

CONVEGNO SID-AMD TOSCANA

L'IMPATTO e i RISCHI delle COMPLICANZE del DIABETE:

dalle **COMPLICANZE TRADIZIONALI**
alle **COMPLICANZE EMERGENTI**

PISA
10 GIUGNO 2023



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Diabete ed Infezioni: un rischio da non sottovalutare

La dottoressa Margherita Occhipinti dichiara di NON aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti, dispositivi medico-chirurgici, ecc.).

Summary

- Cosa sappiamo su Diabete ed Infezioni
- Cosa non abbiamo ancora chiaro
- Cosa è ragionevole fare

Cosa sappiamo

- ✓ I pazienti diabetici sono più predisposti a sviluppare alcuni tipi di infezioni
- ✓ I pazienti diabetici sono più suscettibili a sviluppare alcune complicazioni nel Corso di di infezioni
- ✓ Alcune infezioni rare come l'empiema della colecisti, la pielonefrite enfisematosa, otite sterna e la mucromicosi hanno una prevalenza Maggiore nella popolazione diabetica

Excess Risk of Dying From Infectious Causes in Those With Type 1 and Type 2 Diabetes

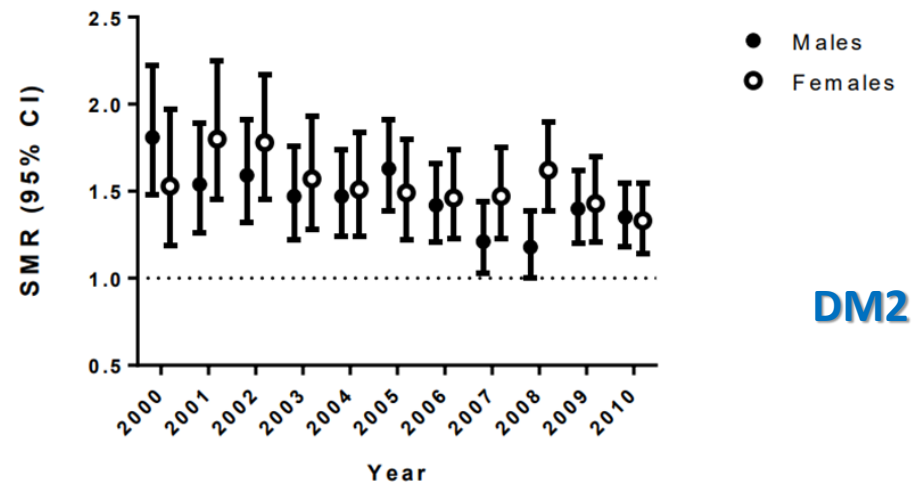


1,108,982 individuals with diabetes who were registered with the Australian Diabetes register between 2000 and 2010 were linked to the National Death Index.

Mortality outcomes were defined as infection-related_{A-B} death (ICD codes A99–B99), pneumonia (J12–J189), septicemia (A40 and A41), and osteomyelitis (M86).

Median follow-up of 6.7 years

Supplementary Figure 2. Standardised mortality ratios (95% confidence intervals) for infection-related_{A-B} mortality by sex across time in type 2 diabetes



Supplementary Figure 3. Standardised mortality ratios (95% confidence intervals) for infection-related_{A-B} mortality across time in type 1 diabetes

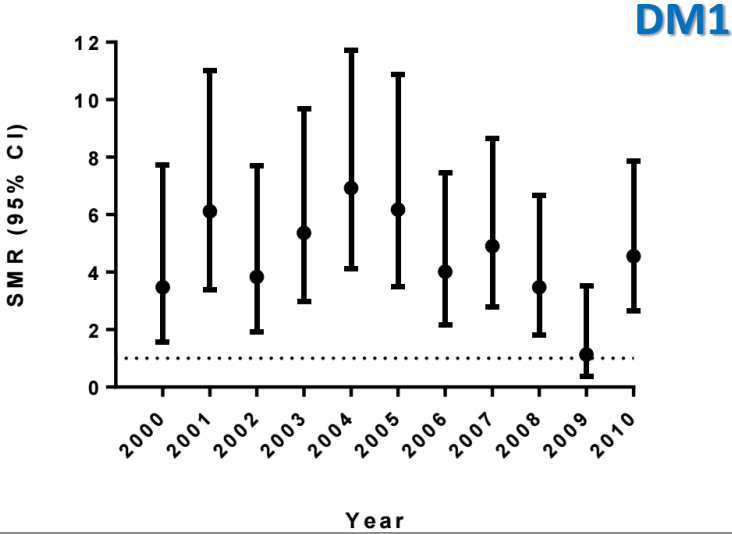


Table 2—SMRs (95% CI) for pneumonia-, septicemia-, and osteomyelitis-related mortality in diabetes by sex and diabetes type

	Males				Females			
	Deaths		SMR	95% CI	Deaths		SMR	95% CI
	Observed	Expected			Observed	Expected		
Type 1 diabetes								
Pneumonia	28	5	6.23	4.3–9.0	13	3	5.0	2.9–8.6
Septicemia	24	2	10.0	6.7–14.9	15	2	9.7	5.9–16.1
Osteomyelitis	3	0*	16.3	5.2–50.4	5	0*	58	24.1–139.3
Type 2 diabetes								
Pneumonia	1,128	913	1.2	1.2–1.3	989	824	1.2	1.1–1.3
Septicemia	646	356	1.8	1.7–2.0	563	291	1.9	1.8–2.1
Osteomyelitis	90	16	3.5	2.9–4.3	49	17	2.9	2.2–3.9

*Rounded to whole number.

ORIGINAL ARTICLE

Diabetes Mellitus, Fasting Glucose,
and Risk of Cause-Specific Death

The Emerging Risk Factors Collaboration*

97 prospective studies

820,900 people

hazard ratios for cause-specific death, according to
baseline diabetes status or fasting glucose level, from
individual-participant data on 123,205 deaths

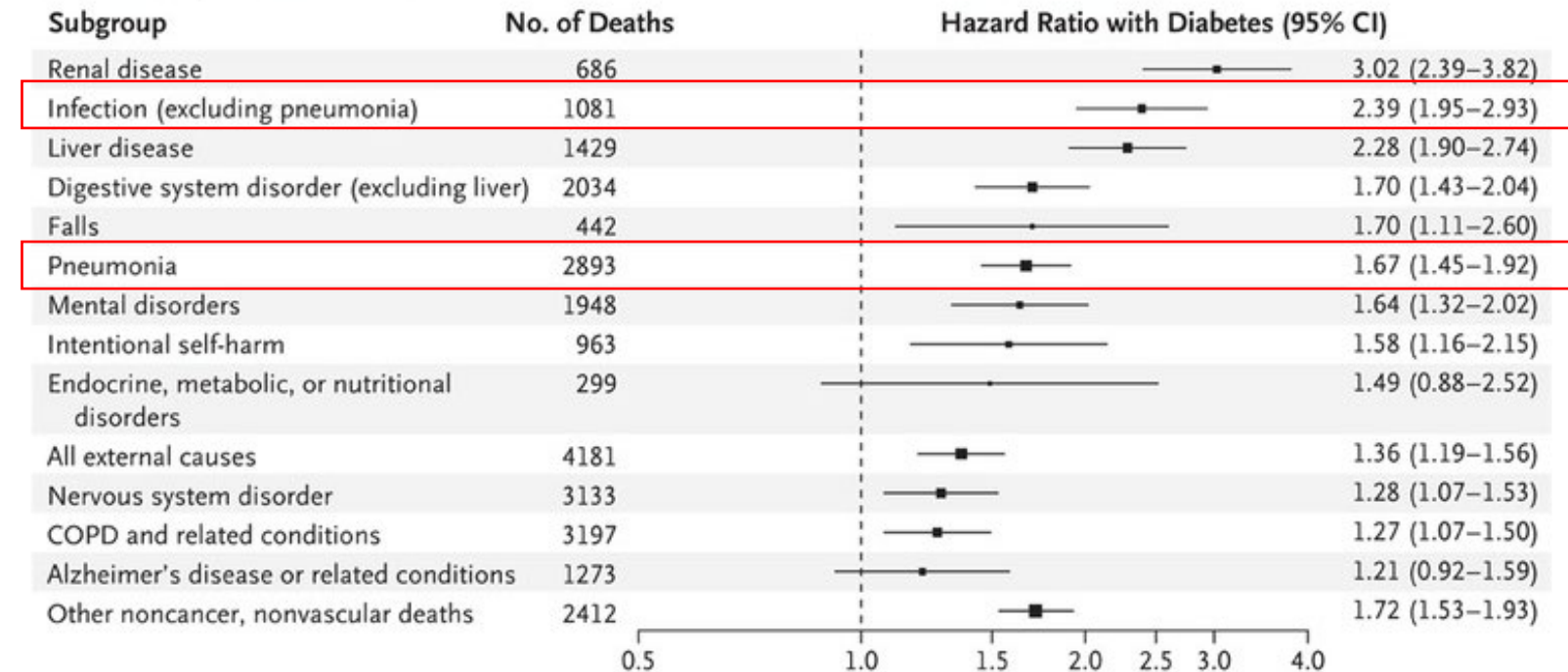
ORIGINAL ARTICLE

Diabetes Mellitus, Fasting Glucose, and Risk of Cause-Specific Death

The Emerging Risk Factors Collaboration*

N Engl J Med. 2011 Mar 3;364(9):829-841. doi: 10.1056/NEJMoa1008862

B Noncancer, Nonvascular Death



Infection-related Hospitalization

Study	DM	Study Type included	Outcome	Risk associated with DM (95% CI)
Fang et al (2021) Atherosclerosis risk in Communities (AIRC)	T1DM ; T2DM	Cohort (12.379) FU 23.8 years	Infection-related hospitalization	HR 1.67
			Hospitalization for foot infection	HR 5.99
Luk et al (2021) (Hong-Kong)	T1DM, T2DM	Cohort (6.164.082)	Hospitalization for Kidney infection (male/female)	RR 2.50 / RR 2.10
			Hospitalization for Tuberculosis (male/female)	RR 2.20/ RR 2.10
			Hospitalization for sepsis (male/female)	RR 2.30 /RR 2.30

From: [The burden and risks of emerging complications of diabetes mellitus](#)

Cosa non abbiamo chiaro

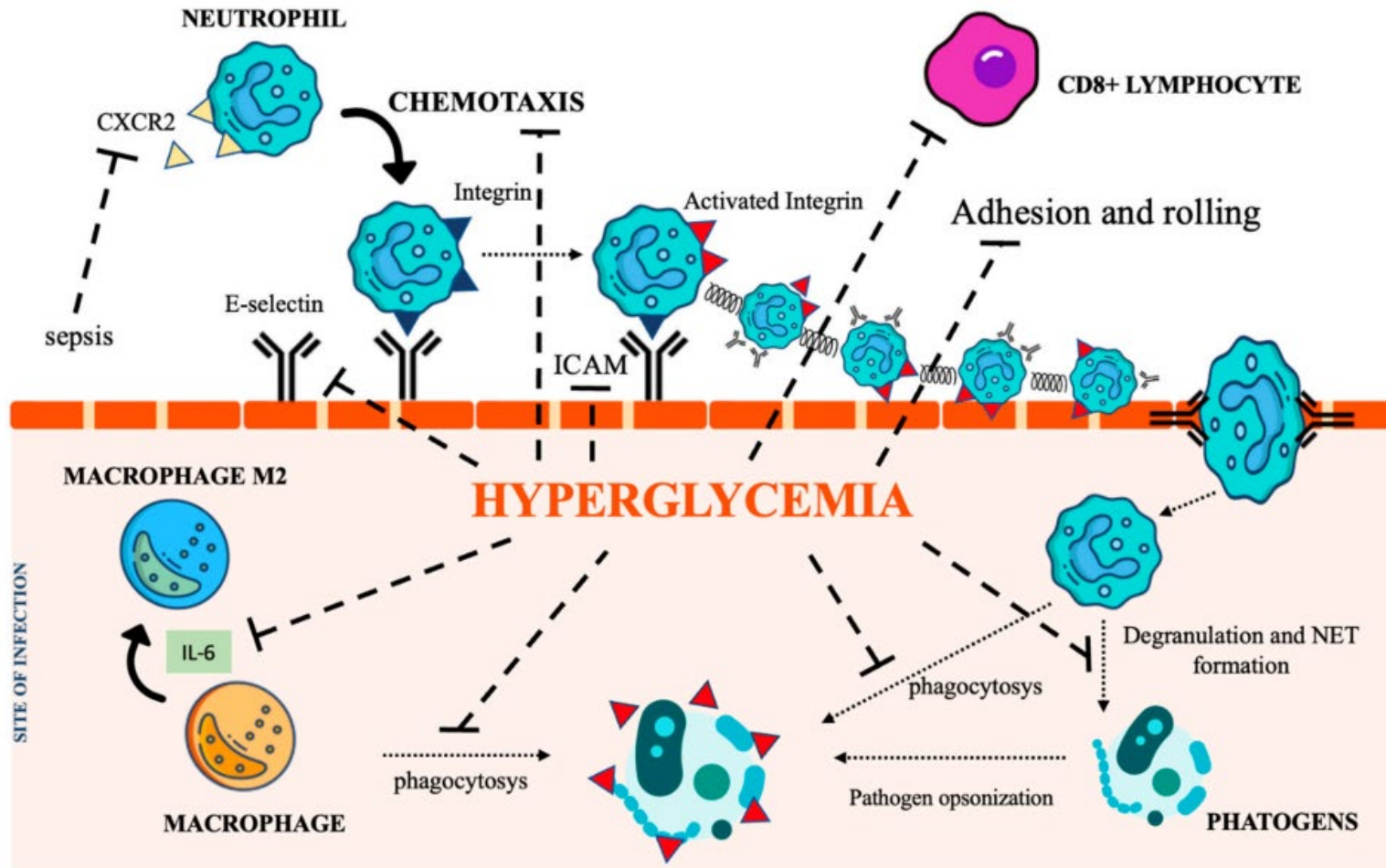
E' colpa del Diabete o dell'Iperglicemia?

E' lo stato infettivo che aumenta la glicemia,
o è la glicemia che favorisce lo stato
infettivo?

GIGI MARZULLO

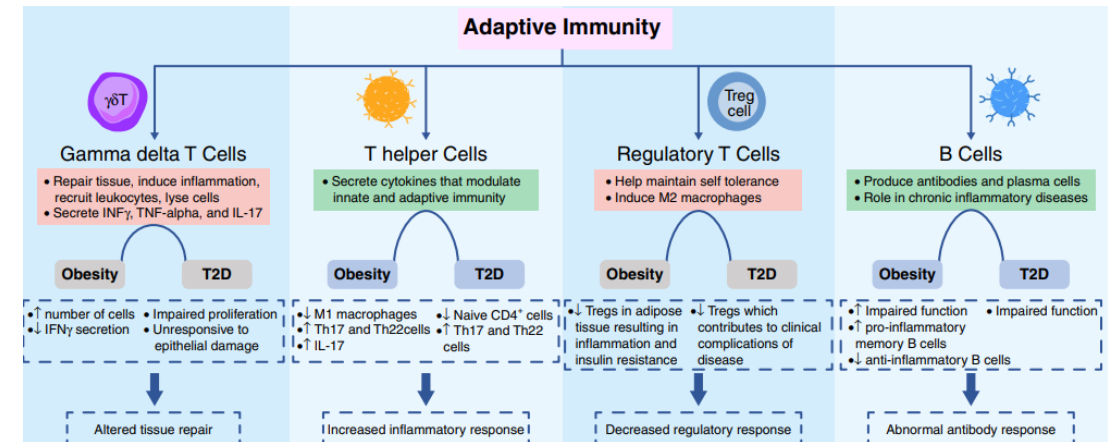
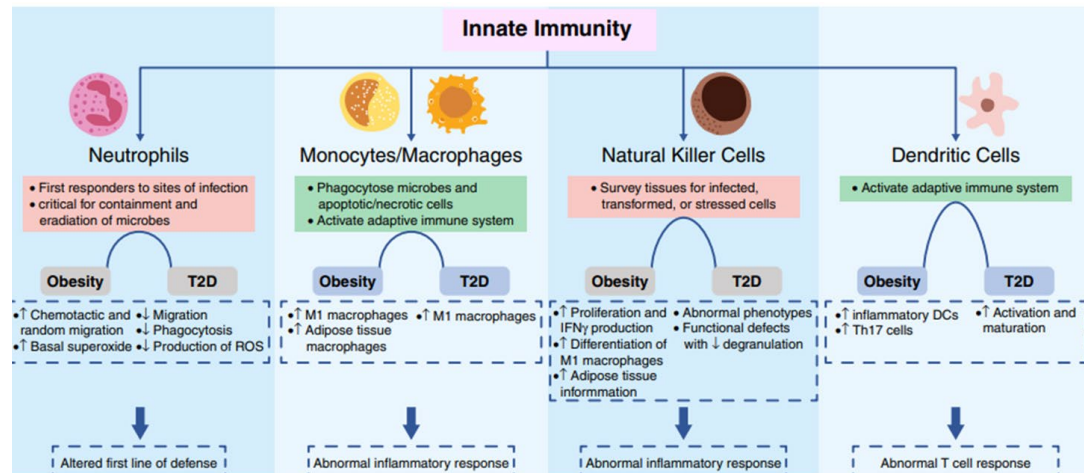


Immunity Impairment in DM



- Remuzzi G, Leukocyte-endothelial interaction is augmented by high glucose concentrations and hyperglycemia in a NF- κ B-dependent fashion Clin Invest 1998;101:1905-1915
- Delamaire M, Impaired leucocyte functions in diabetic patients. Diabet Med 1997;
- Chang F-Y, : Respiratory burst activity of monocytes from patients with non-insulin-dependent diabetes mellitus. Diabetes Res Clin Pract 1995

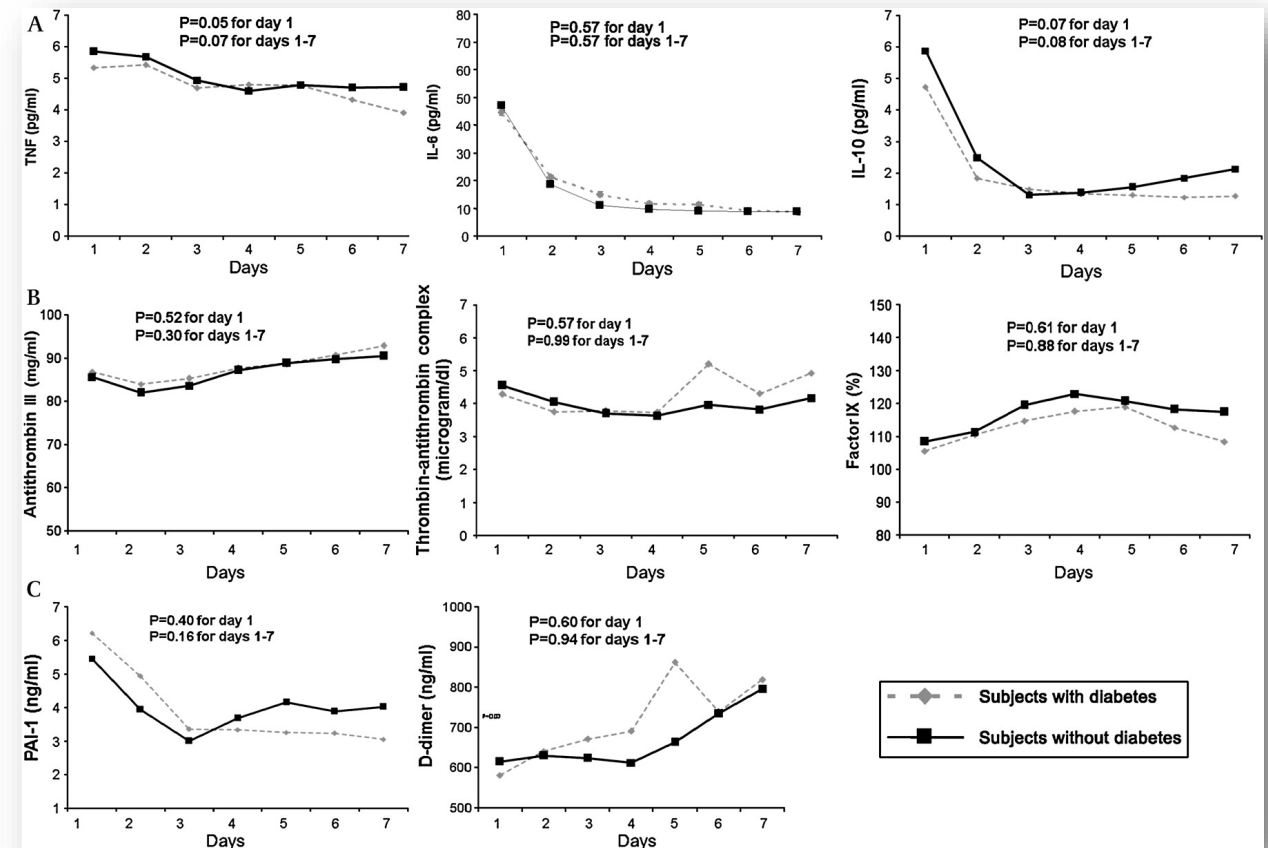
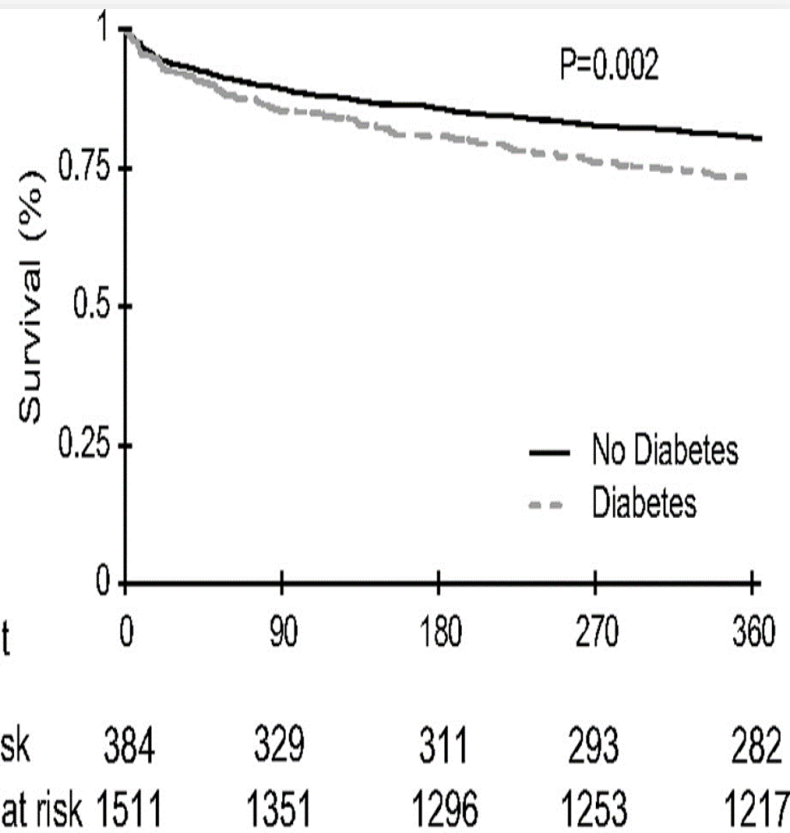
Obesity and type 2 diabetes mellitus drive immune dysfunction, infection development, and sepsis mortality



modified , J Leukoc Biol. 2018;1–10

The influence of pre-existing diabetes mellitus on the host immune response and outcome of pneumonia: analysis of two multicentre cohort studies

- Retrospective analysis of two multicentre cohorts
- 1895 patients
- effect of pre-existing diabetes on the host immune response, acute organ function and mortality in patients hospitalised with community-acquired pneumonia (CAP)
- Measurements included the mortality rate within the first year, risk of organ dysfunction, and immune responses, including circulating inflammatory (tumour necrosis factor, interleukin 6, interleukin 10), coagulation (Factor IX, thrombin–antithrombin complexes, antithrombin), fibrinolysis (plasminogen-activator inhibitor-1 and D-dimer) and cell surface markers (CD120a, CD120b, human leucocyte antigen (HLA)-DR, Toll-like receptor-2 and Toll-like receptor-4).



Pre-existing diabetes was associated with a higher risk of death following CAP. The mechanism is **not due to an altered immune response**, at least as measured by a broad panel of circulating and cell surface markers, but may be **due to worsening of pre-existing cardiovascular and kidney disease**

Diabetes and Infection: Is There a Link?

- *“Considering that diabetes is a complex disease, associated with numerous metabolic disturbances, it is obviously impossible to pin the enhanced susceptibility to infections to a single pathway or cell type”*

Cosa possiamo fare

- Il trattamento intensivo migliora o non è influente sugli outcome?
- Adesione al piano vaccinale

Glycemic Control and Urinary Tract Infections in Women with Type 1 Diabetes: Results from the DCCT/EDIC

Figure 1. Flow of female participants in DCCT/EDIC/UroEDIC

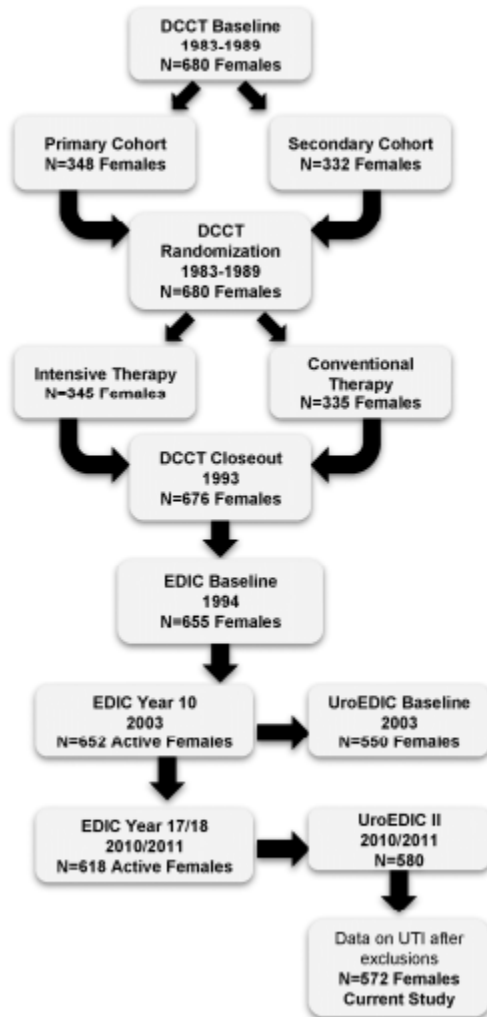
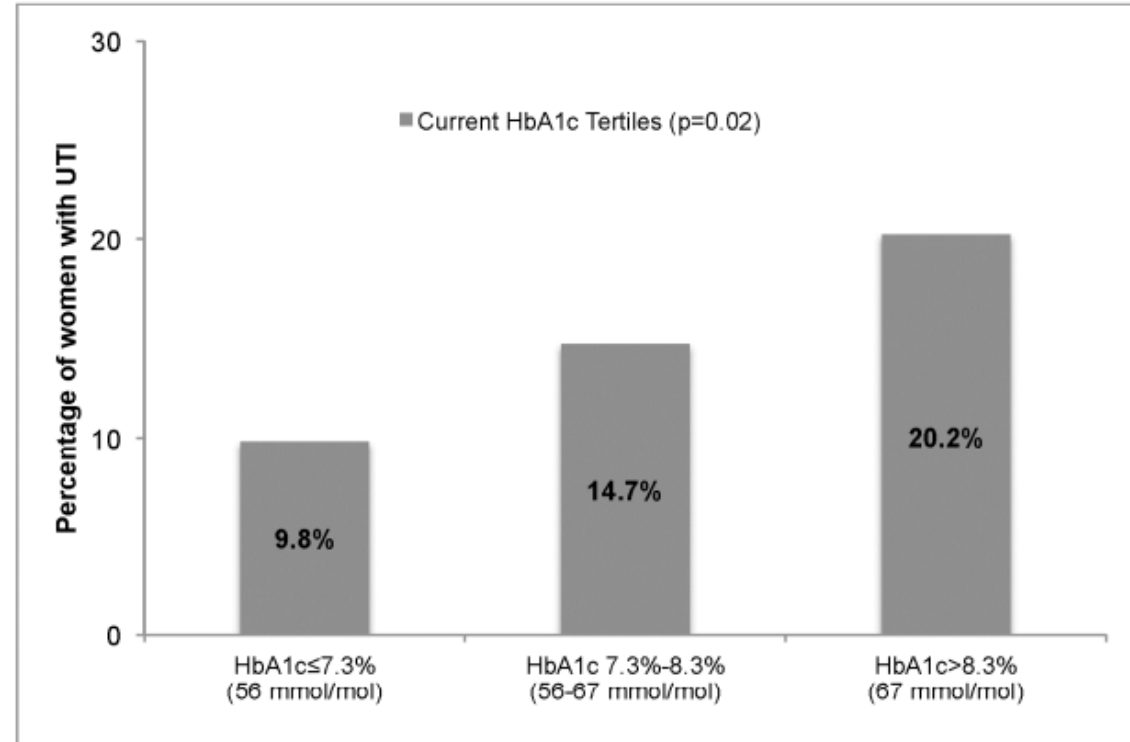


Figure 2. Percentage of women with UTI* at EDIC Year 17 per tertile of current EDIC Year 16 HbA1c



Note: p-values based on Mantel-Haenszel chi square test

* UTI defined as ≥1 episode in past 12 months.

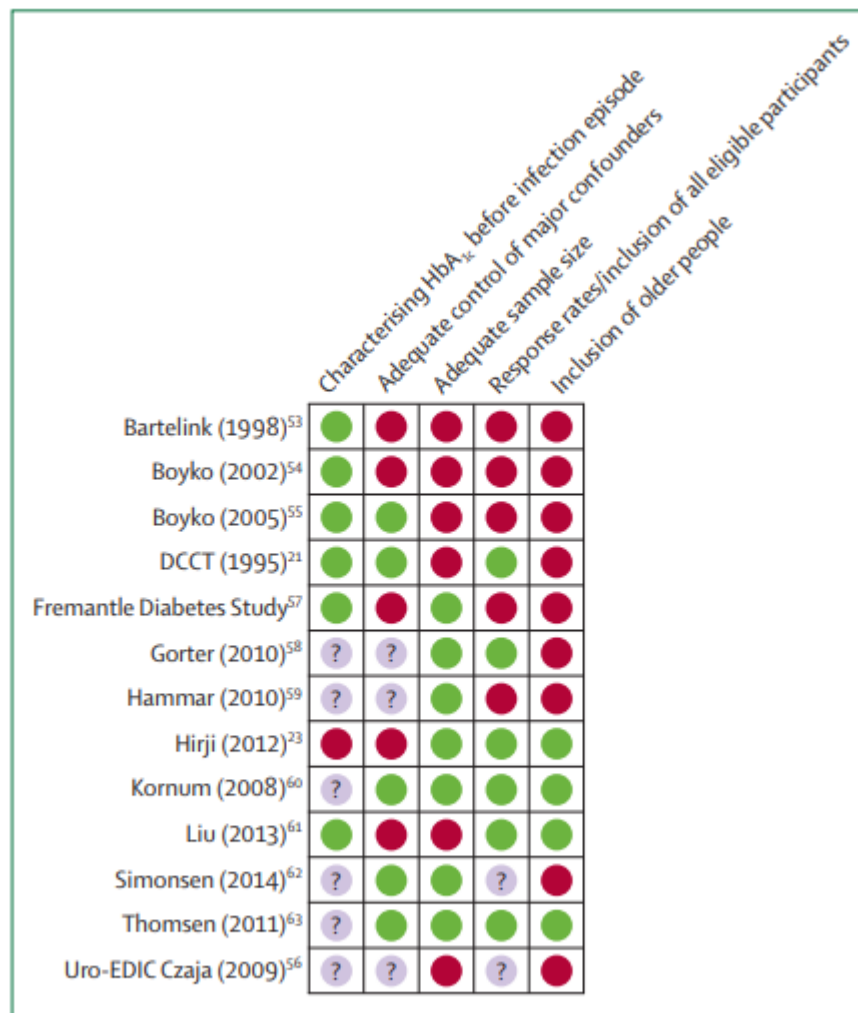


Figure: Summary of robustness and applicability of the evidence from the studies included

Diabetes and infection: assessing the association with glycaemic control in population-based studies



Jonathan Pearson-Stuttard, Samkeliso Blundell, Tess Harris, Derek G Cook, Julia Critchley

Diabetes is a leading cause of morbidity and mortality. The global burden of diabetes is rising because of increased obesity and population ageing. Although preventive and treatment measures are well documented for macrovascular complications, the impact of glycaemic control on infection risk remains unclear. *Lancet Diabetes-Endocrinol* 2015; 5: 111–121

Reported an association between high HbA1c (> 7–8% or > 53–64 mmol/mol) and a 1.5–3.5-fold increased risk of infection in diabetic patients.

Increased infection risk in the elderly with reduced glycaemic control

19 806 people aged 65 years or older with diabetes, with infection rates stratified by glycaemic control

	n/N (%)	Pneumonia (n=113)		Urinary tract infections (n=1169)		Skin and soft tissue infections (n=1487)	
		Odds ratio	p value	Odds ratio	p value	Odds ratio	p value
Overall HbA _{1c} *	19 456/19 806 (98%)†	1.013 (1.003–1.024)	0.011	1.006 (1.002–1.010)	0.005	1.004 (1.000–1.007)	0.0498
Good glycaemic control (HbA _{1c} <7.0% [<53 mmol/mol])‡	10 516/19 456 (54%)	1	..	1	..	1	..
Moderate glycaemic control (HbA _{1c} 7.0–8.5% [53–69 mmol/mol])‡	6 741/19 456 (35%)	1.03 (0.66–1.61)	0.896	1.13 (0.98–1.29)	0.086	1.09 (0.97–1.23)	0.162
Poor glycaemic control (HbA _{1c} >8.5% [>69 mmol/mol])‡	2 199/19 456 (11%)	2.38 (1.44–3.93)	<0.0007	1.28 (1.06–1.55)	0.012	1.30 (1.10–1.54)	0.002

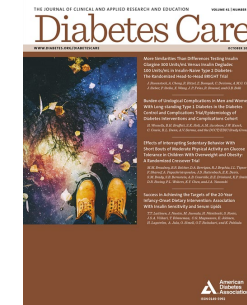
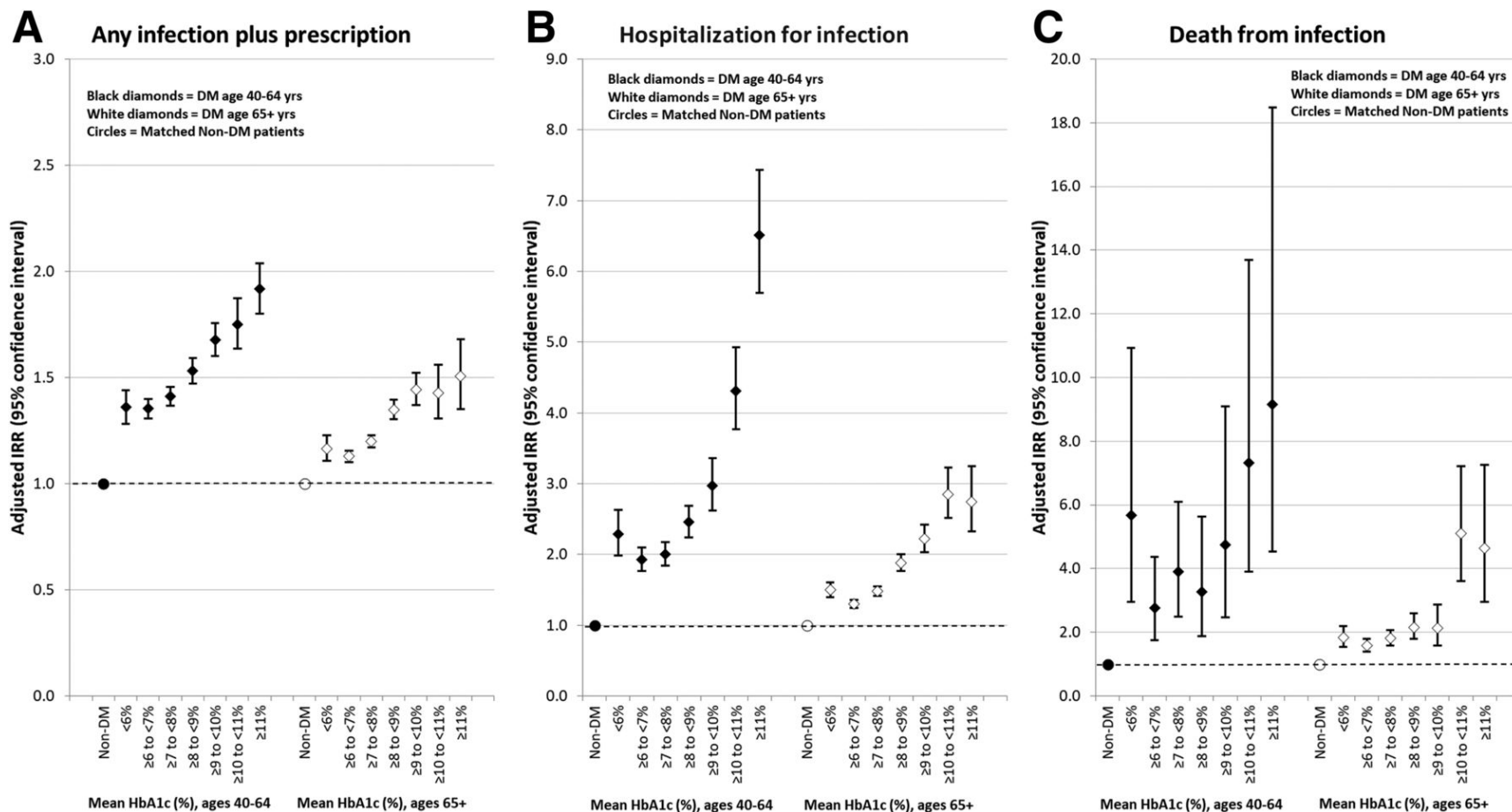
*Models using HbA_{1c} as a linear variable. †We excluded patients whose most recent HbA_{1c} measurements were from more than 3 years before Jan 1, 2014. ‡Models using HbA_{1c} as a categorical variable.

Table: Association between HbA_{1c} value and risk of infections during a 1 year follow-up period (2014) in older people with diabetes, stratified by baseline glycaemic control and adjusted for demographics and comorbidities

Andrew P McGovern, Julia Hine, The Lancet Endocrinology 2016

Glycemic Control and Risk of Infections Among People With Type 1 or Type 2 Diabetes in a Large Primary Care Cohort Study

English primary care data, average glycated hemoglobin (HbA1c) during 2008–2009 was estimated for 85,312 patients with DM ages 40–89 years. Infection rates during 2010–2015 compiled from primary care, linked hospital, and mortality records were estimated across 18 infection categories and further summarized as any requiring a prescription or hospitalization or as cause of death.

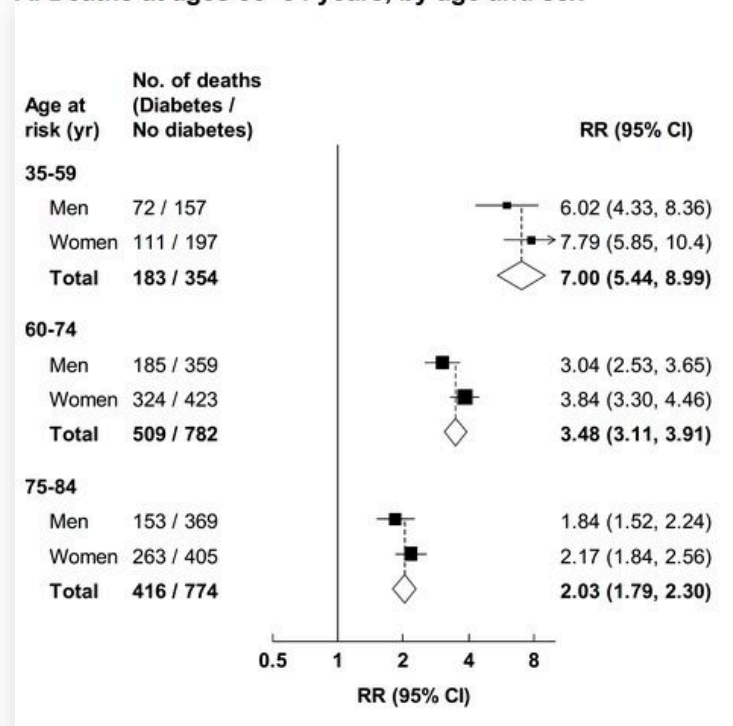


Mexico City

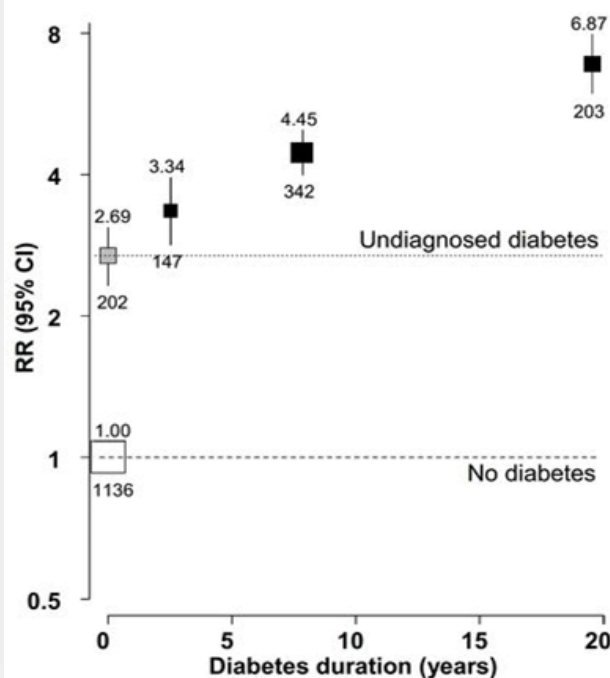
- Studies in high-income countries suggest diabetes is associated with an approximate doubling of the risk of infection-related mortality, but risks are poorly characterized in lower income settings
- In this prospective study of 150 000 Mexican adults, previously diagnosed diabetes was associated with fourfold higher risk of death from infection, and up to 10-fold higher risk of death due to specific infectious causes.
- Relative risks were higher with longer diabetes duration and worse glycemic control.

Relevance of previously diagnosed and undiagnosed diabetes to mortality from any infectious cause by age and sex (A), duration of diabetes (B), and glycemic control (C).

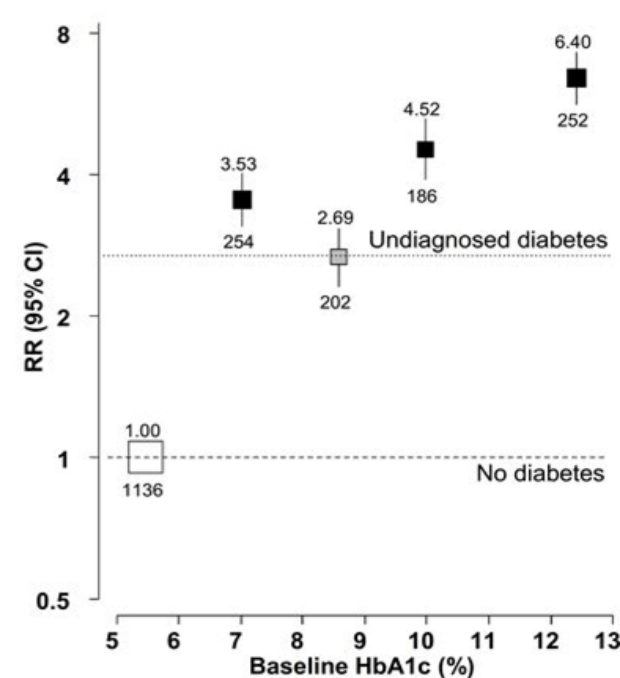
A. Deaths at ages 35–84 years, by age and sex



B. Deaths at ages 35–74 years, by duration of diabetes



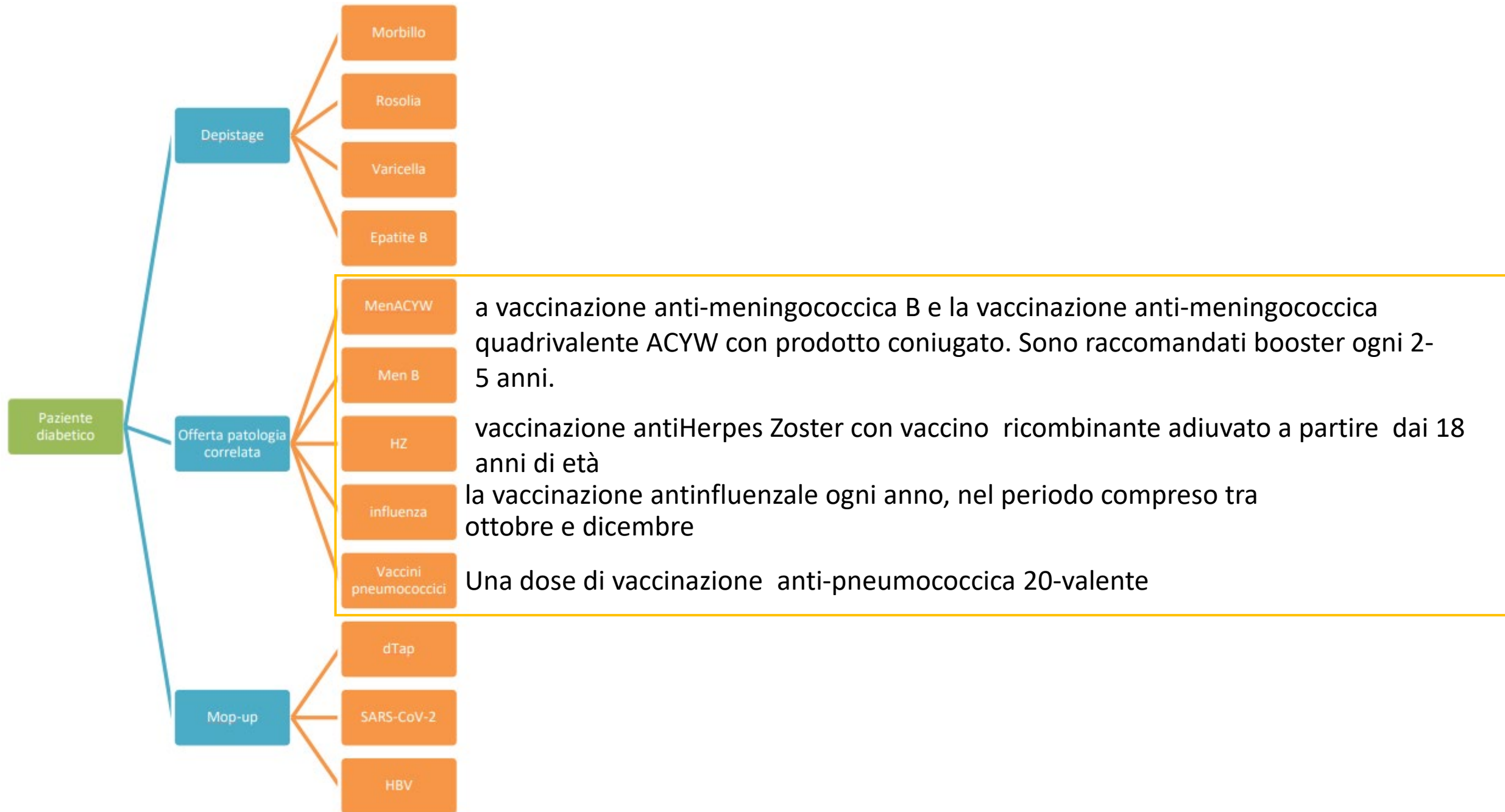
C. Deaths at ages 35–74 years, by HbA1c



RACCOMANDAZIONI PER LA PROFILASSI VACCINALE NEI SOGGETTI AFFETTI DA DIABETE MELLITO DI TIPO 1 E 2

- La pandemia COVID-19 ha portato all'attenzione delle autorità di Sanità Pubblica la condizione di vulnerabilità della popolazione diabetica nei confronti delle patologie infettive
- necessità di implementare idonee strategie vaccinali, attraverso campagne che devono integrare le diverse figure sanitarie di riferimento (MMG, igienista e diabetologo).





Conclusioni

I pazienti diabetici hanno un rischio maggiore di infezioni, gravate da maggior rischio di ospedalizzazione e mortalità

Il compenso glicemico correla con severità delle infezioni e con la relativa mortalità a tutte le età

Tali conseguenze sono sicuramente peggiori in popolazioni a basso livello economico che meritano di essere attenzionate

La prevenzione delle patologie infettive tramite l'adesione al piano vaccinale è da raccomandare a tutti i pazienti

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