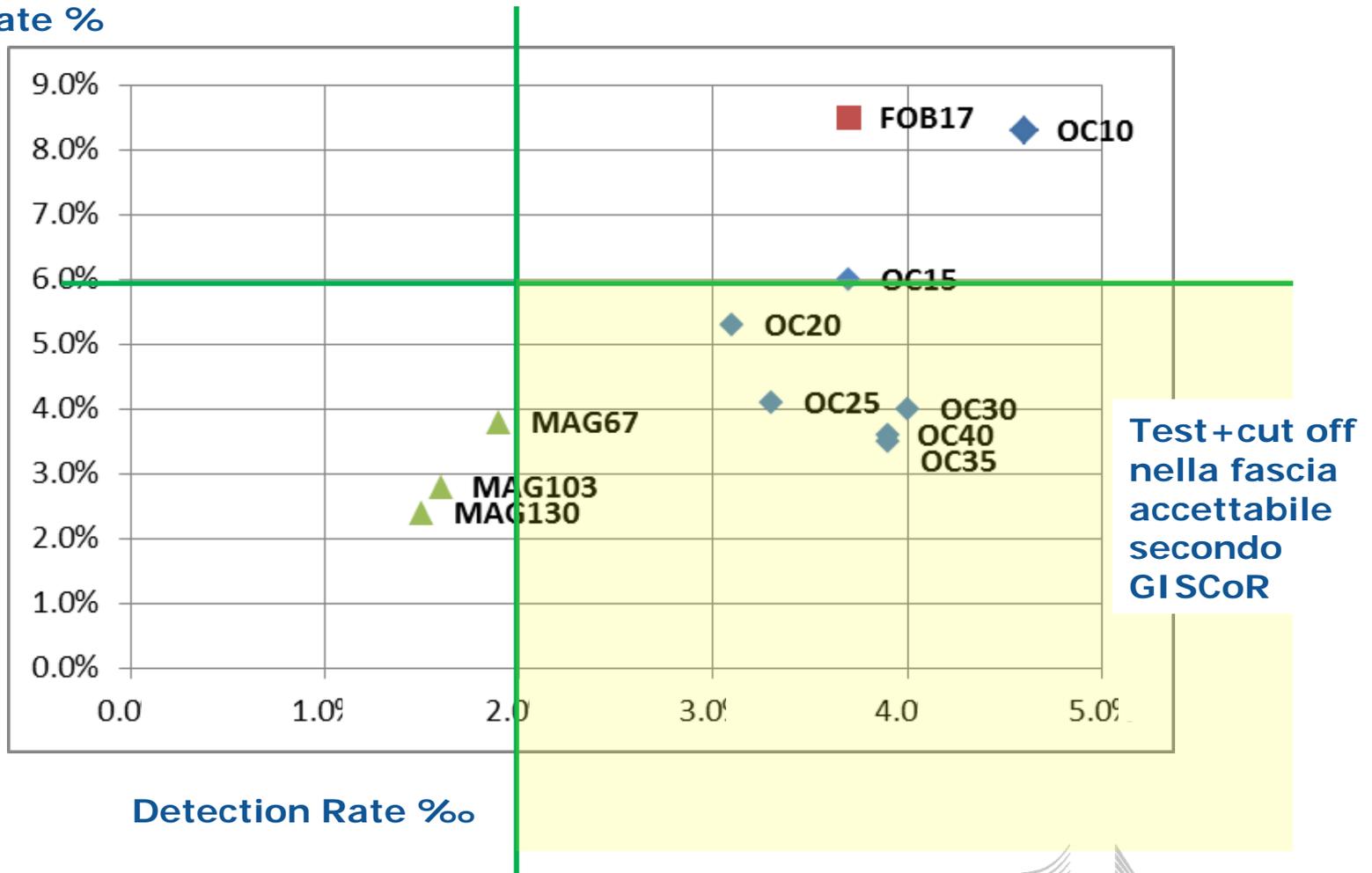


Test+cut off
nella fascia
desiderabile
secondo
GISCOR

Detection Rate %

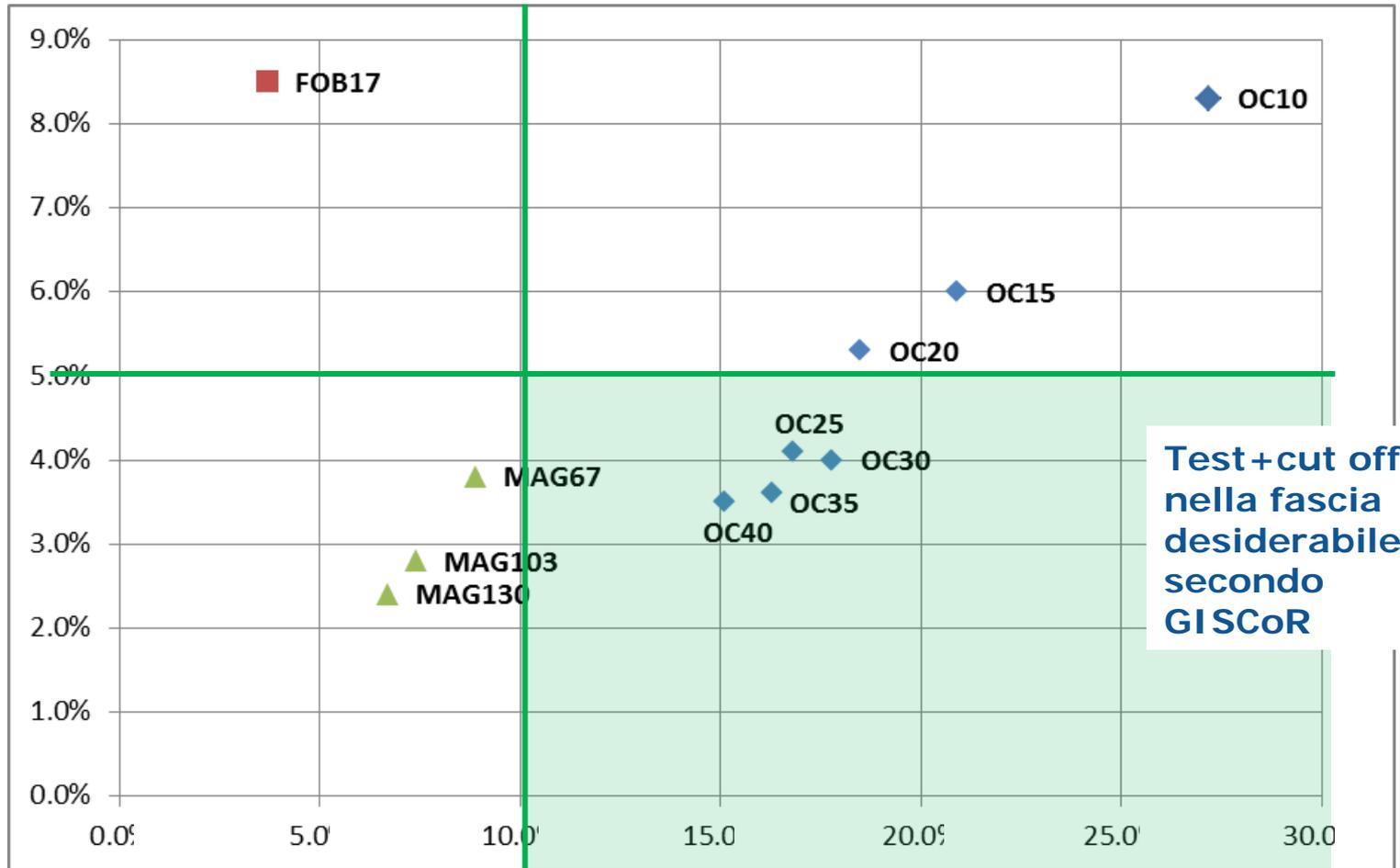
TASSO DI POSITIVITA' VS DETECTION RATE PER CRC – PRIMI ESAMI (2)

Positivity Rate %



TASSO DI POSITIVITA' VS DETECTION RATE PER AA – PRIMI ESAMI

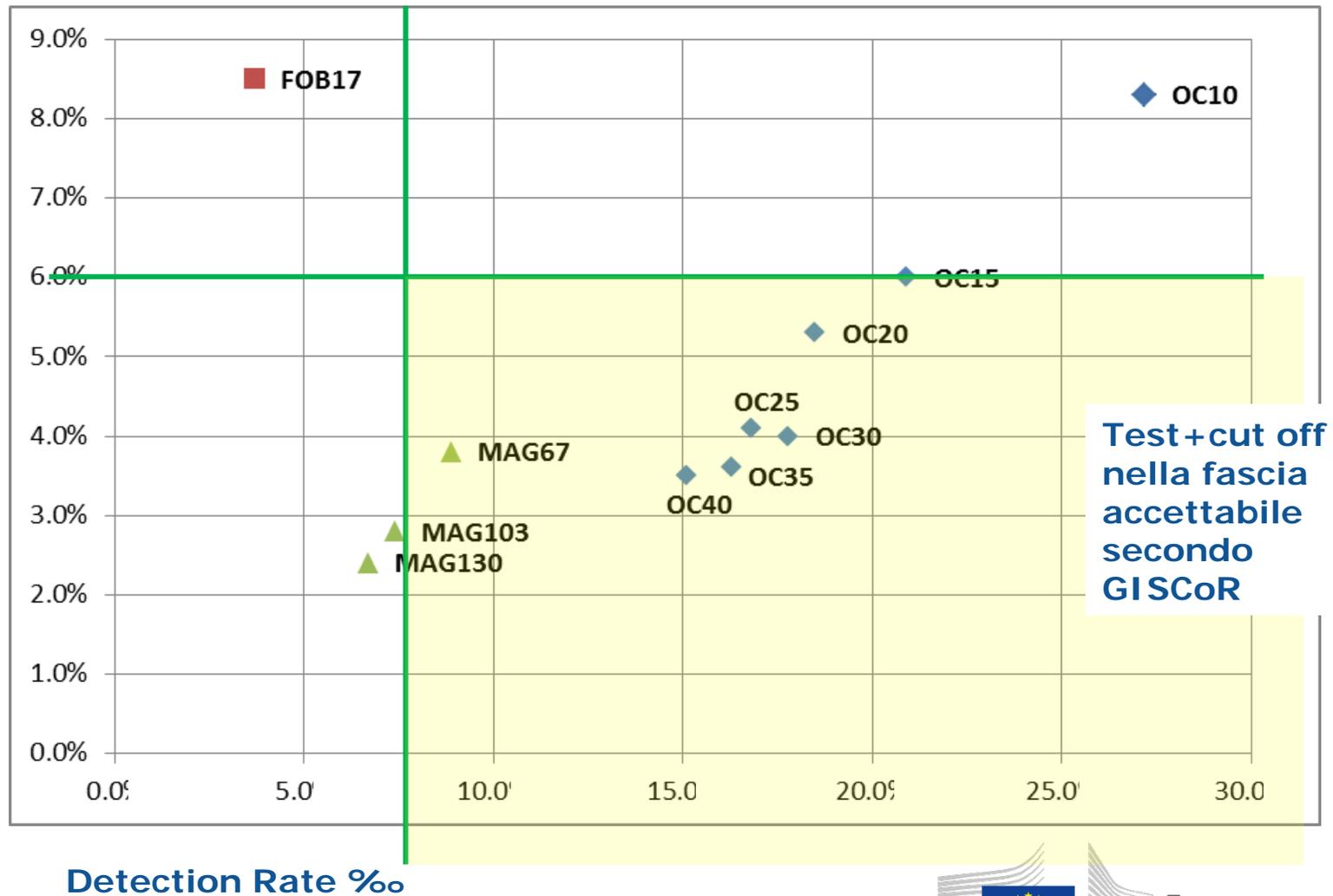
Positivity Rate %



Detection Rate %

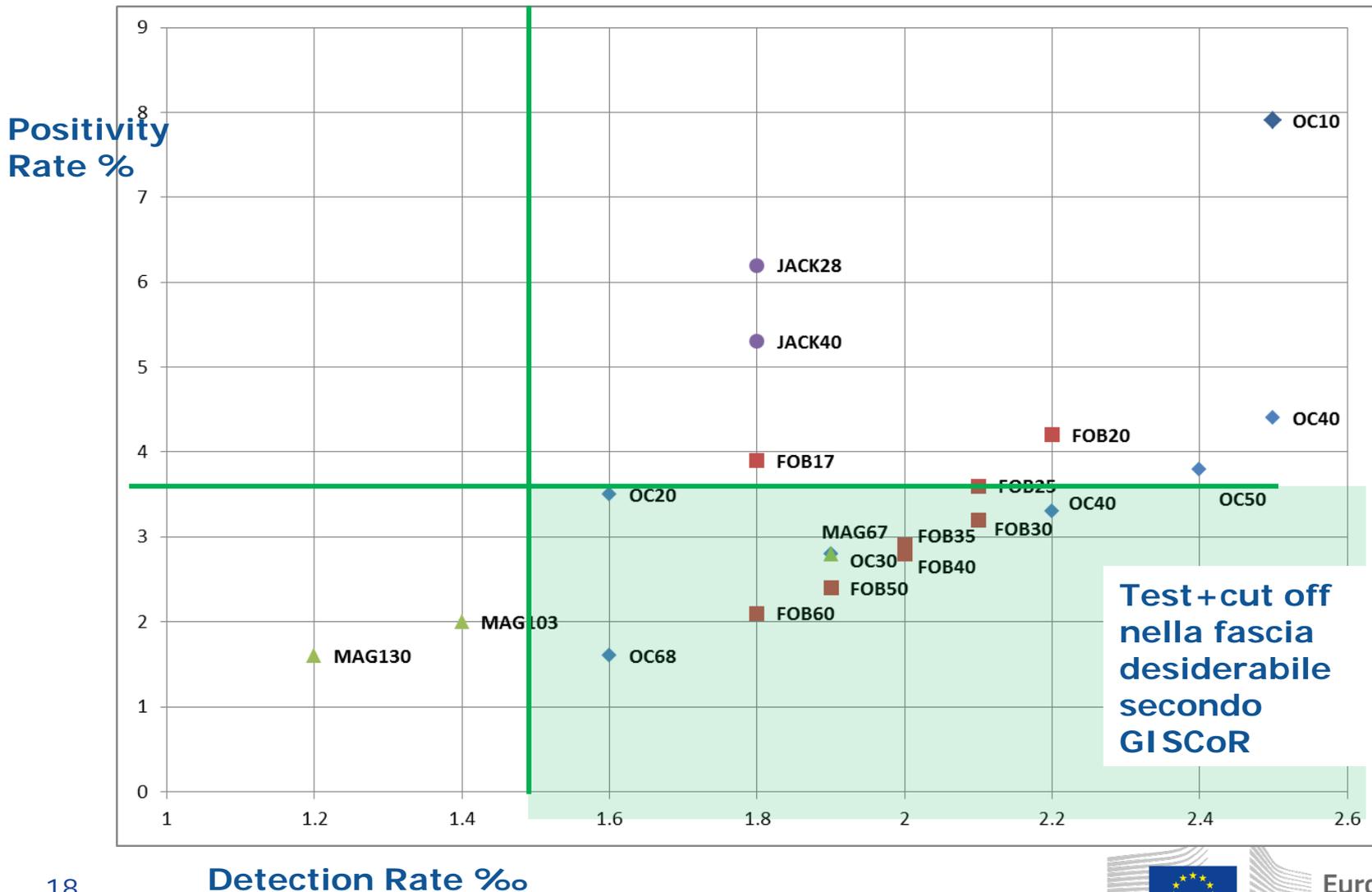
TASSO DI POSITIVITA' VS DETECTION RATE PER AA – PRIMI ESAMI (2)

Positivity Rate %

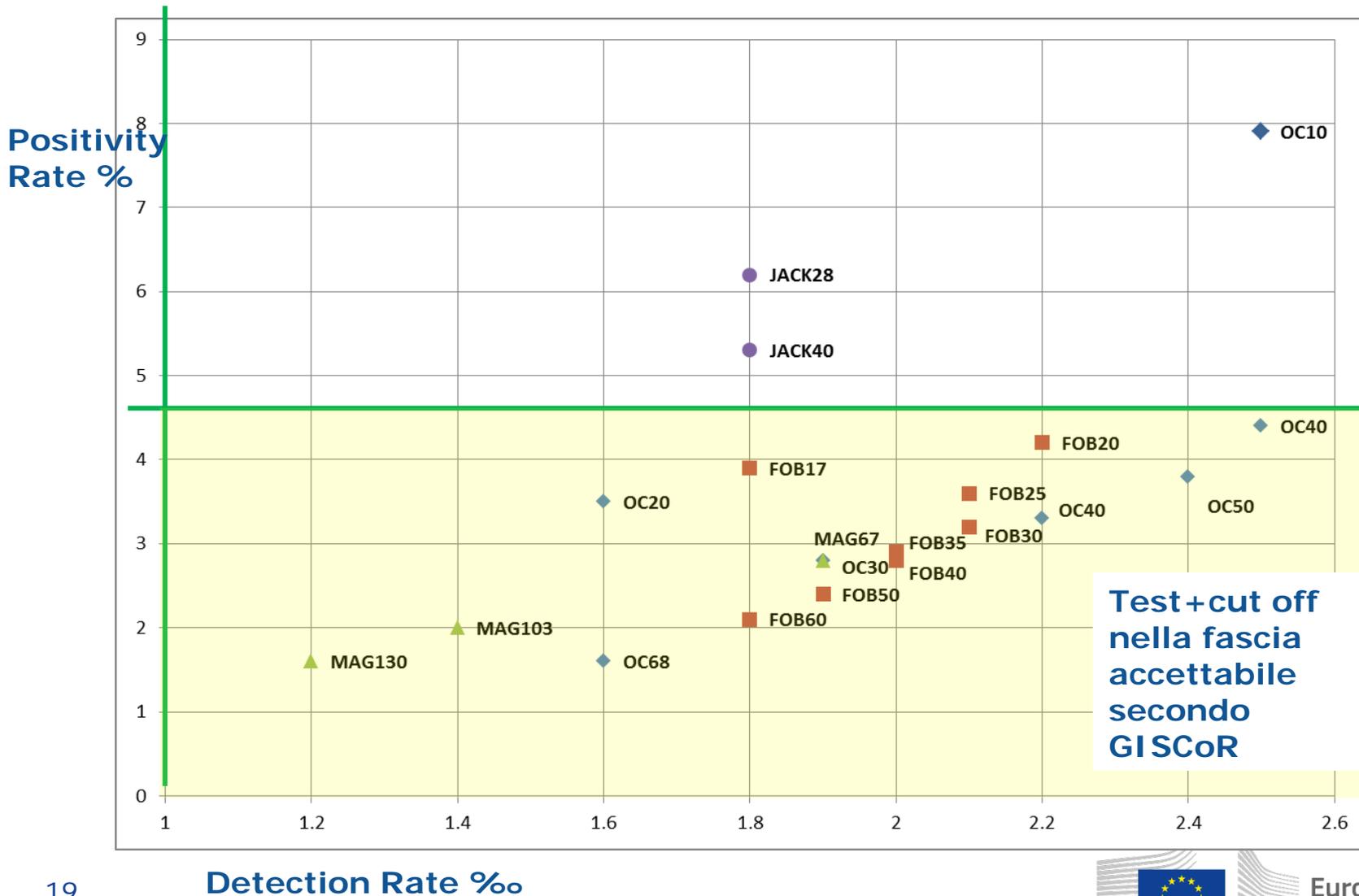


Test+cut off
nella fascia
accettabile
secondo
GISCoR

TASSO DI POSITIVITA' VS DETECTION RATE PER CRC – ESAMI SUCCESSIVI

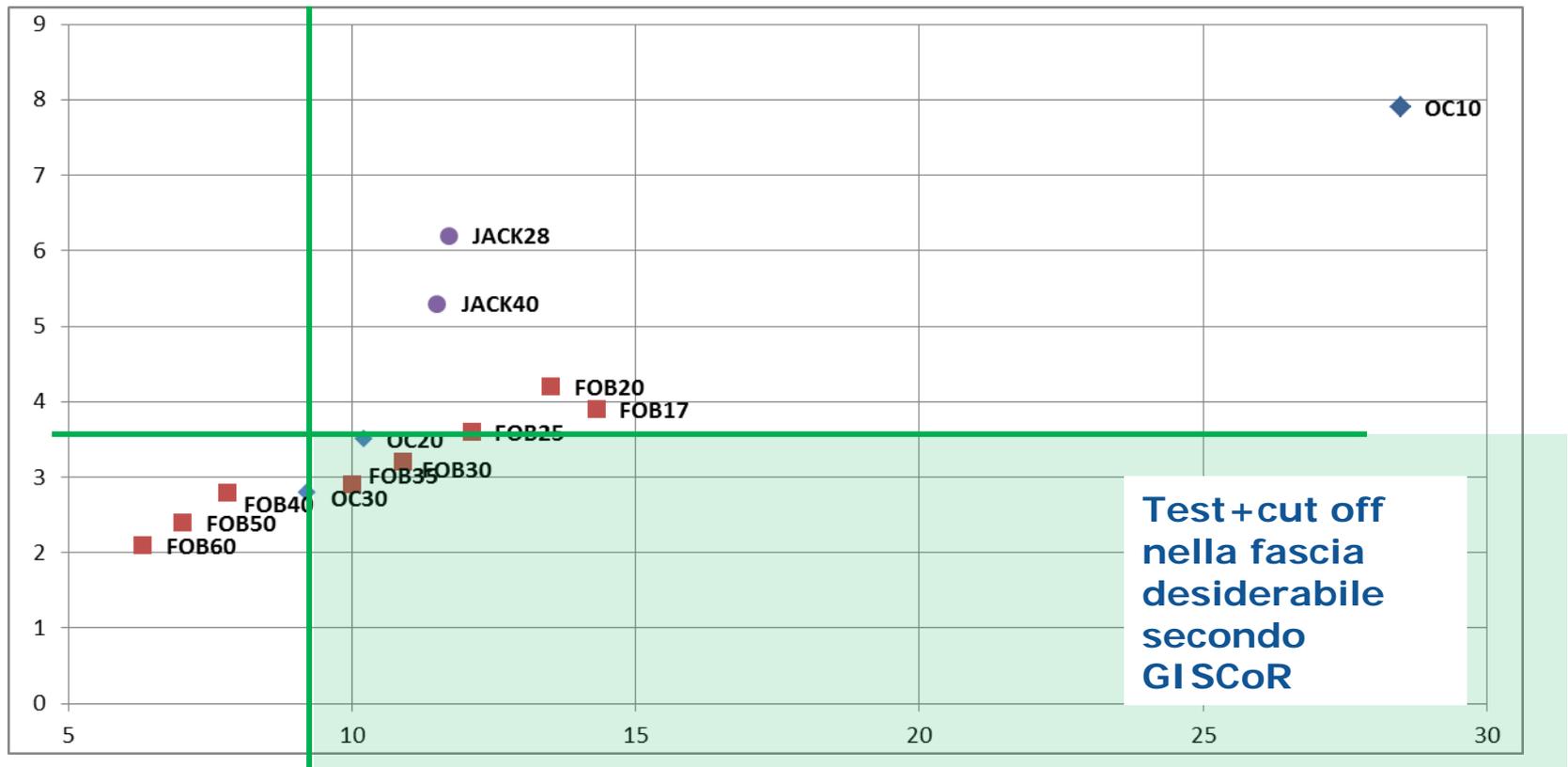


TASSO DI POSITIVITA' VS DETECTION RATE PER CRC – ESAMI SUCCESSIVI (2)



TASSO DI POSITIVITA' VS DETECTION RATE PER AA – ESAMI SUCCESSIVI

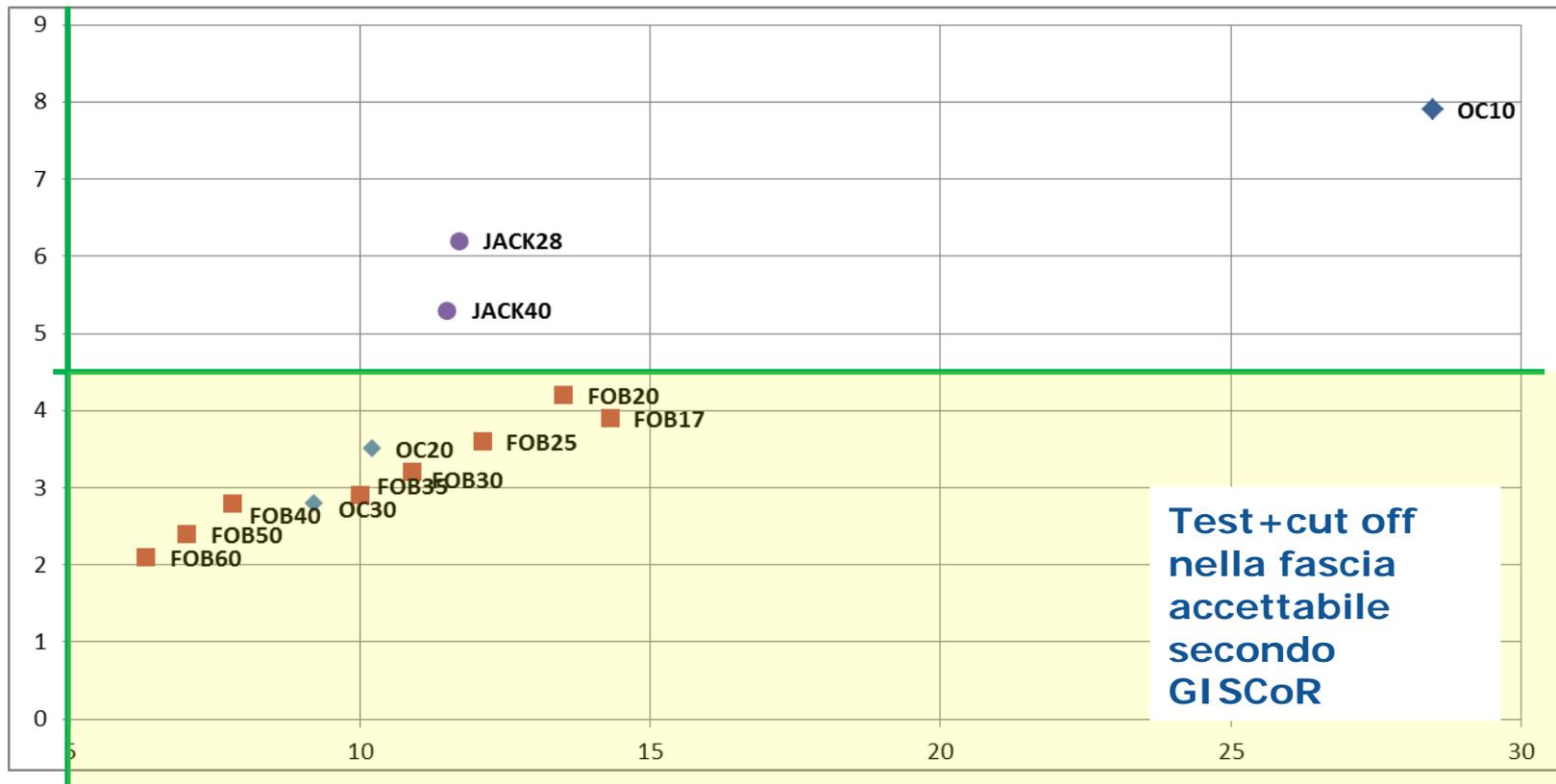
Positivity Rate %



Detection Rate %

TASSO DI POSITIVITA' VS DETECTION RATE PER AA – ESAMI SUCCESSIVI (2)

Positivity Rate %



Detection Rate %

CONCLUSIONI

- Si osservano differenze significative tra test, che in alcuni casi permangono anche dopo l'aggiustamento per le variabili confondenti
- Valutando PR e DR combinate, per i round successivi è sempre disponibile più di una combinazione test + cut-off compatibile con i parametri accettabili GISCoR
- Non si evidenzia un solo test ad un determinato cut-off chiaramente superiore agli altri per tutti i parametri considerati (PR, CRC, AA, etc.)
- La scelta del test e del cut-off dovrebbero tenere conto della performance del test in programmi di popolazione, ottenuta da letteratura, survey GISCoR, etc.

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