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**SICOB ONLINE**


Epidemiologia e meccanismi  
patogenetici dell'interazione  
obesità-cancro

**Francesco S. Papadia, MD, FACS**




# OBESITY


IS A CAUSE OF CANCER TOO



Like smoking, obesity puts millions of adults at greater risk of cancer





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# OBESITY

IS A CAUSE OF CANCER TOO



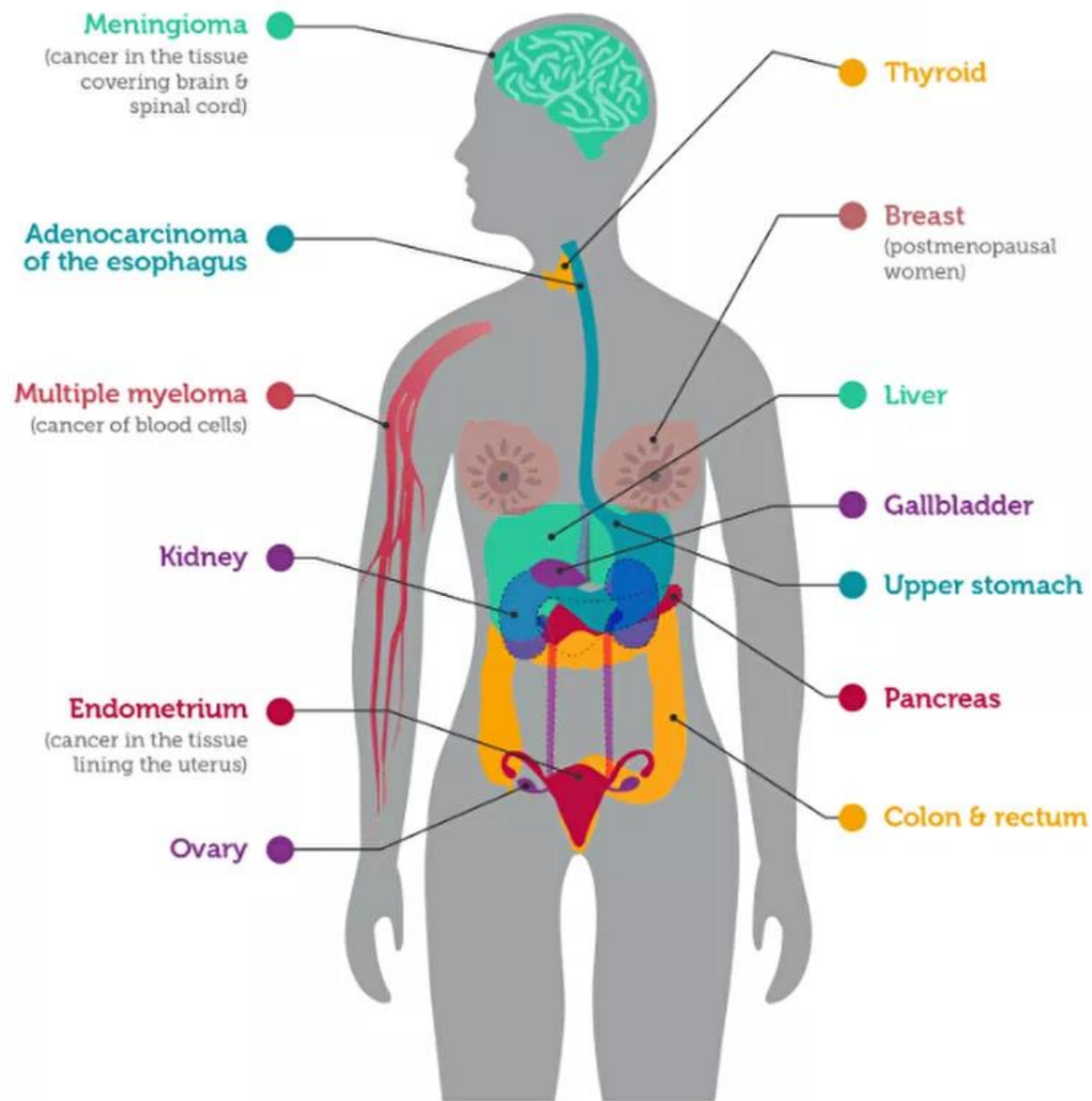
Like smoking, obesity puts millions of adults at greater risk of cancer



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## Cancers Associated with Overweight & Obesity



# Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants



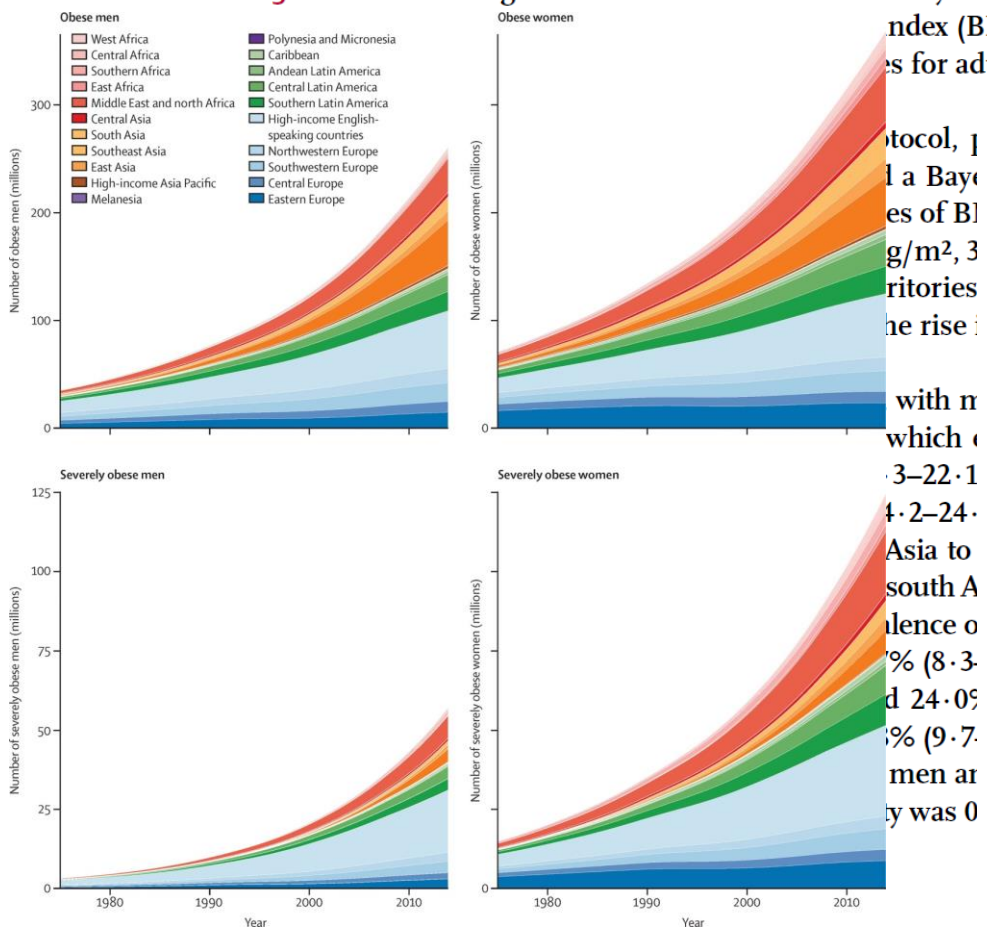
NCD Risk Factor Collaboration (NCD-RisC)\*

## Summary

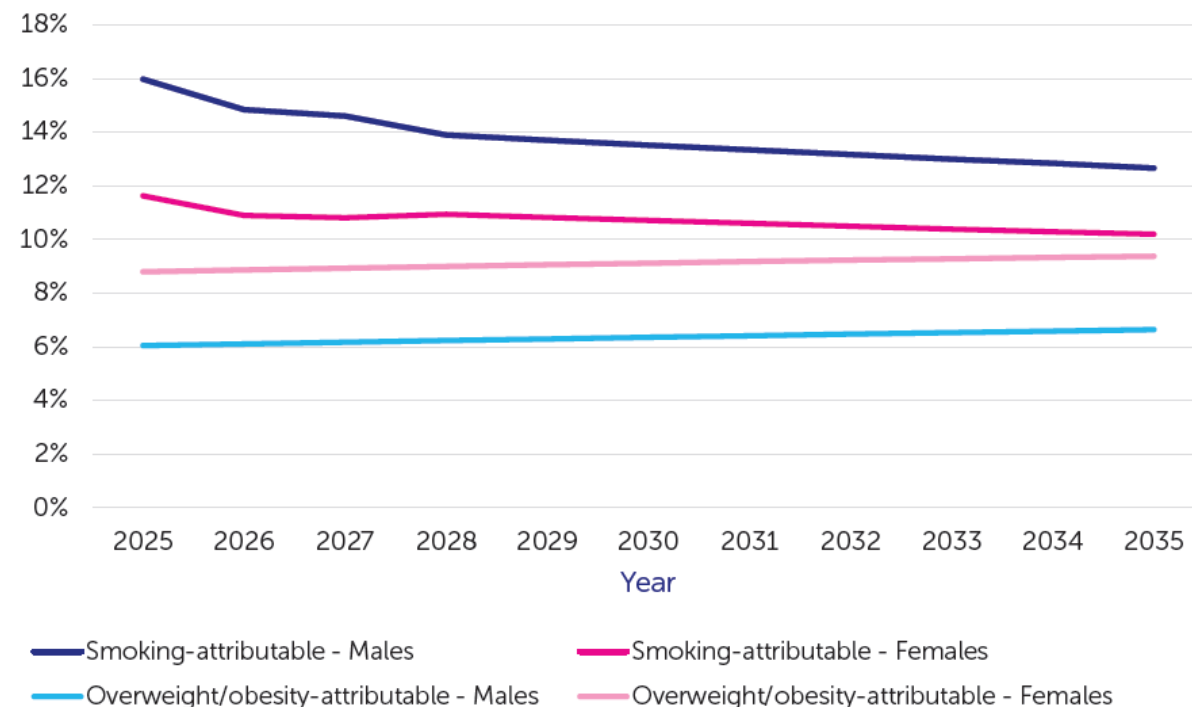
**Background** Underweight and severe and morbid obesity are associated with highly elevated risks of adverse health outcomes. The body-mass index (BMI), which characterises its population distribution, and trends in BMI for adults in all countries.

Lancet 2016; 387: 1377-96

This online publication has been corrected. The corrected version first appeared at



Percentage of UK cancer cases attributable to risk factor





# Commentary: What can Mendelian randomization tell us about causes of cancer?

International Journal of Epidemiology, 2019, 816–821

doi: 10.1093/ije/dyz151

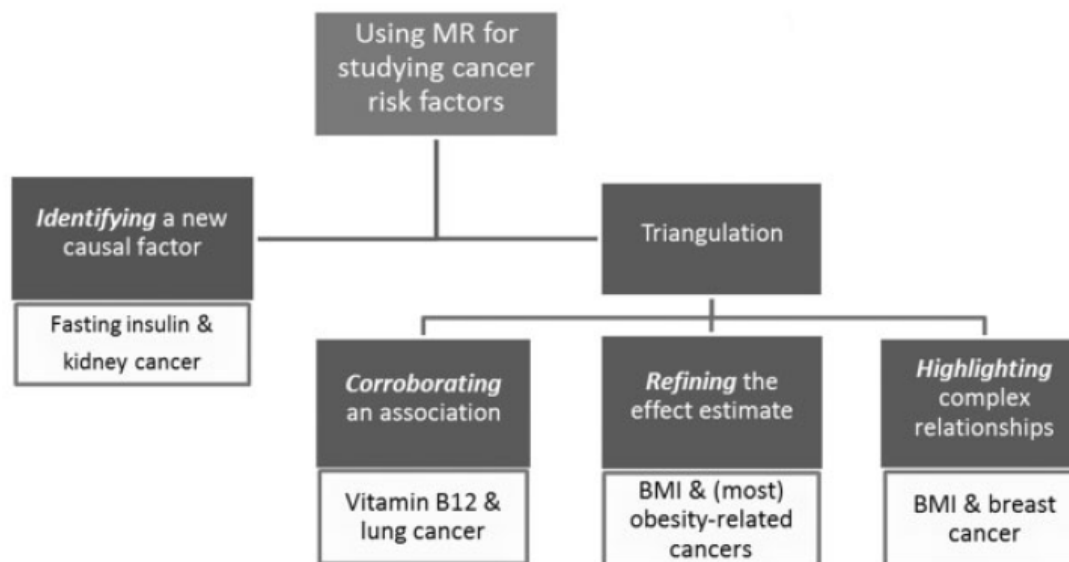


Daniela Mariosa,<sup>1</sup> Robert Carreras-Torres,<sup>1,2</sup> Richard M Martin,<sup>3,4,5</sup> Mattias Johansson<sup>1</sup> and Paul Brennan<sup>1\*</sup>

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Editorial decision 19 June 2019; Accepted 17 July 2019



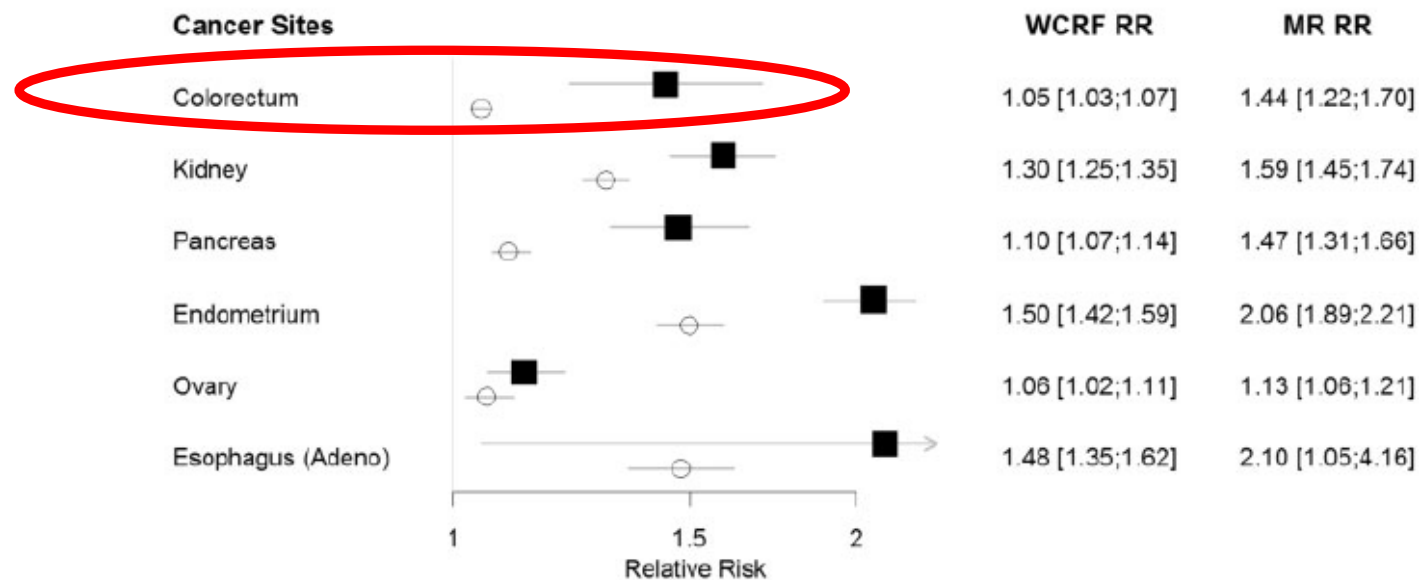
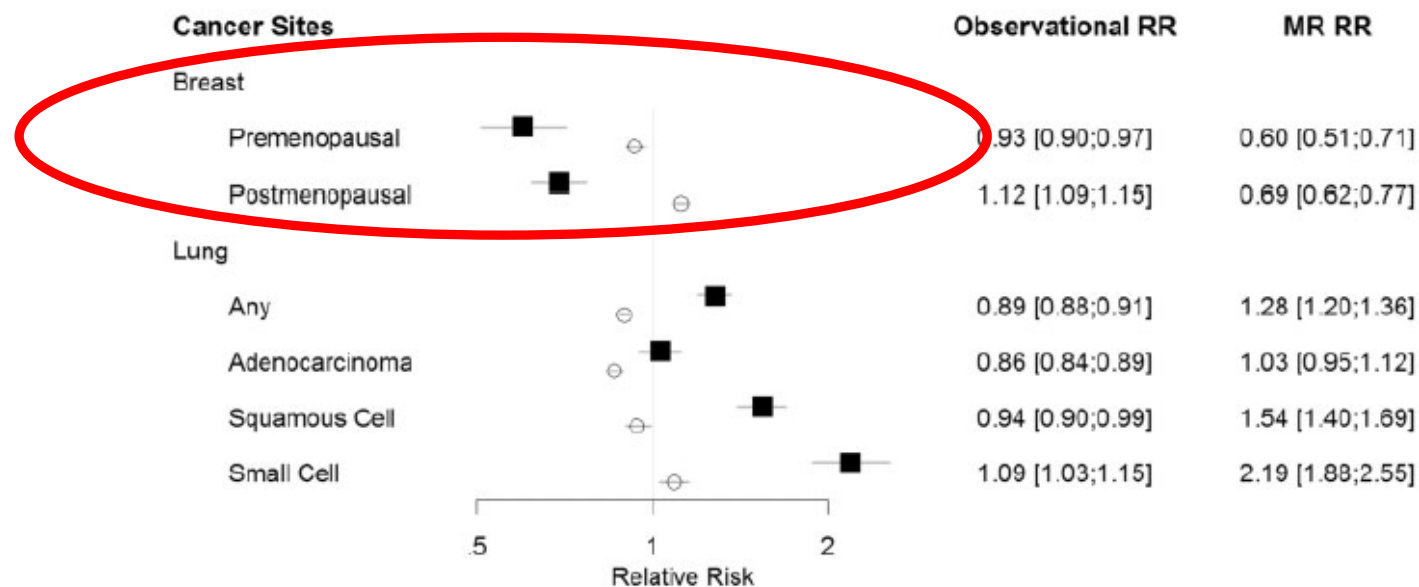


Figure 2. WCRF (circles) and MR (squares) relative risks for the association between a 5-unit BMI increase and cancer risk by cancer site.






# Colorectal Cancer Screening for Average-Risk Adults: 2018 Guideline Update From the American Cancer Society

Andrew M.D. Wolf, MD<sup>1</sup>; Elizabeth T.H. Fontham, MPH, DrPH<sup>2</sup>; Timothy R. Church, PhD<sup>3</sup>; Christopher R. Flowers, MD, MS<sup>4</sup>; Carmen E. Guerra, MD<sup>5</sup>; Samuel J. LaMonte, MD<sup>6</sup>; Ruth Etzioni, PhD<sup>7</sup>; Matthew T. McKenna, MD<sup>8</sup>; Kevin C. Oeffinger, MD<sup>9</sup>; Ya-Chen Tina Shih, PhD<sup>10</sup>; Louise C. Walter, MD<sup>11</sup>; Kimberly S. Andrews, BA<sup>12</sup>; Otis W. Brawley, MD<sup>13</sup>; Durado Brooks, MD, MPH<sup>14</sup>; Stacey A. Fedewa, PhD, MPH<sup>15</sup>; Deana Manassaram-Baptiste, PhD, MPH<sup>16</sup>; Rebecca L. Siegel, MPH<sup>17</sup>; Richard C. Wender, MD<sup>18</sup>; Robert A. Smith, PhD<sup>19</sup>

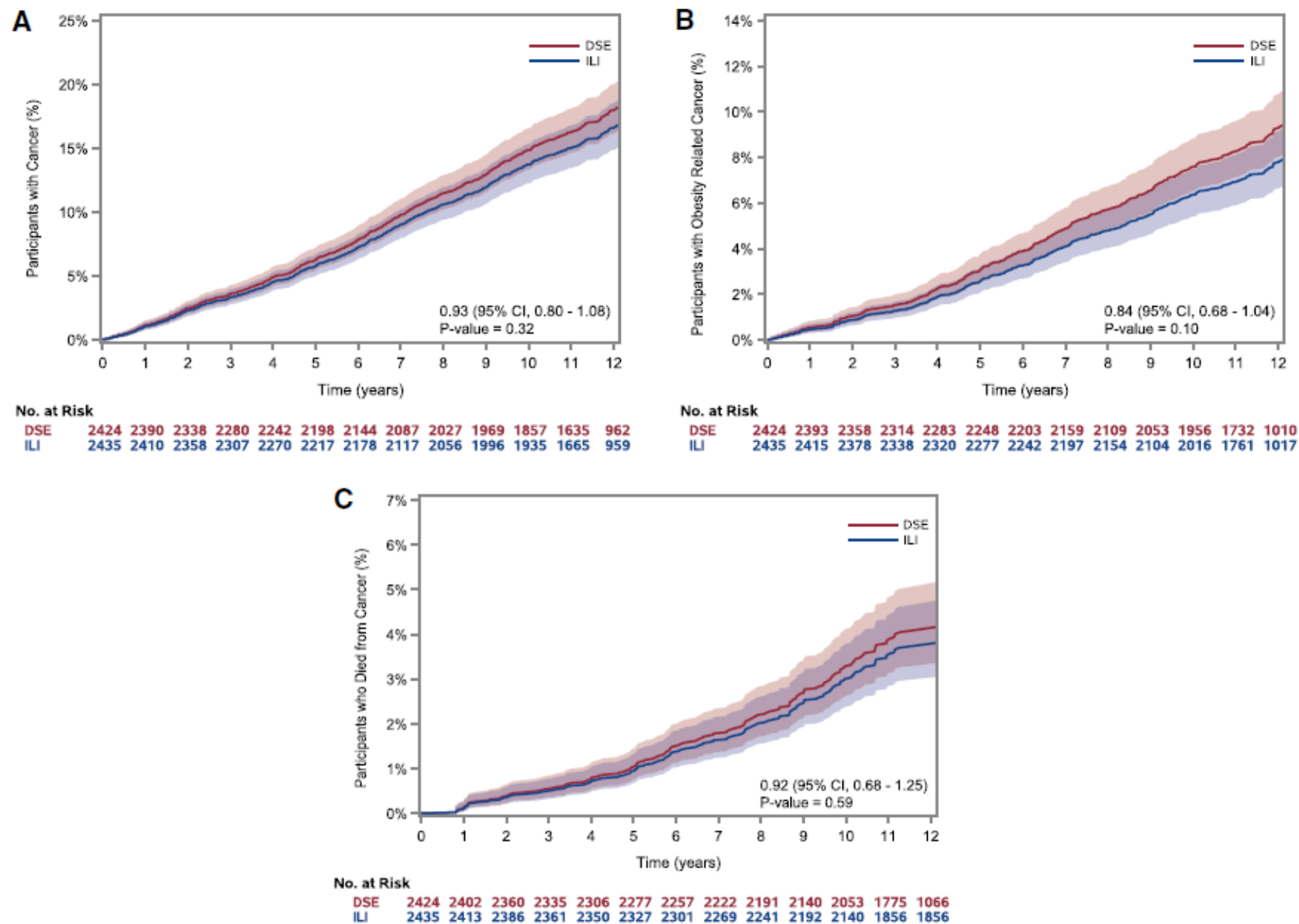
## Riduzione dell'età di screening per CRC negli USA dai 50 ai 45 anni

“more than 1 in 10 colon cancers and nearly 1 in 4 rectal cancers will be diagnosed in people below the traditional screening age”

# Intensive Weight Loss Intervention and Cancer Risk in Adults with Type 2 Diabetes: Analysis of the Look AHEAD Randomized Clinical Trial

*Look AHEAD Research Group, Hsin-Chieh Yeh <sup>1</sup>, John P. Bantle<sup>2</sup>, Maria Cassidy-Begay<sup>3</sup>, George Blackburn<sup>4</sup>, George A. Bray<sup>5</sup>, Tim Byers<sup>6</sup>, Jeanne M. Clark<sup>7</sup>, Mace Coday<sup>8</sup>, Caitlin Egan<sup>9</sup>, Mark A. Espeland<sup>10</sup>, John P. Foreyt<sup>11</sup>, Katelyn Garcia<sup>10</sup>, Valerie Goldman<sup>12</sup>, Edward W. Gregg<sup>13</sup>, Helen P. Hazuda<sup>14</sup>, Louise Hesson<sup>15</sup>, James O. Hill<sup>16</sup>, Edward S. Horton<sup>17</sup>, John M. Jakicic<sup>18</sup>, Robert W. Jeffery<sup>19</sup>, Karen C. Johnson<sup>8</sup>, Steven E. Kahn<sup>20</sup>, William C. Knowler<sup>3</sup>, Mary Korytkowski<sup>21</sup>, Anne Kure<sup>20</sup>, Cora E. Lewis<sup>22</sup>, Christos Mantzoros<sup>4</sup>, Maria Meacham<sup>3</sup>, Maria G. Montez<sup>14</sup>, David M. Nathan<sup>12</sup>, Nicholas Pajewski<sup>10</sup>, Jennifer Patricio<sup>23</sup>, Anne Peters<sup>24</sup>, F. Xavier Pi-Sunyer<sup>23</sup>, Henry Pownall<sup>25</sup>, Donna H. Ryan<sup>5</sup>, Monika Safford<sup>26</sup>, Rebecca L. Sedjo<sup>27</sup>, Helmut Steinburg<sup>28</sup>, Mara Vitolins<sup>29</sup>, Thomas A. Wadden<sup>15</sup>, Lynne E. Wagenknecht<sup>30</sup>, Rena R. Wing<sup>9</sup>, Antonio C. Wolff<sup>31</sup>, Holly Wyatt<sup>32</sup>, and Susan Z. Yanovski<sup>33</sup>*



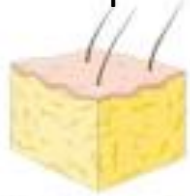


**Figure 2** (A) Cumulative incidence of all cancers. (B) Cumulative incidence of obesity-related cancers. (C) Cumulative probability of cancer mortality.

# Meccanismi biologici obesità-cancro

- 1) iperinsulinemia /IR e alterazioni insulin-like growth factor-I (IGF-I)
- 2) sintesi e metabolismo ormoni sessuali steroidei
- 3) infiammazione cronica subclinica e stress ossidativo
- 4) **alterazioni microambiente/matrice**
- 5) alterazioni del microbioma

Alterata/ridotta produzione adiponectina



↓ adiponectina

Infiemmazione cronica subclinica

↑ citochine pro-infiammatorie, stress ossidativo, IR



Alterazione microbioma



↑ permeabilità intestinale/traslocazione, infiammazione cronica



↑ IR, infiammazione cronica, substrati steroidei

Dieta ricca grassi insaturi

Alterato metabolismo steroidi

↑ estrogeni → endometrio, Mammella post-menopausa



Insulinoresistenza-diabete



↑ IGF, insulina, IGFR, mTOR



↑ angiogenesi, infiammazione cronica, stress ossidativo

Alterazioni microambiente/matrice extracellulare



Promozione  
progressione



# A randomized, phase II, double-blind, placebo-controlled, multicenter, 2x2 factorial design biomarker tertiary prevention trial of low-dose aspirin and metformin in stage I-III colorectal cancer patients. The ASAMET Trial

EudraCT Number: 2015-004824-77

Sponsor's Protocol Code Number: 27UCS2015

Date and Version No: December 18<sup>th</sup>, 2015, Version 0

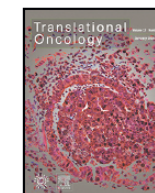
Translational Oncology 13 (2020) 100760



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journal homepage: [www.elsevier.com/locate/tranon](http://www.elsevier.com/locate/tranon)



## Modulating the Distant Spreading of Patient-Derived Colorectal Cancer Cells via Aspirin and Metformin



Gemma Palazzolo<sup>a,\*</sup>, Hilaria Mollica<sup>a</sup>, Valeria Lusi<sup>a</sup>, Mariangela Rutigliani<sup>b</sup>, Martina Di Francesco<sup>a</sup>, Rui Cruz Pereira<sup>a,1</sup>, Marco Filauro<sup>c</sup>, Laura Paleari<sup>d,2</sup>, Andrea DeCensi<sup>e,2</sup>, Paolo Decuzzi<sup>a,2</sup>

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<sup>e</sup> Department of Medicine Area, Medical Oncology Unit, E.O. Ospedali Galliera, Genoa, Italy

## Adipocyte-Induced FABP4 Expression in Ovarian Cancer Cells Promotes Metastasis and Mediates Carboplatin Resistance

Abir Mukherjee<sup>1</sup>, Chun-Yi Chiang<sup>1</sup>, Helen A. Daifotis<sup>1</sup>, Kristin M. Nieman<sup>1</sup>, Johannes F. Fahrmann<sup>2</sup>, Ricardo R. Lastra<sup>3</sup>, Iris L. Romero<sup>1</sup>, Oliver Fiehn<sup>2</sup>, and Ernst Lengyel<sup>1</sup>



Zhao et al. *Journal of Experimental & Clinical Cancer Research* (2020) 39:156  
<https://doi.org/10.1186/s13046-020-01666-z>

Journal of Experimental &  
Clinical Cancer Research

REVIEW

Open Access

## Cancer-associated adipocytes: emerging supporters in breast cancer



Chongru Zhao<sup>†</sup>, Min Wu<sup>†</sup>, Ning Zeng<sup>†</sup>, Mingchen Xiong, Weijie Hu, Wenchang Lv, Yi Yi, Qi Zhang\* and Yiping Wu\*



Review

## Signaling Pathways Induced by Leptin during Epithelial–Mesenchymal Transition in Breast Cancer

Monserrat Olea-Flores<sup>1</sup>, Juan Carlos Juárez-Cruz<sup>1</sup>, Miguel A. Mendoza-Catalán<sup>2</sup> ,  
Teresita Padilla-Benavides<sup>3</sup> and Napoleón Navarro-Tito<sup>1,\*</sup>



RESEARCH ARTICLE

Open Access



# Tall height and obesity are associated with an increased risk of aggressive prostate cancer: results from the EPIC cohort study

Aurora Perez-Cornago<sup>1\*</sup>, Paul N. Appleby<sup>1</sup>, Tobias Pischon<sup>2</sup>, Konstantinos K. Tsilidis<sup>3,4</sup>, Anne Tjønneland<sup>5</sup>, Anja Olsen<sup>5</sup>, Kim Overvad<sup>6</sup>, Rudolf Kaaks<sup>7</sup>, Tilman Kühn<sup>7</sup>, Heiner Boeing<sup>8</sup>, Annika Steffen<sup>8</sup>, Antonia Trichopoulou<sup>9,10</sup>, Pagona Lagiou<sup>9,10,11</sup>, Maria Kritikou<sup>9</sup>, Vittorio Krogh<sup>12</sup>, Domenico Palli<sup>13</sup>, Carlotta Sacerdote<sup>14</sup>, Rosario Tumino<sup>15</sup>, H. Bas Bueno-de-Mesquita<sup>4,16,17</sup>, Antonio Agudo<sup>18</sup>, Nerea Larrañaga<sup>19,20</sup>, Elena Molina-Portillo<sup>20,21</sup>, Aurelio Barricarte<sup>20,22,23</sup>, Maria-Dolores Chirlaque<sup>20,24,25</sup>, J. Ramón Quirós<sup>26</sup>, Pär Stattin<sup>27,28</sup>, Christel Häggström<sup>27,29</sup>, Nick Wareham<sup>30</sup>, Kay-Tee Khaw<sup>31</sup>, Julie A. Schmidt<sup>1</sup>, Marc Gunter<sup>32</sup>, Heinz Freisling<sup>32</sup>, Dagfinn Aune<sup>4</sup>, Heather Ward<sup>4</sup>, Elio Riboli<sup>4</sup>, Timothy J. Key<sup>1</sup> and Ruth C. Travis<sup>1</sup>



RESEARCH ARTICLE

## Adipocyte Secreted Factors Enhance Aggressiveness of Prostate Carcinoma Cells

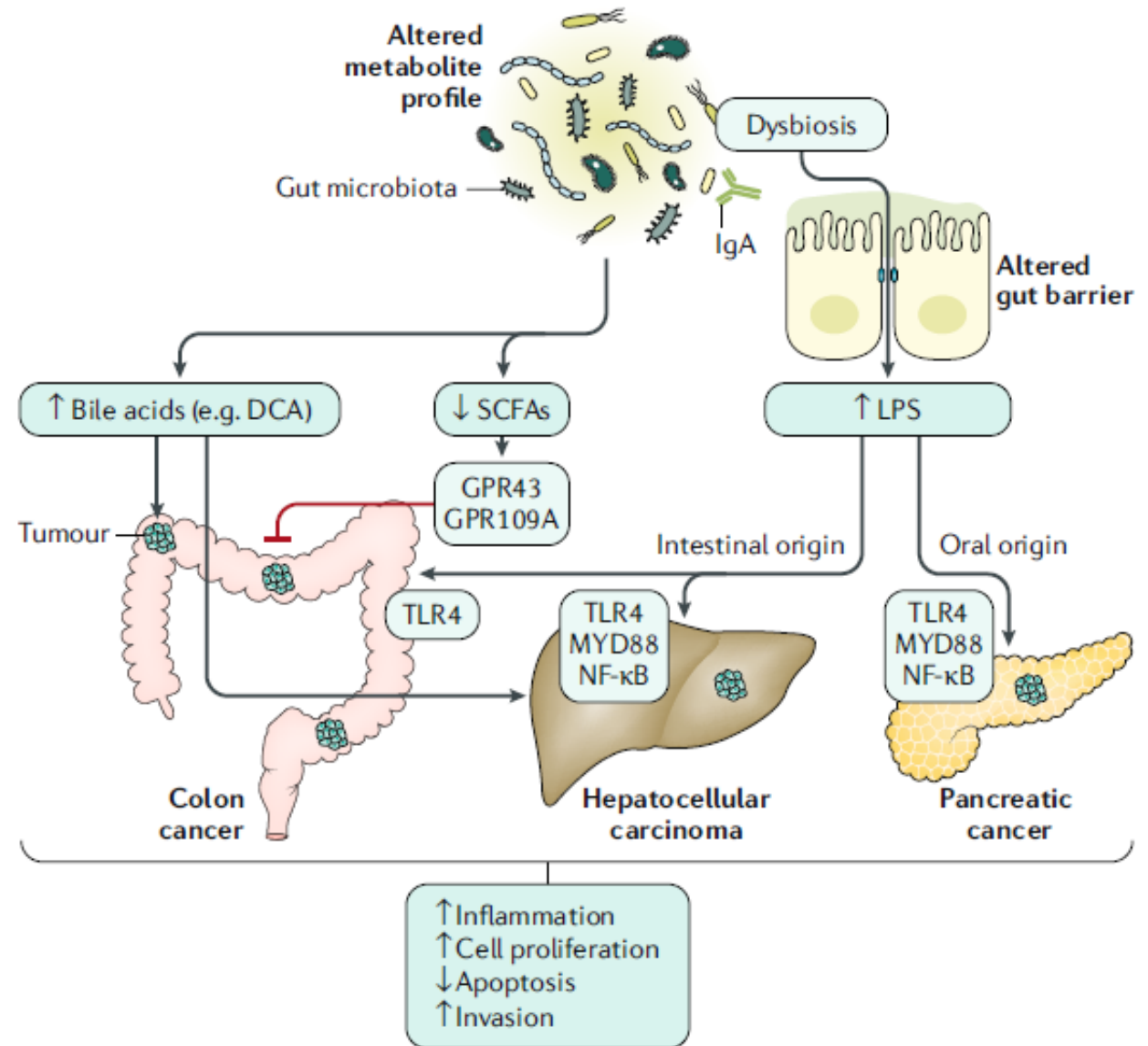
Ângela Moreira<sup>1</sup>, Sofia S. Pereira<sup>1</sup>, Madalena Costa<sup>1</sup>, Tiago Morais<sup>1</sup>, Ana Pinto<sup>1</sup>, Rúben Fernandes<sup>2,3</sup>, Mariana P. Monteiro<sup>1\*</sup>

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Gut microbiota-mediated inflammation in obesity: a link with gastrointestinal cancer



*Grazie per l'attenzione!*

