GISCoR

gruppo italiano screening colorettale

CONVEGNO NAZIONALE GISCoR 2023

Hotel Astoria Palace, Palermo

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CONVEGNO NAZIONALE
GISCoR 2023

Nuove raccomandazioni del Concilio della Unione Europea sullo screening del cancro:

Screening per il cancro colorettale

Nereo Segnan

Gruppo Italiano Screening Colon Retto
GISCoR (Comitato Scientifico)

Palermo 5-6 ottobre 2023

Nessun conflitto di interesse da dichiarare

Council of the European Union

Brussels, 29 November 2022
(OR. en)

14770/22

Interinstitutional File:
2022/0290(NLE)

SAN 608

NOTE

From:	General Secretariat of the Council
To:	Council
Subject:	Council Recommendation on strengthening prevention through early detection: A new EU approach on cancer screening replacing Council Recommendation 2003/878/EC *- Adoption*

Council Recommendation on strengthening prevention through early detection: A new EU approach on cancer screening replacing Council Council Recommendation 2003/878/EC - Adoption.

Colorectal cancer:

- Quantitative faecal immunochemical testing (FIT) is considered the preferred screening test for referring individuals for follow-up colonoscopy between 50 and 74 years old.
- Quantitative information from FIT results might be used on the basis of further research with a view to implement risk-tailored strategies, introducing thresholds defined per sex, age and earlier test results.
- Endoscopy may be adopted as a primary tool to implement combined strategies.

- Quale giustificazione scientifica?
- Neoplasie avanzate non sanguinanti (CRCs and AAD):

- riduzione dell'incidenza del cancro attraverso la polipectomia?

- Aggiornamento delle linee guida regolare e periodico?
- Prevenzione primaria e screening?

Prevention of Colorectal cancer: impact of Behavioral Changes and Screening

- **Cumulative incidence (0-74) in High Income: 3400 per 100,000 (Globocan 2012)**

	Prevented cancer per 100,000	PAF(%)
BC*	1,530	45
Screening	867	26
Screening + BC*	2,007	59

***Updated estimates of cancer preventability (PAF%) by appropriate:**

- **diet,**
- **nutrition,**
- **physical activity,**
- **body fatness**

(http://www.wcrf.org)

Segnan N, Armaroli P. Early detection versus prevention in colorectal cancer screening: Methods estimates and public health implications. Cancer. 2017;123(24):4767-4769.

TABLE 1. Estimates of CRC ADP in 3 Randomized Controlled Trials of Flexible Sigmoidoscopy Screening

		Intervention Group			Control Group			Averted Events			
		Total	Cancers (Ci)	Deaths (Di)	Total	Cancers (Cc)	Deaths (Dc)	Fatality Rate (FRc)	Cancers[a]	Deaths[b]	ADP[c]	ADP %[d]
		No.	No.	No.	No.	No.	No.	Percentage, (95% CI)	No.	No.	No.	Percentage, (95% CI)
ITT	PLCO 2017[6]	77,445	1008	253	77,445	1291	351	27 (25-30)	283	98	77	79 (69-86)
	SCORE 2011[3]	17,136	251	65	17,136	306	83	27 (22-32)	55	18	15	83 (59-96)
	UK Flexible Sigmoidoscopy Screening Trial 2010[1]	57,099	706	189	112,939	1818	538	30 (27-32)	422	164	125	76 (69-82)
	UK Flexible Sigmoidoscopy Screening Trial 2017[2e]	57,098	1230	353	112,936	3253	996	31 (29-32)	820	298	251	84 (80-88)
PP	SCORE 2011[3]	9911	126	33	17,136	306	83	27 (22-32)	88	26	24	92 (75-99)
	UK Flexible Sigmoidoscopy Screening Trial 2010[1]	40,621	445	111	112,939	1818	538	30 (27-32)	581	229	172	75 (69-81)
	UK Flexible Sigmoidoscopy Screening Trial 2017[2e]	40,621	776	215	112,936	3253	996	31 (29-32)	1096	398	335	84 (80-88)

Segnan N, Armaroli P. Early detection versus prevention in colorectal cancer screening: Methods estimates and public health implications. Cancer. 2017;123(24):4767-4769.

The ADP (adverted deaths due to prevention) ranged from **76% to 84%** in the intention-to-treat analysis, and from **75% to 92%** in the per-protocol analysis.

Previous recommandations

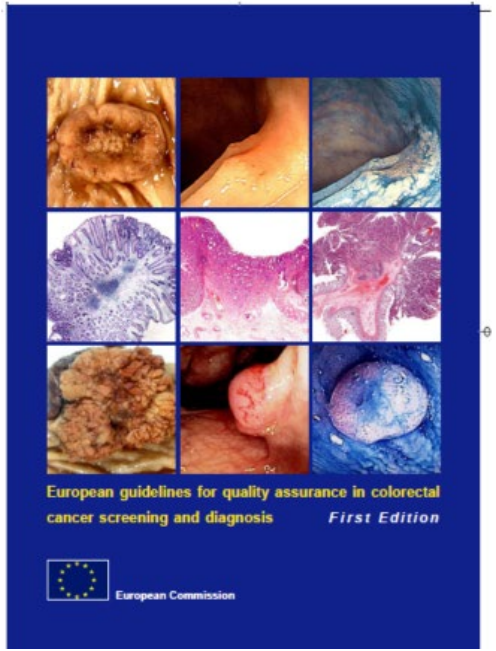
Directorate-General for Health & Consumers

Executive Agency for Health and Consumers

European Partnership Action Against Cancer

European guidelines for quality assurance i
cancer screening and diagnosis

Editors
N. Segnan
J. Patnick
L. von Karsa



2010

. Most of the FOBT randomized trials were performed with guaiac-based tests, but the EU guidelines confirm that faecal immunochemical **testing (FIT) also fulfils the requirements of the EU for primary screening [3, 11].**

At the time of the original publication, **reasonable** evidence for the efficacy of flexible sigmoidoscopy screening was available from a large randomized trial, and there was **limited evidence** for the efficacy of **colonoscopy screening**.

There is now **good** evidence from large randomized trials involving over 300 000 men and women that **screening with flexible sigmoidoscopy can substantially reduce colorectal cancer incidence [4, 6, 7] and mortality [4, 7].**

Recommendations by levels of evidence and strength

	Levels of evidence						
Strength of recommendation		**I**	**II**	**III**	**IV**	**V**	**VI**
	A	**12**	**13**	**23**		**4**	**69**
	B	**13**	**11**	**17**	**2**	**9**	**62**
	C		**3**	**6**	**4**	**4**	**18**
	D		**1**	**5**		**2**	**1**
	E						
	Total	**25**	**28**	**51**	**6**	**19**	**150**

*including recommendations reported just once

European Guidelines for Quality Assurance in Colorectal Cancer Screening – first edition *

Volume 1 – 10 Chapters, 386 pages

- Introduction
- Organisation
- Evaluation
- FOBT
- Endoscopy
- Training
- Pathology
- Clinical Management
- Surveillance
- Communication

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Volume 2 – Evidence 1.000 pages,500 tables of evidence

*Financial support of
EU Health Programme

Previous EU recommendations

Armaroli P, Villain P, Suonio E, Almonte M, Anttila A, Atkin WS, Dean PB, de Koning HJ, Dillner L, Herrero R, Kuipers EJ, Lansdorp-Vogelaar I, Minozzi S, Paci E, Regula J, Törnberg S, Segnan N.

- European Code against Cancer, 4th Edition: Cancer screening. Cancer Epidemiol. 2015 Dec;39 Suppl 1:S139-52.

Box 2

Primary test, age and interval between tests for colorectal, breast and cervical screening in organized European programs.

Colorectal cancer screening:

- men and women starting at age 50–60 years,
- and from then on, every 2 years if the screening test is the guaiac-based faecal occult blood test (gFOBT) or the fecal immunochemical test (FIT),
- or every 10 years or more if the screening test is flexible sigmoidoscopy (FS) or colonoscopy (TC).
- Most programs continue sending invitations to screening up to age 70–75 years.

Council Recommendation on strengthening prevention through early detection: A new EU approach on cancer screening replacing Council Recommendation 2003/8 Brussels, 29 November 2022

Quantitative information from FIT results might be used on the basis of further research with a view to implement risk-tailored strategies, introducing thresholds defined per sex, age and earlier test results

Senore C, Zappa M, Campari C, Crotta S, Armaroli P, Arrigoni A, Cassoni P, Colla R, Fracchia M, Gili F, Grazzini G, Lolli R, Menozzi P, Orione L, Polizzi S, Rapi S, Riggi E, Rubeca T, Sassatelli R, Visioli C, Segnan N. Faecal haemoglobin concentration among subjects with negative FIT results is associated with the detection rate of neoplasia at subsequent rounds: a prospective study in the context of population based screening programmes in Italy. Gut. 2020 Mar;69(3):523-530

Table 4 CRC DR at the third FIT* and IC risk during the 36 months following second negative FIT by cumulative f-Hb concentration over two consecutive FITs—screenees from three centres

Sum f-Hb µg/g	Not invited†	Non-attenders	Screened	Uptake‡	SD CRCs		Interval CRC		
FIT1 + FIT2	N	N	N	%	N	%	N	%	IR§ (95% CI)
0	4382	2990	29553	90.8	15	0.05	9	0.02	9.84 (5.12 to 18.99)
0.1–3.9	2972	1584	14925	90.4	11	0.07	9	0.05	10.88 (4.53 to 26.15)
4–9.9	1825	932	9637	91.2	17	0.18	16	0.13	50.48 (29.90 to 85.23)
10–14.9	559	284	2522	89.9	9	0.36	6	0.18	39.37 (12.70 to 122.08)
15–19.9	290	142	1285	90.0	7	0.54	4	0.23	75.54 (24.36 to 234.21)
≥20	122	65	556	89.5	12	2.16	5	0.67	238.07 (89.35 to 634.31)
Total	10150	5997	58478	90.7	71	0.12	49	0.07	21.30 (15.50 to 29.27)

*Examinations performed within 36 months since the second FIT.
†Subjects no longer eligible for the third invitation (older than 69, dead or emigrated).
‡Proportion of subjects having performed a second FIT who had a third examination within 3 years. Subjects diagnosed with an IC were not eligible for the third test.
§Incidence rate x100 000 PYs. Each subject contributed to the time at risk until the date of death, emigration, third FIT or 31 December 2012, whichever came first . The follow-up time was at least 36 months for all subjects. Only IC diagnosed within 36 months since the last negative FIT were considered.
CRCs, colorectal cancers; DR, detection rate; f-Hb, faecal haemoglobin; FIT, faecal immunochemical test; IC, interval CRC; PYs, person-years; SD, screen detected.

Stratifiction by gender,age and delay from last screening episode

			Pop	%	Compliers	N	CCR DR	CRC	RR
M	<60 yr	<26 m	10000	0.1	0.533	5330	0.00065	3.46	1.08
		27-38 m	7000	0.07	0.45	3150	0.0007	2.21	1.17
		>39 m	8000	0.08	0.4	3200	0.00085	2.72	1.42
		<26 m	9000	0.09	0.65	5850	0.00175	10.24	2.92
M	>=60 yr	27-38 m	6000	0.06	0.55	3300	0.00185	6.11	3.08
		>39 m	7000	0.07	0.45	3150	0.0025	7.88	4.17
F	<60 yr	<26 m	11000	0.11	0.644	7084	0.0006	4.25	1.00
		27-38 m	8000	0.08	0.6	4800	0.00065	3.12	1.08
		>39 m	9500	0.095	0.45	4275	0.00075	3.21	1.25
		<26 m	10000	0.1	0.7	7000	0.001	7.00	1.67
F	>=60 yr	27-38 m	7000	0.07	0.65	4550	0.0013	5.92	2.17
		>39 m	7500	0.075	0.5	3750	0.00155	5.81	2.58
delay			60000		tot	55439	0.00111674	61.91	
Tot			100000						

Some risk indicators for risk stratification

1. **Age**
2. **Gender**
3. Screening interval between tests
4. **Interval from last screening/Never screened**
5. Lower/higher cut-off.
6. **Faecal haemoglobin concentration among subjects with negative FIT results**
7. Life years gained
8. **Risk scores**

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Tot			100000						

Comparative effectiveness studies nested in the screening programmes

We suggest to adapt the IT system, classifying the target population in different risk groups, using the available current information (age ,gender, interval from last screening episode, Hb concentration in subjects with previuos negative FIT …..) in the active screening programmes

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Proposal of comparative effectiveness evaluation

Prospective sequential randomized trial

comparing CRC risk groups in each screening programme with a sample of the target population not stratified by risk, in each screening programme

- Risk groups should be updated, according to the intermediate outcomes, as well as the risk categories.
- An individual should change the risk group from the lower to higher or viceversa, according to the screening events and results

Outcomes by risk groups

- Detection rate of CRC and AAD
- Stage at diagnosis,
- FIT positivity rate
- Interval cases

- DALY’s in intervention arm and in control arm

Gastroenterology
Volume 162, Issue 3, March 2022, Pages 668-674

Commentary

Comparing Colorectal Cancer Screening Outcomes in the International Cancer Screening Network: A Consortium Proposal

Nereo Segnan, Evelien Dekker, V.Paul Doria-Rose, Carlo Senore, Linda Rabeneck, Iris Lansdorp-Vogelaar, International Cancer Screening Network Colorectal Cancer Screening Working Group

EU Cost Action

We applied to structure **an International multidisciplinary Consortium of CRC screening programs** aiming to implement a common accessible database, in order to generate comparable estimates of indicators and outcomes of CRC across different programs and countries.
Such consortium will promote the collaboration…… for:

1. Harmonising and bringing together the data from the different programs in one database,

2. Defining a computational approach to extract the relevant indicators accounting for differences between programs

3. Addressing ethical and legal aspects related to data sharing for the purposes of comparative evaluation, benchmarking and research, in the context of international initiatives.

4. Maintaining a sustainable collaborative network that ensures optimal exchange of knowledge to keep CRC screening up-to-date

Grazie per l'attenzione

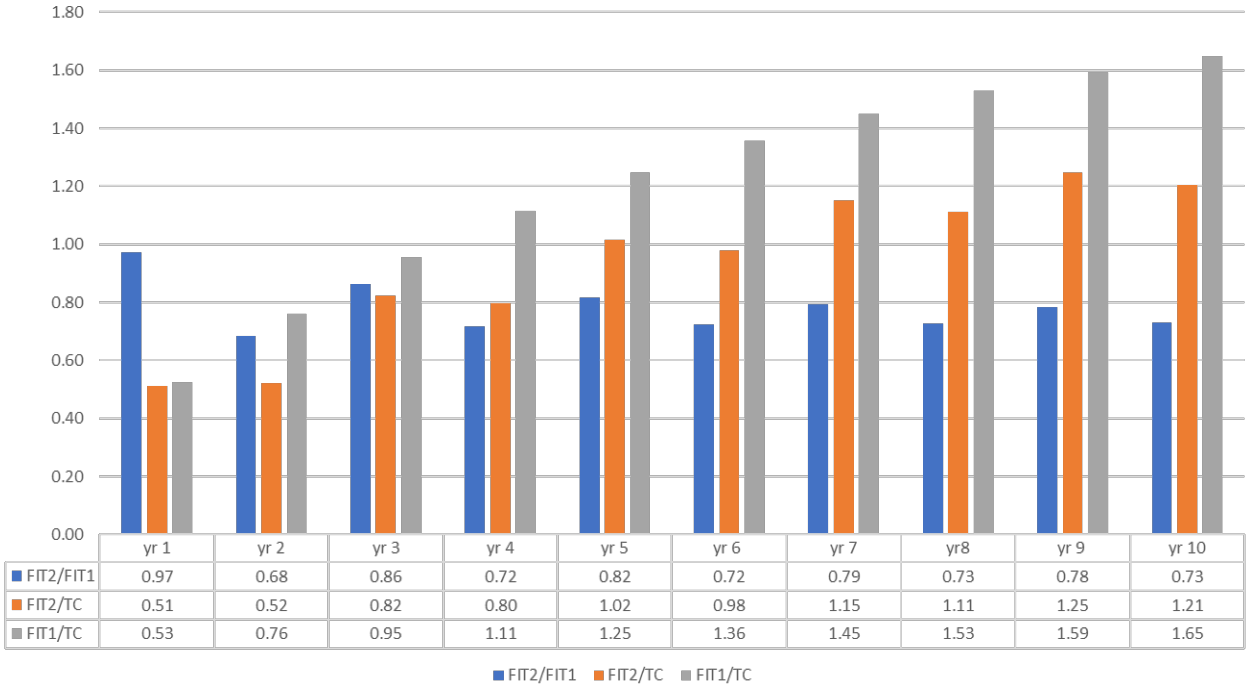
Table 2. Yearly and cumulative workload of total colonoscopies (TCs) in FIT2, FIT1 and TC screening programmesrogramme .

	yr 1	yr 2	yr 3	yr 4	yr 5	yr 6	yr 7	yr8	yr 9	yr 10
FIT2										
# TC per year	388	44	335	38	313	36	291	33	271	31
Cum # TC	388	432	767	806	1118	1154	1445	1479	1749	1780
FIT1										
# TC per year	430	415	286	276	266	256	246	237	228	219
Cum # TC	430	845	1131	1406	1672	1927	2174	2411	2638	2857
TC										
# TC test per year	3900	306	298	290	283	275	267	260	252	245
cum # TC tests	3900	4206	4504	4794	5077	5352	5619	5879	6131	6376

Number of CRCs and Detection Rates in 2, and 1 yr FIT and in TC screenings

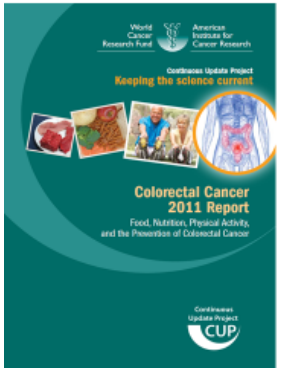
FIT2	yr 1	yr 2	yr 3	yr 4	yr 5	yr 6	yr 7	yr 8	yr 9	yr 10
CRC cases	9.95	1.16	7.66	0.89	7.36	0.85	7.06	0.82	6.74	0.78
cum CRC cases	9.95	11.10	19.10	19.99	27.35	28.21	35.27	36.08	42.83	43.61
cum DR in attenders %	0.1457	0.1502	0.1405	0.1398	0.1362	0.1359	0.1349	0.1348	0.1348	0.1348
cum DR in target pop %	0.1020	0.0577	0.0670	0.0533	0.0591	0.0514	0.0559	0.0507	0.0542	0.0503
FIT1										
CRC cases	10.24	6.02	5.89	5.76	5.63	5.50	5.37	5.24	5.10	4.97
cum CRC cases	10.24	16.25	22.14	27.90	33.53	39.03	44.39	49.63	54.73	59.70
cum DR in attenders %	0.1500	0.1212	0.1120	0.1078	0.1055	0.1042	0.1034	0.1030	0.1028	0.1027
cum DR in target pop %	0.1050	0.0844	0.0777	0.0743	0.0724	0.0712	0.0703	0.0697	0.0692	0.0689
TC										
cum CRC cases	19.50	21.35	23.20	25.05	26.91	28.77	30.62	32.48	34.34	36.19
cum DR in attenders %	0.5000	0.5075	0.5150	0.5225	0.5300	0.5375	0.5450	0.5525	0.5600	0.5675
cum DR in target pop %	0.2000	0.1109	0.0814	0.0668	0.0581	0.0525	0.0485	0.0456	0.0434	0.0418

ORs of cumulative CRC DRs within the 3 cohorts



	yr 1	yr 2	yr 3	yr 4	yr 5	yr 6	yr 7	yr8	yr 9	yr 10
FIT2/FIT1	0.97	0.68	0.86	0.72	0.82	0.72	0.79	0.73	0.78	0.73
FIT2/TC	0.51	0.52	0.82	0.80	1.02	0.98	1.15	1.11	1.25	1.21
FIT1/TC	0.53	0.76	0.95	1.11	1.25	1.36	1.45	1.53	1.59	1.65

Cancer preventability estimates for diet, nutrition, body fatness, and physical activity (http://www.wcrf.org)



Colorectum Cancer	PAF%*			
Appropriate behaviours	**USA**	**UK**	**Brazil**	**China**
Foods containing fibre	11	**12**	11	n/a
Red meat	5	**5**	7	7
Processed meat	12	**10**	5	1
Alcoholic drinks	5	**7**	2	1
Physical activity (colon)	15	**12**	15	7
Body fatness	16	**14**	10	8
Totals	*47*	***45***	*41*	*22*

*Updated estimates of cancer preventability (PAF%) by appropriate diet, nutrition, physical activity, and body fatness in four countries