Tratamiento de la Diabetes en personas con Cáncer: Opciones y Consideraciones

SOCHIDIAB

Curso Diabetes y Cáncer:
UN DESAFÍO COMPARTIDO

Dr. Gonzalo Galván Escobar
Medicina Interna
Nutrición Clínica y Diabetes

- **Sin conflicto de interés**

Temario Presentación

01	Introducción
02	*Outcomes* en DM2 y Cáncer
03	Terapias Específicas e Hiperglucemia
04	Manejo de la Diabetes
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06	Manejo Interdisciplinario
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Introducción

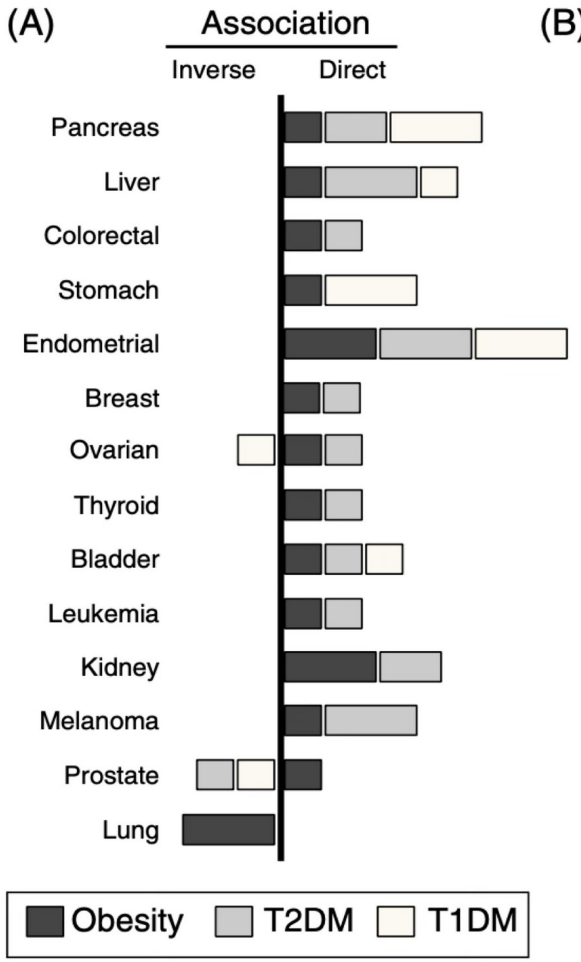
Diabetes y Cáncer : su relación e importancia

Introducción

- La **diabetes y el cáncer** son dos patologías que han ido aumentando en el tiempo con un importante **impacto en la salud pública**.
- Múltiples estudios observacionales muestran una **mayor mortalidad en paciente con DM2 y cáncer**.
- Los pacientes con diabetes muestran un **curso neoplásico más agresivo.**
- Una optimización del control metabólico es crucial, ya que **previene retrasos** en procedimientos diagnósticos (ej. PET), **reduce las suspensiones** de tratamientos oncológicos.
- Abordar estas patologías de manera efectiva exige un paradigma de **manejo integral e interdisciplinario.**

ESMO Open, December 2023 , Volume 8, Issue 6

Asociación DM2 y Cáncer



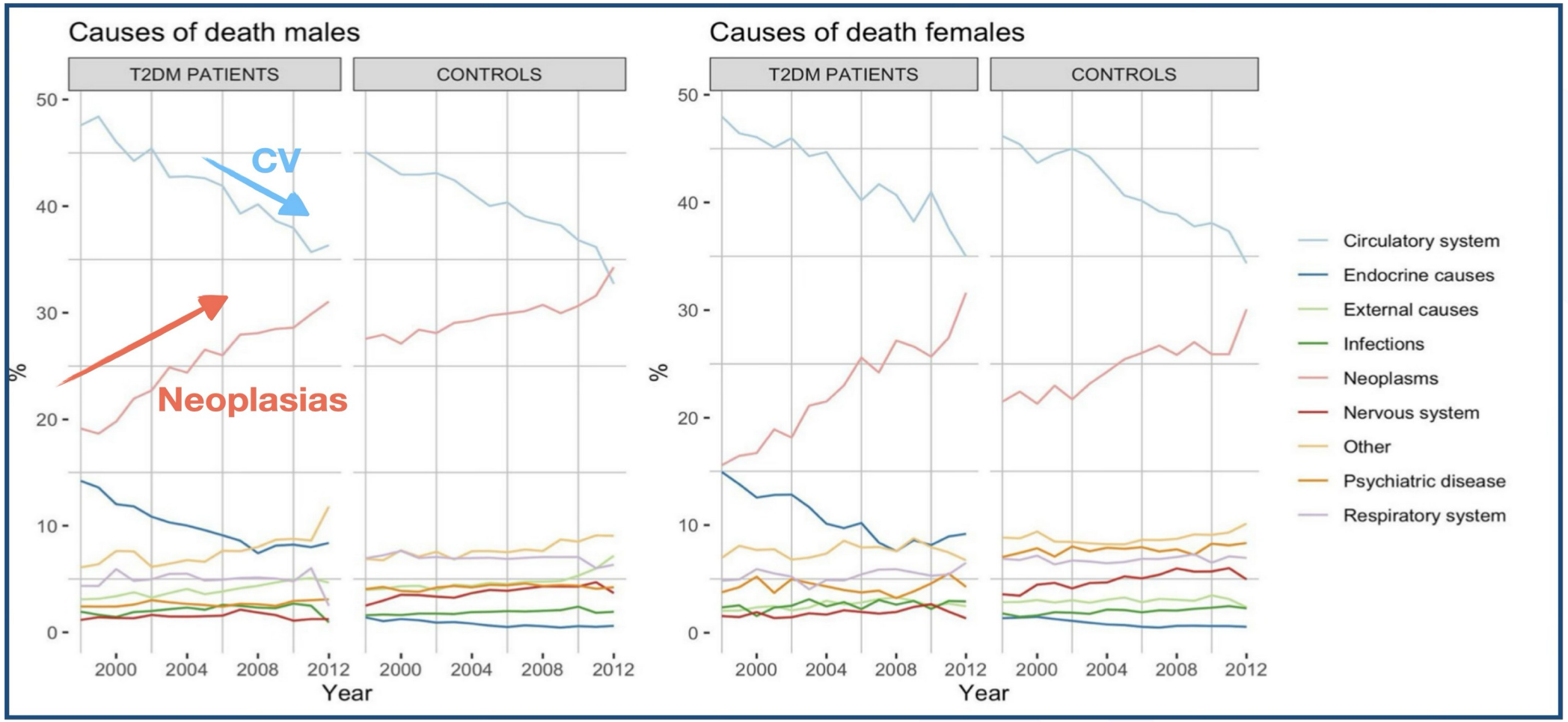
(B)

	Obesity	T2DM	T1DM
	RR (95% CI) [Ref.]	RR (95% CI) [Ref.]	RR (95% CI) [Ref.]
Pancreas	1.48 (1.15 – 1.92) [8]	1.95 (1.66 – 2.28) [20]	2.00 (1.37 – 3.01) [24]
Liver	1.35 (1.24 – 1.47) [9]	2.31 (1.87 – 2.84) [20]	1.59 (0.30 –4.71) [25]
Colorectal	1.32 (1.18 – 1.48) [10]	1.27 (1.21 – 1.34) [20]	1.10 (0.60 – 1.70) [24]
Stomach	1.13 (1.03 – 1.24) [16]	1.09 (0.98 – 1.22) [20]	2.30 (1.10 – 4.10) [24]
Endometrial	2.54 (2.11 – 3.06) [6]	1.97 (1.71 – 2.27) [20]	2.70 (1.40 – 4.70) [24]
Breast	1.42 (1.30 – 1.45) [11]	1.20 (1.12 – 1.28) [20]	1.00 (0.80 – 1.30) [24]
Ovarian	1.30 (1.10 – 1.50) [12]	1.17 (1.02 – 1.34) [20]	0.80 (0.40 – 1.50) [24]
Thyroid	1.29 (1.18 – 1.41) [13]	1.16 (0.97 – 1.39) [20]	1.20 (0.60 – 2.20) [24]
Bladder	1.10 (1.06 – 1.42) [14]	1.35 (1.17 – 1.56) [20]	1.60 (0.70 – 3.10) [24]
Leukemia	1.26 (1.17 – 1.37) [19]	1.28 (1.05 – 1.57) [20]	1.30 (0.70 – 2.20) [24]
Kidney	1.77 (1.68 – 1.87) [7]	1.38 (1.10 – 1.72) [20]	0.80 (0.20 – 2.10) [24]
Melanoma	1.31 (1.19 – 1.44) [19]	2,16(1.14 – 4.35) [23]	0.80 (0.50 – 1.10) [24]
Prostate	1.16 (1.08 – 1.24) [15]	0.96(0.74 – 1.26) [23]	0.33 (0.01 – 1.89) [25]
Lung	0.79 (0.73 – 0.85) [22]	1.03 (0.94 – 1.13) [20]	1.10 (0.50 – 1.90) [24]

Diabetes Care 2020;43:2313–2322

Cambio en el Perfil de Mortalidad

Cohorte Sueca 1998-2012



Scientific Reports Nature, (2020) 10:17376

Cambio en el Perfil de Mortalidad

Cohorte de Escocia 2009 y 2014

Table 2 | Cause of death for patients with type 2 diabetes by sex

Cause of death	Men	Women	Total
Cancer	29.6% (342)	25.6% (246)	27.8% (588)
Heart disease	25.7% (297)	22.1% (212)	24.1% (509)
Respiratory	12.4% (143)	13.8% (133)	13.0% (276)
Stroke	7.6% (88)	9.6% (92)	8.5% (180)
Sepsis	5.0% (58)	7.0% (67)	5.9% (125)
Decompensated diabetes	4.2% (48)	4.7% (45)	4.4% (93)
Mental health	3.1% (36)	5.1% (49)	4.0% (85)
Renal failure	2.3% (27)	2.8% (27)	2.6% (54)
Accident/liver/neurological/other	10.0% (116)	9.4% (90)	9.7% (206)
Total	1,155	961	2,116

1er causa muerte

J Diabetes Investig 2020; 11: 55–61

Peores *Outcomes* con DM2

Importancia de un tratamiento oportuno

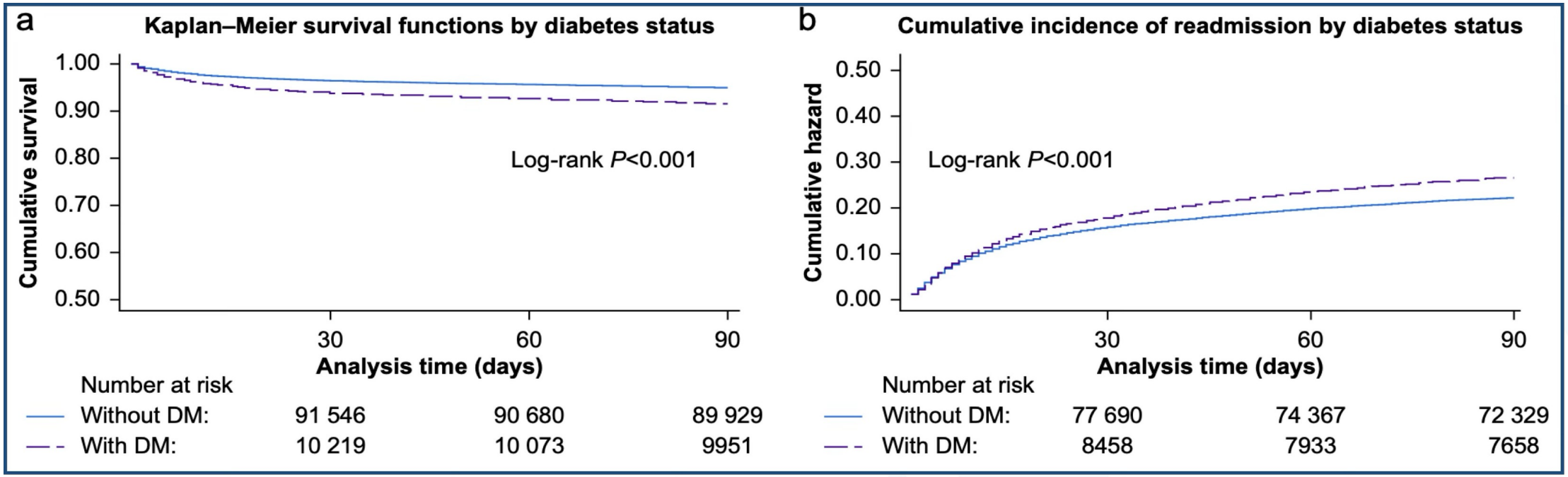
Peor Sobrevida con DM2

	No diabetes					Type 2 diabetes					Adjusted relative mortality	
Cancer site	Cases	Deaths	*n*/PKPY	Mean (95% CI), years	Median (SE), years	Cases	Deaths	*n*/PKPY	Mean (95% CI), years	Median (SE), years	HR (95% CI)	*P*
Overall	104,016	42,602	120.7	9.5 (9.4–9.5)	7.1 (0.9)	8,392	3,780	171.5	7.0 (6.7–7.3)	4.6 (0.1)	1.24 (1.20–1.29)	<0.001
Bladder	5,968	2,287	102.5	9.4 (9.1–9.7)	7.8 (0.3)	675	268	113.4	8.3 (7.5–9.1)	6.2 (0.4)	1.16 (1.02–1.32)	0.027
Breast	24,393	4,796	38.8	14.3 (14.1–14.4)	19.6 (0.4)	1,182	328	76.9	10.4 (9.5–11.3)	9.4 (0.8)	1.32 (1.17–1.49)	<0.001
Colorectal	13,388	5,742	136.8	8.6 (8.4–8.8)	5.5 (0.2)	1,285	532	147.5	7.3 (6.6–8)	5.1 (0.3)	1.00 (0.91–1.10)	0.992
Liver	1,217	876	742.0	2.4 (2.0–2.8)	0.5 (0.0)	243	163	661.0	2.4 (1.5–3.2)	0.7 (0.1)	0.88 (0.74–1.05)	0.157
Lung	11,611	8,916	870.9	1.8 (1.7–1.9)	0.5 (0.0)	856	595	689.2	2.2 (1.8–2.6)	0.7 (0.0)	0.84 (0.77–0.92)	<0.001
Ovary/endometrium	4,732	1,832	111.9	9.9 (9.6–10.3)	7.9 (0.5)	394	136	112.7	8.6 (7.3–9.8)	8.4 (0.9)	0.87 (0.72–1.04)	0.120
Pancreas	1,944	1,532	1,343.6	1.2 (1–1.4)	0.3 (0.0)	364	288	1,184.1	1.1 (0.8–1.3)	0.3 (0.0)	0.98 (0.86–1.12)	0.764
Prostate	15,256	4,894	89.3	9.1 (8.8–9.3)	7.9 (0.1)	1,385	465	105.5	7.5 (6.9–8.0)	6.7 (0.2)	1.19 (1.08–1.31)	0.001
Other	25,507	11,727	143.8	8.6 (8.4–8.7)	5.2 (0.2)	2,008	1,005	208.0	6.1 (5.6–6.5)	3.2 (0.3)	—	—

KPY, per thousand patient-years. *Cox model specification: age at baseline, sex, smoking history, Charlson comorbidity index, and year of diagnosis.

Diabetes Care 35:299–304, 2012

Peores *Outcomes* en Cirugía Oncológica



British Journal of Anaesthesia, 133 (1): 67e76 (2024)

Cohorte Inglesa 2010-2020

Terapias Específicas e Hiperglucemia

La importancia de la interacción Oncólogo Diabetólogo

Type of SACT	Drug examples	Risk of diabetes/hyperglycaemia (range of any grade)	Type of diabetes most likely to develop
Targeted therapy			
mTOR inhibitors	Everolimus[49,50]	12%–50%	T2DM
	Temsirolimus[50]	26%	
PI3K inhibitors	Alpelisib[51]	37%	T2DM
	Idelalisib[52]	28%/30%	
EGFR inhibitor	Osimertinib[53]	2%	T2DM
	Panitumumab[54,55]	1%–10%	
Multikinase inhibitor	Sunitinib[56–58]	0%–8%	Reverses T1/T2DM but also causes hyperglycaemia
	Pazopanib[58]	Risk of hypoglycaemia	
Tyrosine kinase inhibitor (TKI)	Nilotinib[59]	6%	T2DM
	Ponatinib[60]	3%	
ALK inhibitor	Ceritinib[61]	49%	T2DM
FLT3 inhibitor	Midostaurin[62,63]	7%–20%	T2DM
	Gilteritinib[64]	13%	
Monoclonal antibody	Gemtuzumab (anti-CD33) **inpatient use*[65]	10%	T2DM
Somatostatin analogues	Octreotide, lanreotide[66]	Up to 30%	T2DM, but risk of hypoglycaemia
Chemotherapy			
Anti-metabolite	5-fluorouracil[67,68]	Up to 10%	T2DM
	Pemetrexed[69,70]	4%	
	Decitadine/azacitidine[71]	6%–33%	
Alkylating agents	Busulfan[72]	66%–67%	
Platinum based	Oxaliplatin[73,74]	4%	
Anthracyclines	Doxorubicin[68,75]	Up to 10%	
Other	Arsenic trioxide[76]	45%	
ICPs			
PD-1	Nivolumab[27]	<1%	T1DM
	Pembrolizumab[28]	1%–2.2%	
CTLA-4	Ipilimumab[27]	0.02%	
	Combination ICP[77]	4%	

Diabetic Medicine. 2022;39:e14636.

DM tipo 2:

Inhibidores mTOR: 12-50%

PI3K : 28-37%

Inhibidores ALK: 49%

Análogos Somatostatina: hasta 30%

Alquilantes: 66-67%

ICPs: 1-2% pero tipo DM1

Corticoides : Anticiparnos a la Hiperglucemia

Pre-existing type 1 or type 2 diabetes
Family history of diabetes
Obesity
Increasing age
Ethnic minorities
Impaired fasting glucose or impaired glucose tolerance
Polycystic ovarian syndrome
Previous gestational diabetes
Previous development of hyperglycaemia on glucocorticoid therapy
Concurrent cytotoxic therapy known to cause hyperglycaemia

Factores de riesgo para HIPERGLUCEMIA

Glucocorticoid (steroid)	Potency (equivalent doses)	Duration of action (half-life, in hours)
Hydrocortisone	20 mg	8
Prednisolone	5 mg	16–36
Methylprednisolone	4 mg	18–40
Dexamethasone	0.8 mg	36–54
Betamethasone	0.8 mg	26–54

Potencia y duración corticoides (efecto puede durar desde 8 hrs hasta 54 hrs)

Diabetic Medicine. 2022;39:e14636

Manejo de la Diabetes

Derivación oportuna para optimizar manejo y outcomes

Generalidades Tratamiento

- En paciente con QMT siempre considerar **efectos adversos gastrointestinales**: GLP1a, Metformina, Acarbosa.

- En **contexto hipercatabólico** buscar alternativas: aGLP1, iSGLT2, metformina. **Insulina** sería de elección.

- **Metformina:** evaluar **riesgo deshidratación y/o nefrotoxicidad** por QMT o medios de contraste.

- **iSGLT2:** evaluar **riesgo de deshidratación por QMT y posibilidad infecciones urinarias** en contexto inmunosupresión.

- **Insulina:** requiere educación, automonitoreo (SMBG/MCG) y riesgo de hipoglucemias.

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

		CANCER PRE-TREATMENT	CANCER TREATMENT	POST CANCER TREATMENT/ SURVIVORSHIP CARE
1	 Patients with normal glycaemic control	Risk factors for both diabetes and cancer (obesity, physical inactivity, smoking habit)	Iatrogenic hyperglycaemia and secondary diabetes diagnosis related to corticosteroids and specific cancer treatments Pancreatic cancer resection Destruction of the pancreatic tissue containing the islets of Langerhans	Increased risk of cancer relapse and progression Diabetes-related complications
2	 Patients with undiagnosed diabetes	Diabetes-related comorbidities and long-term complications	Hyperglycaemic crisis and related life-threatening conditions Limited compliance with treatment protocol Increased incidence and severity of treatment toxicities Worst prognosis	Increased risk of diabetes-related comorbidities and long-term complications Reduced quality of life
3	 Patients with a history of diabetes	Increased risk of developing some types of cancer Delay in cancer diagnosis Diabetes-related comorbidities	Hyperglycaemia-associated metabolic alterations Dehydration (hyperglycaemia, vomiting, diarrhoea) Increased risk of infections and sepsis Hyperglycaemia management Less aggressive cancer treatment Discontinuation of cancer treatments Surgical complications Catabolic weight loss Increased incidence of some treatment toxicities Worst prognosis Low cumulative survival rate in patients undergoing insulin treatments Aggressiveness of neoplastic cell growth related to chronic hyperinsulinemia and hyperglycaemia Delayed wound healing	Increased risk of cancer relapse and progression Increased risk of diabetes-related comorbidities

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Table 1. Recommendations for DM screening before starting cancer therapy
Basal assessment
FPG, PPG, HbA1c,* lipid panel, uric acid, and BP
Follow-up assessment
Patients without previously known diabetes, especially if at increased risk* • FPG every 2 weeks during the first month, then monthly for 6-12 months • BP monitoring at every visit • HbA1c after 3 months (together with lipid panel and uric acid), and then annually if normal • Education for early recognition of symptoms of hyperglycaemia and DKA, if on ICIs
Patients with already known diabetes • FPG, HbA1c, LDL-C, triglycerides, and BP every 3 months • Reinforce SMBG (basal and postprandial); consider FGM/CGM • Revise diabetes self-management education and support • Consider overall CV risk
Patients who develop hyperglycaemia on ICIs • Urine/capillary ketones • ICA, anti-GAD, anti-insulin Ab • Insulin, C-peptide • Pancreatic amylase and lipase

Nuevas perspectivas

Antidiabéticos como terapias adyuvantes

Trends in Cancer

CellPress
OPEN ACCESS

Review

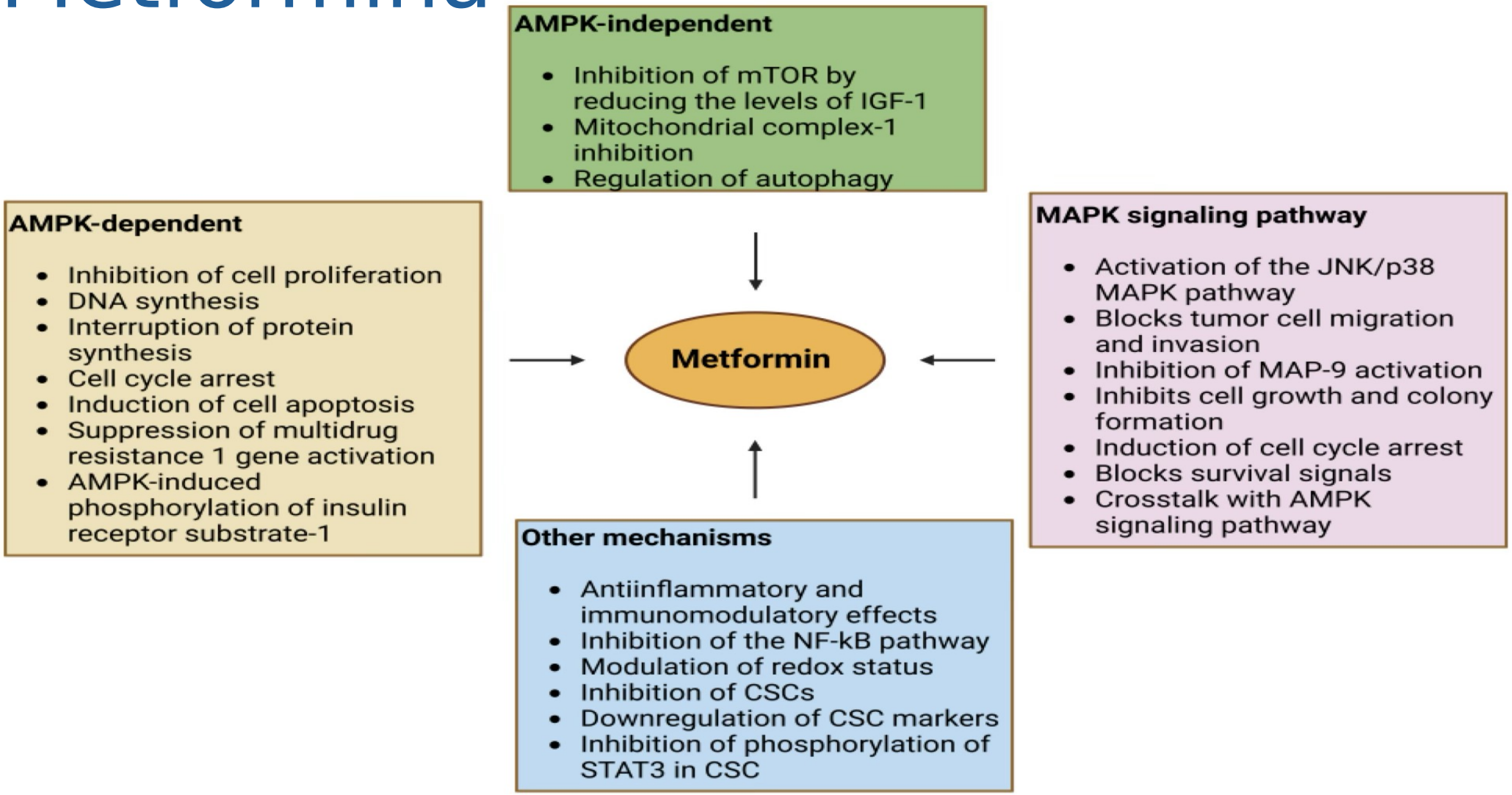
Repurposing glucose-lowering drugs for cancer therapy

Michaela Luconi [1,*], Giulia Cantini [1,*], and Clara Crescioli [2,*]

The metabolic interplay between cancer cells and the TME, which supports the continuous adaptation of cancer to potential organism response, represents an emerging target for anticancer therapies such as GLDs [1]. Targeting the metabolic vulnerabilities of cancer cells and TME components, as well as tumor-sustaining metabolism at the systemic level (Figure 2), with metabolism-oriented drugs could provide more effective cancer treatment strategies acting on **cancer metabolism reprogramming**.

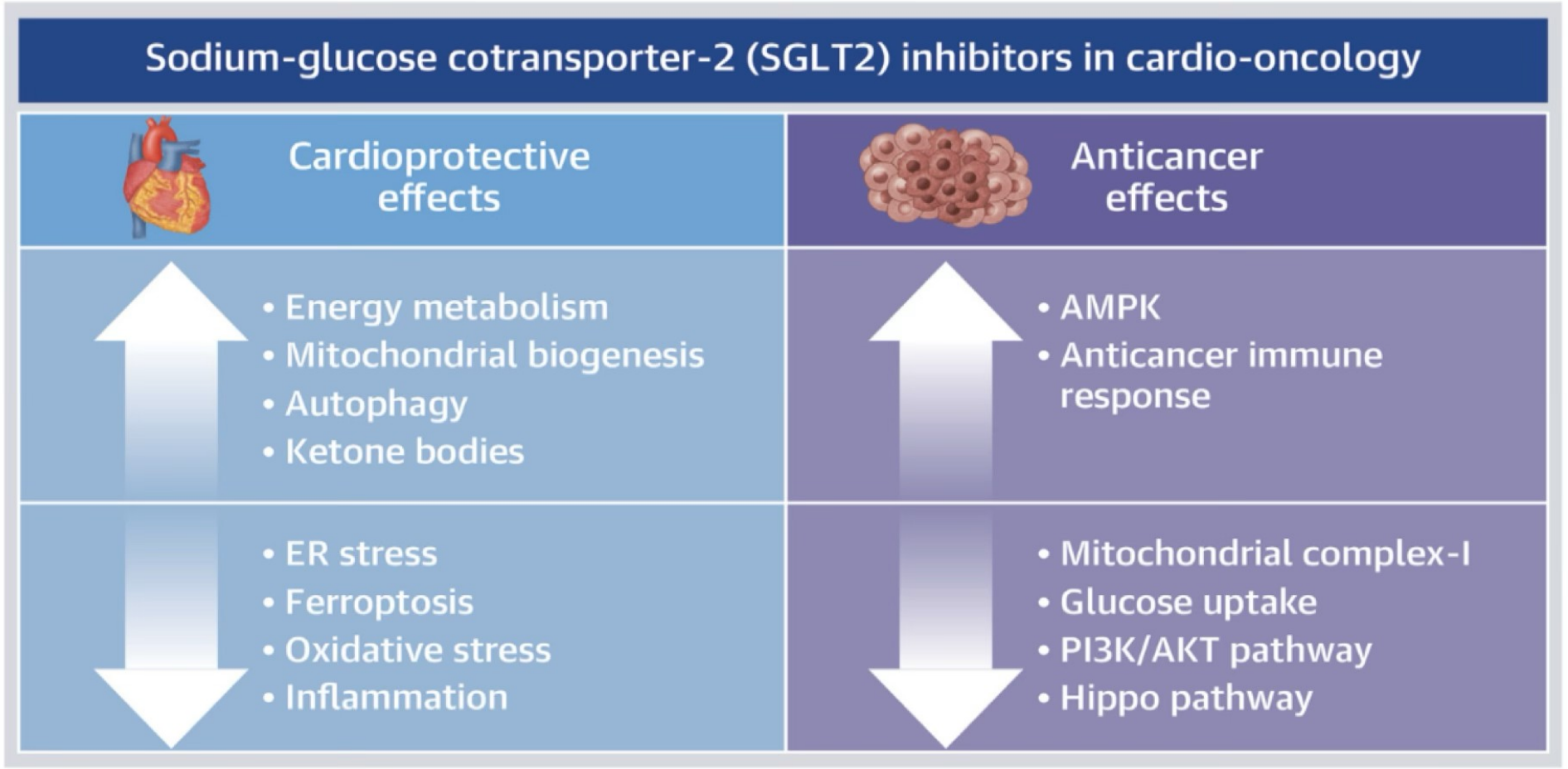
Trends in Cancer, July 2025, Vol. 11, No. 7

Metformina



Dhas et al. Molecular Biomedicine (2024) 5:40

iSGLT2



Dabour MS, et al. J Am Coll Cardiol CardioOnc. 2024;6(2):159-182.

iSGLT2

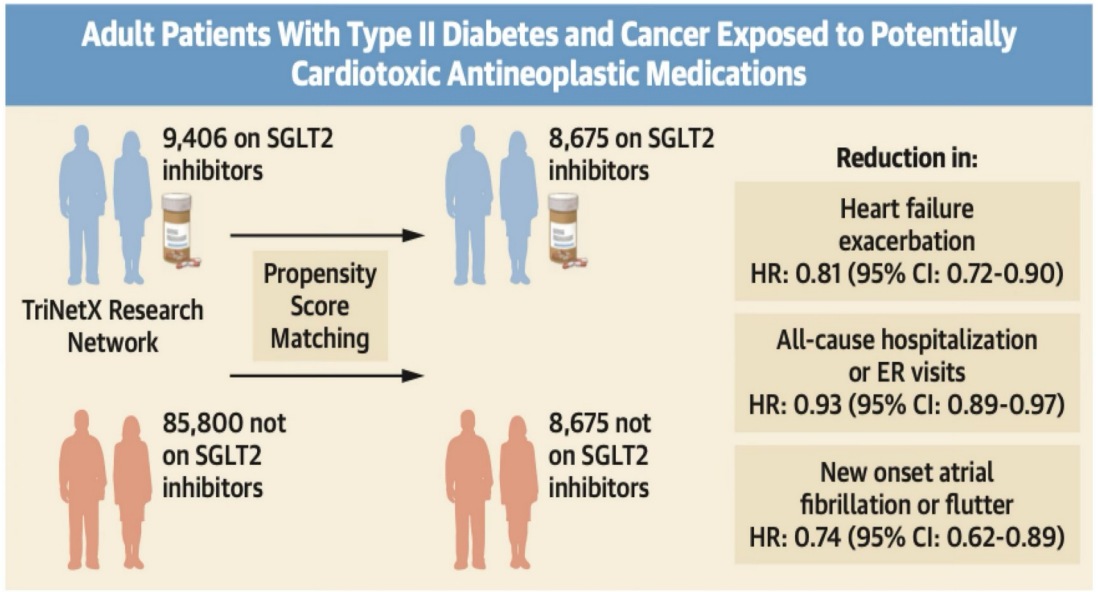
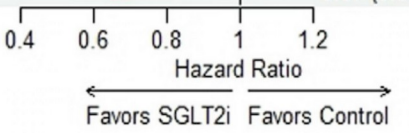


FIGURE 1 Forest Plot for Subgroup Analysis

Effect of SGLT2i on Cancer Therapy-Related Cardiac Dysfunction

Outcomes	Events (Treatment vs Control)	HR	P-value
Primary analysis			
Cancer therapy-related cardiac dysfunction	646 vs 948	0.76 (0.69-0.84)	<0.001
Subgroup analysis			
Anthracycline therapy	179 vs 301	0.70 (0.58-0.85)	<0.001
Monoclonal Ab therapy	90 vs 123	0.81 (0.66-0.98)	0.03
Proteasome inhibitors	158 vs 162	0.88 (0.67-1.15)	0.37
Antimetabolites	76 vs 113	0.75 (0.65-0.86)	<0.001
Alkylating agents	37 vs 70	0.63 (0.53-0.76)	<0.001
Small molecule TKI	106 vs 179	0.67 (0.54,0.83)	<0.001

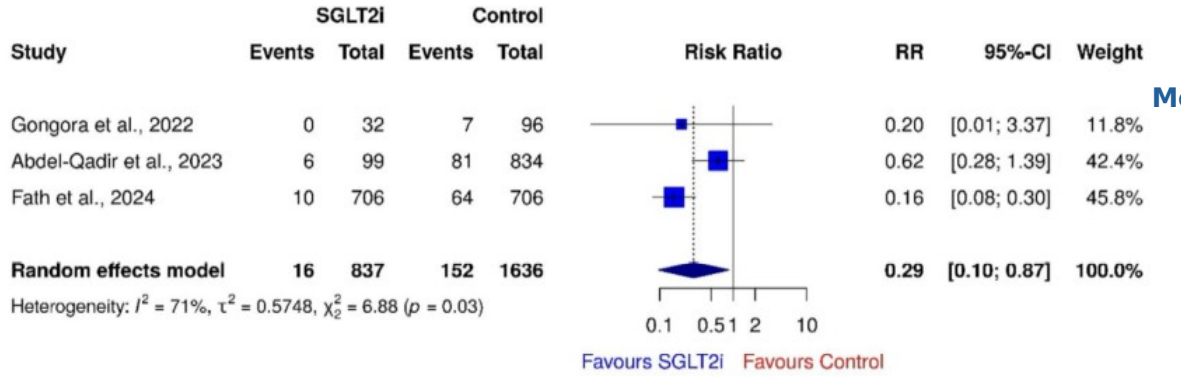


JACC: CARDIOONCOLOGY, VOL. 6, NO. 6, 2024
DECEMBER 2024:863-875

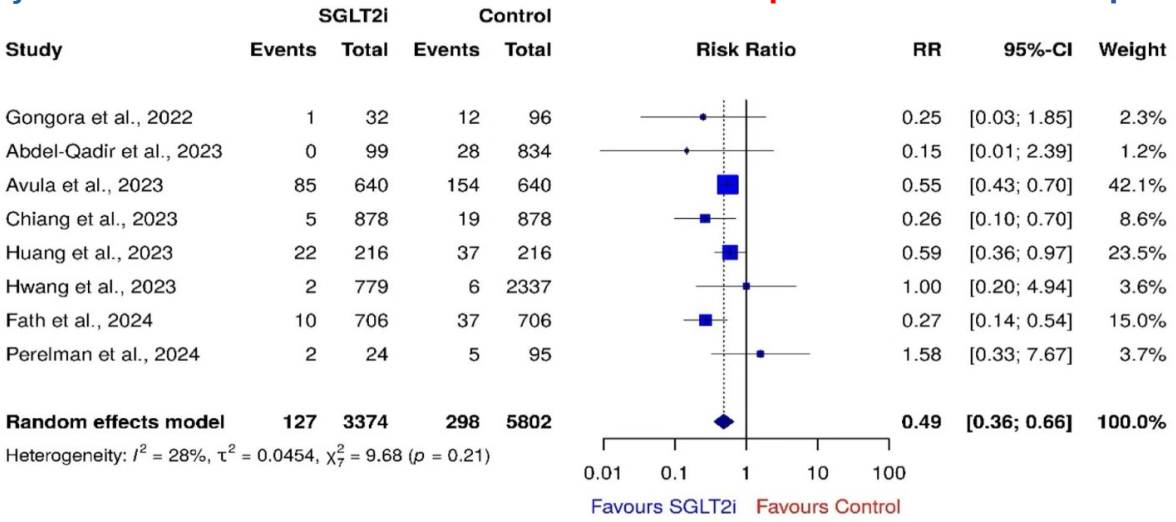
iSGLT2

ESC European Society of Cardiology

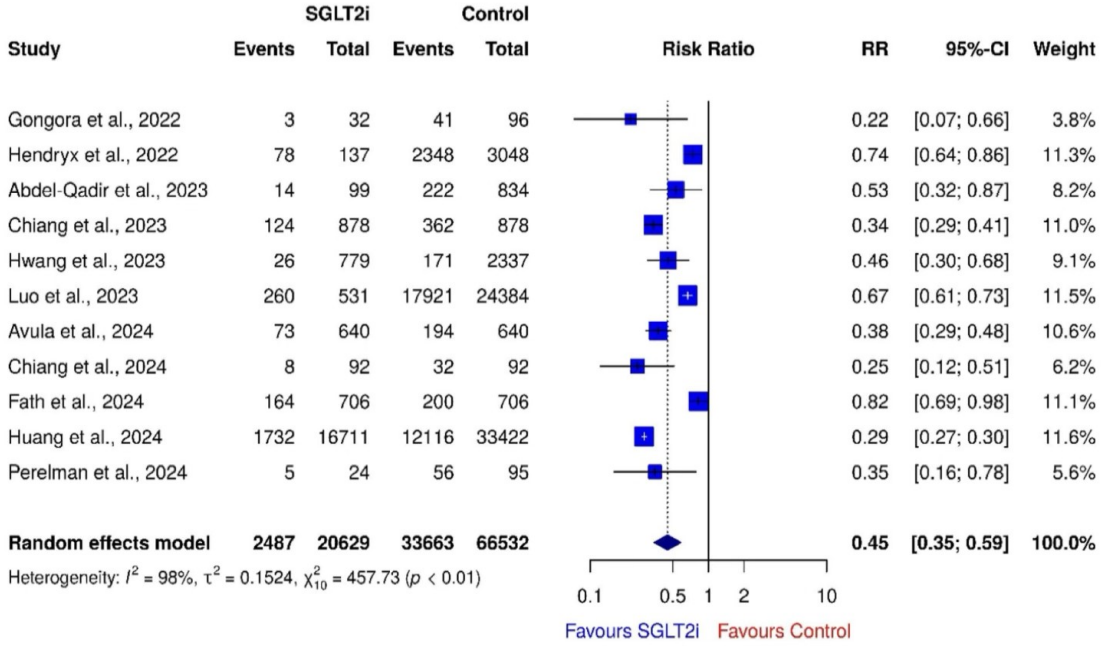
ta-Analysis of new or incident heart failure in cancer patients using SGLT2 inhibitor



ta-analysis of SGLT2 inhibitor studies on heart failure hospitalizations in cancer patients.

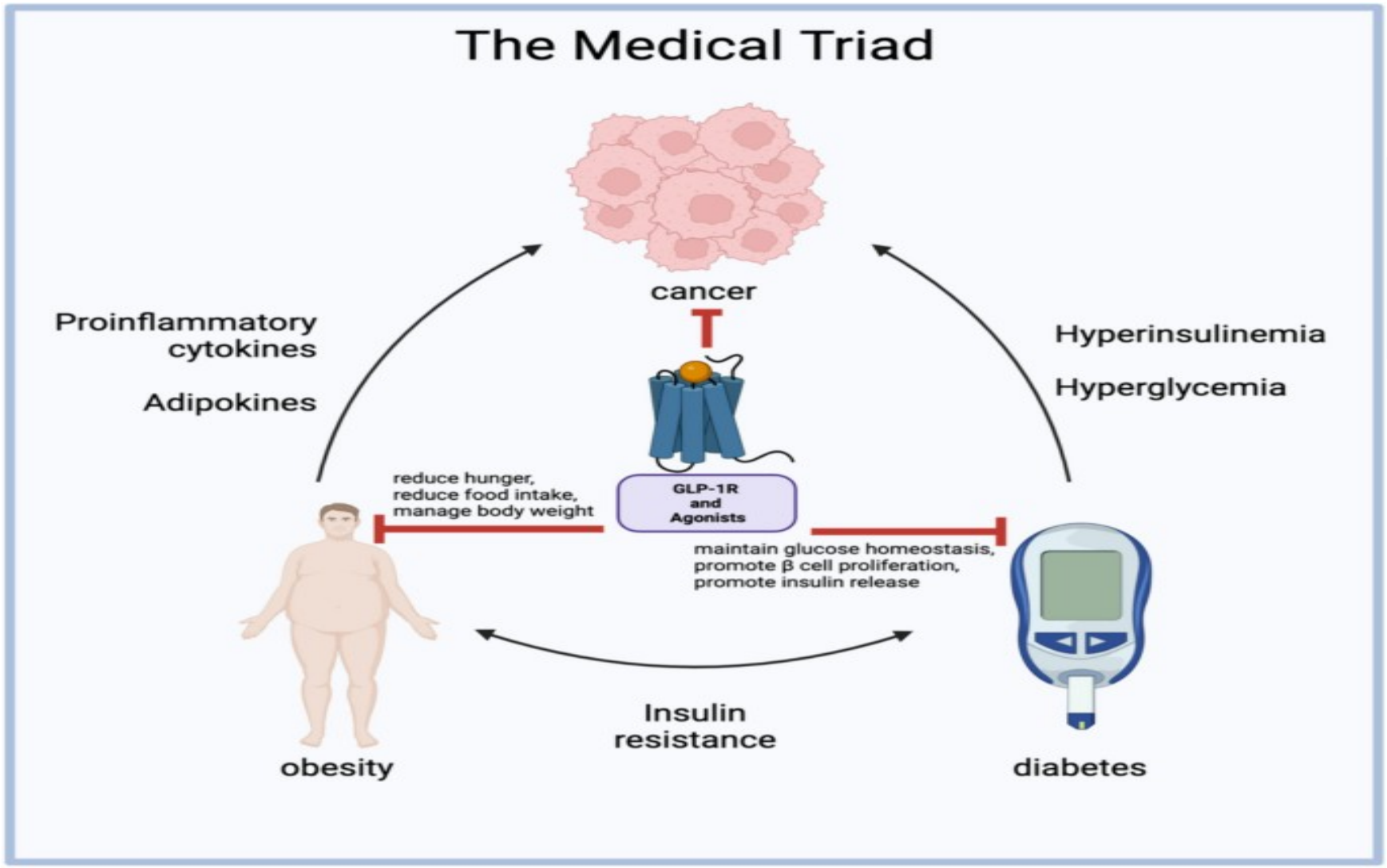


Meta-Analysis of all-cause mortality in cancer patients using SGLT2 inhibitors



European Journal of Preventive Cardiology (2025) **00**, 1–13
https://doi.org/10.1093/eurjpc/zwaf026

GLP1a

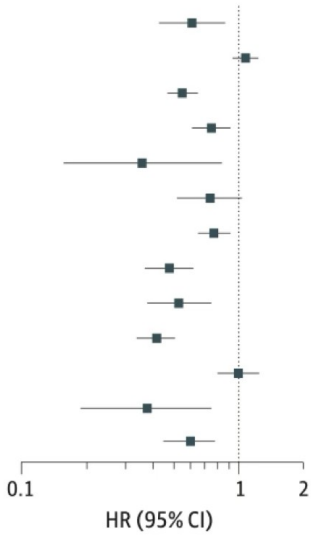


Cancer Metastasis Rev 43, 1297–1314 (2024)

GLP1a

Figure 2. Risk of 13 Obesity-Associated Cancers Among Patients Receiving Glucagon-Like Peptide 1 Receptor Agonists (GLP-1RAs) vs Those Receiving Insulins

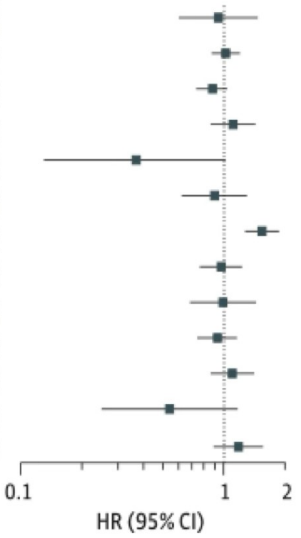
Outcome (N = 1 651 452)	Group prescribed GLP-IRAs but not insulin, No (%) (n = 48 983)	Group prescribed insulin but not GLP-IRAs, No (%) (n = 1 044 745)	HR (95% CI)
Esophageal cancer (n = 48 437)	49 (0.10)	77 (0.16)	0.60 (0.42-0.86)
Breast cancer (n = 13 768)	427 (3.08)	379 (2.94)	1.07 (0.93-1.23)
Colorectal cancer (n = 48 443)	223 (0.46)	391 (0.81)	0.54 (0.46-0.64)
Endometrial cancer (n = 25 750)	160 (0.62)	210 (0.82)	0.74 (0.60-0.91)
Gallbladder cancer (n = 48 587)	<10 (<0.02)	19 (0.04)	0.35 (0.15-0.83)
Stomach cancer (n = 48 449)	56 (0.12)	75 (0.16)	0.73 (0.51-1.03)
Kidney cancer (n = 48 322)	223 (0.46)	284 (0.59)	0.76 (0.64-0.91)
Hepatocellular carcinoma (n = 48 397)	79 (0.16)	167 (0.35)	0.47 (0.36-0.61)
Ovarian cancer (n = 25 739)	51 (0.20)	94 (0.37)	0.52 (0.37-0.74)
Pancreatic cancer (n = 48 490)	123 (0.25)	290 (0.60)	0.41 (0.33-0.50)
Thyroid cancer (n = 48 527)	154 (0.32)	149 (0.31)	0.99 (0.79-1.24)
Meningioma (n = 48 518)	11 (0.02)	29 (0.06)	0.37 (0.18-0.74)
Multiple myeloma (n = 48 527)	80 (0.17)	131 (0.27)	0.59 (0.44-0.77)



GLP1a vs Insulina : disminuye riesgo 10/13 cánceres asociados a obesidad

Figure 4. Risk of 13 Obesity-Associated Cancers Among Patients Receiving Glucagon-Like Peptide 1 Receptor Agonists (GLP-1RAs) vs Those Receiving Metformin

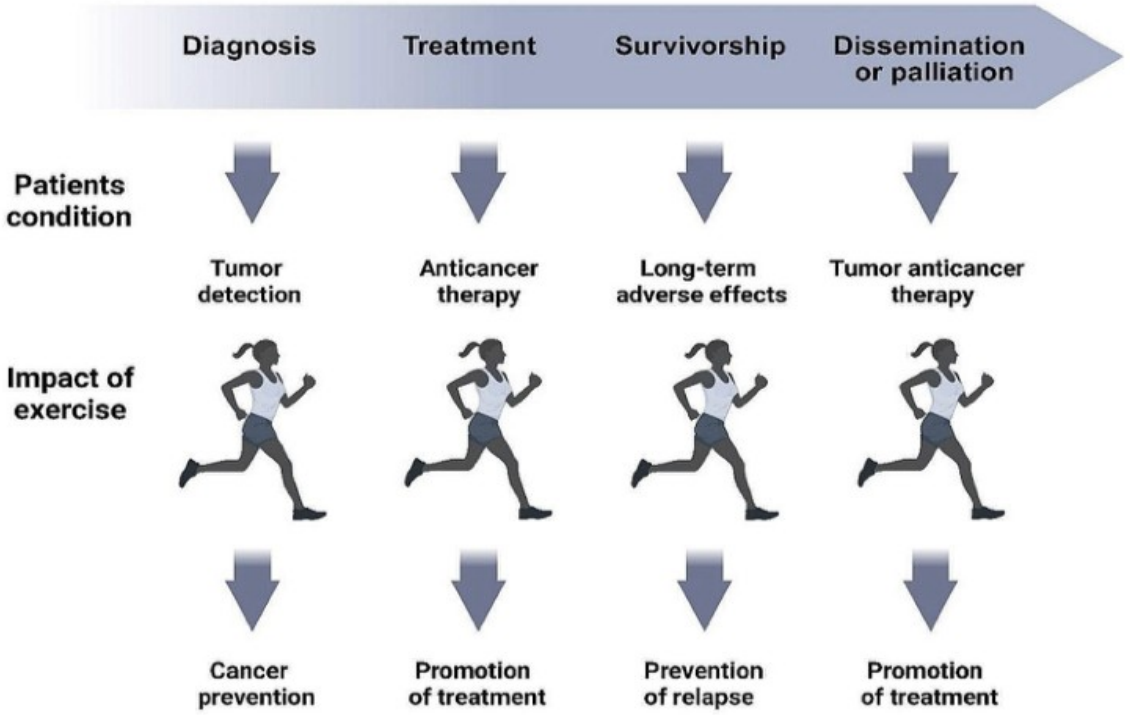
Outcome (N = 1 651 452)	Group prescribed GLP-IRAs but not metformin, No (%) (n = 32 365)	Group prescribed metformin but not GLP-IRAs, No (%) (n = 856 160)	HR (95% CI)
Esophageal cancer (n = 32 263)	37 (0.12)	42 (0.13)	0.94 (0.60-1.47)
Breast cancer (n = 10 419)	295 (2.8)	320 (3.1)	1.02 (0.87-1.20)
Colorectal cancer (n = 32 275)	228 (0.71)	279 (0.86)	0.88 (0.73-1.04)
Endometrial cancer (n = 17 168)	122 (0.71)	119 (0.69)	1.11 (0.86-1.43)
Gallbladder cancer (n = 32 261)	<10 (<0.03)	14 (0.04)	0.37 (0.13-1.02)
Stomach cancer (n = 32 267)	52 (0.16)	60 (0.19)	0.90 (0.62-1.30)
Kidney cancer (n = 32 162)	252 (0.78)	178 (0.55)	1.54 (1.27-1.87)
Hepatocellular carcinoma (n = 32 267)	125 (0.39)	142 (0.44)	0.97 (0.76-1.23)
Ovarian cancer (n = 17 197)	54 (0.31)	59 (0.34)	0.99 (0.68-1.44)
Pancreatic cancer (n = 32 271)	142 (0.44)	166 (0.51)	0.93 (0.74-1.16)
Thyroid cancer (n = 32 259)	127 (0.39)	121 (0.38)	1.10 (0.86-1.41)
Meningioma (n = 32 263)	<10 (<0.03)	20 (0.06)	0.54 (0.25-1.17)
Multiple myeloma (n = 32 256)	104 (0.32)	95 (0.30)	1.18 (0.89-1.56)

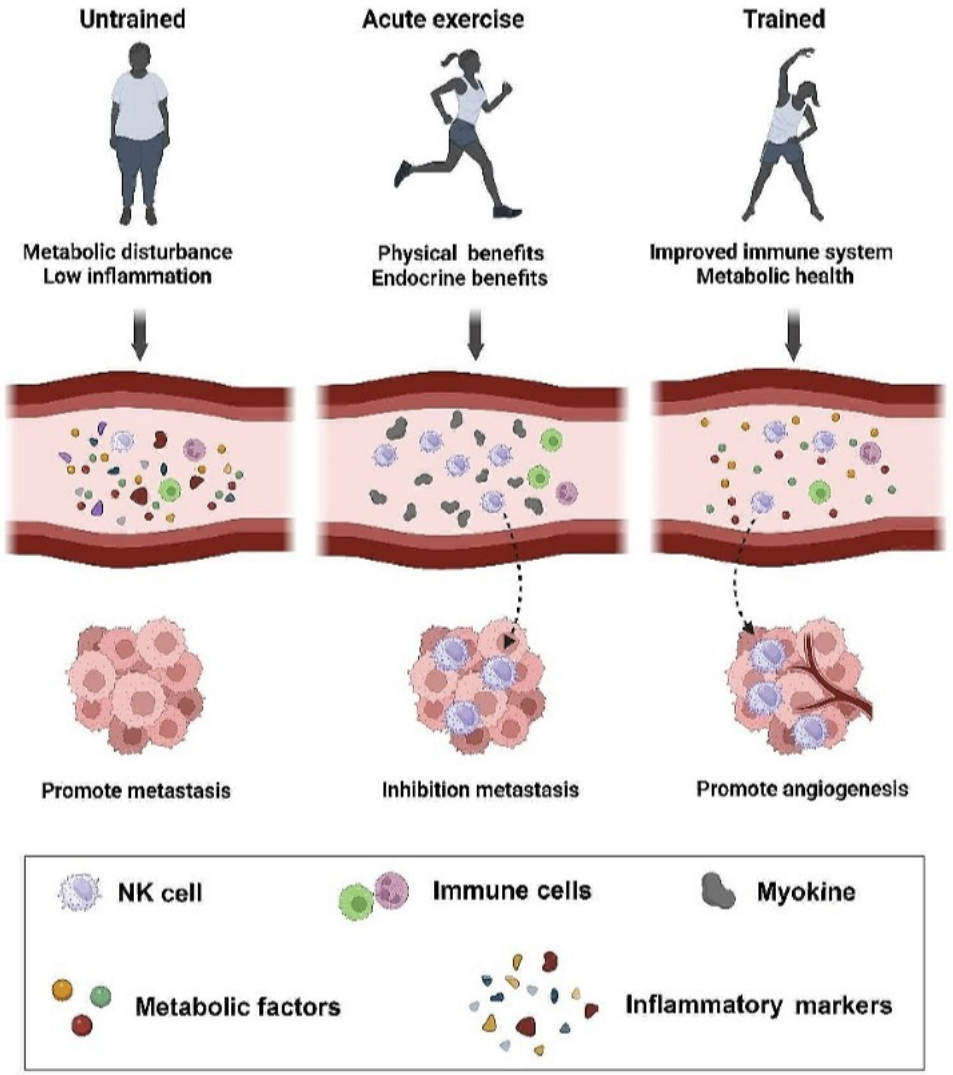


GLP1a vs Metformina: efecto similar salvo Ca renal

JAMA Network Open. 2024;7(7)

Ejercicio





Xu et al. Cell Communication and Signaling (2024) 22:260

Ejercicio

ORIGINAL ARTICLE

Structured Exercise after Adjuvant Chemotherapy for Colon Cancer

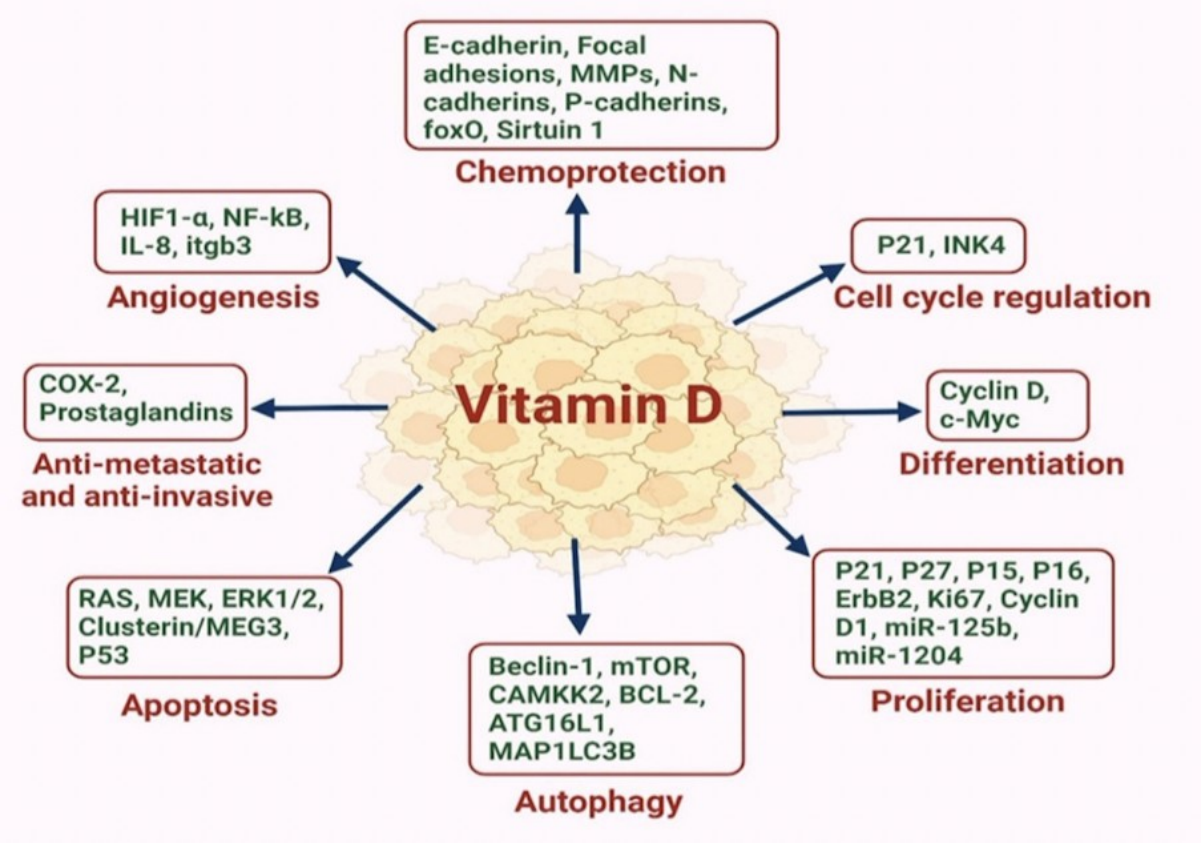
Kerry S. Courneya, Ph.D.,[1] Janette L. Vardy, M.D., Ph.D.,[2,3]

CONCLUSIONS

A 3-year structured exercise program initiated soon after adjuvant chemotherapy for colon cancer resulted in significantly longer disease-free survival and findings consistent with longer overall survival. (Funded by the Canadian Cancer Society and others; CHALLENGE ClinicalTrials.gov number, NCT00819208.)

This article was published on June 1, 2025, at NEJM.org.

Vitamina D



Cancers **2025**, *17*(23), 3751

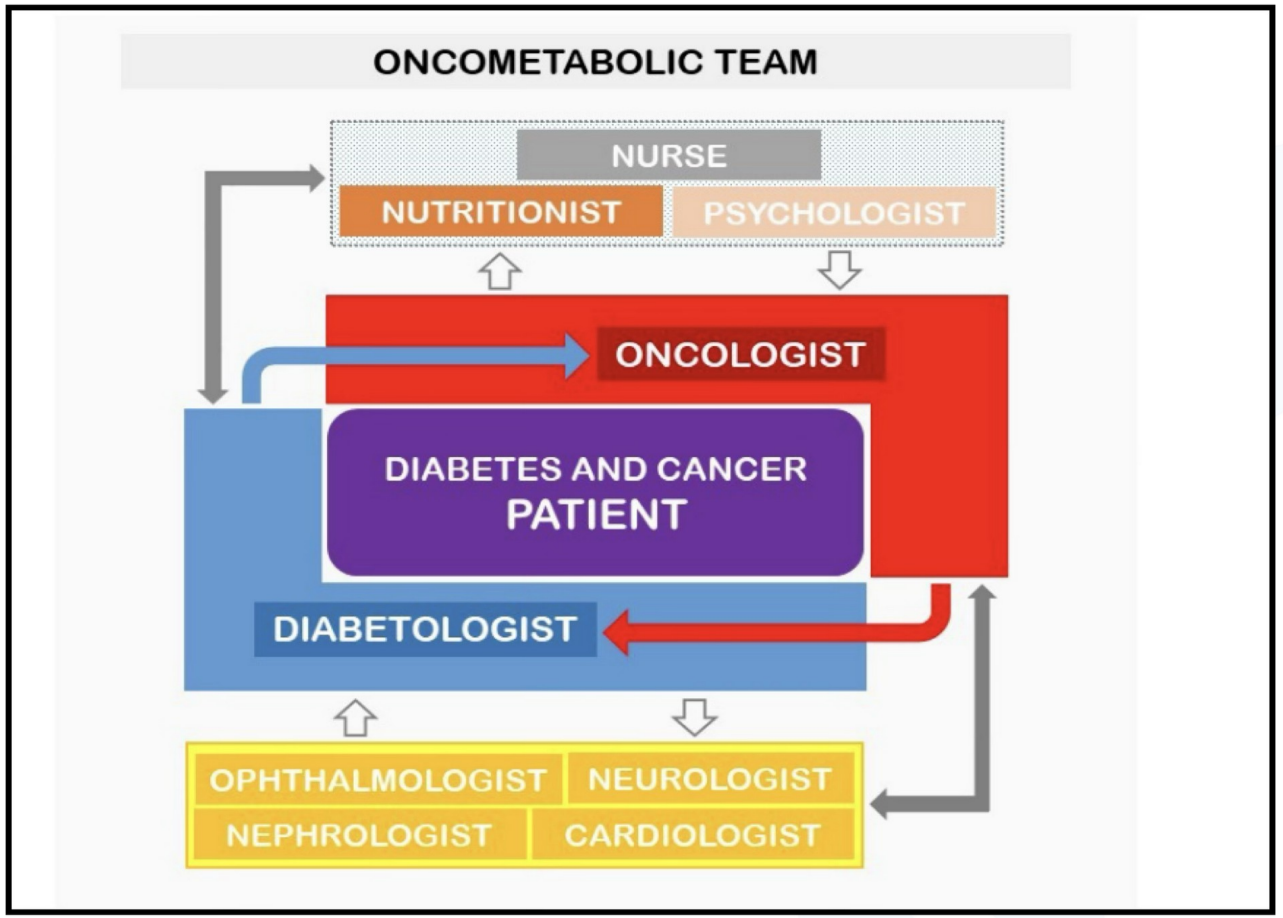
Disminución incidencia Cáncer : **SIN EVIDENCIA CONTUNDENTE**

Disminución Mortalidad: meta-análisis **RESULTADOS INCONSISTENTES**.

Manejo Interdisciplinario

Hacia donde debemos apuntar

Equipo OncoDIABETES



Explor Med. 2020;1:184-204

Conclusiones

- La coexistencia de Diabetes y Cáncer nos plantea **un gran desafío**, tanto en su **prevención como en su manejo**.
- La compleja relación entre estas dos entidades nos obliga a realizar un **manejo multidisciplinario y colaborativo**.
- Ideal desarrollar **protocolos de manejo y derivación oportuna** para facilitar el flujo y optimizar tiempos de atención.
- **Conducta activa**.
- Siempre: **PREVENCIÓN.**

Fin ...
Muchas Gracias !

ggalvanescobar@gmail.com