Medicina di precisione e modelli di predizione nel diabete di tipo 2

Vincenzo Trischitta

IRCCS "Casa Sollievo della Sofferenza", San Giovanni Rotondo

Dichiaro di NON aver ricevuto negli ultimi due anni compensi o finanziamenti da aziende farmaceutiche e/o diagnostiche e di non soffrire di altri tipi di conflitti d'interesse inerenti questa relazione

Vincenzo Trischitta

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Precision medicine in affected individuals aims to identify patients at different risk of…

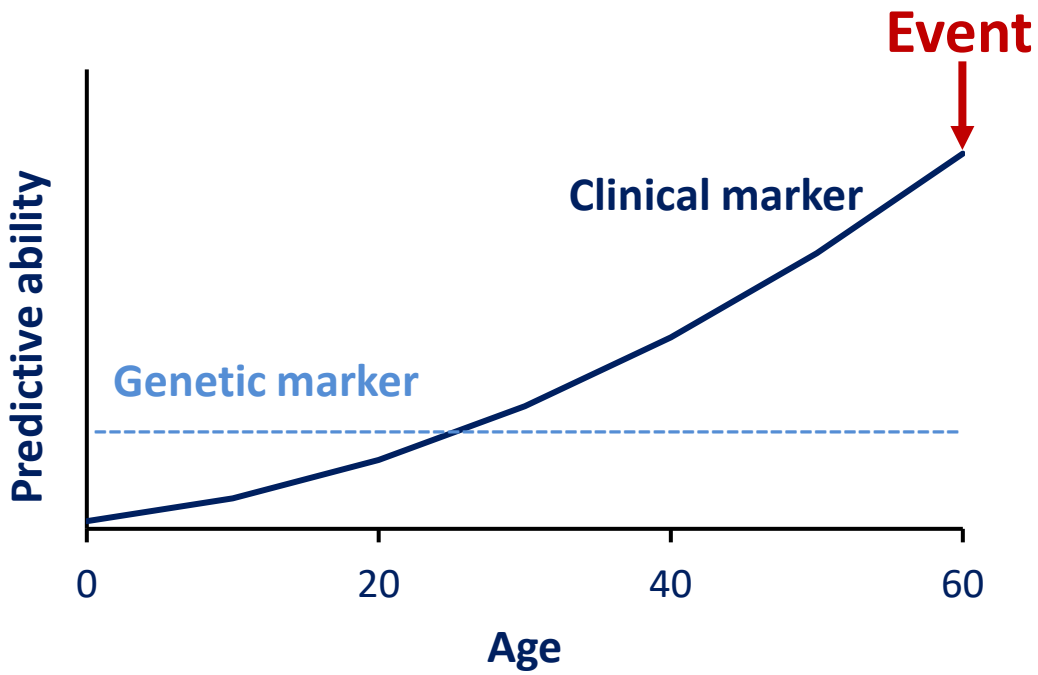
…belonging to different disease subtypes (differential diagnosis)
Precision diagnosis

…developing a given clinical outcome (complications, events)
Precision prediction

…responding to a given treatment (efficacy, side effects)
Precision intervention/treatment

Precision medicine aims to find the most appropriate management at a given time, in a given place, for a given person.

Markers of genetic susceptibility, clinical risk factors and risk estimation at a given time



Precision medicine aims to find the most appropriate management for a given person at a given time, in a given place.

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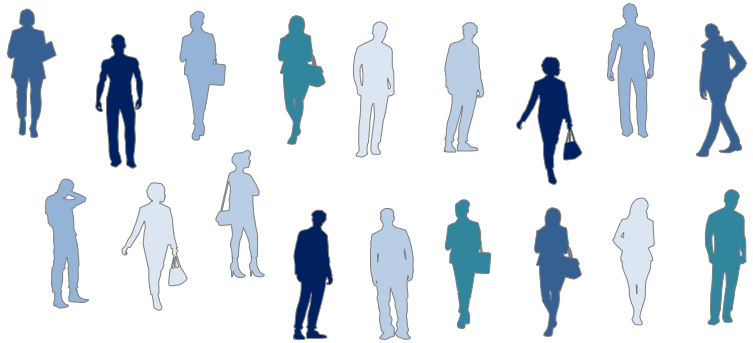
Clinical prediction requires individual risk measurement



Gradient of individual risk

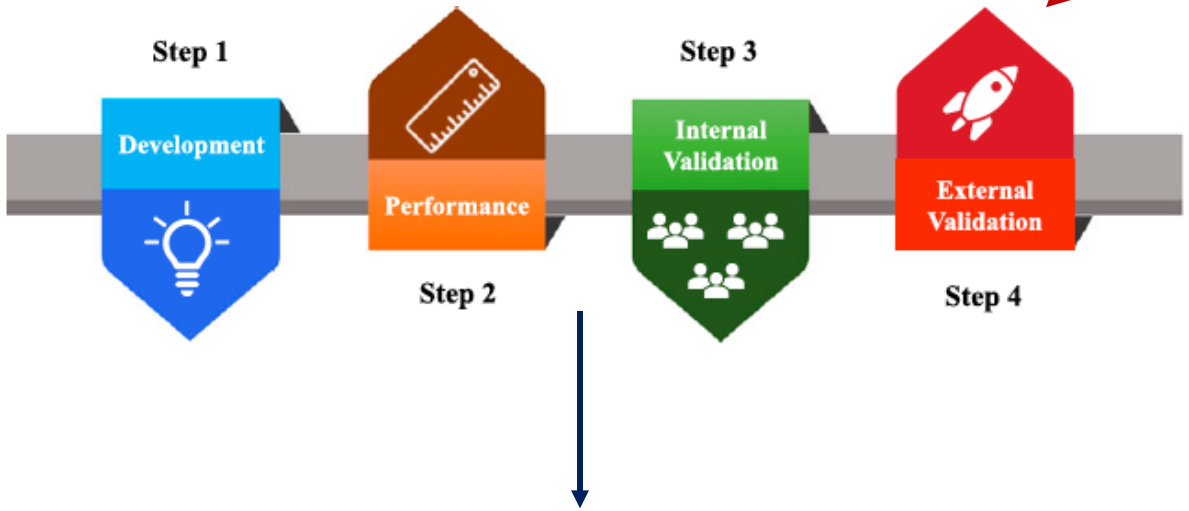
We do need prediction models able to assign a numerical score to each individual.
This approach is the gold standard for optimal risk stratification and therefore for the implementation of precision medicine.

Trischitta V, Diabetes 2023;72:1057

Moving Toward the Implementation of Precision Medicine Needs Highly Discriminatory, Validated, Inexpensive and Easy-to-Use Prediction Models

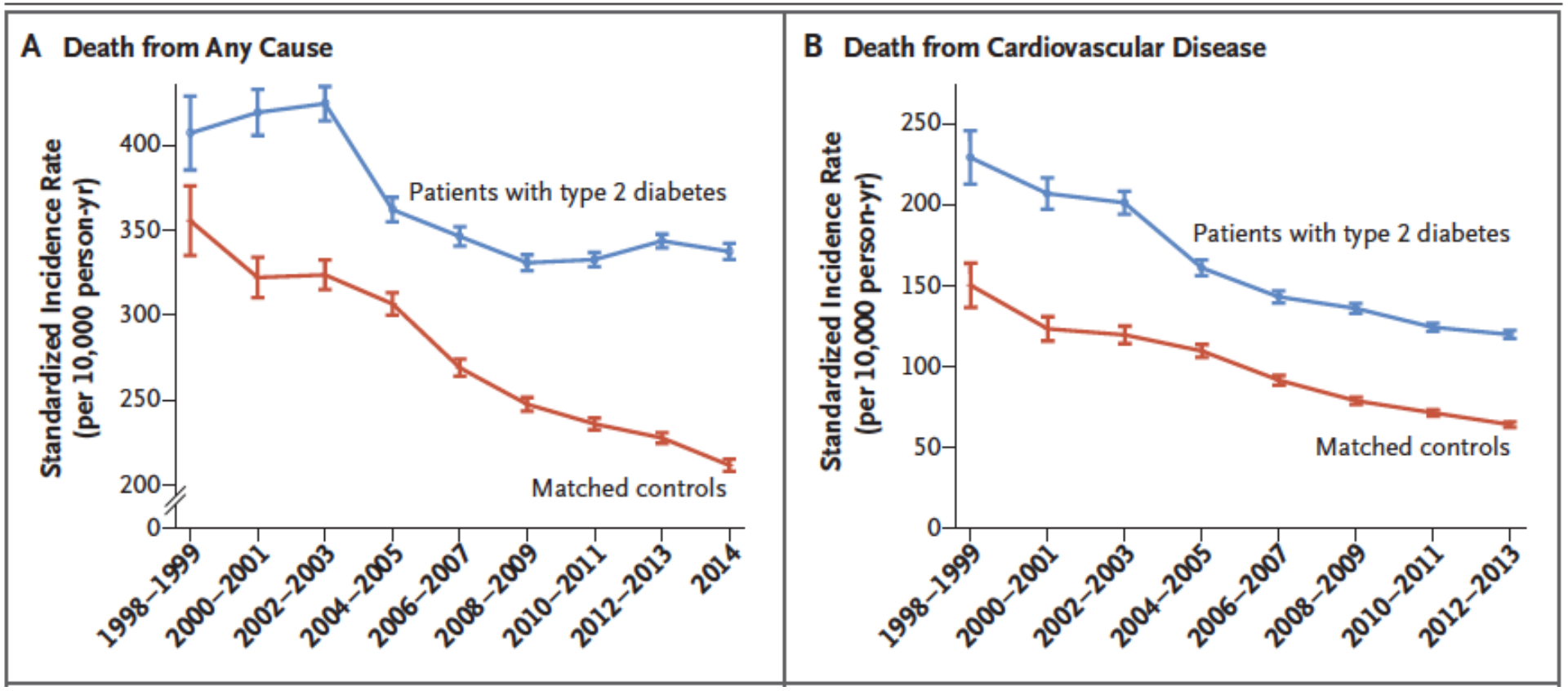
Trischitta V & Copetti M, Diabetes Care 2020

Ideally, to be checked in each new context



You first create and validate a clinical model and then try improve it with additional markers (i.e., studies on the so-called omics or even non omics)

The risk of mortality in patients with T2D



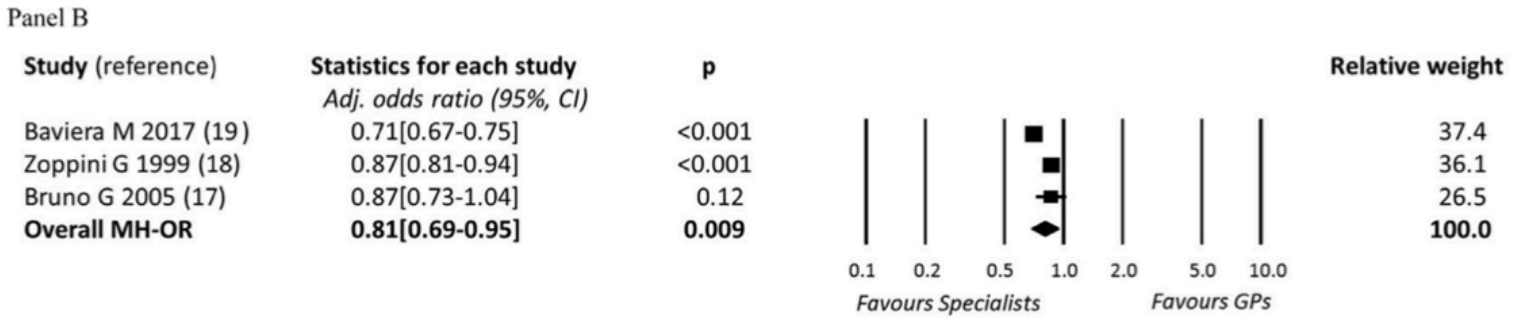
Rawshani A, N Engl J of Med 2017

Attending Diabetes Clinic and all-cause mortality in T2D

Table 1 Main characteristics of the studies included in the meta-analysis.

First author (year)	Enrolment (year)	Follow-up (years)	Patients (No.)		Mean age (years)		Gender (Male, %)		Insulin (%)		Deaths (No.)	
			DC	noDC	DC	noDC	DC	noDC	DC	noDC	DC	noDC
Zoppini G. 1999 [17]	1986	10	4047	3101	67	67	47	47	8	4	1564	1332
Bruno G. 2005 [18]	1991	11	1097	316	68	72	44	42	19	11	502	180

To customize different types of care for different people, **well-performing risk prediction models are indispensable**. They better be parsimonious, especially if they are to be used in contexts with limited resources.



Bonora E, Nutrition, Metabolism & Cardiovascular Diseases, 2018

ENFORCE
(EstimatioN oF mORtality risk in type2 diabetiC patiEnts)

Development and validation of a predicting model of all-cause mortality in patients with type 2 diabetes mellitus
De Cosmo S, Copetti M et al, Diabetes Care 2013

EstimatioN oF mORtality risk in type2 diabetiC patiEnts (ENFORCE): an inexpensive, parsimonious and easy-to-use prediction model
Copetti M et al, J Clin Endocrinol and Metab 2019

- Accurate discrimination (C statistic=80%)
- Validated in several independent samples
  including patients with early-stage T2D
- Well calibrated
- Parsimonious (only 9, very common variables)
- Easy to use (1 minute per patient)
- Freely available on the web

http://www.operapadrepio.it/enforce/enforce.php

http://www.siditalia.it/clinica/formule-e-calcolatori

https://aemmedi.it/strumenti-del-diabetologo/

Age
Anti-hypertension Tx
DBP
Insulin Tx
HDL Cholesterol
ACR
LDL Cholesterol
BMI
Triglycerides

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Trischitta V & Copetti M, Diabetes Care 2020

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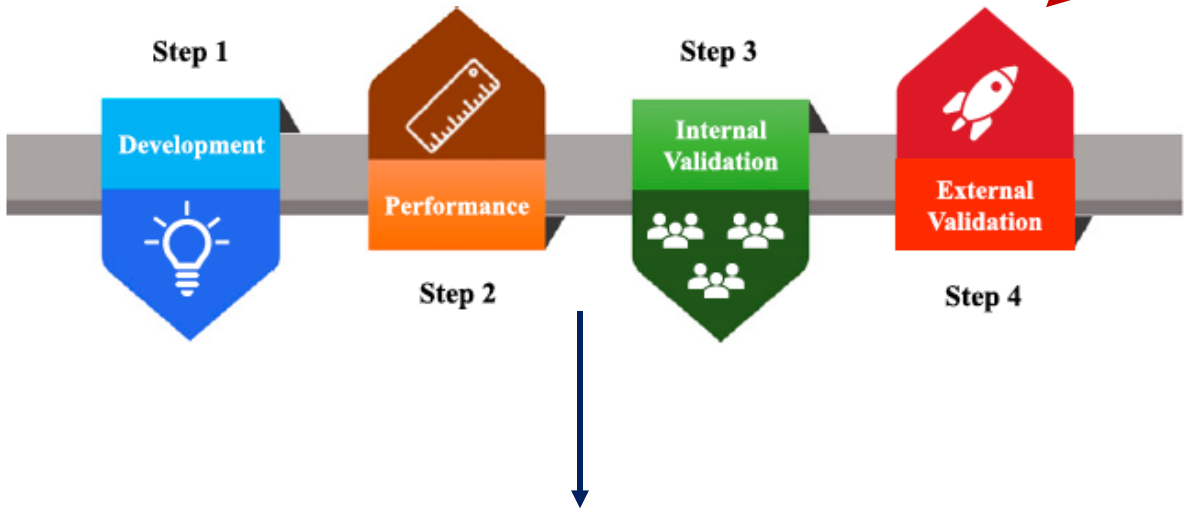

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https://doi.org/10.1210/clinem/dgae593
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Clinical Research Article

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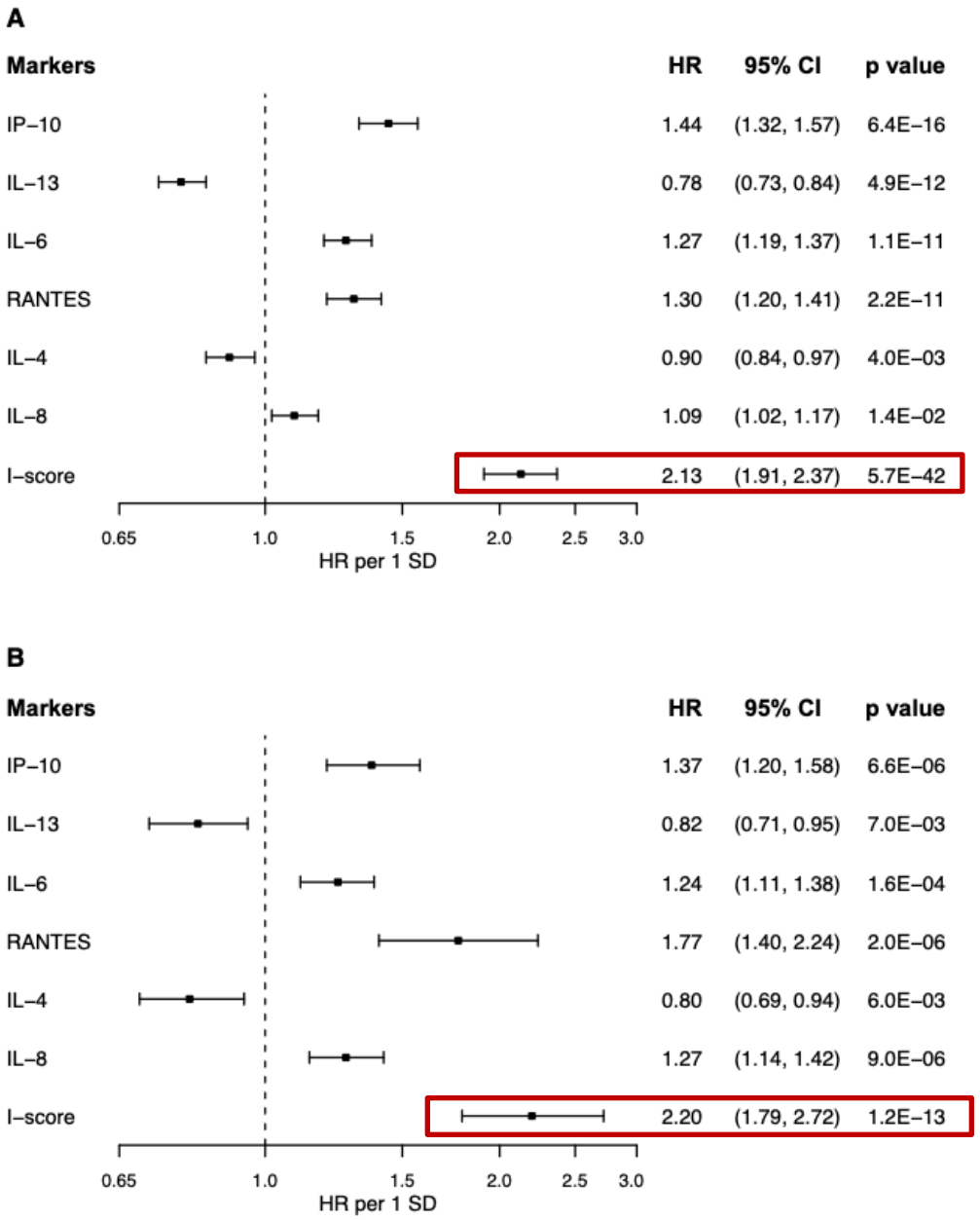
Independent association of cytokines (and the derived I-score) with mortality in the aGMS (A) and the FMS (B)



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	HR	95% CI		*P*
I score	2.13	1.91	2.37	5.7×10^{-42}
Males vs females	1.39	1.19	1.61	1.9×10^{-5}
Age at recruitment (per 10 years)	2.04	1.88	2.26	9.4×10^{-44}
Smoking habit (yes vs no)	1.72	1.39	2.12	5.7×10^{-7}
BMI (per 1 unit)	1.02	1.00	1.03	1.60×10^{-2}
HbA1c (per 1 unit)	1.02	1.03	1.11	1.00×10^{-2}
Disease duration (per 10 years)	1.02	0.94	1.13	5.6×10^{-1}
eGFR (per 10 mL/min/m^2)	1.12	1.07	1.17	5.2×10^{-7}
Antihypertension therapy (yes vs no)	1.29	1.08	1.54	4.0×10^{-3}
Insulin therapy (yes vs no)	1.48	1.25	1.74	4.0×10^{-6}
Statins therapy (yes vs no)	0.92	0.79	1.06	2.5×10^{-1}

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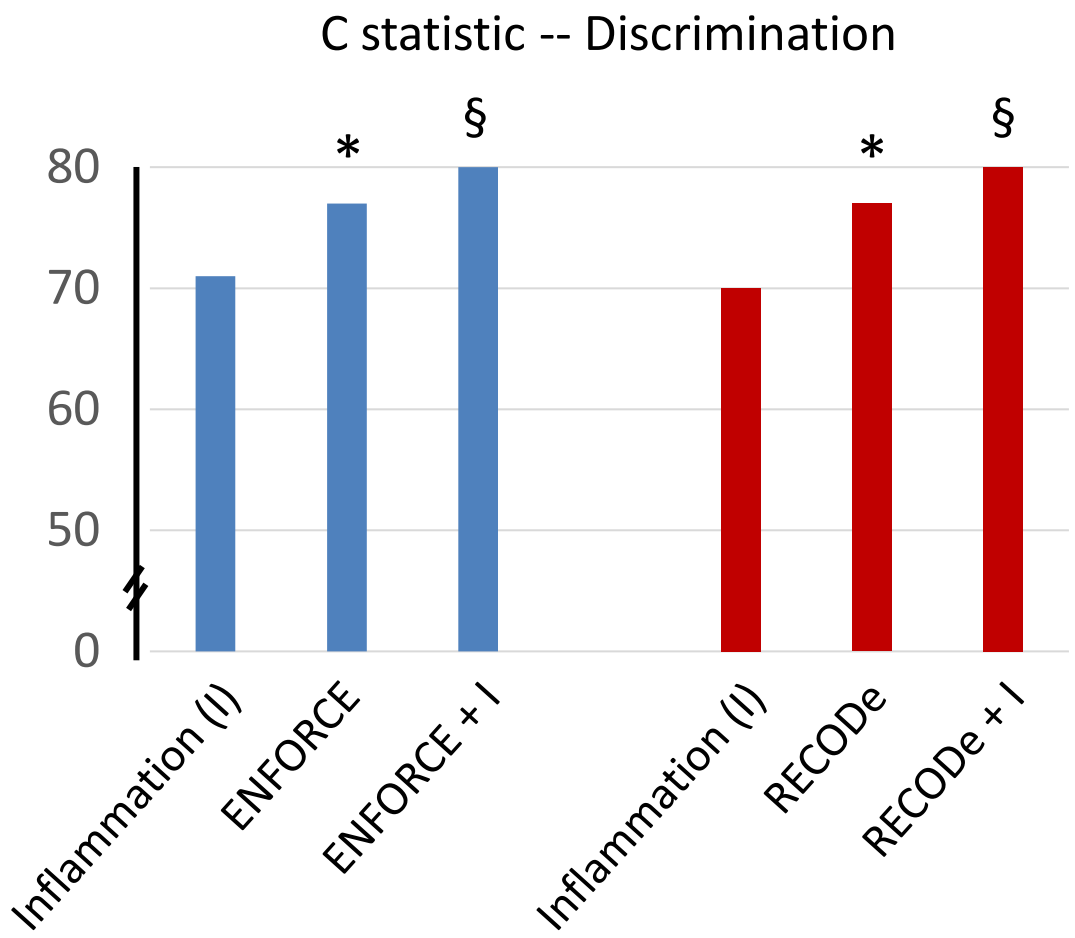

** vs inflammation*
§ vs clinical model w/o inflammation

The future that will come (or that we hope will come) …

We need clinical prediction models that are validated, parsimonious, easy to use and…free of charge!

Clinicians should be educated to use and interpret them (not to take for granted). The same goes for public health professionals!

Further science (omic- and non-omic-studies) is needed to unravel new markers capable of improving clinical prediction models.

SAPIENZA
UNIVERSITÀ DI ROMA

CASA SOLLIEVO DELLA SOFFERENZA
SAN GIOVANNI ROTONDO

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Ministero della Salute

Ministero dell'Università e della Ricerca

EFSD European Foundation for the Study of Diabetes