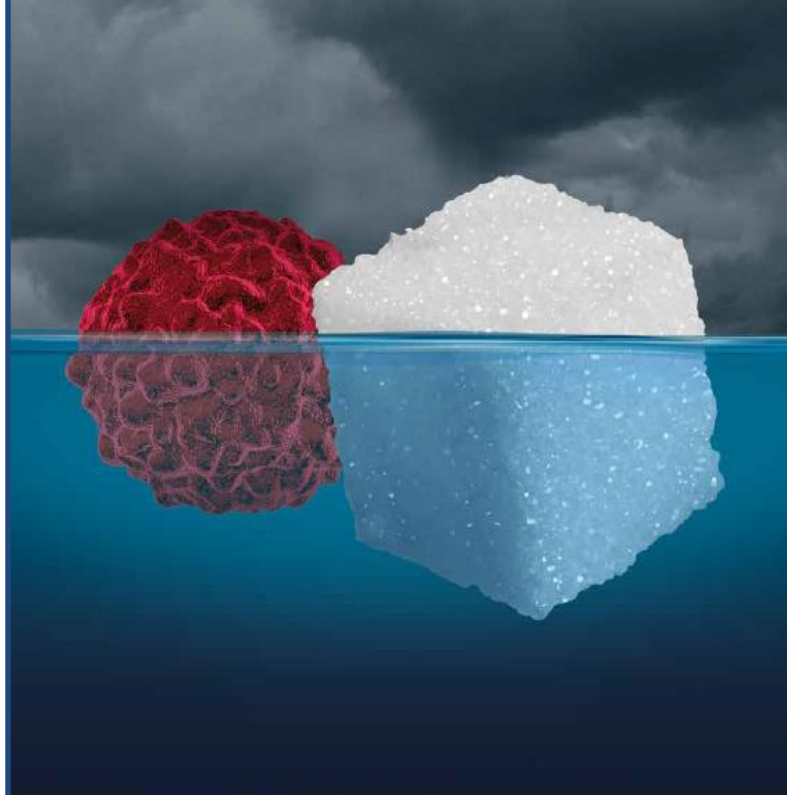




**DIABETE E TUMORI NELLA PRATICA CLINICA:
RILEVANZA, CRITICITÀ, SOLUZIONI**

ROMA, 9 Novembre 2019

UNAHOTELS DECÒ
Via Giovanni Amendola, 57



**Diabete e tumori : aspetti
epidemiologici nazionali e
internazionali.**

*Valeria Manicardi
Coordinatore Annali AMD
Roma 9 nov 2019*

Modulo dichiarazione conflitto di interessi

Tutti i rapporti finanziari intercorsi negli ultimi due anni devono essere dichiarati.

- ☐ Non ho rapporti (finanziari o di altro tipo) con le Aziende del farmaco
- ☒ Ho / ho avuto rapporti (finanziari o di altro tipo) con le Aziende del farmaco

Relationship	Company/Organization
Docenza	MSD
Docenza	Roche Diagnostic
Docenza	Astrazeneca



Diabete e tumori : aspetti epidemiologici nazionali e internazionali.

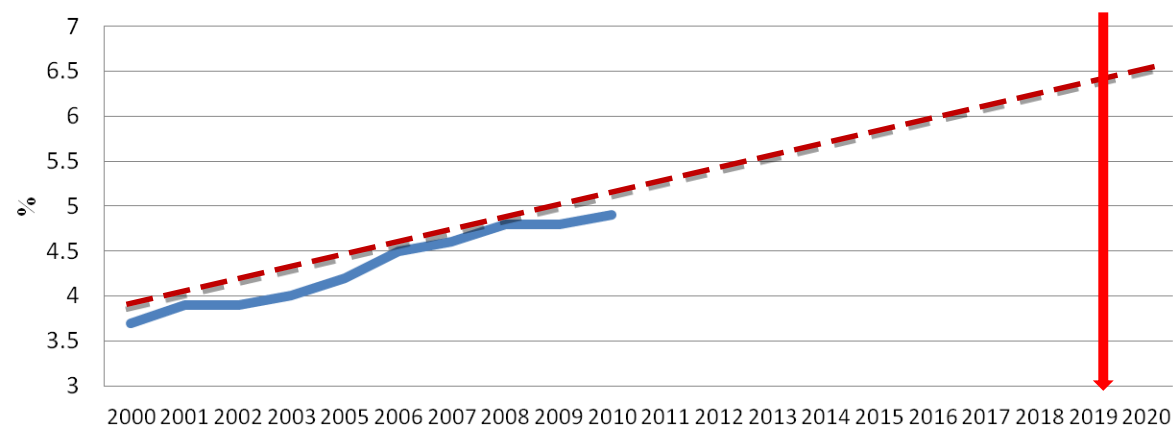


- **Nel 1960 una associazione tra le due patologie venne evidenziata per la prima volta** da Joslin et al. (Joslin Clinic)
- **Nel 2010 – Nicolucci et al hanno pubblicato su ACTA DIABETOLOGICA una REVIEW su Diabete e Neoplasie , analizzate per sede, dimostrando l'aumentato rischio per molte sedi, e la riduzione del rischio per il T. della Prostata**
- **Nel 2010 – Diabetes and Cancer : A consensus Report – Am Diabetes Association and Am Cancer Society - CA CANCER J Clin 2010;60:207 -221**
- **L'AACE (American Association Clinical Endocrinology) in una review (Endocr Pract 2013) ha confermato l'associazione tra obesità, diabete di tipo 2 e diversi tipo di cancro.**



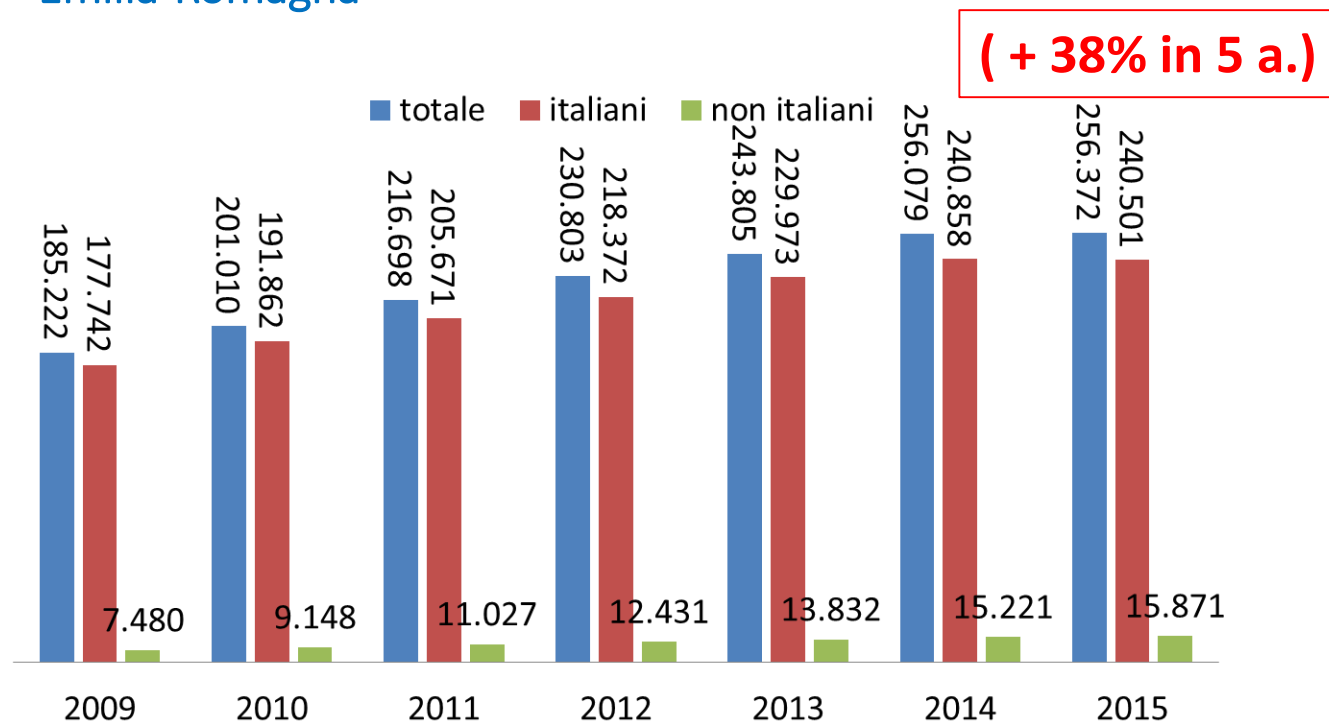
Il diabete: una pandemia

Andamento della prevalenza del diabete in Italia:
2001-2010 (ISTAT)



3,1% → 4,9% → 7%

Popolazione adulta con diabete (≥ 18 anni), residente in Emilia-Romagna



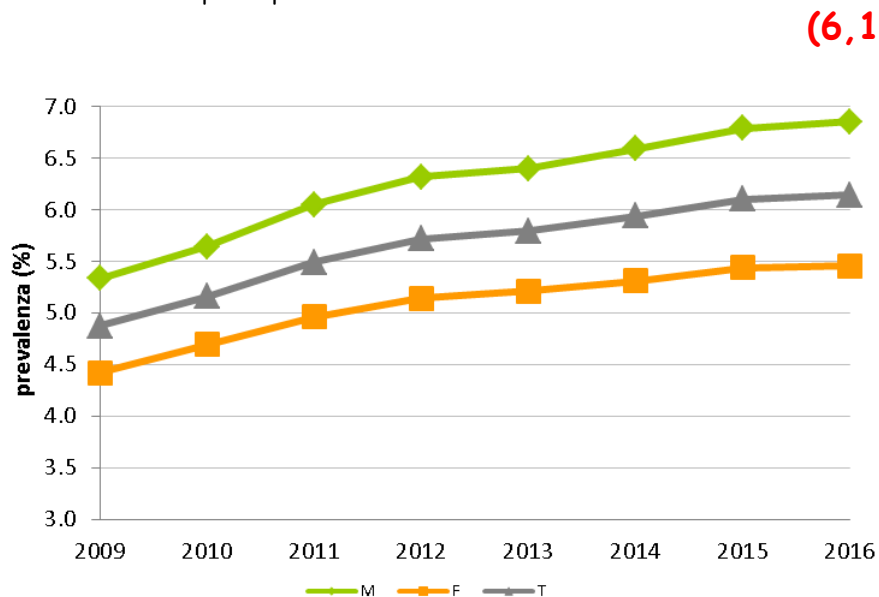
Lucia Nobilio
Agenzia Sanitaria e Sociale Regionale



PREVALENZA a REGGIO E.



Trend temporali per anno



(6,1%)



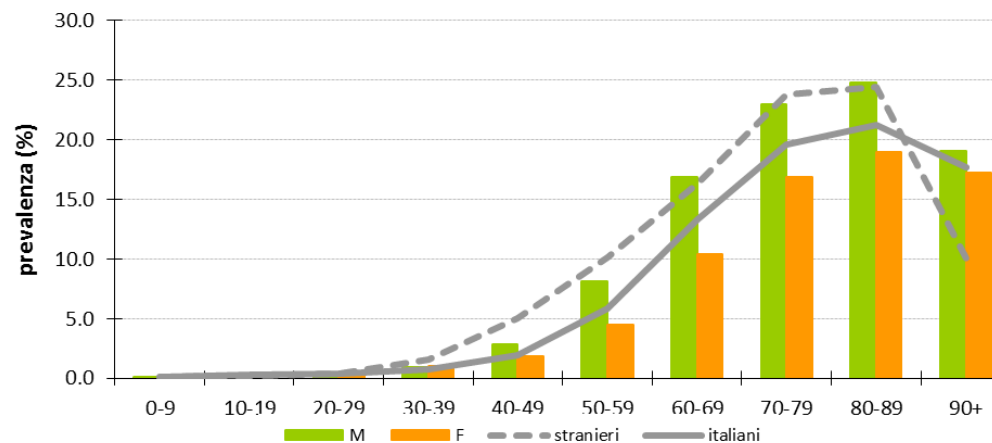
Anno 2016

- 2583 (4%) stranieri
- 30148 (6,5%) italiani)

Prevalenza ed Età

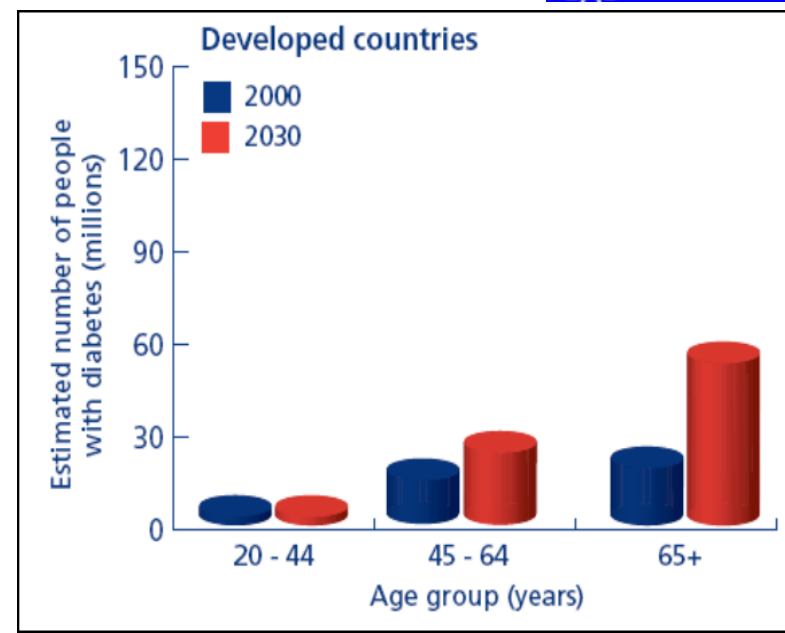
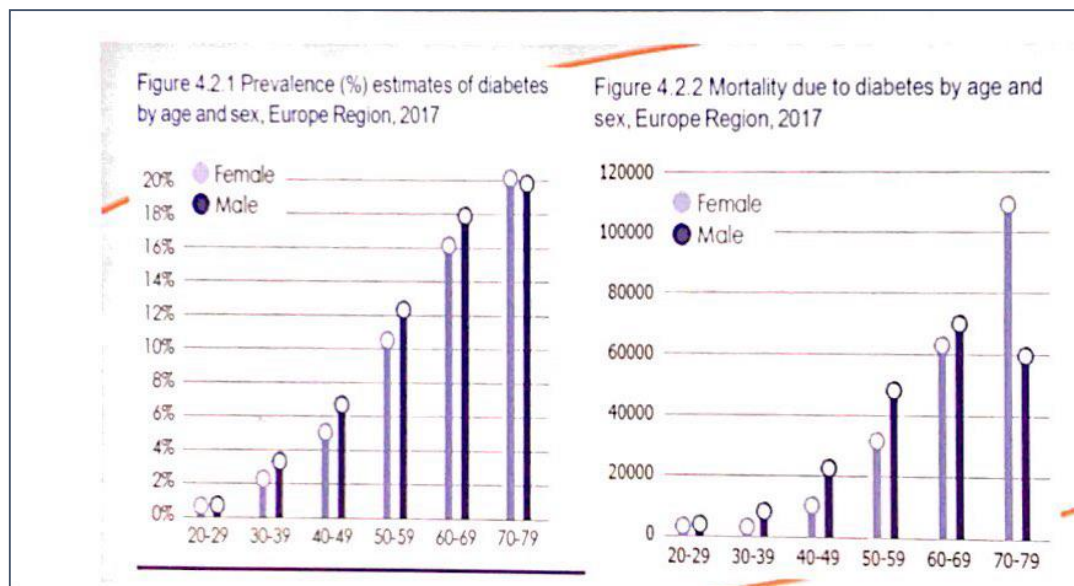
Anno 2016

- 17924 (6,9%) maschi
- 14807 (5,5%) femmine
- 32731 (6,1%) totale (intera provincia di RE)





Il Diabete negli anziani in Europa





Diabete e Tumori : I numeri



Giovannucci E, Diabetes Care 2010; 33: 1674– 1685

Nicolucci A, Acta Diabetol 2010; 47: 87– 95

Jemal A, CA Cancer J Clin 2011; 61: 69– 90

Diabete

- 287 milioni di casi (6.6%) nel mondo
- Dodicesima causa principale di morte
- **Prevalenza in età > 65 anni: 17%**

- 8-18% dei pazienti neoplastici è diabetico

- **L'ETA' può spiegare l'aumento di associazione ?**

Cancro

- 12.7 milioni di nuove diagnosi/ anno nel mondo
- Seconda causa principale di morte: 7.8 milioni/ anno
- **60% dei casi diagnosticati in età > 65 anni**



Esistono fattori di rischio comuni fra diabete e neoplasie ?



Giovannucci E, Diabetes Care 2010; 33: 1674– 1685

NON MODIFICABILI

Età
Sesso
Razza/ etnia

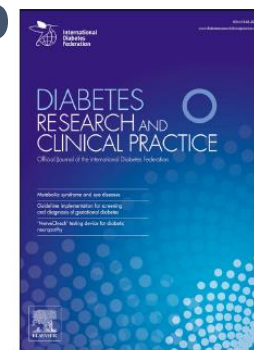
MODIFICABILI

- Obesità sovrappeso
- Abitudini dietetiche
- Sedentarietà
- Fumo di tabacco

Review

What the oncologist can learn from diabetes studies: epidemiology, prevention, management, cure

Adriana Albini, Marco Gallo



High sugar content of various foods is a “carcinogen”, linked to metabolic syndrome, obesity and diabetes [17, 18] and high IGF levels are associated with elevated cancer risk. Thus, the oncologist could learn from the diabetes field. *Diabetes Research and Clinical Practice* (2018),



Diabetes and Cancer: A Consensus Report

Edward Giovannucci, MD, ScD¹; David M. Harlan, MD²; Michael C. Archer, MA, PhD, DSC³; Richard M. Bergenstal, MD⁴; Susan M. Gapstur, PhD⁵; Laurel A. Habel, PhD⁶; Michael Pollak, MD⁷; Judith G. Regensteiner, PhD⁸; Douglas Yee, MD⁹

Abstract

Epidemiologic evidence suggests that cancer incidence is associated with diabetes as well as certain diabetes risk factors and treatments. This consensus statement of experts assembled jointly by the American Diabetes Association and the American Cancer Society reviews the state of science concerning 1) the association between diabetes and cancer incidence or prognosis; 2) risk factors common to both diabetes and cancer; 3) possible biologic links between diabetes and cancer risk; and 4) whether diabetes treatments influence the risk of cancer or cancer prognosis. In addition, key unanswered questions for future research are posed. *CA Cancer J Clin* 2010;60:207-221. © 2010 by the American Diabetes Association and the American Cancer Society, Inc.

the American Diabetes Association and the American Cancer Society convened a consensus development conference in December 2009. After a series of scientific presentations by experts in the field, the writing group independently developed this consensus report to address the following questions:

- 1) Is there a meaningful association between diabetes and cancer incidence or prognosis?
- 2) What risk factors are common to both diabetes and cancer?
- 3) What are possible biologic links between diabetes and cancer risk?
- 4) Do diabetes treatments influence the risk of cancer or cancer prognosis?
- 5) Metformina e prevenzione del cancro
- 6) Insulina e aumento del rischio di cancro



Diabete e tumori

Quale relazione ?

TABLE 1. Summary and Recommendations

● Diabetes (primarily type 2) is associated with an increased risk of some cancers (<u>liver, pancreas, endometrium, colon/rectum, breast, and bladder</u>). Diabetes is associated with a <u>reduced risk of prostate cancer</u>. For some other cancer sites, there appears to be no association or the evidence is inconclusive.
● The association between diabetes and some cancers may be due in part to shared risk factors between the 2 diseases such as aging, obesity, diet, and physical inactivity.
● Possible mechanisms for a direct link between diabetes and cancer include hyperinsulinemia, hyperglycemia, and inflammation.
● Healthful diet, physical activity, and weight management reduce the risk and improve outcomes of type 2 diabetes and some forms of cancer and should be promoted for all.
● Patients with diabetes should be strongly encouraged by their health care professionals to undergo appropriate cancer screenings as recommended for all people of their age and sex.
● The evidence for specific drugs affecting cancer risk is limited, and observed associations may have been confounded by indications for specific drugs, effects on other cancer risk factors such as body weight and hyperinsulinemia, and the complex progressive nature of hyperglycemia and pharmacotherapy in type 2 diabetes.
● Although still limited, early evidence suggests that metformin is associated with a lower risk of cancer and that exogenous insulin is associated with an increased cancer risk. Further research is needed to clarify these issues and evaluate if insulin glargine is more strongly associated with cancer risk compared with other insulins.
● Cancer risk should not be a major factor when choosing between available diabetes therapies for the average patient. For selected patients with a very high risk of cancer occurrence (or for recurrence of specific cancer types), these issues may require more careful consideration.



Obesità, sovrappeso: FdR comune tra diabete e tumori



Diabete

- Obesità
- Obesità viscerale
- Insulino resistenza

Neoplasie

- Incidenza associata a sovrappeso:
 - *Mammella in post menopausa*
 - *Colon/ retto*
 - *Endometrio*
 - *Pancreas*
 - *Esofago*
 - *Rene*
 - *Colecisti*
 - *Fegato*
- Incidenza associata a incremento ponderale:
 - *Mammella*
- Incidenza associata a obesità viscerale:
 - *Colon*
- Aumento di mortalità associato a sovrappeso:
 - *Prostata*

Epidemiological aspects of neoplasms in diabetes

Antonio Nicolucci

- La relazione tra Diabete e Cancro non si limita ai fattori Casuali .
- Il metabolismo del Glucosio è un fattore di rischio indipendente per la insorgenza di cancro nel DT2:
 - iperglicemia
 - Insulino - Resistenza
 - iperinsulinismo

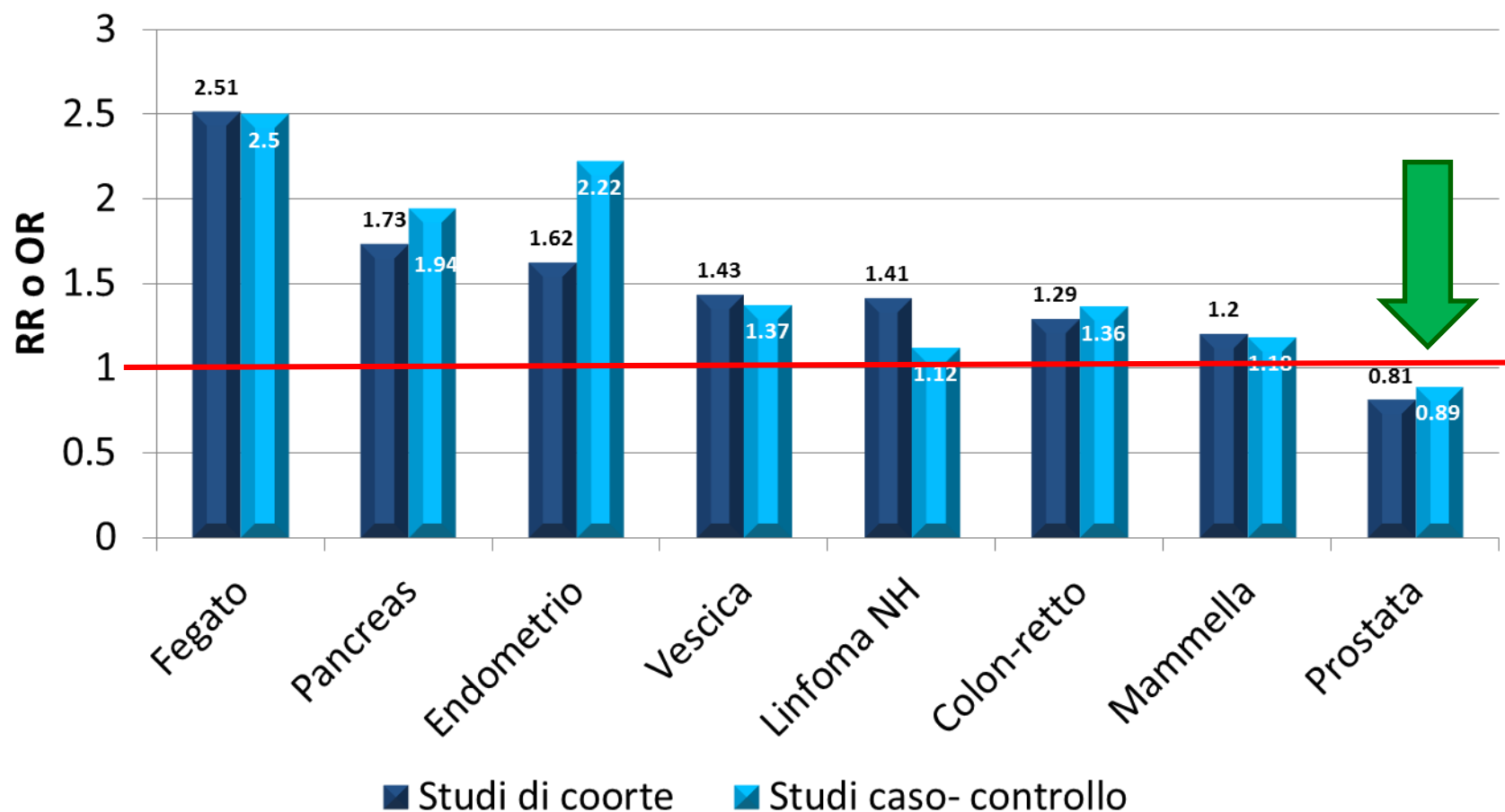
Table 1 Risk of developing different neoplasms for individuals with diabetes when compared to controls: results of meta-analyses

Cancer site	Relative risk (RR or OR)	Reference
<i>Pancreas</i>		
Cohort studies (<i>N</i> = 19)	1.73 (1.59–1.88)	6
Case-control studies (<i>N</i> = 17)	1.94 (1.53–2.46)	
<i>Colon-rectum</i>		
Cohort studies (<i>N</i> = 9)	1.29 (1.16–1.43)	9
Case-control studies (<i>N</i> = 6)	1.36 (1.23–1.50)	
<i>Liver</i>		
Cohort studies (<i>N</i> = 7)	2.51 (1.9–3.2)	12
Case-control studies (<i>N</i> = 13)	2.50 (1.8–3.5)	
<i>Breast</i>		
Cohort studies (<i>N</i> = 15)	1.20 (1.11–1.30)	16
Case-control studies (<i>N</i> = 5)	1.18 (1.05–1.32)	
<i>Endometrium</i>		
Cohort studies (<i>N</i> = 3)	1.62 (1.21–2.16)	22
Case-control studies (<i>N</i> = 13)	2.22 (1.80–2.74)	
<i>Bladder</i>		
Cohort studies (<i>N</i> = 3)	1.43 (1.18–1.74)	24
Case-control studies (<i>N</i> = 7)	1.37 (1.04–1.80)	
<i>Prostate</i>		
Cohort studies (<i>N</i> = 10)	0.81 (0.71–0.92)	19
Case-control studies (<i>N</i> = 9)	0.89 (0.72–1.11)	
<i>Non-Hodgkin's lymphoma</i>		
Cohort studies (<i>N</i> = 5)	1.41 (1.07–1.88)	23
Case-control studies (<i>N</i> = 11)	1.12 (0.95–1.31)	





Il diabete tipo 2 è associato ad un aumento del rischio di alcune neoplasie

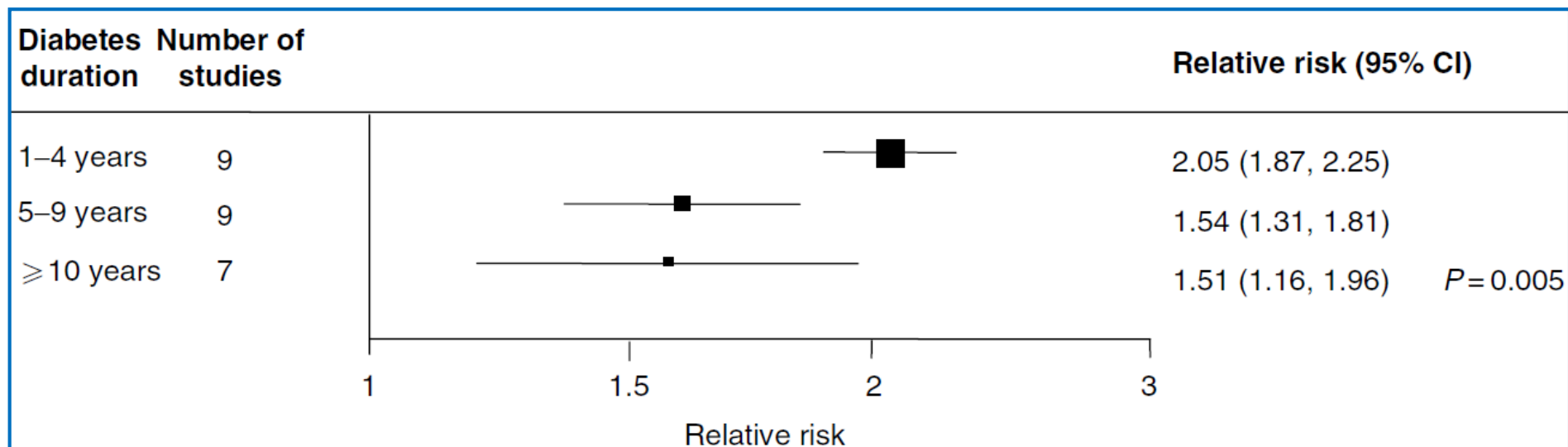




Carcinoma del **pancreas**: causa o effetto?

Durata del diabete e Reverse causality

Relative risk of pancreatic cancer by duration of diabetes



Huxley R, British Journal of Cancer 2005; 92: 2076– 2083

E' insorto prima il Diabete o il Tumore ?



HCC e diabete: fattori confondenti

Table 2 Results from separate multiple logistic regression analyses examining the risk of HCC (v non-cancer controls) with each of diabetes, HCV, HBV, alcoholic liver disease, and haemochromatosis

	Adjusted OR	95% CI	p Value
Diabetes	3.08	2.74–3.46	<0.0001
Excluding HCV (n=7758)	2.99	2.64–3.40	<0.0001
Excluding HBV (n=8048)	3.11	2.76–3.50	<0.0001
Excluding alcoholic liver disease (n=7769)	2.94	2.59–3.34	<0.0001
Excluding haemochromatosis (n=8156)	3.08	2.73–3.47	<0.0001
Excluding patients without any of the above risk factors (n=7042)	2.87	2.49–3.30	<0.0001
HCV without diabetes	24.42	17.49–34.11	<0.0001
HCV and diabetes	36.88	2.64–3.40	<0.0001
HBV	23.94	13.65–41.99	<0.0001
Alcohol liver disease	69.62	44.92–107.90	<0.0001
Haemochromatosis	8.88	5.24–15.07	<0.0001

HCC, hepatocellular carcinoma; HBV, hepatitis B virus; HCV, hepatitis C virus; OR, odds ratio; 95% CI, 95% confidence interval.

All models adjusted for age, sex, race, SEER registry, and Medicare/Medicaid dual enrolment (n=8244).

Interaction terms between HBV and diabetes, alcoholic liver disease and diabetes, and haemochromatosis and diabetes were not significant at a p value of <0.05.



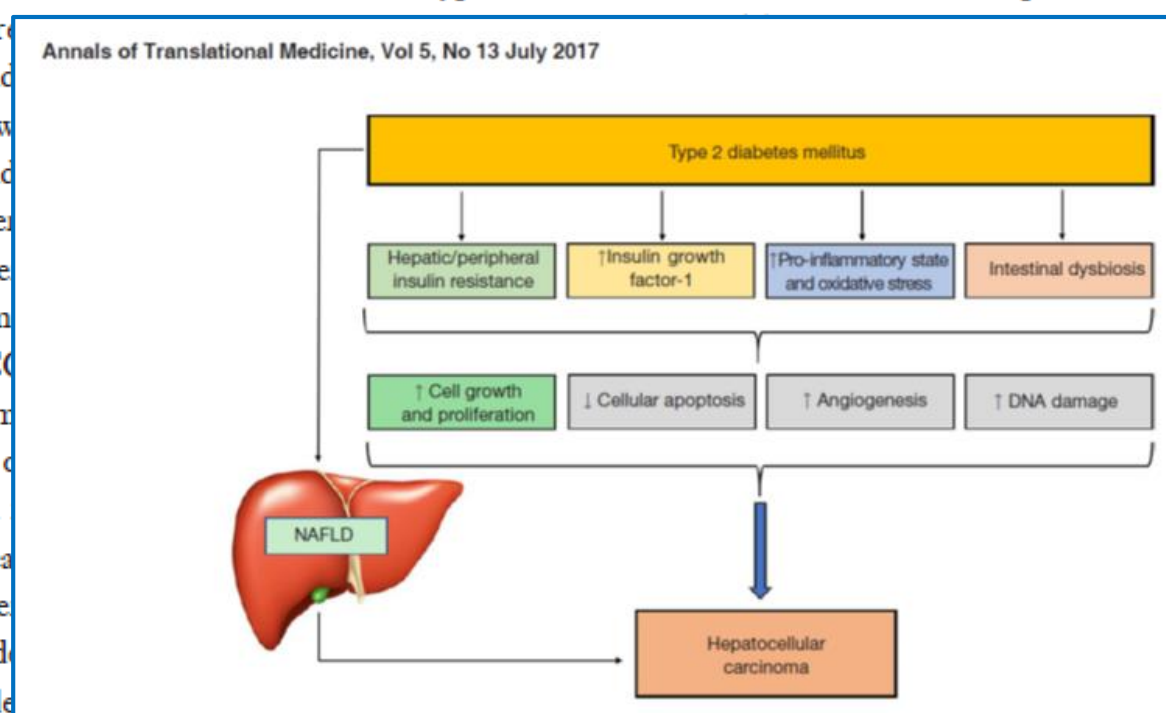
Type 2 diabetes mellitus and risk of hepatocellular carcinoma: spotlight on nonalcoholic fatty liver disease

Alessandro Mantovani, Giovanni Targher

Abstract: The incidence of both type 2 diabetes mellitus (T2DM) and multiple cancer types are rapidly

increasing. There is a positive association between increased risk of hepatocellular carcinoma (HCC) and T2DM, obesity and causes the release of putative agents on the risk of developing HCC.

Annals of Translational Medicine, Vol 5, No 13 July 2017



with an increased relative association. However, due to selection bias and confounding, a number of studies have shown a lower risk of HCC in individuals with T2DM or insulin resistance. In this review, we discuss the putative mechanisms underlying the association between T2DM, obesity and causes the release of putative agents on the risk of developing HCC.

Keywords: Diabetes; cancer; hepatocellular carcinoma (HCC); nonalcoholic fatty liver disease (NAFLD)



HCC , NAFLD e Diabete



REVIEW

Ann Transl Med 2017;5(13):270

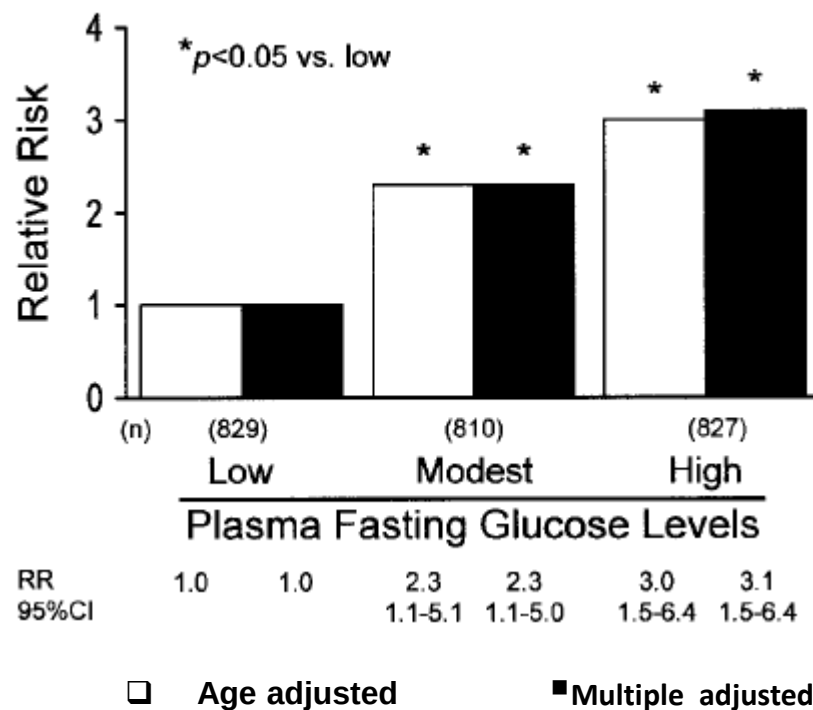
- Tutti gli studi sono concordi nel dimostrare l'aumento di rischio di HCC nel DT2 (x 2 , x 3)
- La presenza di **NAFLD** (e di **NASH** con vari gradi di fibrosi) aumenta il rischio di HCC
- Il rischio è aumentato nei trattati con SU e Insulina
- Ed è ridotto nei trattati con Metformina



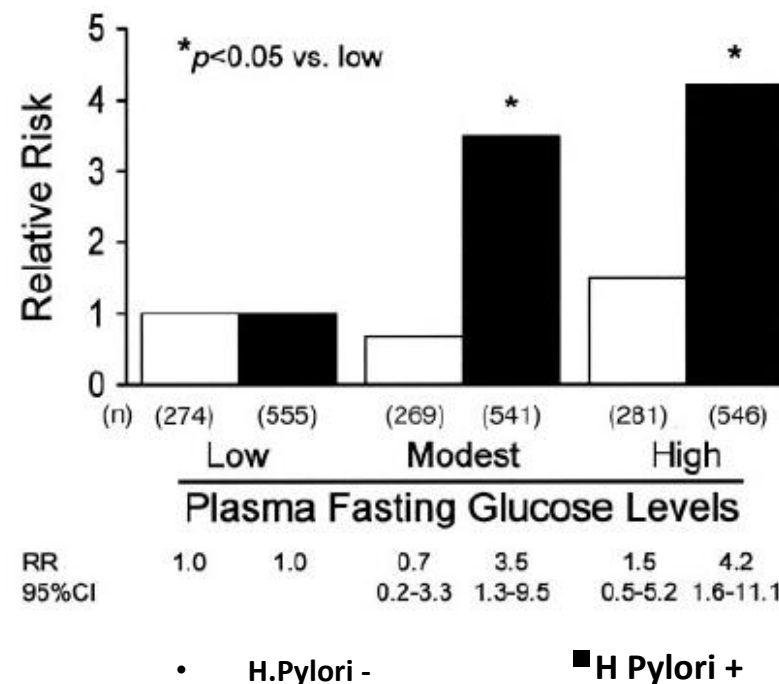
Carcinoma dello stomaco

Hisayama Study

Glicemia e incidenza di carcinoma gastrico



Glicemia, H. pylori ed incidenza di carcinoma gastrico



Yamagata H, Diabetes Care 2005; 28: 789– 794



Diabetes Mellitus Increases Risk of Gastric Cancer After *Helicobacter pylori* Eradication: A Territory-wide Study With Propensity Score Analysis

<https://doi.org/10.2337/dc19-0437>

Ka Shing Cheung,¹ Esther W. Chan,²
Lijia Chen,¹ Wai Kay Seto,¹ Ian C.K. Wong,^{2,3}
and Wai K. Leung¹

Studio retrospettivo
Paz trattati per HP
Follow up di 7 anni

RESEARCH DESIGN AND METHODS

This was a territory-wide cohort study of patients aged ≥ 45 years who had received clarithromycin-based triple therapy for HP infection between 2003 and 2012 in Hong Kong. Data were retrieved from a public electronic health database. Observation started from receipt of therapy for HP infection to GC diagnosis, death, or the end

Table 3—Association between DM and GC (sensitivity analysis including GC cases diagnosed within 1st year and patients requiring retreatment but excluding all other malignancy)

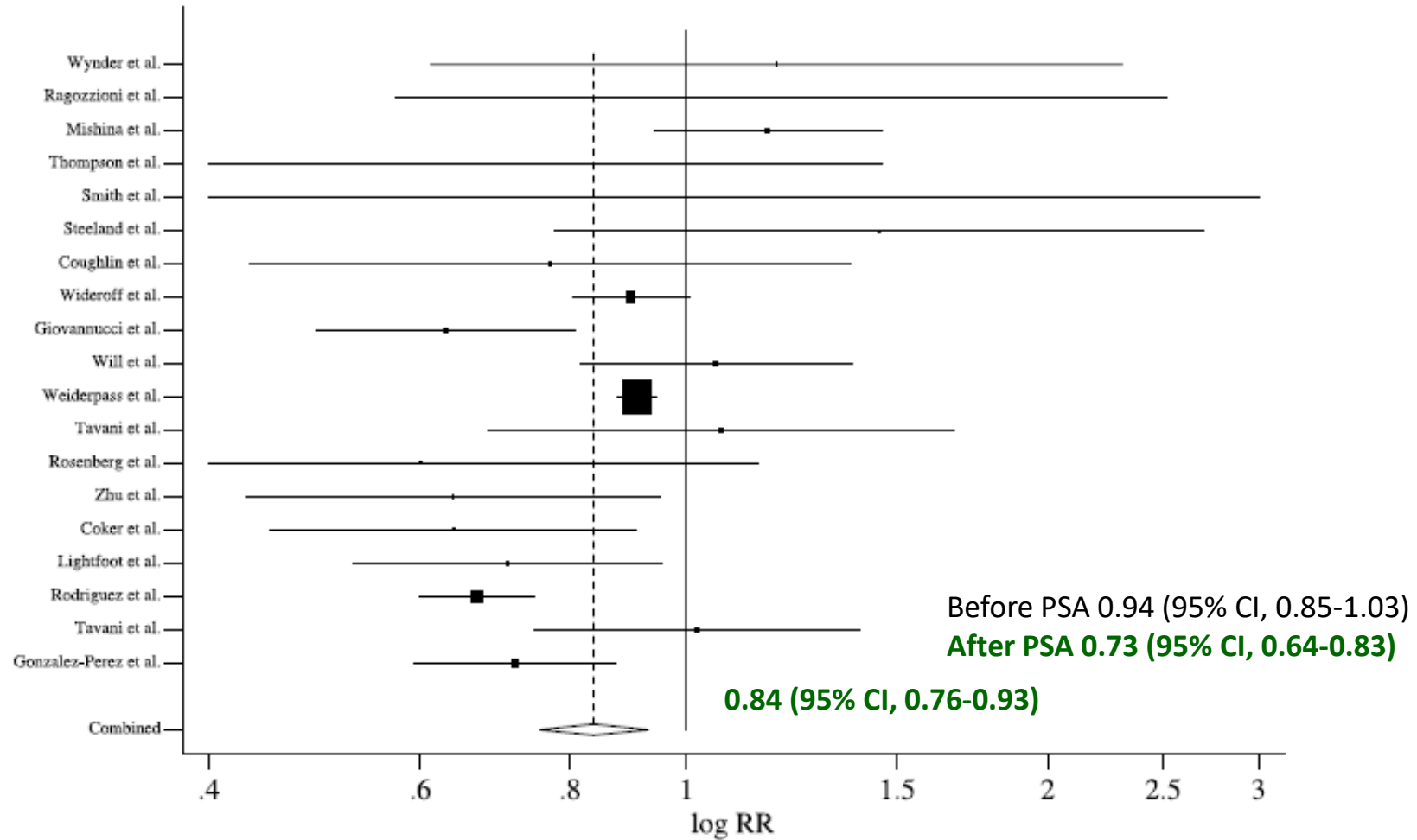
	Patients without DM and GC, n	Patients with DM and GC, n	Adjusted HR*	95% CI	P value
Entire cohort# (n = 48,211; GC = 320)	40,598 (GC = 250)	7,613 (GC = 70)	2.12	1.54–2.93	<0.001
<i>H. pylori</i> treatment status#					
Single-treatment group (n = 41,932; GC = 265)	35,764 (GC = 210)	6,168 (GC = 55)	1.98	1.37–2.85	<0.001
Retreatment group (n = 6,279; GC = 55)	4,834 (GC = 40)	1,445 (GC = 15)	2.54	1.27–5.07	0.008

*Adjustment for age at receipt of *H. pylori* eradication therapy, sex, smoking, alcohol use, history of gastric and duodenal ulcers, other comorbidities

Il DMT2 è un FdR per Comparsa di Cancro del Cardias (HR:3.4), soprattutto in paz mal controllati e senza ter con Metformina (2.59 vs 1.28)



Carcinoma della prostata



ARTICLE

Cancer incidence in persons with type 1 diabetes: a five-country study of 9,000 cancers in type 1 diabetic individuals

Bendix Carstensen¹ · Stephanie H Read² · Søren Friis³ · Reijo Sund⁴ · Ilmo Keskimäki⁵ · Ann-Marie Svensson⁶ · Rickard Ljung⁷ · Sarah H Wild² · Joannes J Kerssens⁸ · Jessica L Harding⁹ · Dianna J Magliano⁹ · Soffia Gudbjörnsdóttir⁶ ·
on behalf of the Diabetes and Cancer Research Consortium

Diabetologia (2016) 59:980–988

Abstract

Aims/hypothesis An excess cancer incidence of 20–25% has been identified among persons with diabetes, most of whom have type 2 diabetes. We aimed to describe the association between type 1 diabetes and cancer incidence.

Methods Persons with type 1 diabetes were identified from five nationwide diabetes registers: Australia (2000–2008), Denmark (1995–2014), Finland (1972–2012), Scotland (1995–2012) and Sweden (1987–2012). Linkage to national cancer registries provided the numbers of incident cancers in people with type 1 diabetes and in the general population. We used Poisson models with adjustment for age and date of follow up to estimate hazard ratios for total and site-specific cancers.

Results A total of 9,149 cancers occurred among persons with type 1 diabetes in 3.9 million person-years. The median age at cancer diagnosis was 51.1 years (interquartile range 43.5–59.5). The hazard ratios (HRs) (95% CIs) associated with type

1 diabetes for all cancers combined were 1.01 (0.98, 1.04) among men and 1.07 (1.04, 1.10) among women. HRs were increased for cancer of the stomach (men, HR 1.23 [1.04, 1.46]; women, HR 1.78 [1.49, 2.13]), liver (men, HR 2.00 [1.67, 2.40]; women, HR 1.55 [1.14, 2.10]), pancreas (men, HR 1.53 [1.30, 1.79]; women, HR 1.25 [1.02, 1.53]), endometrium (HR 1.42 [1.27, 1.58]) and kidney (men, HR 1.30 [1.12, 1.49]; women, HR 1.47 [1.23, 1.77]). Reduced HRs were found for cancer of the prostate (HR 0.56 [0.51, 0.61]) and breast (HR 0.90 [0.85, 0.94]). HRs declined with increasing diabetes duration.

Conclusion Type 1 diabetes was associated with differences in the risk of several common cancers; the strength of these associations varied with the duration of diabetes.

Keywords Cancer incidence · Cancer rate ratio · Cancer subtypes · Diabetes duration

5 registri Nazionali : 9149 eventi in 3,9 mln di anni – persona

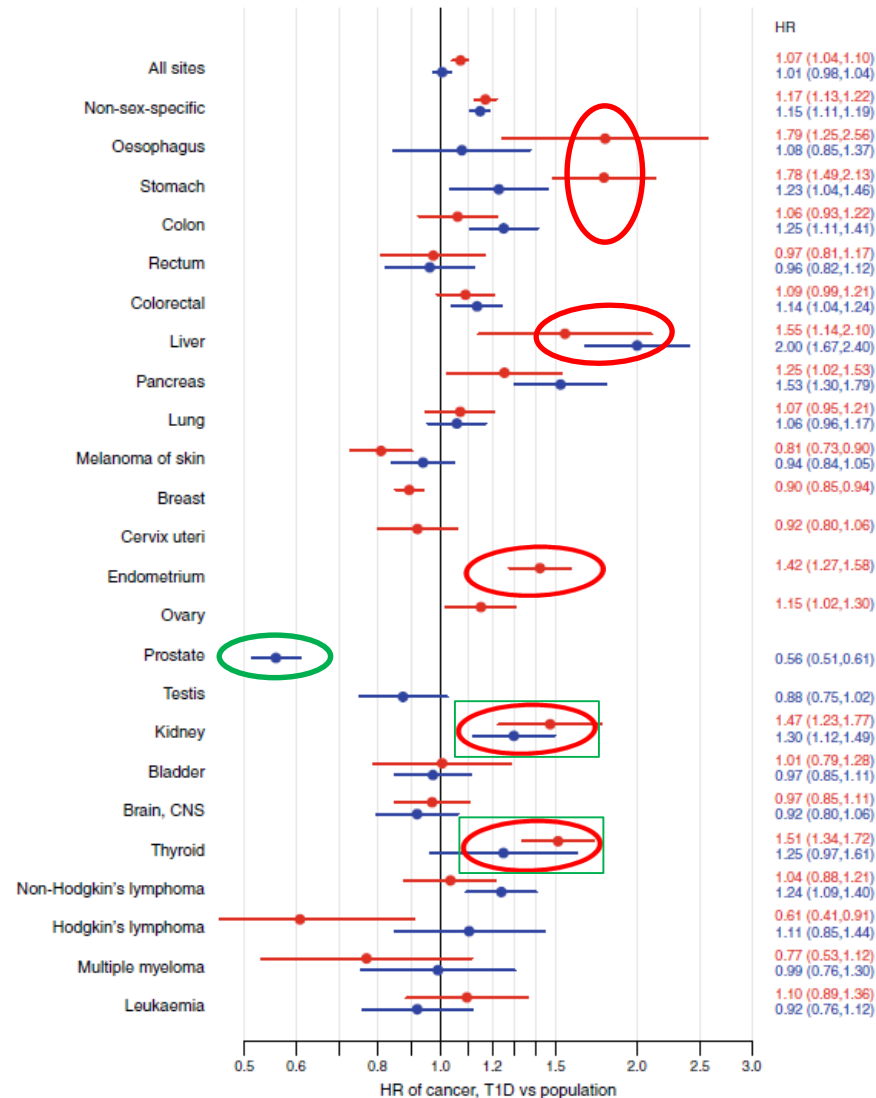
Diabete e Cancro nel DT1

Diabetologia (2016) 59:980–988

Diabetologia (2016) 59:980–988

985

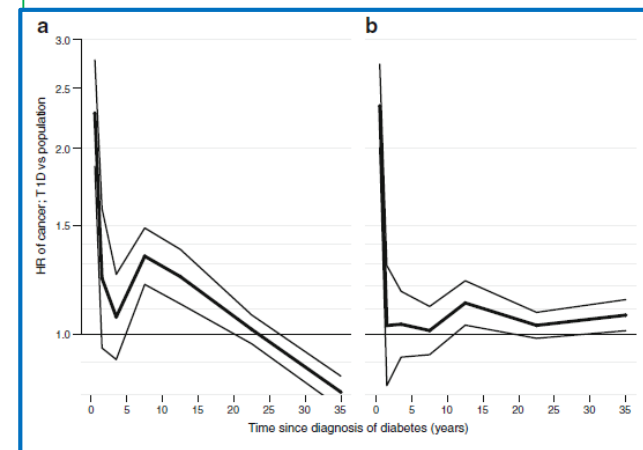
Fig. 2 HRs (with 95% CIs) of site-specific cancers associated with type 1 diabetes in men (blue) and women (red) obtained from the analysis of combined country data. HRs are presented on a logarithmic scale. CNS, central nervous system; T1D, type 1 diabetes



DT1: stesse sedi del DT2

Incidenza molto più alta alla diagnosi, poi in riduzione

Fig. 3 HR (95% CI) of all cancers by duration of diabetes in men (a) and women (b)





Diabetologia (2010) 53:1867–1876

DOI 10.1007/s00125-010-1796-7

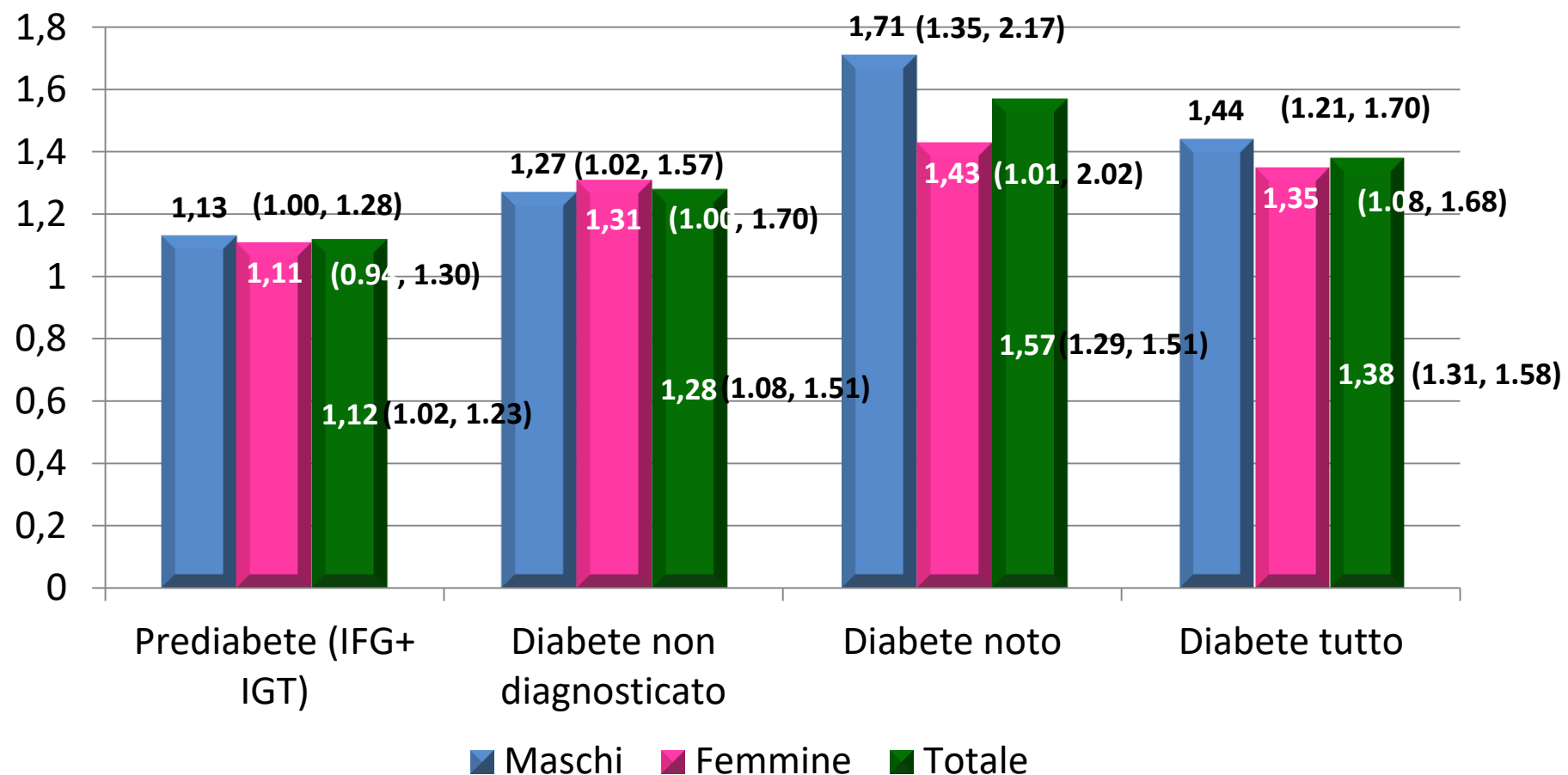
ARTICLE

Diabetes, prediabetes and cancer mortality

**X. H. Zhou • Q. Qiao • B. Zethelius • K. Pyörälä •
S. Söderberg • A. Pajak • C. D. A. Stehouwer •
R. J. Heine • P. Jousilahti • G. Ruotolo • P. M. Nilsson •
G. Calori • J. Tuomilehto •
for the DECODE Study Group**



HR per mortalità per neoplasie per categorie di tolleranza ai CHO



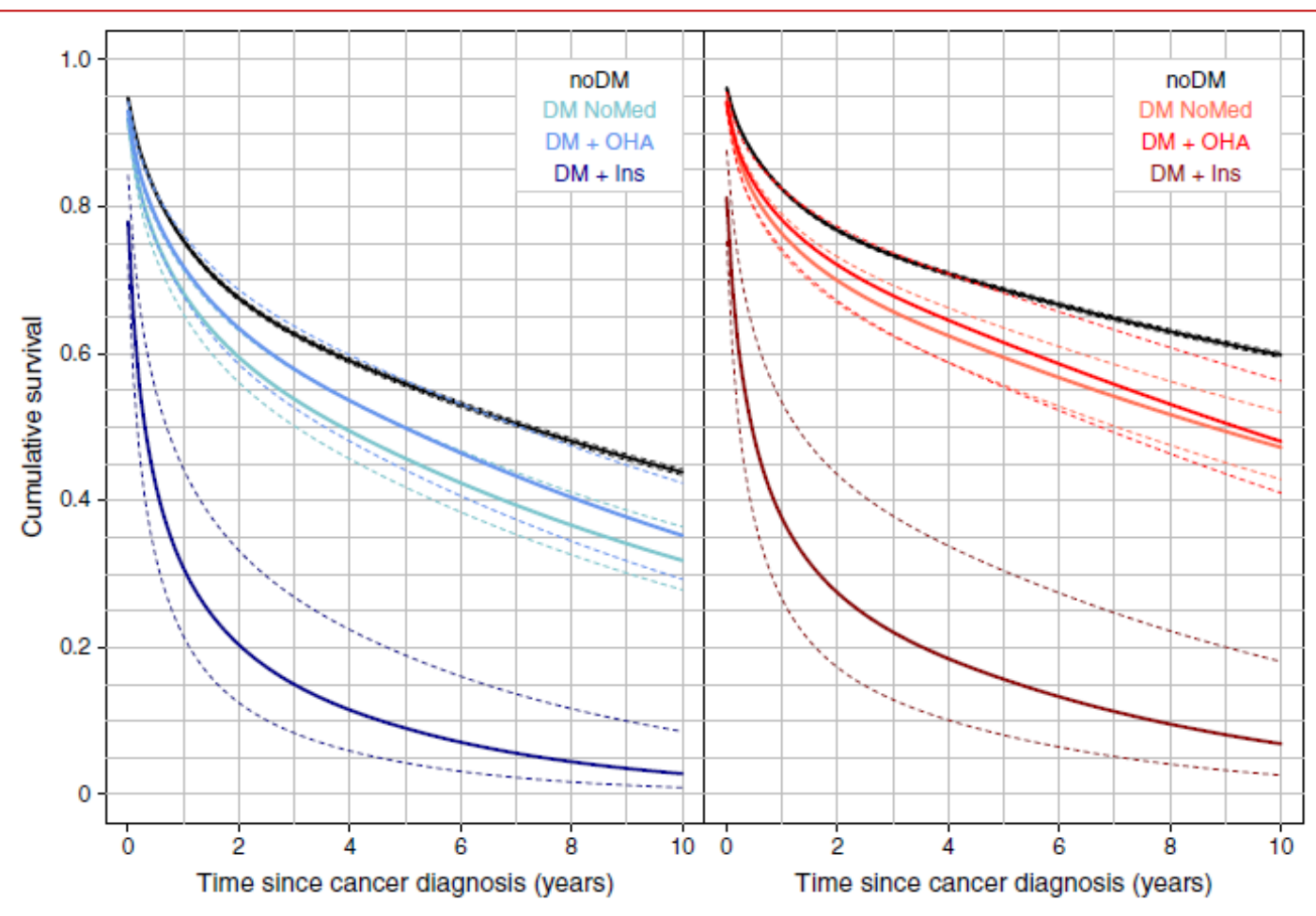
Zhou XH Diabetologia 2010; 53: 1867– 1876



Mortality after cancer among patients with diabetes mellitus: effect of diabetes duration and treatment

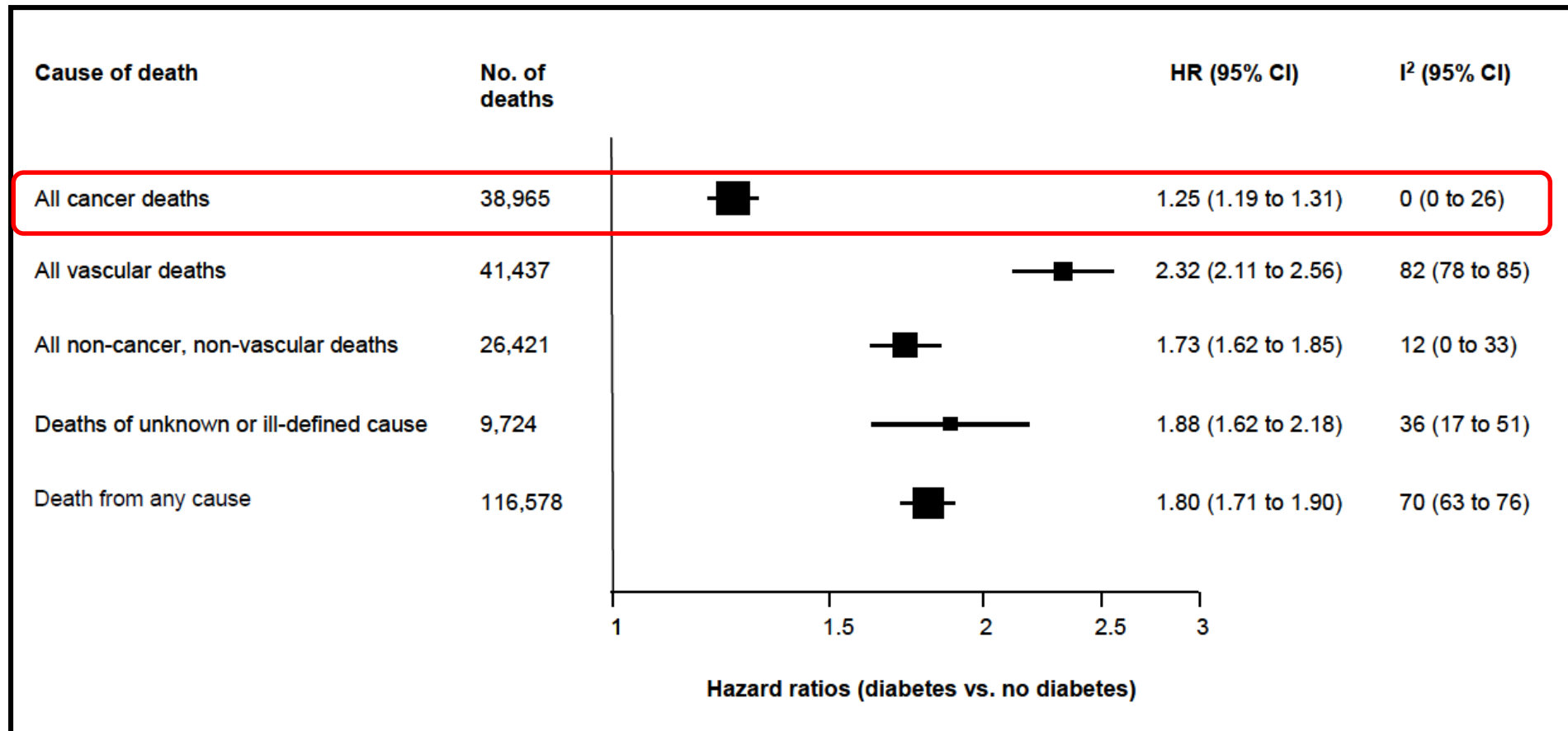
Kristina Ranc • Marit E. Jørgensen • Søren Friis •
Bendix Carstensen

Diabetologia 2014





HR per le principali cause di morte nel diabete

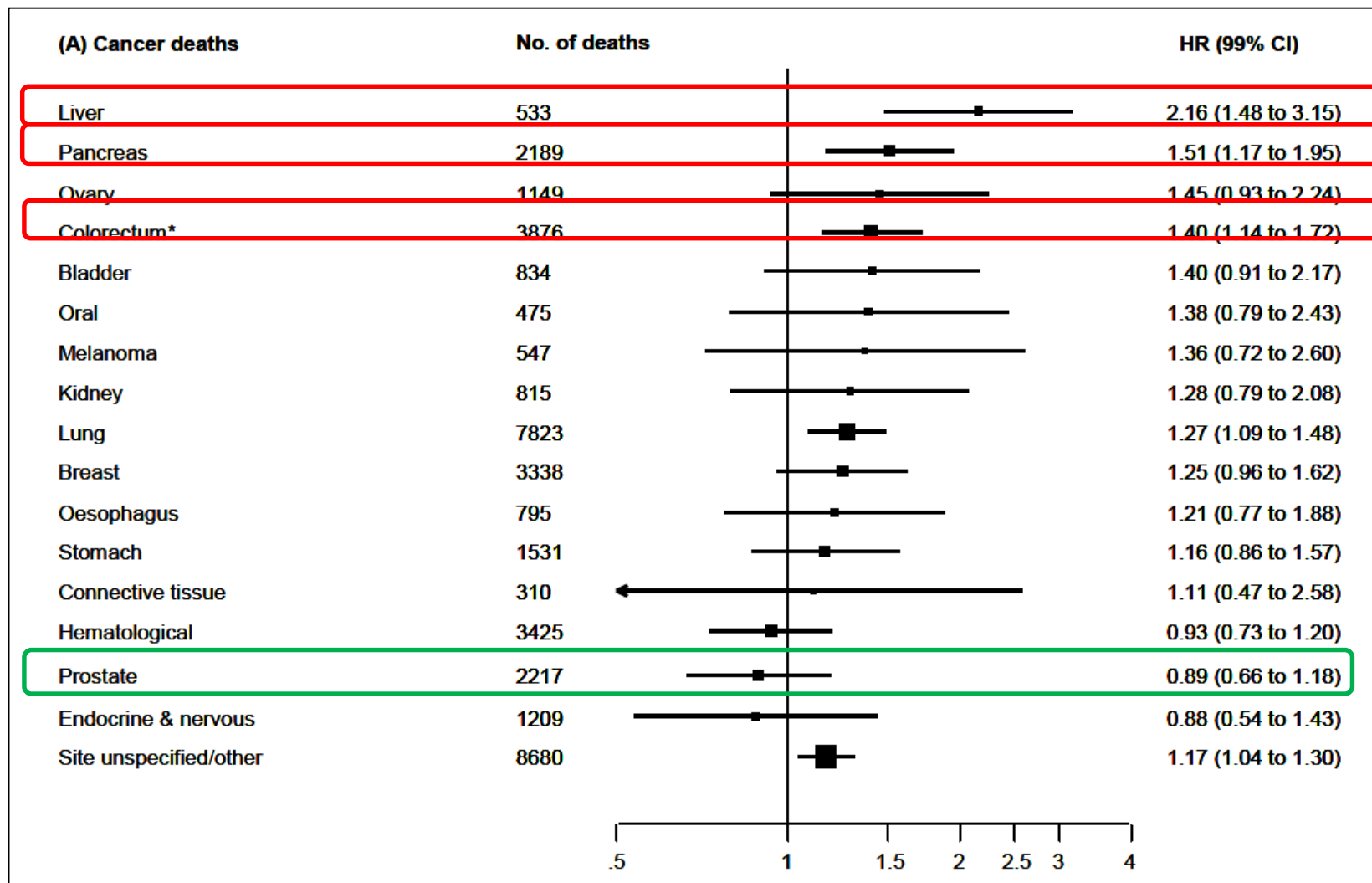




HR per mortalità per neoplasie in sedi diverse in diabetici vs. non diabetici



123.205 morti, fra 820.900 persone, in 97 studi prospettici.





Registri di patologia a Reggio E

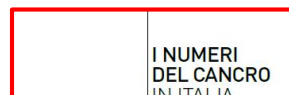


REGISTRO TUORI

- Dal 1996 esiste il Registro Tumori a RE
- Costruito secondo i criteri AIRTUM
- Segue :
Incidenza,
Prevalenza,
Mortalità

I Numeri:

- 2019 :371.000
- Mort 2016: 179
- Trend in aumento al Nord che al Sud
- EmR e Toscana 65% F a 5 anni.



REGISTRO DIABETE

- Dal 2009 è stato costruito il Registro Diabete
- Attraverso il Link di 6 banche Dati
- Approvato dal CE
- Validata la metodologia





RESEARCH ARTICLE

Open Access

Diabetes and risk of cancer incidence: results from a population-based cohort study in northern Italy



Paola Ballotari¹, Massimo Vicentini^{1*}, Valeria Manicardi², Marco Gallo³, Sofia Chiatamone Ranieri⁴, Marina Greci⁵ and Paolo Giorgi Rossi¹

Background: Aim of this study was to compare cancer incidence in populations with and without diabetes by cancer site. Furthermore, we aimed at comparing excess risk of cancer according to diabetes type, diabetes duration and treatment, the latter as regards Type 2 diabetes.

Methods: By use of the Reggio Emilia diabetes registry we classified the resident population aged 20–84 at December 31st 2009 into two groups: with and without diabetes. By linking with the cancer registry we calculated the 2010–2013 cancer incidence in both groups. The incidence rate ratios (IRR) by cancer site, type of diabetes, diabetes duration, and as concerns Type 2 diabetes, by treatment regimen were computed using Poisson regression model and non-diabetic group as reference.



RESEARCH ARTICLE

Open Access



Diabetes and risk of cancer incidence: results from a population-based cohort study in northern Italy

Paola Ballotari¹, Massimo Vicentini^{1*}, Valeria Manicardi², Marco Gallo³, Sofia Chiatamone Ranieri⁴, Marina Gred⁵ and Paolo Giorgi Rossi¹



Article in BMC Cancer · October 2017

DOI: 10.1186/s12885-017-3696-4

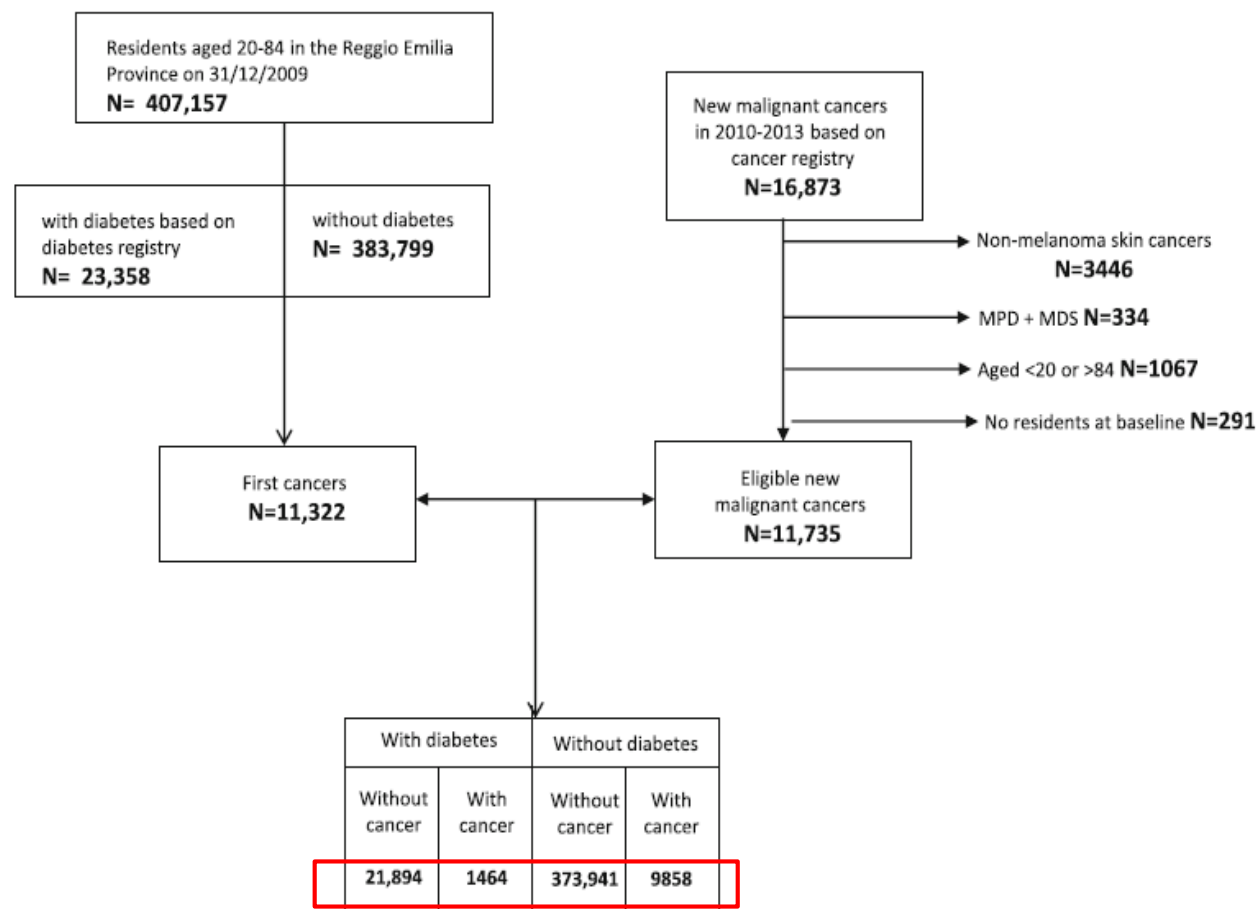


Fig. 1 Flowchart portraying the linkage process for all sites analysed. MPD = chronic myeloproliferative disorders; MDS = myelodysplastic syndromes



Diabete e Cancro a Reggio Emilia - BMC Cancer ,ott 2017

Table 2 No. of subjects with cancer by diabetes status, Incidence Rate Ratios (IRR) and 95% Confidence Intervals (95%CI) for subjects with diabetes vs subjects without diabetes

Cancer site ^a	Total				Females				Males			
	No DM	DM	IRR	95% CI	No DM	DM	IRR	95% CI	No DM	DM	IRR	95% CI
All sites	9858	1464	1.22	1.15–1.29	4851	563	1.25	1.15–1.37	5007	901	1.17	1.05–1.39
C16: Stomach	396	58	0.95	0.72–1.26	139	20	1.17	0.72–1.88	257	38	0.87	0.66–2.21
C18-C20: Colon-rectum	956	177	1.32	1.12–1.55	455	59	1.12	0.85–1.49	501	118	1.44	1.25–2.60
C22: Liver	207	99	3.37	2.63–4.32	61	23	3.26	2.00–5.35	146	76	3.40	2.40–7.16
C24: Biliary tract	69	16	1.41	0.81–2.45	28	7	1.76	0.76–4.04	41	9	1.22	0.07–4.58
C25: Pancreas	340	101	2.00	1.60–2.51	155	48	2.49	1.79–3.46	185	53	1.68	0.65–2.61
C33-C34: Lung	1047	177	1.10	0.93–1.29	329	36	1.01	0.71–1.43	718	141	1.11	0.67–1.47
C50: Breast	1643	148	1.05	0.89–1.26	1633	147	1.06	0.89–1.26	10	1	-	-
C54: Corpus uteri	-	-	-	-	249	44	1.84	1.33–2.56	-	-	-	-
C56: Ovary	-	-	-	-	139	21	1.56	0.97–2.49	-	-	-	-
C61: Prostate	-	-	-	-	-	-	-	-	938	134	0.86	0.72–1.04
C64-C66; C68: Kidney	377	60	1.20	0.67–2.14	111	19	1.55	0.94–2.54	266	41	1.02	0.74–1.44
C67;D09: Bladder	627	138	1.39	1.16–1.68	126	25	1.72	1.11–2.66	501	113	1.33	1.08–1.64
C73: Thyroid	504	27	1.00	0.67–1.49	368	18	1.05	0.64–1.70	136	9	0.88	0.44–1.77
C82-C85; C96: NHL ^b	425	56	1.09	0.82–1.44	180	20	1.14	0.71–1.82	245	36	1.05	0.74–1.50
Other sites ^c	2252	277	1.09	0.96–1.23	1001	102	1.11	0.89–1.36	1251	175	1.07	0.91–1.25

^aOnly first primary cancers are listed. Non-melanoma skin cancer (C44), chronic myeloproliferative disorders and myelodysplastic syndromes (D45-D47) were not counted as a cancer diagnosis; ^bNon-Hodgkin lymphoma; ^cCancers not in any mentioned group. IRR = calculated using Poisson model, adjusted for age, foreign status, and sex (when no stratified). People without diabetes were used as reference



Diabete e Cancro a Reggio E. in relazione al Tipo di Diabete e al trattamento



Table 3 Population, No. of cancer, Incidence Rate Ratios (IRR) and 95% Confidence Intervals (95% CI) for type of diabetes, treatment (only for type 2 diabetes), and diabetes duration vs subjects without diabetes

	Person-years	N cancer	IRR	95% CI
Without diabetes	1,499,890	9858	1.00	-
With diabetes	85,953	1464	1.22	1.15–1.29
By type of diabetes:				
Type 1 diabetes	3017	15	0.88	0.53–1.47
Secondary diabetes ^a	393	10	2.04	1.10–3.80
Type 2 diabetes	82,542	1439	1.22	1.15–1.29
By treatment:				
Diet only	22,900	349	1.10	1.00–1.23
OHAs only	44,637	792	1.22	1.14–1.32
Insulin only	7738	161	1.32	1.13–1.54
OHAs + insulin	7267	137	1.37	1.16–1.62
By diabetes duration (years):				
0–1	24,553	361	1.10	0.99–1.23
2–5	24,710	403	1.23	1.11–1.36
6–10	17,033	337	1.44	1.29–1.61
11+	19,658	363	1.15	1.04–1.30

IRR = calculated using Poisson model, adjusted for age, foreign status, and sex

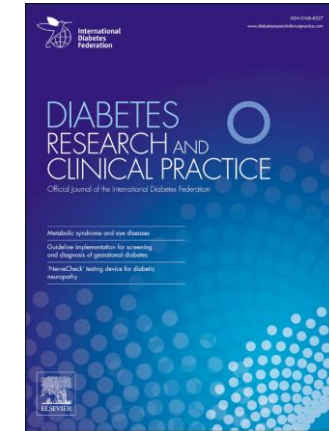
Conclusions: Our study indicates that the strength of association depends on specific cancer site. Insulin, monotherapy or combined therapy, per se or as an indication of poor blood glucose control, in addition to diabetes duration, may play a role in the association of diabetes and cancer.



Effect of different glucose-lowering therapies on cancer incidence in type 2 diabetes: an observational population-based study

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<https://doi.org/10.1016/j.diabres.2018.04.036>



17026 DT2 : 7460 con Metformina → 887 eventi di cancro di cui 348 con Metf.

Il rischio di Cancro è risultato simile nei DT2 trattati con Metformina rispetto ai DT2 in sola dieta.

- **prostate (IRR=0.65; 95%CI:0.36;1.17), liver (IRR=0.82; 95%CI:0.36;1.85) - breast (IRR=0.77; 95%CI:0.43;1.40) cancers only was slightly reduced;**
- for lung (IRR=1.52; 95%CI:0.92;2.50), pancreas IRR=1.51; 95%CI:0.59;3.89) and colon-rectum (IRR=1.71; 95%CI:0.94;3.08) the risk was slightly increased

Highlights

- No effect of [metformin](#) on all-sites cancer incidence.
- A possible protective effect for **breast, liver** and [prostate cancer](#) incidence.
- Our study's time-related bias-free results were consistent with those from RCTs.





Conclusioni



I dati epidemiologici internazionali e nazionali confermano la associazione tra Diabete e Tumori , in particolare per il DT2 con aumento di rischio per alcune sedi:

- **Fegato**
- **Pancreas**
- **Colon-retto**
- **Endometrio**

E confermano la riduzione di rischio per il tumore della

- **Prostata**

Nel DT1 – *modello ideale per studiare il rapporto tra Insulina Esogena e cancro* - i dati sono di meno, a volte non univoci, ma quando i numeri sono adeguati si conferma lo stesso tipo di rischio visto per il DT2.

Da comprendere pienamente il ruolo della Insulina esogena.



Stanislao Farri, *La Stazione Reggio Emilia AV Mediopadana di Santiago Calatrava*, 2013

Grazie dell'attenzione !