

# GISCoR

gruppo italiano screening coloretale



T Hotel, Cagliari  
6-7 Novembre 2025

# XVIII CONGRESSO NAZIONALE 2025

# Lo screening stratificato sul rischio: primi risultati dello studio BIOFIT

Gianluigi Ferrante

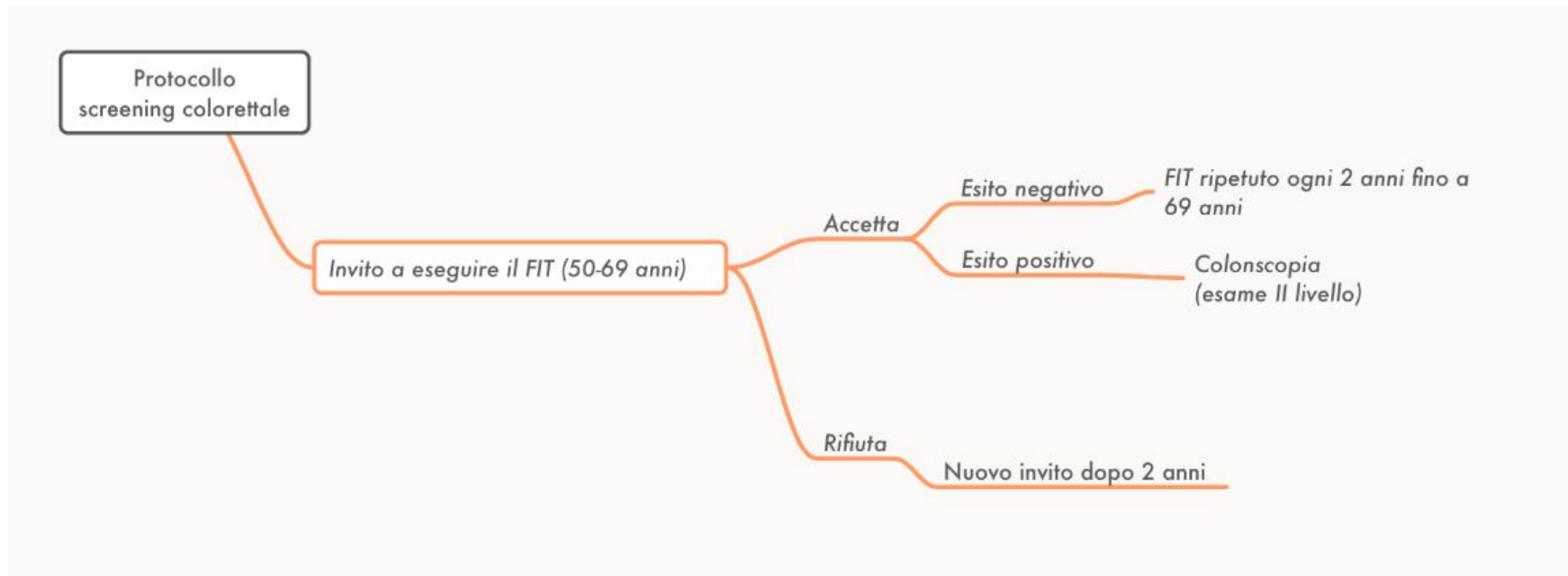
*AOU Città della Salute e della Scienza di Torino - CPO Piemonte*

# CONTESTO

13.12.2022	EN	Official Journal of the European Union	C 473/1
<p>I</p> <p><i>(Resolutions, recommendations and opinions)</i></p> <p>RESOLUTIONS</p> <p>COUNCIL</p> <p>COUNCIL RECOMMENDATION</p> <p><b>of 9 December 2022</b></p> <p><b>on strengthening prevention through early detection: A new EU approach on cancer screening</b></p> <p><b>replacing Council Recommendation 2003/878/EC</b></p> <p><i>(2022/C 473/01)</i></p>			

Council Recommendation of 9 december 2022 on strengthening prevention through early detection: a new EU approach on cancer screening replacing Council Recommendation 2003/878/EC 2022/C 473/01. [https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022H1213\(01\)](https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32022H1213(01))

# PROGRAMMA ORGANIZZATO DI SCREENING COLORETTALE



## CARATTERISTICHE TEST IMMUNOCHIMICO FIT



Provetta del Test immunochimico per la ricerca del sangue occulto fecale (FIT)

- Il test FIT è costo-efficace, ma la **sensibilità** del singolo round di screening del FIT è **bassa** per gli **adenomi avanzati**
- Abbassare il cut-off del test avrebbe un impatto negativo sulla sostenibilità dei programmi di screening
- Il FIT risulta falsamente positivo in circa la metà dei casi e induce una quota importante di colonscopie non necessarie

## RAZIONALE STUDIO (sperimentale)

> [Eur J Cancer](#). 2019 Jan;107:53-59. doi: 10.1016/j.ejca.2018.11.004. Epub 2018 Dec 10.

### Changes in FIT values below the threshold of positivity and short-term risk of advanced colorectal neoplasia: Results from a population-based cancer screening program

Andrea Buron<sup>1</sup>, Marta Román<sup>2</sup>, Josep M Augé<sup>3</sup>, Francesc Macià<sup>2</sup>, Jaume Grau<sup>4</sup>, Maria Sala<sup>2</sup>, Javier Louro<sup>2</sup>, Montserrat Martinez-Alonso<sup>5</sup>, Cristina Alvarez-Urturi<sup>6</sup>, Montserrat Andreu<sup>6</sup>, Xavier Bessa<sup>6</sup>, Diana Zaffalon<sup>6</sup>, Antoni Castells<sup>7</sup>, Maria Pellisé<sup>7</sup>, Marta Aldea<sup>4</sup>, Liseth Rivero<sup>7</sup>, Cristina Hernández<sup>8</sup>, Isabel Torá-Rocamora<sup>4</sup>, Xavier Castells<sup>2</sup>

Affiliations + expand

PMID: 30544059 DOI: [10.1016/j.ejca.2018.11.004](#)

> [Gut](#). 2020 Mar;69(3):523-530. doi: 10.1136/gutjnl-2018-318198. Epub 2019 Aug 27.

### 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

Carlo Senore<sup>1</sup>, Marco Zappa<sup>2</sup>, Cinzia Campari<sup>3</sup>, Sergio Crotta<sup>4</sup>, Paola Armaroli<sup>5</sup>, Arrigo Arrigoni<sup>6</sup>, Paola Cassoni<sup>7</sup>, Rossana Colla<sup>3</sup>, Mario Fracchia<sup>8</sup>, Fabrizio Gili<sup>9</sup>, Grazia Grazzini<sup>10</sup>, Roberto Lolli<sup>11</sup>, Patrizia Menozzi<sup>3</sup>, Lorenzo Orione<sup>12</sup>, Salvatore Polizzi<sup>13</sup>, Stefano Rapi<sup>14</sup>, Emilia Riggi<sup>5</sup>, Tiziana Rubeca<sup>10</sup>, Romano Sassatelli<sup>3</sup>, Carmen Visioli<sup>2</sup>, Nereo Segnan<sup>5</sup>

Affiliations + expand

PMID: 31455608 DOI: [10.1136/gutjnl-2018-318198](#)

> [Gut](#). 2023 Jan;72(1):101-108. doi: 10.1136/gutjnl-2022-327188. Epub 2022 May 10.

### Faecal occult blood loss accurately predicts future detection of colorectal cancer. A prognostic model

Reinier G S Meester<sup>1</sup>, Hilliene J van de Schootbrugge-Vandermeer<sup>2</sup>, Emilie C H Breekveldt<sup>2</sup>, Lucie de Jonge<sup>2</sup>, Esther Toes-Zoutendijk<sup>2</sup>, Arthur Kooyker<sup>2</sup>, Daan Nieboer<sup>2</sup>, Christian R Ramakers<sup>3</sup>, Manon C W Spaander<sup>4</sup>, Anneke J van Vuuren<sup>4</sup>, Ernst J Kuipers<sup>4</sup>, Folkert J van Kemenade<sup>5</sup>, Iris D Nagtegaal<sup>6</sup>, Evelien Dekker<sup>7</sup>, Monique E van Leerdam<sup>8</sup>, Iris Lansdorp-Vogelaar<sup>2</sup>; Dutch colorectal cancer screening working group

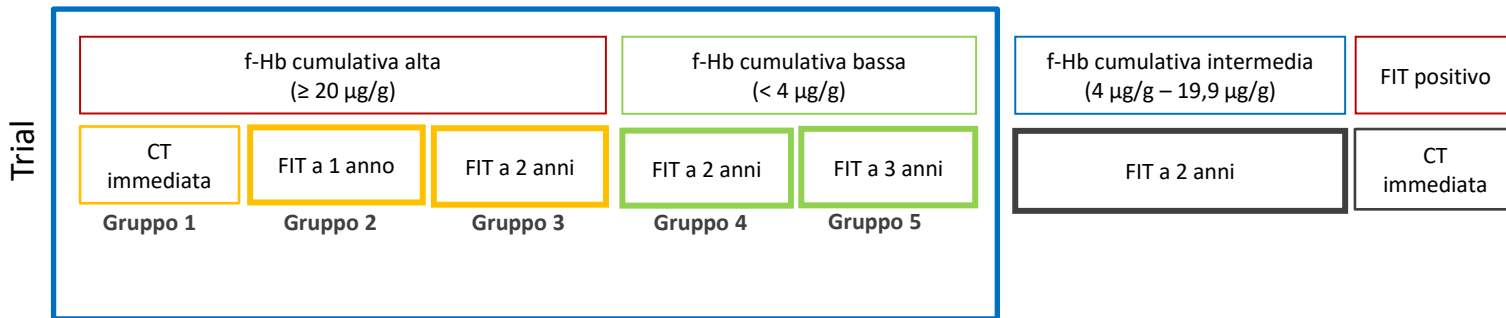
Affiliations + expand

PMID: 35537811 PMCID: [PMC9763180](#) DOI: [10.1136/gutjnl-2022-327188](#)

## OBIETTIVI DELLO STUDIO (sperimentale)

- Valutare l'impatto di un protocollo di screening che preveda l'adozione di percorsi differenziati **in base al livello di rischio**, definito dalla **sommatoria della concentrazione di emoglobina fecale (f-Hb)** misurata negli ultimi due FIT consecutivi.

# DISEGNO DELLO STUDIO (sperimentale)



Vantaggi per il gruppo 1

CT  
immediata

anticipare la diagnosi di una eventuale lesione

Vantaggi per il gruppo 2

FIT a 1 anno

prevenire una lesione o di individuarla precocemente con uno screening più frequente

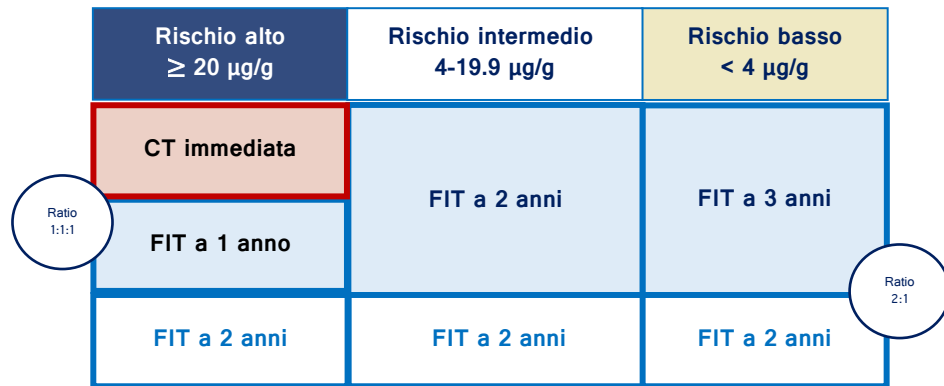
Vantaggi per il gruppo 5

FIT a 3 anni

avere una minore probabilità di eseguire colonscopie inutili



# DISEGNO DELLO STUDIO (sperimentale)



Endpoint



Tasso rilevamento di adenomi av. e CRC

Tasso positività CT

VPP di adenomi av. e CRC



Il rischio è valutato in funzione della concentrazione cumulativa di emoglobina fecale (f-Hb) degli ultimi due FIT consecutivi

# MATERIALI E METODI

**PREVENZIONE SERENA** 

studio BI OFI T



**QUALI VANTAGGI**  
potrei avere dalla  
partecipazione a  
questo studio?

Se il suo rischio risulterà nella media, non cambierà nulla rispetto allo standard.

Se farà parte del gruppo 1 (colonscopia) avrà il vantaggio di anticipare la diagnosi di una eventuale lesione evitando di dover ripetere lo screening in futuro.

Se farà parte del gruppo 2 farà uno screening più frequente con una maggiore possibilità di prevenire la malattia o di individuarla precocemente.

Se farà parte del gruppo 3 o 4, non cambierà nulla rispetto allo standard attuale, che è già molto protettivo.

Se farà parte del gruppo 5 farà uno screening meno frequente, riducendo così la possibilità di avere risultati falsamente positivi con conseguenti colonscopie inutili.

Se il suo rischio risulterà nella media, non cambierà nulla rispetto allo standard.

Se farà direttamente la colonscopia avrà quel rischio minimo di complicazioni che esiste per questo tipo di esame.

Se avrà uno screening più frequente rispetto allo standard (gruppo 2) potrebbe incorrere più facilmente in risultati falsamente positivi.

Se avrà uno screening meno frequente rispetto allo standard (gruppo 5) potrebbe avere un ritardo nell'individuazione di eventuali lesioni. Questo effetto è però mitigato dal basso rischio di avere lesioni.

**QUALI SVANTAGGI**  
potrei avere dalla  
partecipazione a  
questo studio?

**COSA SUCCEDDE**  
se decido di **NON**  
partecipare?

L'adesione è volontaria ed è possibile ritirarsi in qualunque momento senza fornire giustificazioni. Se non desidera prendere parte allo studio non si preoccupi: seguirà gli intervalli e le procedure attualmente previste dal programma di screening e le sarà sempre garantita la migliore assistenza.

**DOVE POSSO TROVARE**  
maggiori informazioni?

Se ha dubbi o desidera avere maggiori informazioni può collegarsi al sito del **CPO Piemonte** - Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica in Piemonte:  
<https://www.cpo.it/it/>







































































































































































































































































studio BI OFI T

**PREVENZIONE SERENA** 



**PERCHÉ**

Il nuovo metodo **BI OFI T**                                                                                                                                                                                                                                                                       

# STATO RECLUTAMENTO (studio sperimentale)



Nov 2022 Inizio studio  
Nov 2023 Aggiornamento  
metodo reclutamento



74,6%

ha aderito all'invito al programma di screening

29,1%

ha dato il consenso alla partecipazione  
allo studio e alla randomizzazione

## I round del progetto

	n.	CT	AA
GR1 - CT immediata	71	47	8
GR2 - FIT a 1 anno	70	--	--
GR3 - FIT a 2 anni	65	--	--
GR4 - FIT a 2 anni	5.012	--	--
GR5 - FIT a 3 anni	10.020	--	--
<b>Totale</b>	<b>15.238</b>		

## II round del progetto

	n.	FIT+	CT	AA
GR1 - CT immediata	4	2	2	2
GR2 - FIT a 1 anno	29	9	6	2
GR3 - FIT a 2 anni	9	1	1	1
GR4 - FIT a 2 anni	341	7	6	2
GR5 - FIT a 3 anni	79	5	4	0
<b>Totale</b>	<b>462</b>			

VPP per adenomi avanzati  
20,4% (10 AA/49 CT)

# RAZIONALE (studio caso-controllo)

Multicenter Study > [Gastroenterology](#). 2023 Sep;165(3):582-599.e8.

doi: 10.1053/j.gastro.2023.05.037. Epub 2023 May 30.

## A Fecal MicroRNA Signature by Small RNA Sequencing Accurately Distinguishes Colorectal Cancers: Results From a Multicenter Study

Barbara Pardini<sup>1</sup>, Giulio Ferrero<sup>2</sup>, Sonia Tarallo<sup>3</sup>, Gaetano Gallo<sup>4</sup>, Antonio Francavilla<sup>5</sup>, Nicola Licheri<sup>6</sup>, Mario Trompetto<sup>7</sup>, Giuseppe Clerico<sup>7</sup>, Carlo Senore<sup>8</sup>, Sergio Peyre<sup>9</sup>, Veronika Vymetalkova<sup>10</sup>, Ludmila Vodickova<sup>10</sup>, Vaclav Liska<sup>11</sup>, Ondrej Vycital<sup>11</sup>, Miroslav Levy<sup>12</sup>, Peter Macinga<sup>13</sup>, Tomas Huc<sup>13</sup>, Eva Budinska<sup>14</sup>, Pavel Vodicka<sup>10</sup>, Francesca Cordero<sup>6</sup>, Alessio Naccarati<sup>15</sup>

Affiliations + expand

PMID: 37263306 DOI: [10.1053/j.gastro.2023.05.037](#)

> [BMC Cancer](#). 2015 Apr 30;15:329. doi: 10.1186/s12885-015-1327-5.

## Circulating miRNAs miR-34a and miR-150 associated with colorectal cancer progression

Sinéad T Aherne<sup>1</sup>, Stephen F Madden<sup>2</sup>, David J Hughes<sup>3</sup>, Barbara Pardini<sup>4</sup>, Alessio Naccarati<sup>5, 6</sup>, Miroslav Levy<sup>7</sup>, Pavel Vodicka<sup>8</sup>, Paul Neary<sup>9</sup>, Paul Dowling<sup>10, 11</sup>, Martin Clynes<sup>12</sup>

Affiliations + expand

PMID: 25924769 PMCID: [PMC4417244](#) DOI: [10.1186/s12885-015-1327-5](#)

> [Nat Med](#). 2019 Apr;25(4):667-678. doi: 10.1038/s41591-019-0405-7. Epub 2019 Apr 1.

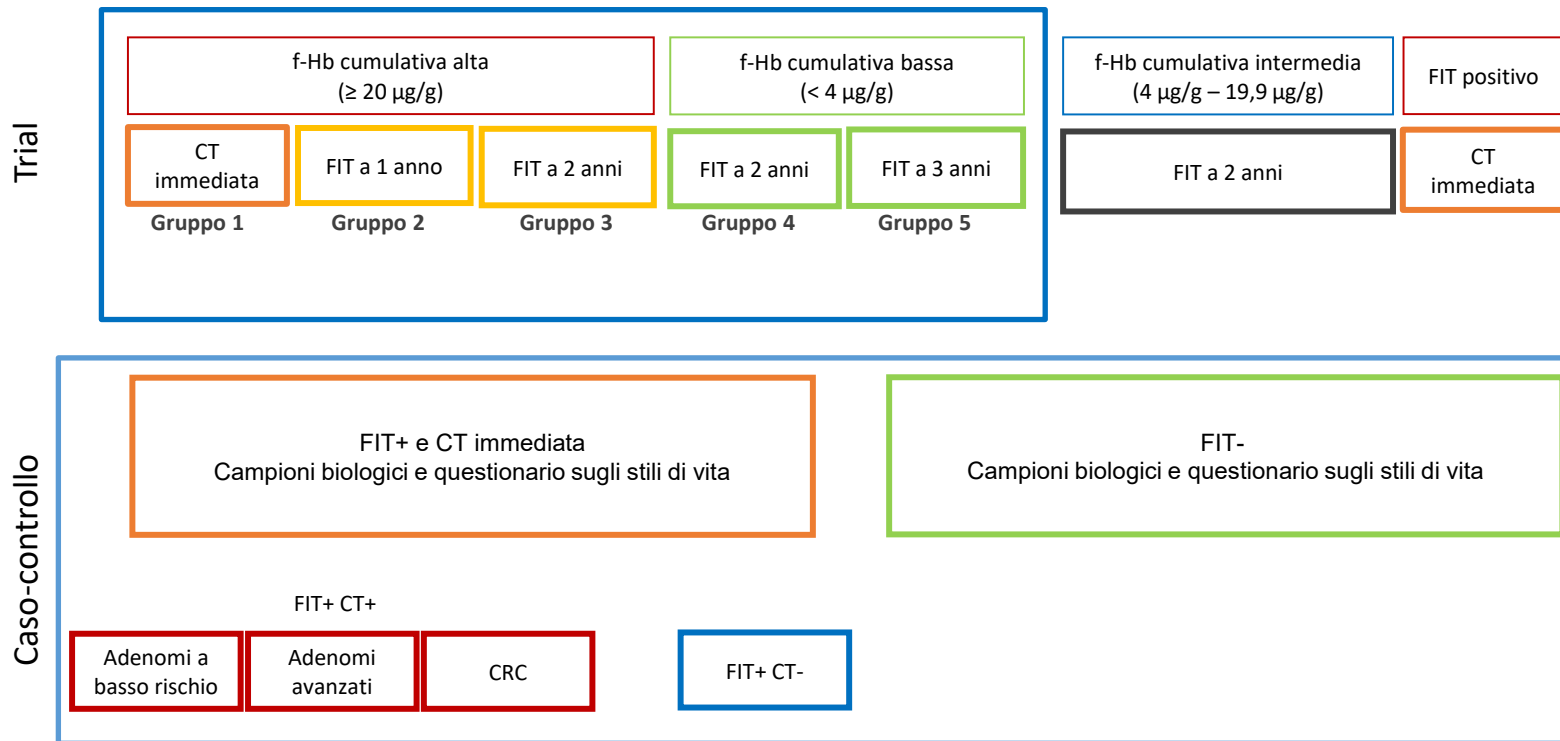
## Metagenomic analysis of colorectal cancer datasets identifies cross-cohort microbial diagnostic signatures and a link with choline degradation

Andrew Maltez Thomas<sup># 1 2 3</sup>, Paolo Manghi<sup># 1</sup>, Francesco Asnicar<sup>1</sup>, Edoardo Pasolli<sup>1</sup>, Federica Armanini<sup>1</sup>, Moreno Zolfo<sup>1</sup>, Francesco Beghini<sup>1</sup>, Serena Manara<sup>1</sup>, Nicolai Karcher<sup>1</sup>, Chiara Pozzi<sup>4</sup>, Sara Gandini<sup>4</sup>, Davide Serrano<sup>4</sup>, Sonia Tarallo<sup>5</sup>, Antonio Francavilla<sup>5</sup>, Gaetano Gallo<sup>6 7</sup>, Mario Trompetto<sup>7</sup>, Giulio Ferrero<sup>8</sup>, Sayaka Mizutani<sup>9 10</sup>, Hirotugu Shiroma<sup>9</sup>, Satoshi Shiba<sup>11</sup>, Tatsuhiro Shibata<sup>11 12</sup>, Shinichi Yachida<sup>11 13</sup>, Takuji Yamada<sup>9 14</sup>, Jakob Wirbel<sup>15</sup>, Petra Schrotz-King<sup>16</sup>, Cornelia M Ulrich<sup>17</sup>, Hermann Brenner<sup>16 18 19</sup>, Manimozhiyan Arumugam<sup>20 21</sup>, Peer Bork<sup>15 22 23 24</sup>, Georg Zeller<sup>15</sup>, Francesca Cordero<sup>8</sup>, Emmanuel Dias-Neto<sup>3 25</sup>, João Carlos Setubal<sup>2 26</sup>, Adrian Tett<sup>1</sup>, Barbara Pardini<sup>5 27</sup>, Maria Rescigno<sup>28</sup>, Levi Waldron<sup>29 30</sup>, Alessio Naccarati<sup>5 31</sup>, Nicola Segata<sup>32</sup>

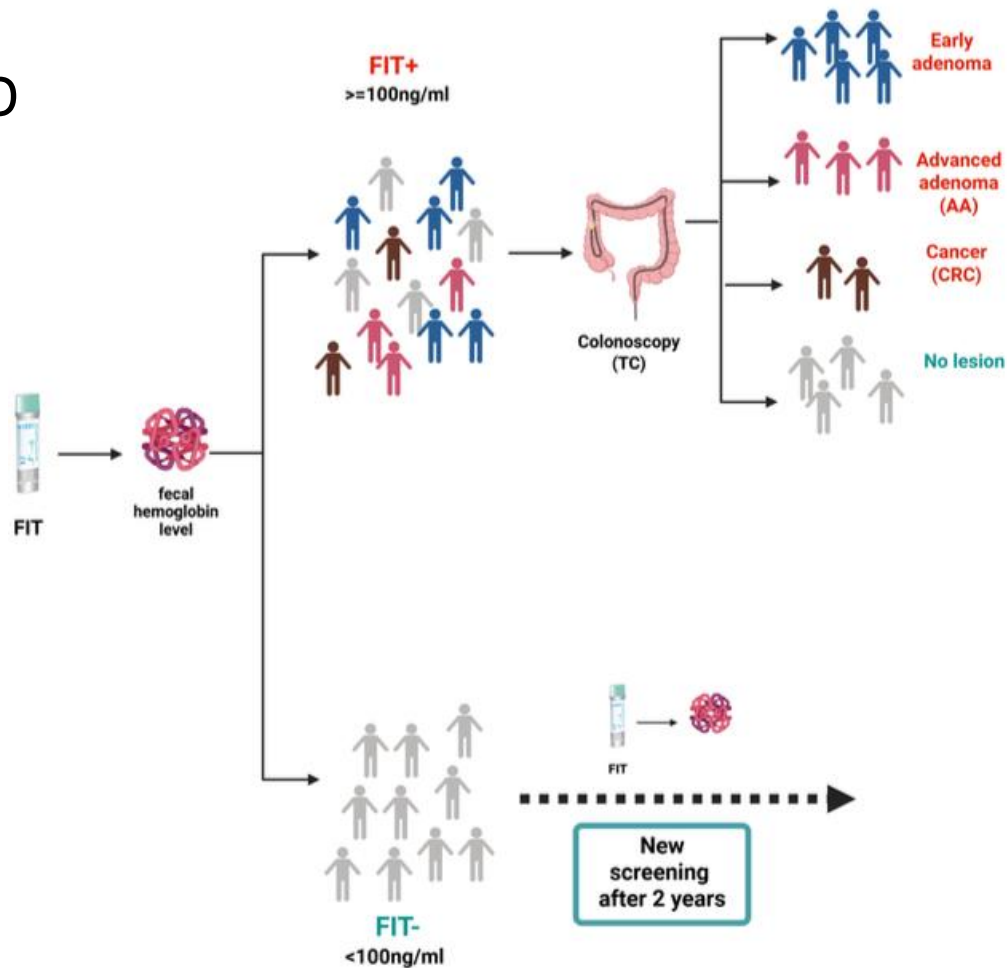
Affiliations + expand

PMID: 30936548 PMCID: [PMC9533319](#) DOI: [10.1038/s41591-019-0405-7](#)

# DISEGNO DELLO STUDIO (caso-controllo)

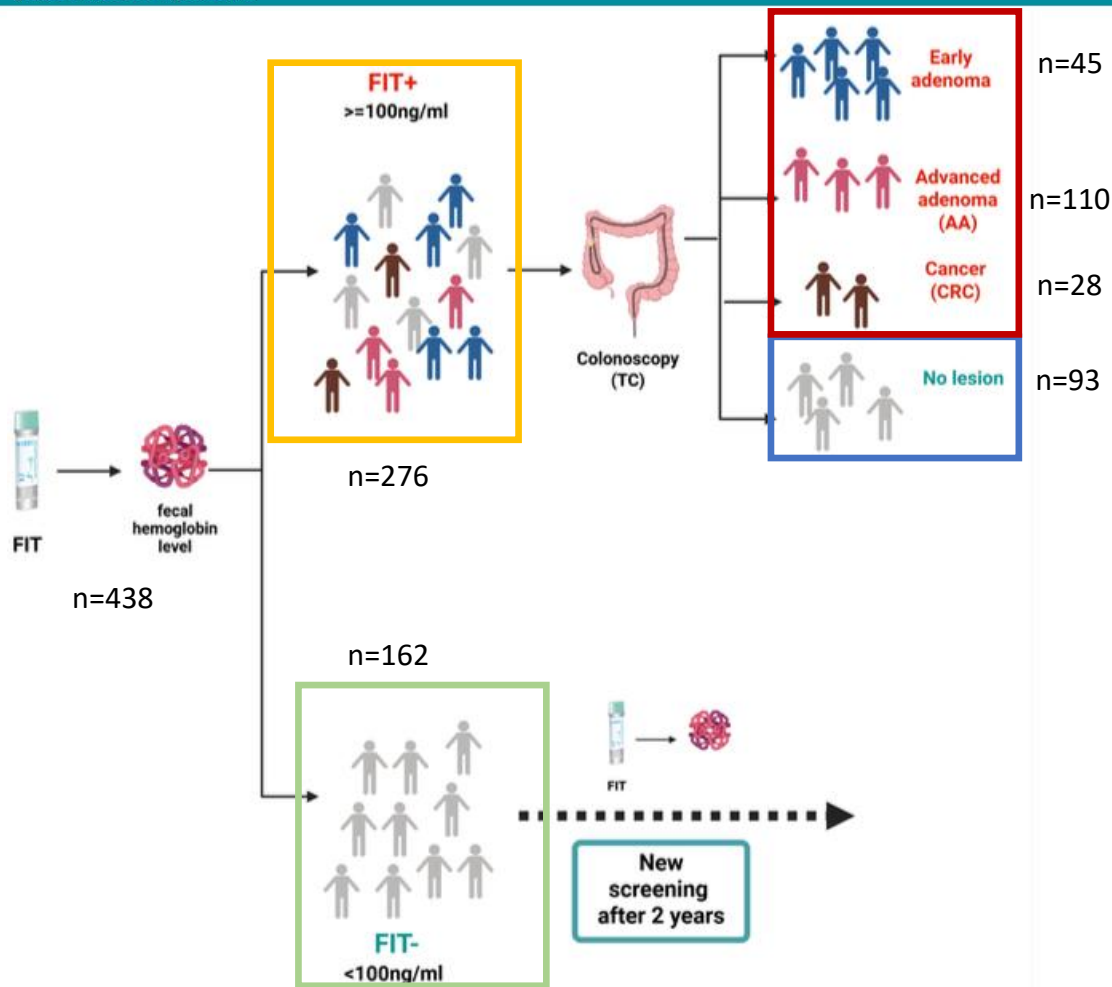


# STUDIO CASO-CONTROLLO



## OBIETTIVI DELLO STUDIO (caso-controllo)

- Valutare se i **miRNA** rilevati nei **leftover del FIT**, attraverso la tecnica del Next-Generation Sequencing (**NGS**), possano funzionare da **biomarcatori di triage** nello screening coloretale.
- Indagare la capacità delle **firme molecolari di miRNA** di predire adenomi o CRC **nei successivi round di screening**.
- Valutare il valore predittivo di alcuni **biomarcatori fecali** insieme a uno **score di rischio calcolato a partire da questionari ad-hoc sugli stili di vita**, per il rischio di adenomi avanzati (AA) e carcinomi colorettali (CRC).



## STUDIO CASO-CONTROLLO (biomarcatori triage)

### CONFRONTI

**FIT+ CT+** vs. **FIT+ CT-**

**FIT+ LR Adenoma** vs. **FIT+ CT-**

**FIT+ HR Adenoma** vs. **FIT+ CT-**

**FIT+ CRC** vs. **FIT+ CT-**

**FIT+ vs. FIT-**

**FIT+ CT-** vs. **FIT-**

**FIT+ LR Adenoma** vs. **FIT-**

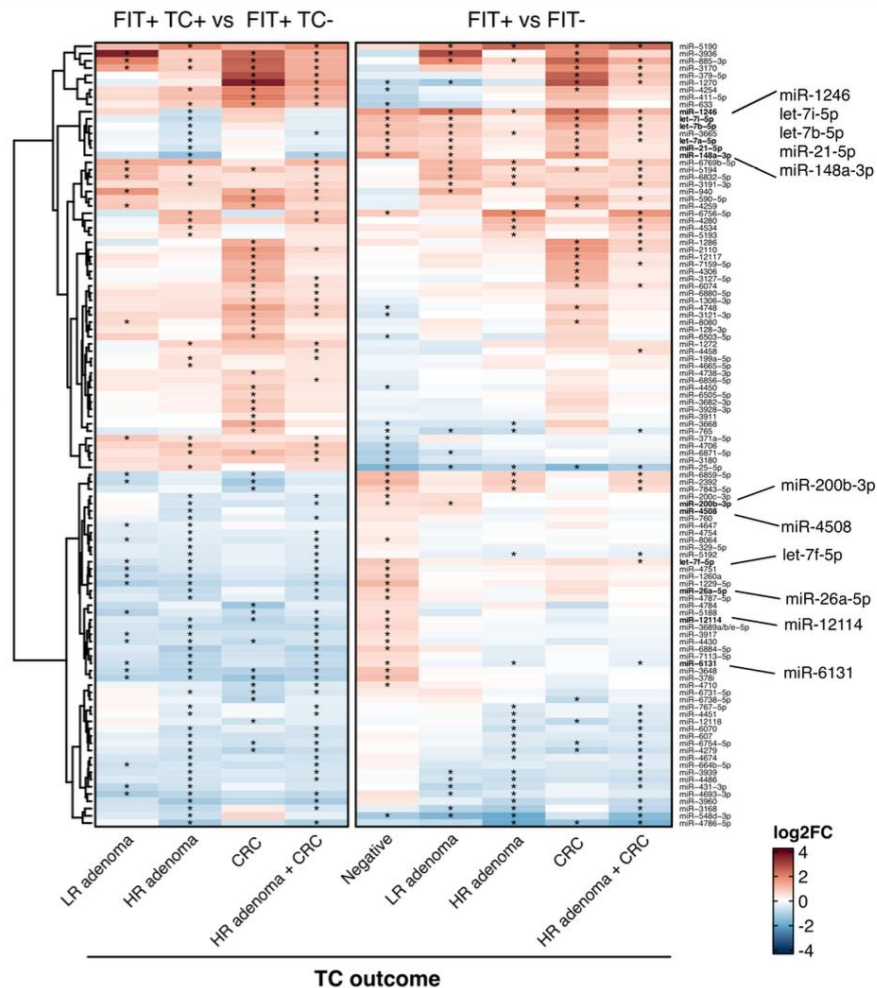
**FIT+ HR Adenoma** vs. **FIT-**

**FIT+ CRC** vs. **FIT-**

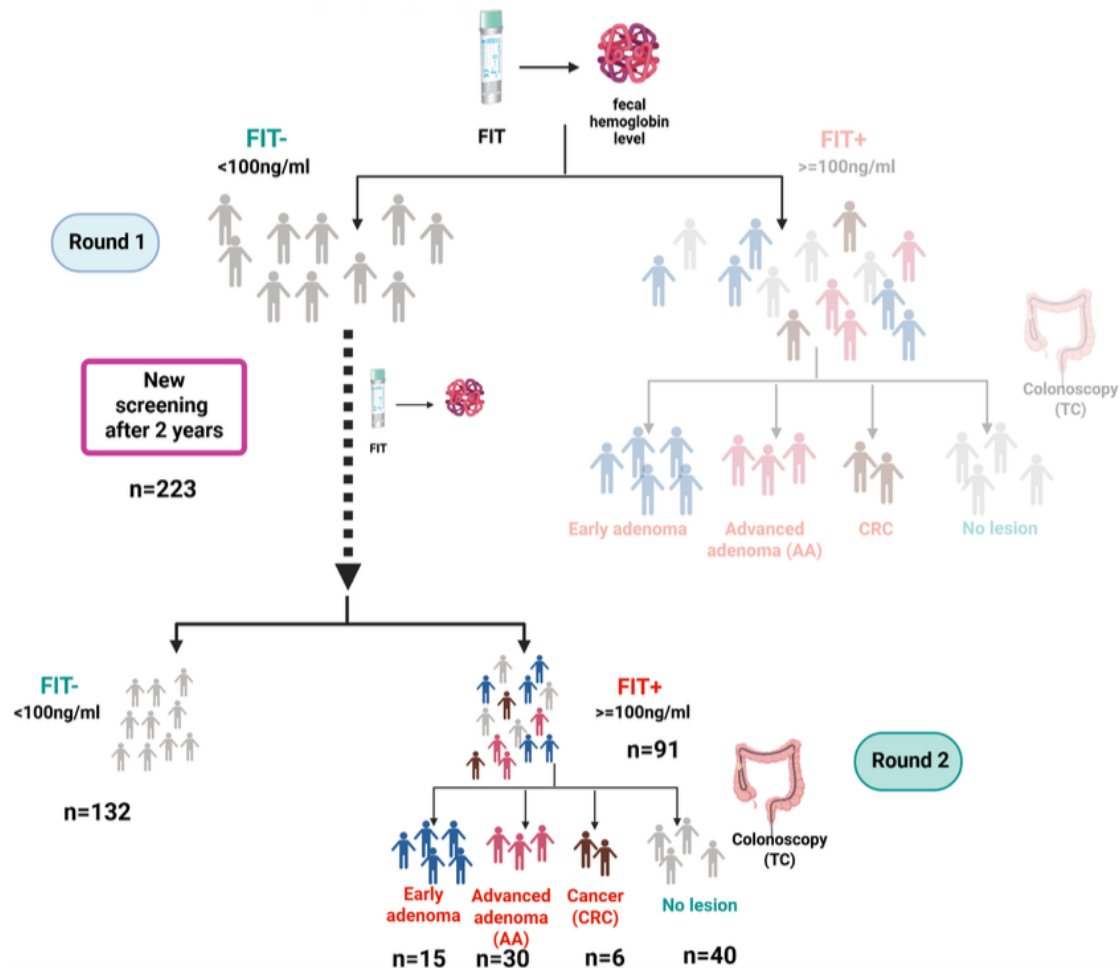


# RISULTATI (biomarcatori triage)

Figura. Heatmap che rappresenta i miRNA DE dal confronto tra campioni FIT+ con/senza lesioni e campioni FIT- (lato destro) o tra FIT+ con/senza lesioni versus FIT+ senza lesioni (lato sinistro).



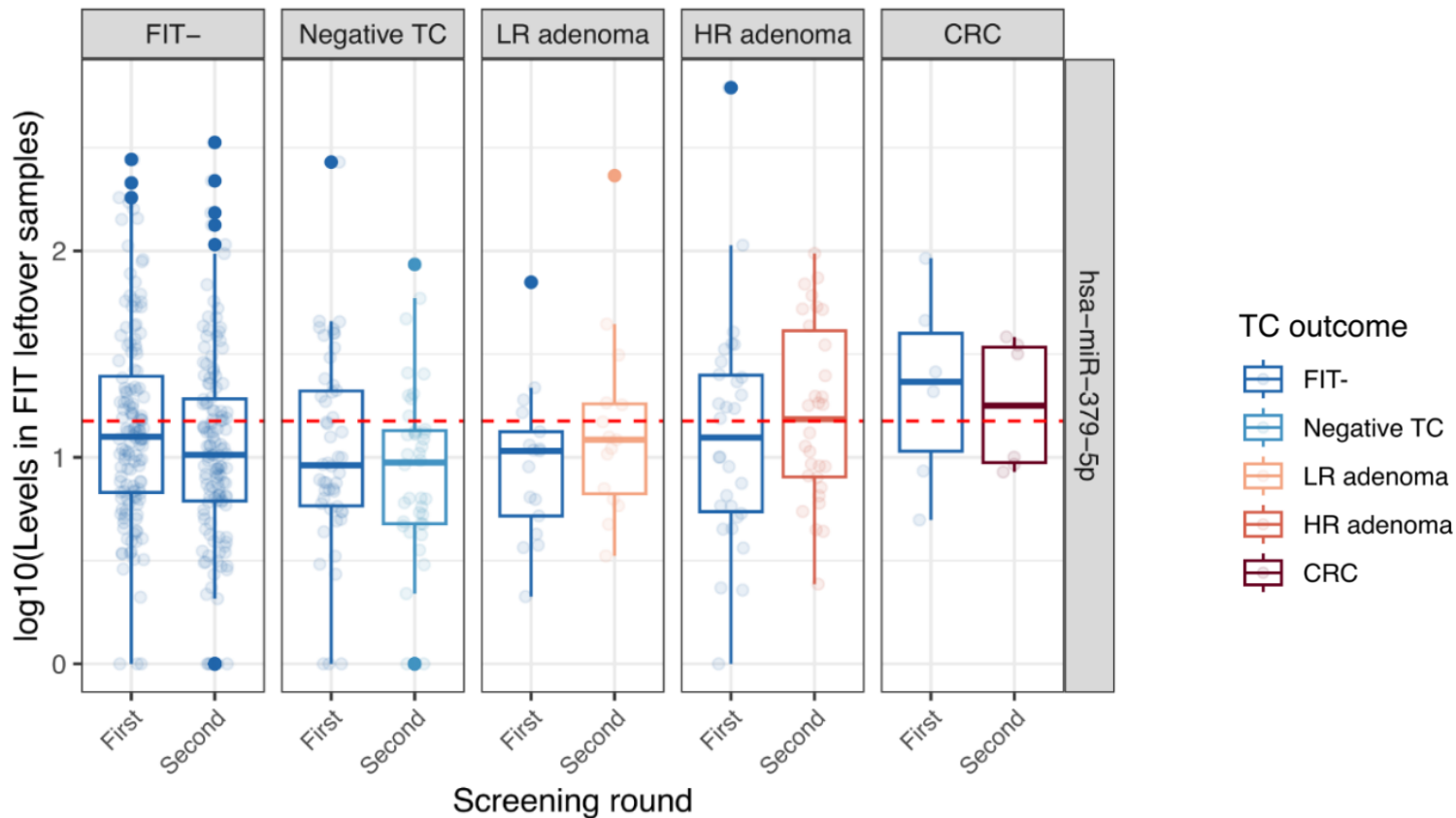
# STUDIO CASO-CONTROLLO (biomarcatori predittivi CRC)



## RISULTATI (biomarcatori predittivi CRC)

- Confrontando i livelli di espressione dei miRNA tra il primo e il secondo round di screening e stratificando per gli esiti della CT, **22 miRNA risultavano già espressi in modo differenziale** circa 2 anni prima del rilevamento della lesione.
- Tra questi, **miR-379-5p** e **miR-12118** hanno mostrato un significativo trend di diminuzione/aumento dei livelli quando si passa da campioni FIT- a FIT+ senza lesioni e a FIT+ con lesioni.

## RISULTATI (biomarcatori predittivi CRC)



## CONCLUSIONI

- I **miRNA delle feci**, potrebbero in futuro essere utilizzati come biomarcatori per migliorare lo screening di popolazione e per anticipare la diagnosi di cancro del colon-retto (CRC).
- Lo studio ha individuato **108 miRNA** che hanno livelli diversi nelle persone con cancro o altre lesioni precancerose rispetto a quelle sane.

## CONCLUSIONI

- I miRNA **miR-12118** e **miR-379-5p** hanno mostrato un cambiamento significativo e graduale nei loro livelli quando si passava da persone sane (FIT-) a persone con test FIT positivo ma sane (FIT+ senza lesioni) fino a persone con lesioni (FIT+ con lesioni).
- Per confermare questi risultati e renderli applicabili nella pratica, sono necessarie **ulteriori analisi su gruppi di persone più ampi e indipendenti**, possibilmente utilizzando strumenti di machine learning (apprendimento automatico) per analizzare i dati.

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