Terapia all’esordio: uno nessuno centomila...

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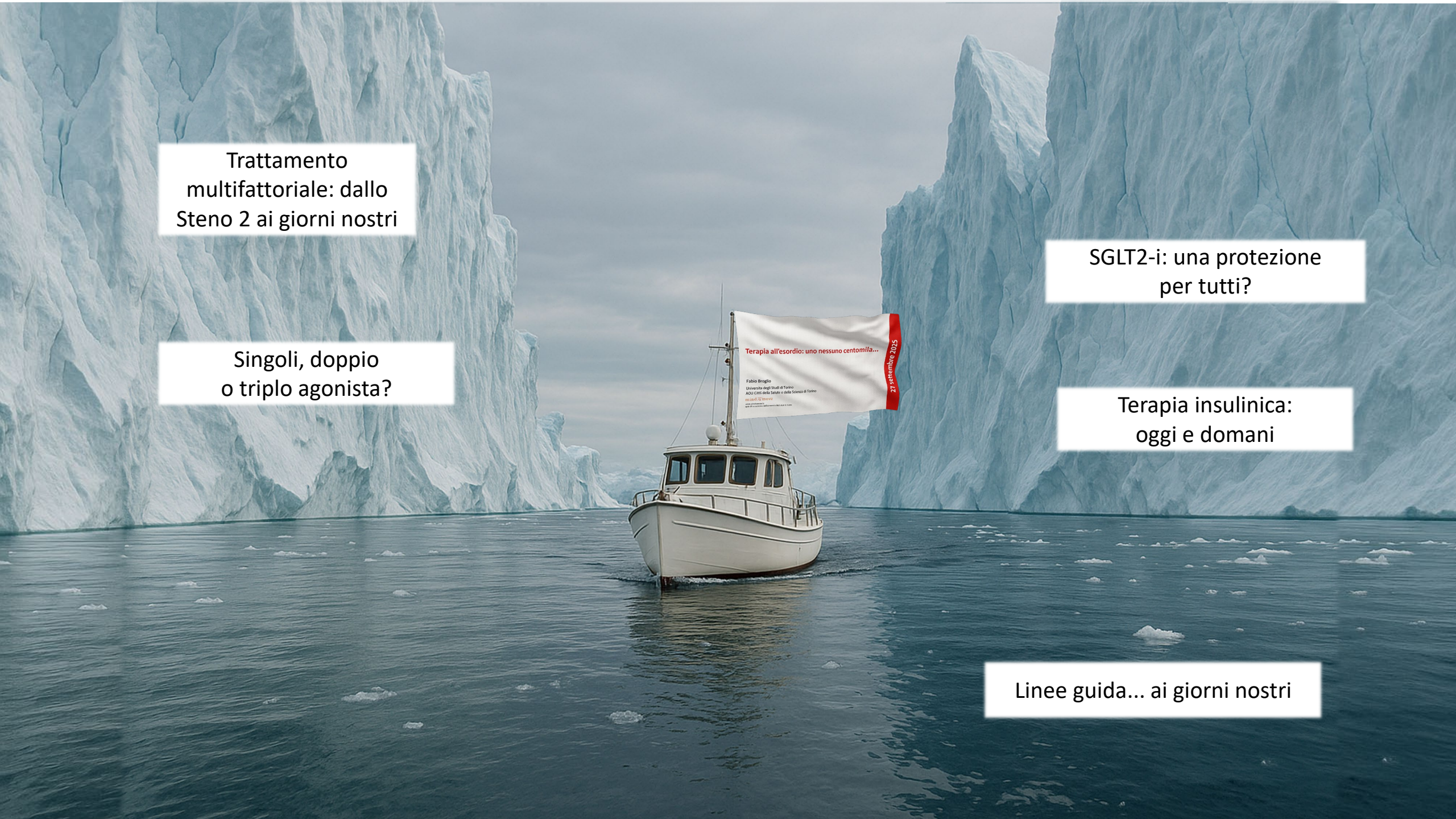
mind To move

www.mindtomove.it
spin-off accademico dell’Università degli Studi di Torino

27 settembre 2025


Trattamento multifattoriale: dallo Steno 2 ai giorni nostri
Singoli, doppio o triplo agonista?
SGLT2-i: una protezione per tutti?
Terapia insulinica: oggi e domani
Linee guida... ai giorni nostri
Terapia all'esordio: uno nessuno centomila...
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uno

Caratteristiche differenziali del diabete tipo 1 e tipo 2

	TIPO 1	TIPO 2
Prevalenza	Circa 0,3%	Circa 5%
Sintomatologia	Sempre presente Spesso eclatante e a inizio brusco	Spesso modesta o assente
Tendenza alla chetosi	Presente	Assente
Peso	Generalmente normale	Generalmente in eccesso
Età all'esordio	Più comunemente < 30 anni	Più comunemente > 40 anni
Comparsa di complicanze croniche	Non prima di alcuni anni dopo la diagnosi	Spesso presenti al momento della diagnosi
Insulina circolante	Ridotta o assente	Normale o aumentata
Autoimmunità	Presente	Assente
Terapia	Insulina necessaria sin dall'esordio	Dieta, farmaci orali, analoghi GLP-1, insulina

Standard AMD/SID 2010

“

this hypothetical basis, we woul
intervene therapeutically to atte
excursions of blood glucose, par
symptomatic glycosuria and hypo

Standards of Medical Care in Diabetes–2006

American Diabetes Association

“The goal of therapy is to achieve an A1C as close to normal as possible in the absence of hypoglycemia. However, this goal is difficult to achieve with present therapies”.

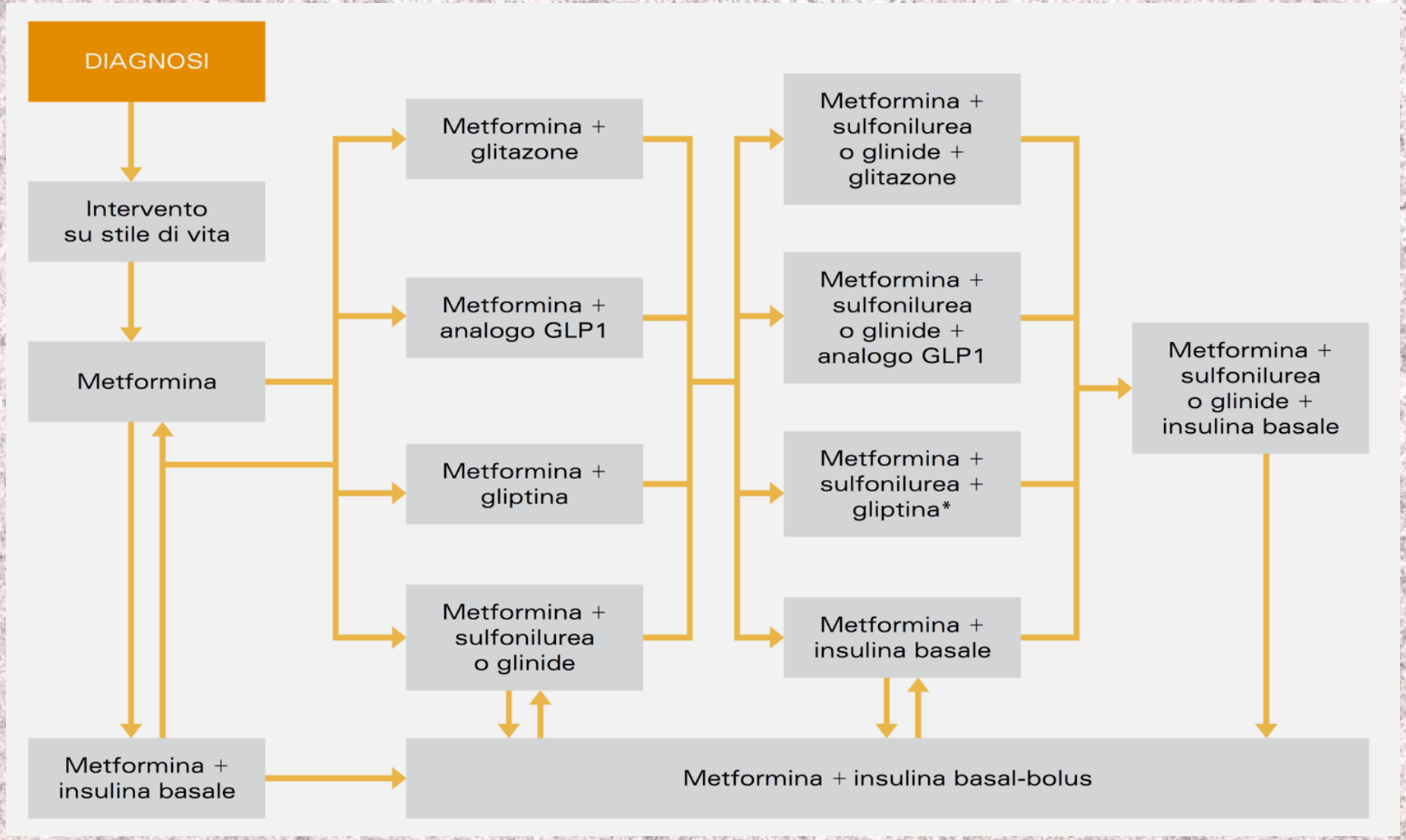
“More stringent goals (i.e., a normal A1C, 6%) should be considered in individual patients based on epidemiological analyses suggesting that there is no lower limit of A1C at which further lowering does not reduce the risk of complications”.

LO SCOPO

LO SCOPO NEGLI ANNI ‘00

STANDARD ITALIANI PER LA CURA DEL DIABETE MELLITO

2009-2010

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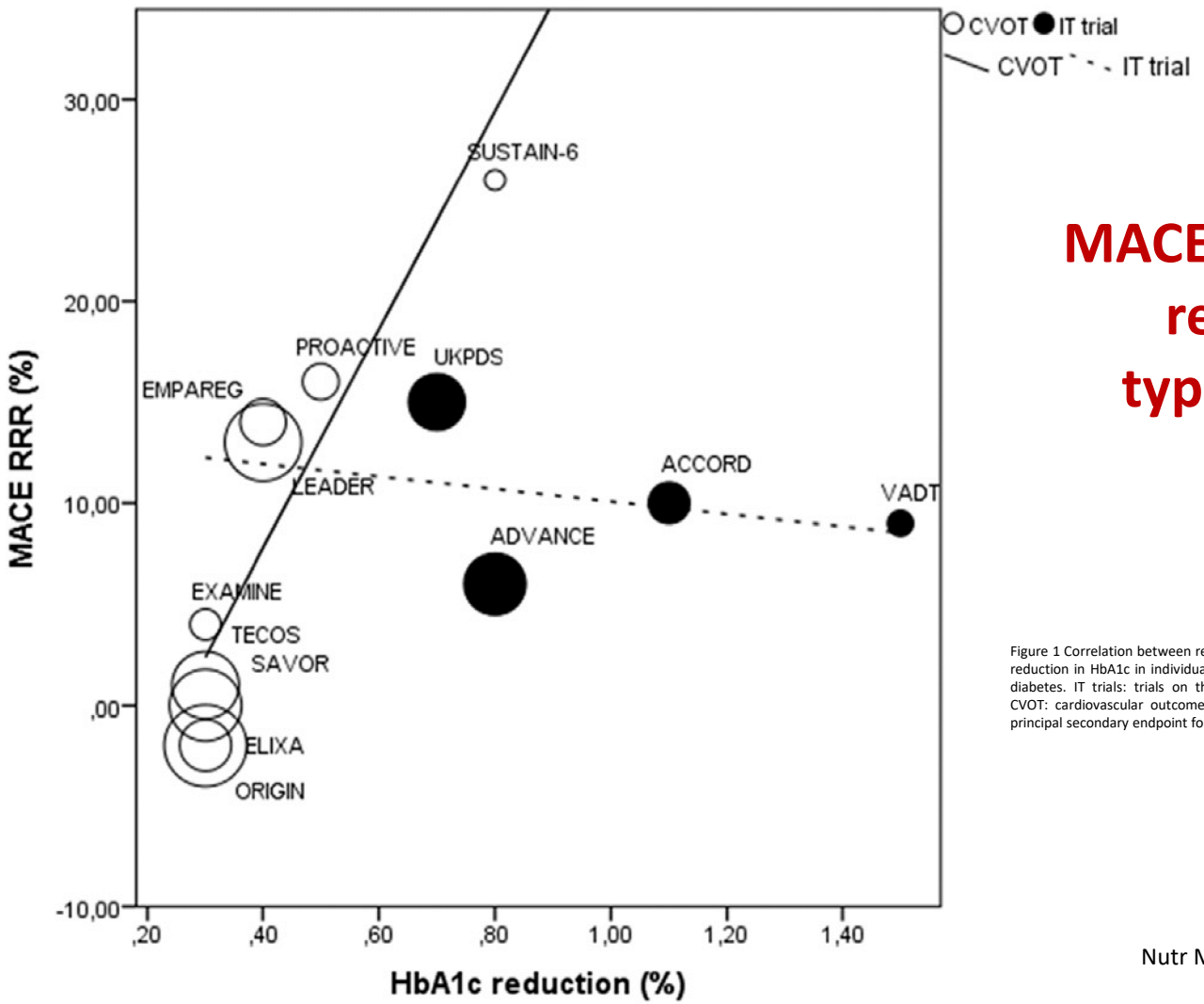
Back to glycemic control: An alternative look at the results of cardiovascular outcome trials in type 2 diabetes

E. Mannucci*, M. Monami



MACE RRR vs HbA1c reduction in type 2 Diabetes Mellitus

Figure 1 Correlation between relative risk reduction (RRR) for MACE and reduction in HbA1c in individual cardiovascular outcome trials in type 2 diabetes. IT trials: trials on the effects of intensification of therapy. CVOT: cardiovascular outcome trials on individual drugs. PROACTIVE: principal secondary endpoint for MACE.

Nutr Metab Cardiovasc Dis. 2017 Apr;27(4):375-377

Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Aidin Rawshani, M.D., Araz Rawshani, M.D., Ph.D., Stefan Franzén, Ph.D., Naveed Sattar, M.D., Ph.D., Björn Eliasson, M.D., Ph.D., Ann-Marie Svensson, Ph.D., Björn Zethelius, M.D., Ph.D., Mervete Miftaraj, M.Sc., Darren K. McGuire, M.D., M.H.Sc., Annika Rosengren, M.D., Ph.D., and Soffia Gudbjörnsdottir, M.D., Ph.D.

5 risk factors: elevated HbA1c, elevated LDL, albuminuria, smoking, and elevated blood pressure

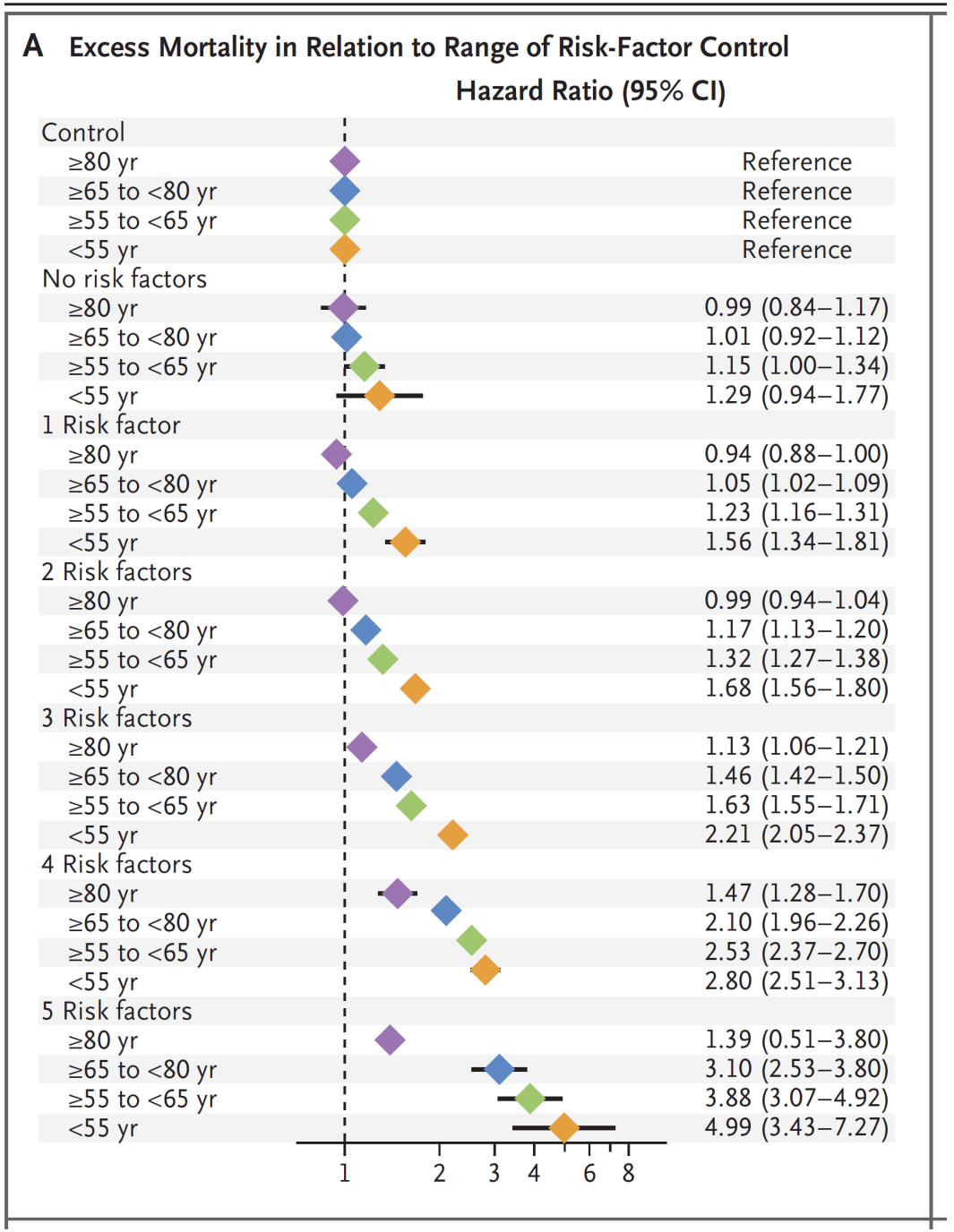


Figure 1 (facing page). Adjusted Hazard Ratios for Outcomes, According to Age Category and Number of Risk-Factor Variables outside Target Ranges, among Patients with Type 2 Diabetes, as compared with Matched Controls. Hazard ratios show the excess risk of each outcome among patients with type 2 diabetes, as compared with matched controls from the general population, according to age categories and to the number of riskfactor variables (scale, none to five) that were outside target ranges currently recommended in guidelines. The analysis included patients ith type 2 diabetes and controls matched for age, sex, and county in Sweden. We constructed a Cox hazards model for each ge category, and these models were adjusted for the covariable category"; this covariable denotes the number of risk-factor variables that were within target ranges. These Cox model analyses were performed on five imputed data sets for each age ategory, and hazard ratios were pooled from all the data sets with the use of Rubin's rule.

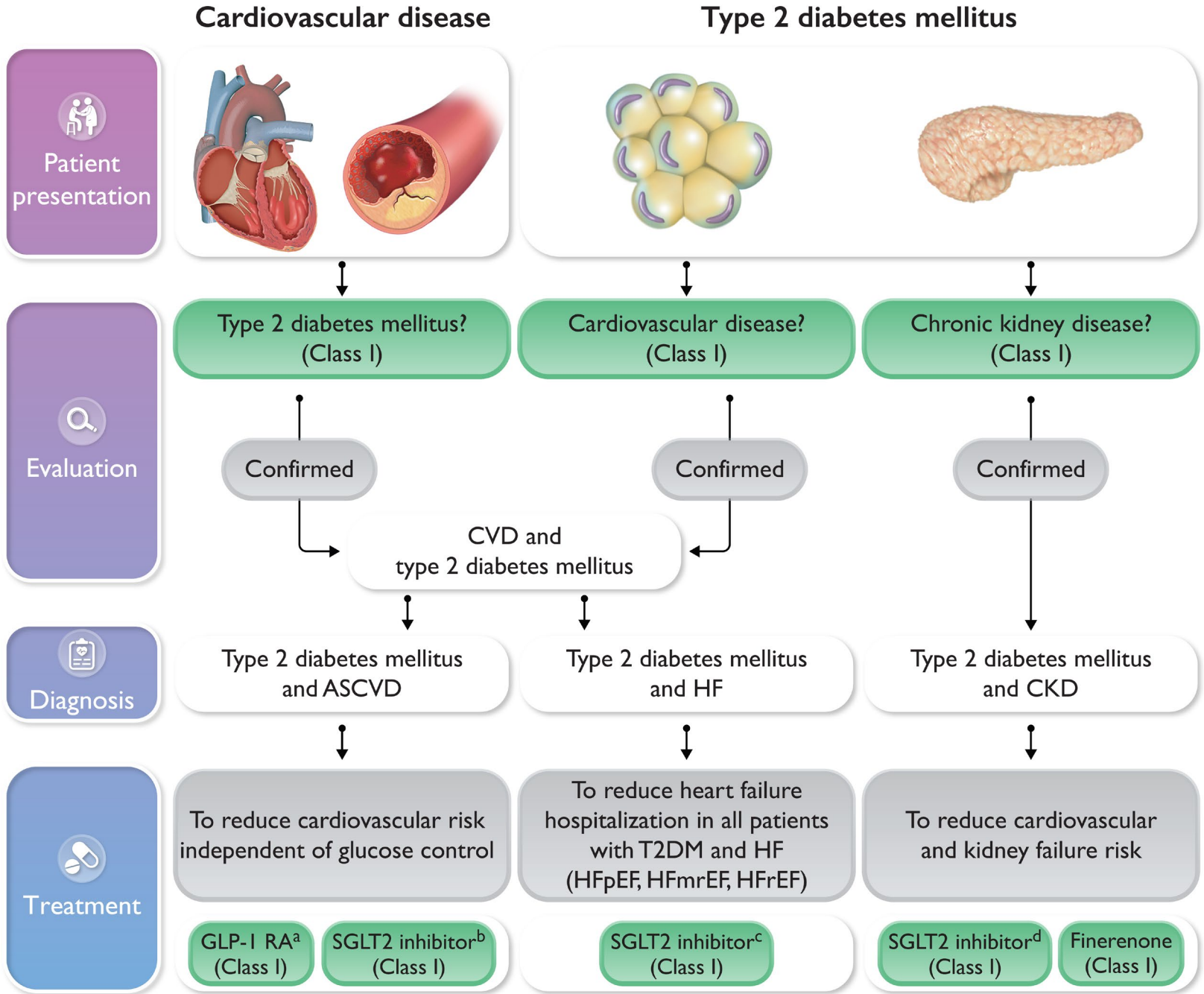
N Engl J Med 2018;379:633-44.

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC)

ESC European Society of Cardiology

European Heart Journal (2023) **00**, 1–98 https://doi.org/10.1093/eurheartj/ehad192



Standards of Care in Diabetes 2025

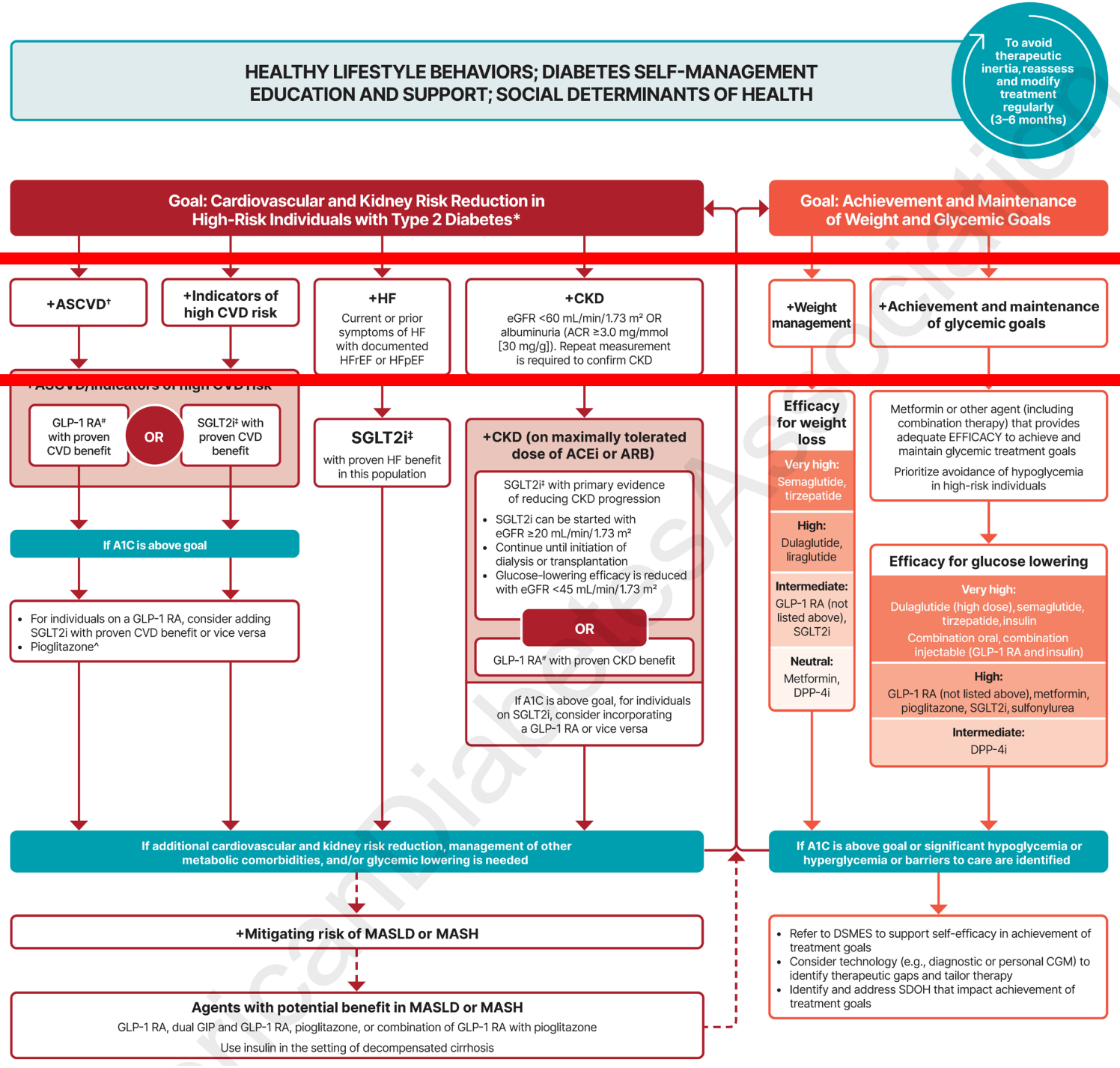
American Diabetes Association.
ISSN 0149-5992

Table 2 Prevalence of chronic complications of diabetes

Complication	Prevalence (%)
Overall cardiovascular disease	18.9
Prior clinical cardiovascular disease	11.2
Ischemic ECG	5.6
Carotid stenosis >40%	6.0
Lower limb stenosis (any)	6.6
Chronic kidney disease (eGFR <60 mL/min/1.73 m^2)	8.8
Albuminuria (micro or macro)	13.2
Microalbuminuria	11.9
Macroalbuminuria	1.3
Distal symmetric polyneuropathy	21.2
Cardiovascular autonomic neuropathy	18.6
Retinopathy of any type	4.9
Background retinopathy	4.2
Proliferative retinopathy	0.7

eGFR, estimated glomerular filtration rate.

BMJ Open Diab Res Care 2020;8:e001549



Standards of Care in Diabetes 2025

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HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT; SOCIAL DETERMINANTS OF HEALTH

To avoid therapeutic inertia, reassess and modify treatment regularly (3–6 months)

ESC GUIDELINES

2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes

Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC)

Very high CV risk	Patients with T2DM with: • Clinically established ASCVD or • Severe TOD or • 10-year CVD risk ≥20% using SCORE2-Diabetes
High CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk 10 to <20% using SCORE2-Diabetes
Moderate CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk 5 to <10% using SCORE2-Diabetes
Low CV risk	Patients with T2DM not fulfilling the very high-risk criteria and a: • 10-year CVD risk <5% using SCORE2-Diabetes

ESC European Society of Cardiology

European Heart Journal (2023) 00, 1–98 https://doi.org/10.1093/eurheartj/ehad192

Goal: Cardiovascular and Kidney Risk Reduction in High-Risk Individuals with Type 2 Diabetes*

- **CVD†**
- **+Indicators of high CVD risk**
- **+HF**
  Current or prior symptoms of HF with documented HFrEF or HFpEF
- **+CKD**
  eGFR <60 mL/min/1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). Repeat measurement is required to confirm CKD

D/indicators of high CVD risk≈

-1 RA# proven benefit **OR** SGLT2i‡ with proven CVD benefit

If A1C is above goal

iduals on a GLP-1 RA, consider adding with proven CVD benefit or vice versa one^

SGLT2i‡
with proven HF benefit in this population

+CKD (on maximally tolerated dose of ACEi or ARB)

SGLT2i‡ with primary evidence of reducing CKD progression
- SGLT2i can be started with eGFR ≥20 mL/min/1.73 m²
- Continue until initiation of dialysis or transplantation
- Glucose-lowering efficacy is reduced with eGFR <45 mL/min/1.73 m²

OR

GLP-1 RA# with proven CKD benefit

If A1C is above goal, for individuals on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiovascular and kidney risk reduction, management of other metabolic comorbidities, and/or glycemic lowering is needed

+Mitigating risk of MASLD or MASH

Agents with potential benefit in MASLD or MASH
GLP-1 RA, dual GIP and GLP-1 RA, pioglitazone, or combination of GLP-1 RA with pioglitazone
Use insulin in the setting of decompensated cirrhosis

Goal: Achievement and Maintenance of Weight and Glycemic Goals

- **+Weight management**
- **+Achievement and maintenance of glycemic goals**

Efficacy for weight loss

Very high: Semaglutide, tirzepatide

High: Dulaglutide, liraglutide

Intermediate: GLP-1 RA (not listed above), SGLT2i

Neutral: Metformin, DPP-4i

Metformin or other agent (including combination therapy) that provides adequate EFFICACY to achieve and maintain glycemic treatment goals

Prioritize avoidance of hypoglycemia in high-risk individuals

Efficacy for glucose lowering

Very high: Dulaglutide (high dose), semaglutide, tirzepatide, insulin
Combination oral, combination injectable (GLP-1 RA and insulin)

High: GLP-1 RA (not listed above), metformin, pioglitazone, SGLT2i, sulfonylurea

Intermediate: DPP-4i

If A1C is above goal or significant hypoglycemia or hyperglycemia or barriers to care are identified

- Refer to DSMES to support self-efficacy in achievement of treatment goals
- Consider technology (e.g., diagnostic or personal CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of treatment goals

Lifetime risk of cardiovascular-renal disease in type 2 diabetes: a population-based study in 473,399 individuals

Ruiqi Zhang[1,2], Jil Billy Mamza[2], Tamsin Morris[2], George Godfrey[2], Folkert W. Asselbergs[3,4,5], Spiros Denaxas[3,6], Harry Hemingway[3,6] and Amitava Banerjee[3,6,7,8*]

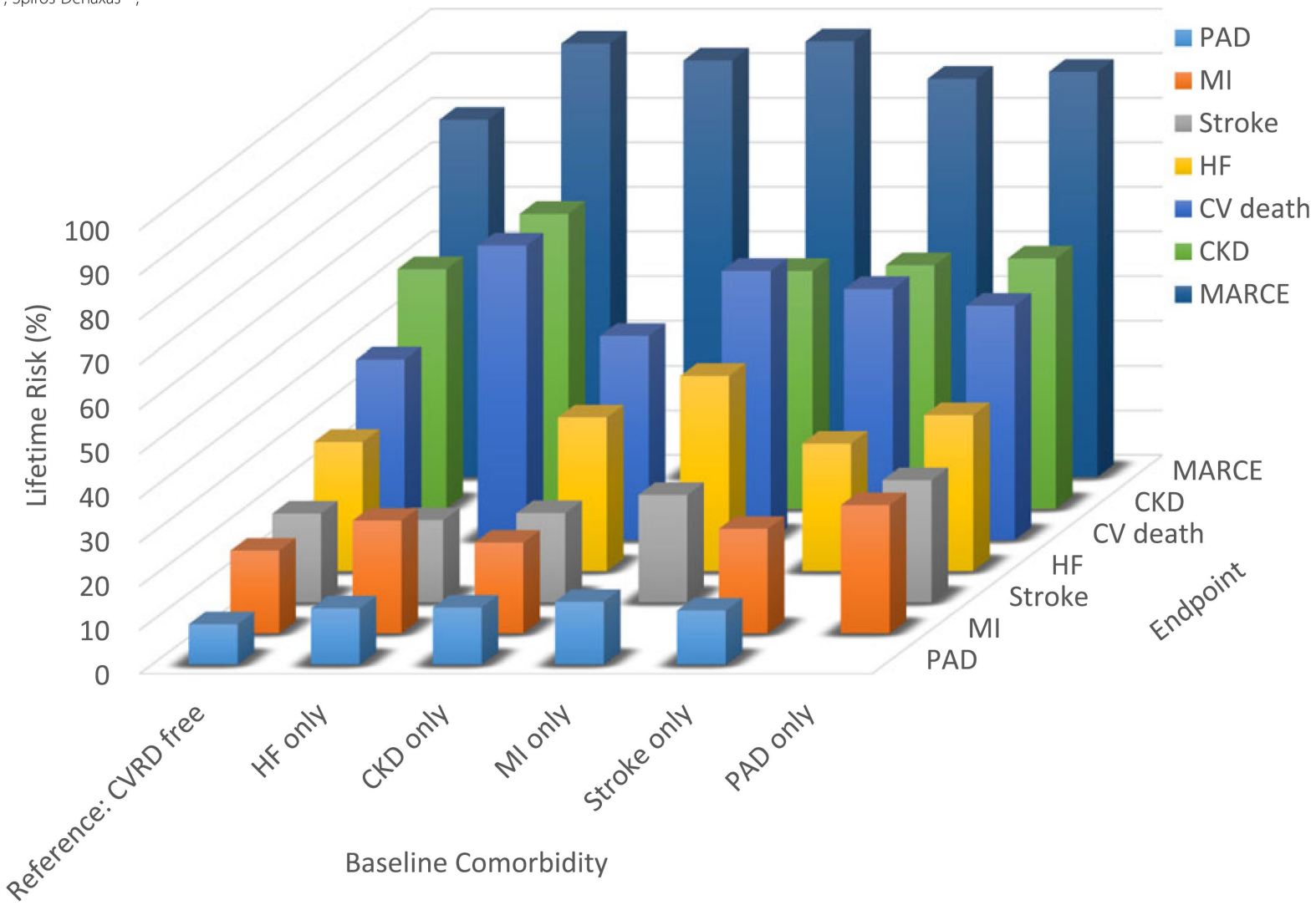


Fig. 3 Lifetime risk of individual and composite major adverse renal and cardiovascular events. Abbreviations: cardiovascular and renal diseases, CVRD; heart failure, HF; chronic kidney disease, CKD; myocardial infarction, MI; peripheral artery disease, PAD


centomila

Phenotypic and genetic classification of diabetes

Aaron J. Deutsch[1,2,3,4] · Emma Ahlqvist[5] · Miriam S. Udler[1,2,3,4]

Strategies for identifying diabetes subtypes

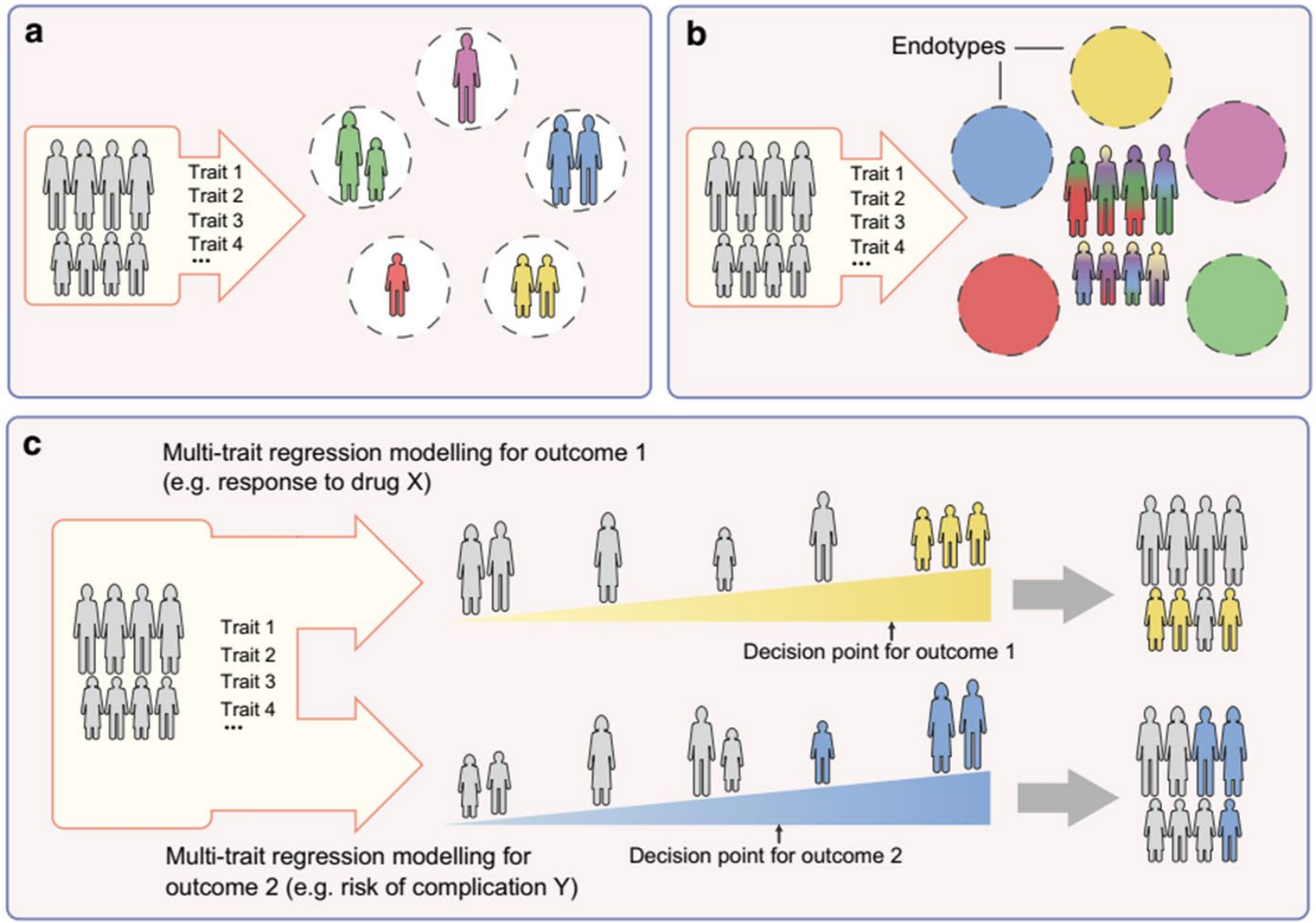


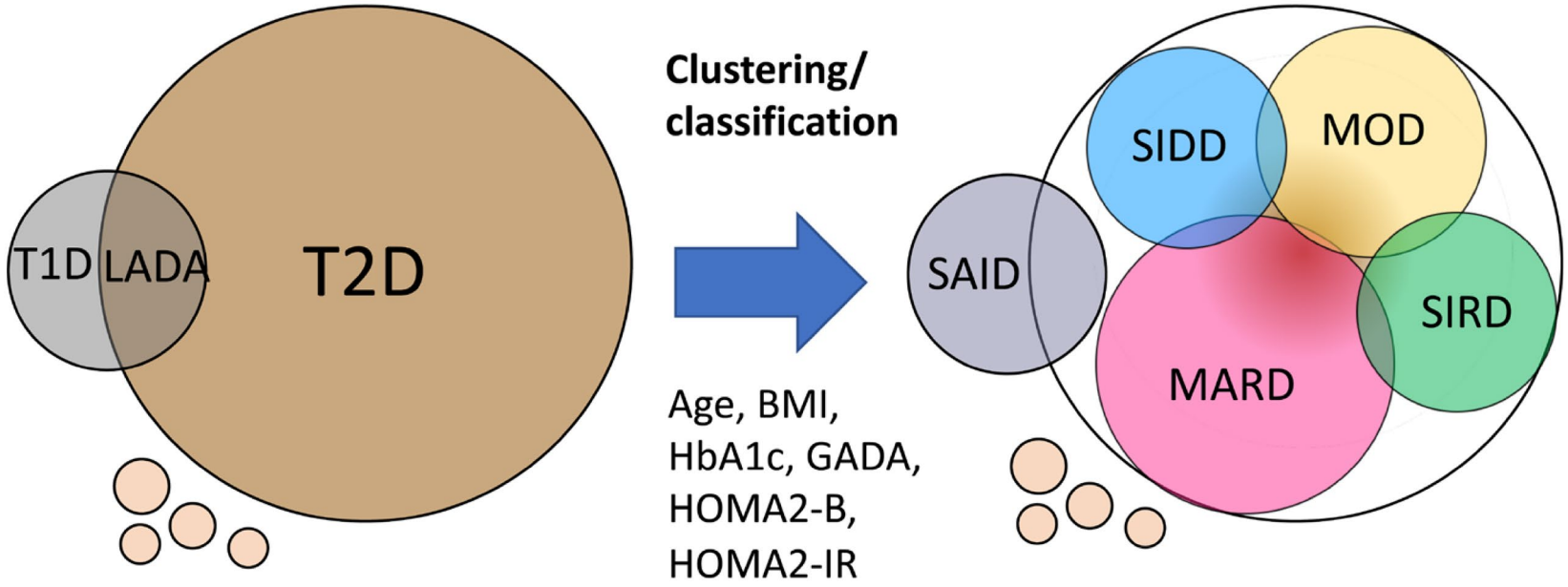
Fig. 2 Strategies for identifying diabetes subtypes. (a) Hierarchical ('hard') clustering istributes people into discrete subtypes. These clusters are defined using a series of raits, which may include phenotypic and/or genotypic criteria. (b) In a 'soft' clustering pproach, discrete subtypes are also defined using a series of traits; however, people ay have features belonging to more than one cluster. Clusters that represent a distinct athobiological mechanism may be referred to as endotypes. (c) Alternatively, clinical raits may be integrated into a regression model, yielding a continuous measurement of arious outcomes (e.g. response to a certain drug or risk of developing a certain omplication). Clinical decisions (e.g. to start a certain medication) are implemented for eople who fall above a specified threshold

Diabetologia (2022) 65:1758–1769

Towards improved precision and a new classification of diabetes mellitus

Emma Ahlqvist[1], Rashmi B Prasad[1,2] and Leif Groop[1,2]

Subclassification of individuals with adult-onset diabetes



SAID (Severe AutoImmune Diabetes)

early-onset disease, relatively low BMI, poor metabolic control, insulin deficiency, and presence of GADA

SIDD (Severe Insulin-Deficient Diabetes)

GADA negative, low age at onset, relatively low BMI, low insulin secretion (low HOMA2-B index), and poor metabolic control.

MOD (Mild Obesity-related Diabetes)

obesity but not by insulin resistance

SIRD (Severe Insulin Resistant Diabetes)

insulin resistance (high HOMA2-IR index), high BMI.

MARD (Mild Age-Related Diabetes)

older than patients in other clusters, only modest metabolic derangements

Journal of Endocrinology (2021) 252, R59–R70

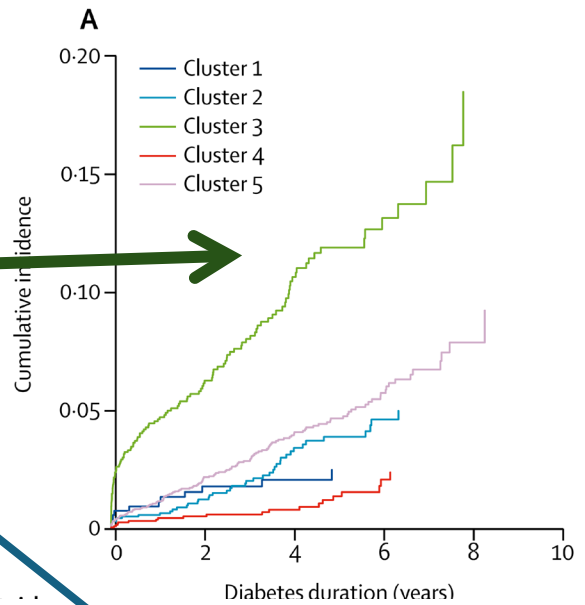
Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables

Emma Ahlqvist, Petter Storm, Annemari Käräjämäki, Mats Martinell*, Mozhgan Dorkhan, Annelie Carlsson, Petter Vikman, Rashmi B Prasad, Dina Mansour Aly, Peter Almgren, Ylva Wessman, Nael Shaat, Peter Spégel, Hindrik Mulder, Eero Lindholm, Olle Melander, Ola Hansson, Ulf Malmqvist, Åke Lernmark, Kaj Lahti, Tom Forsén, Tiinamaija Tuomi, Anders H Rosengren, Leif Groop*

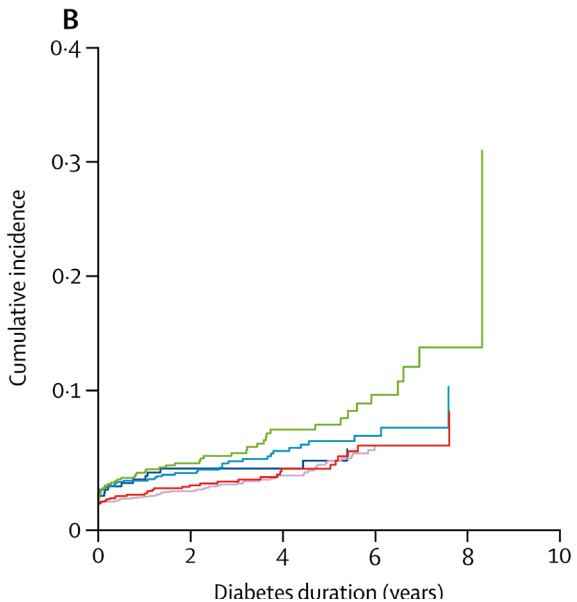
Cluster 3 (severe insulin resistant diabetes - SIRD): insulin resistance (high HOMA2-IR index), high BMI.

Cluster 2 (severe insulin-deficient Diabetes - SIDD): GADA negative, low age at onset, relatively low BMI, low insulin secretion (low HOMA2-B index), and poor metabolic control.

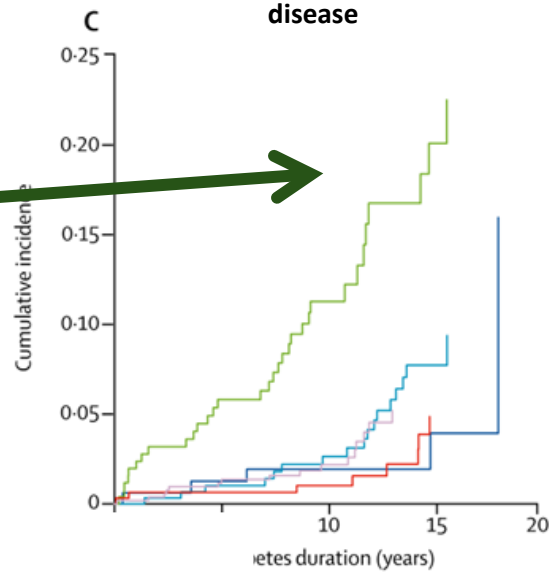
Time to chronic kidney disease (at least stage 3B)



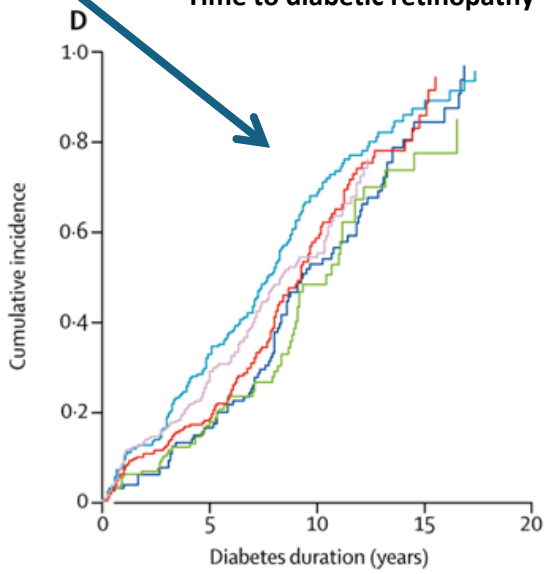
Time to macroalbuminuria



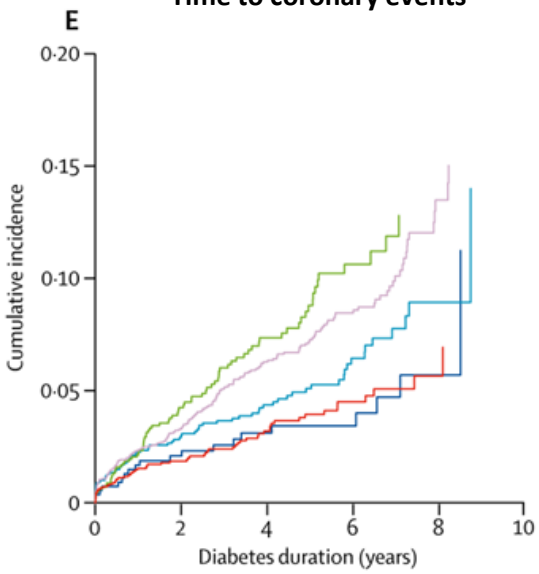
Time to end-stage renal disease



Time to diabetic retinopathy



Time to coronary events

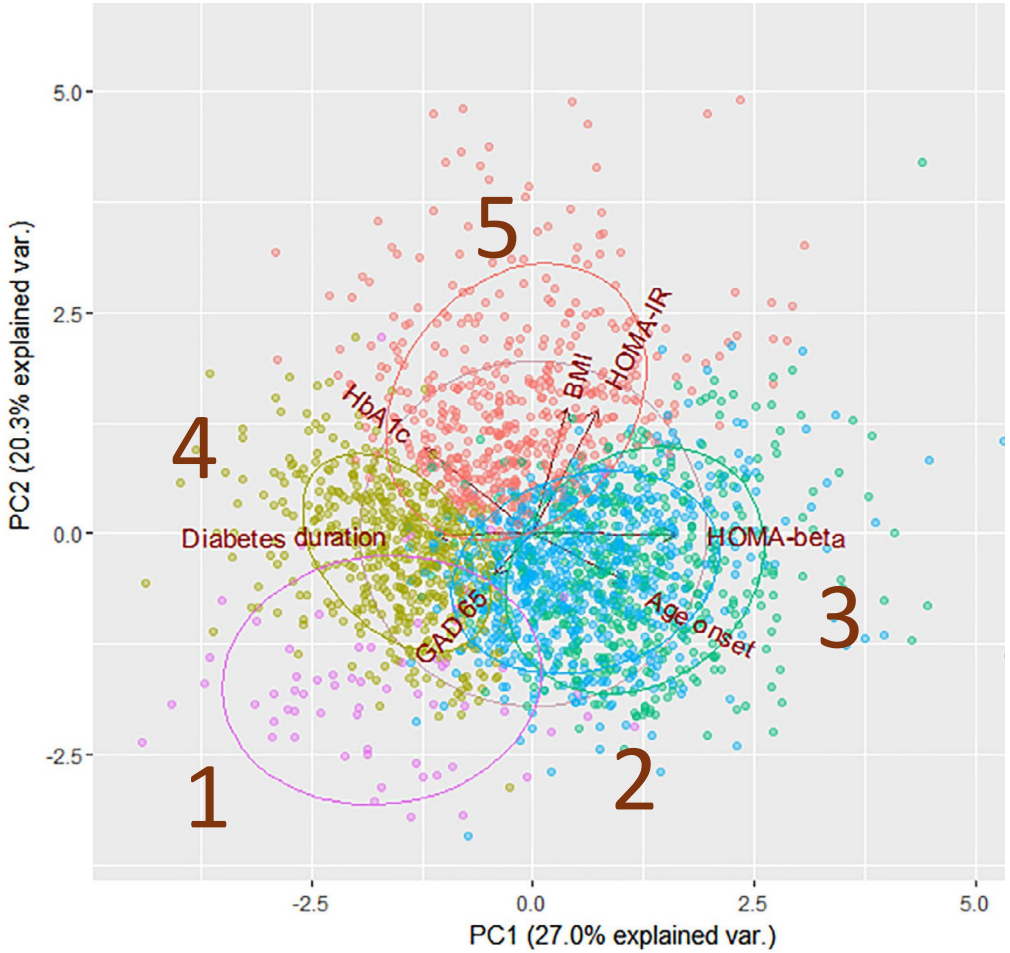


Lancet Diabetes Endocrinol 2018; 6: 361–69

Stratification of type 2 diabetes based on routine clinical markers

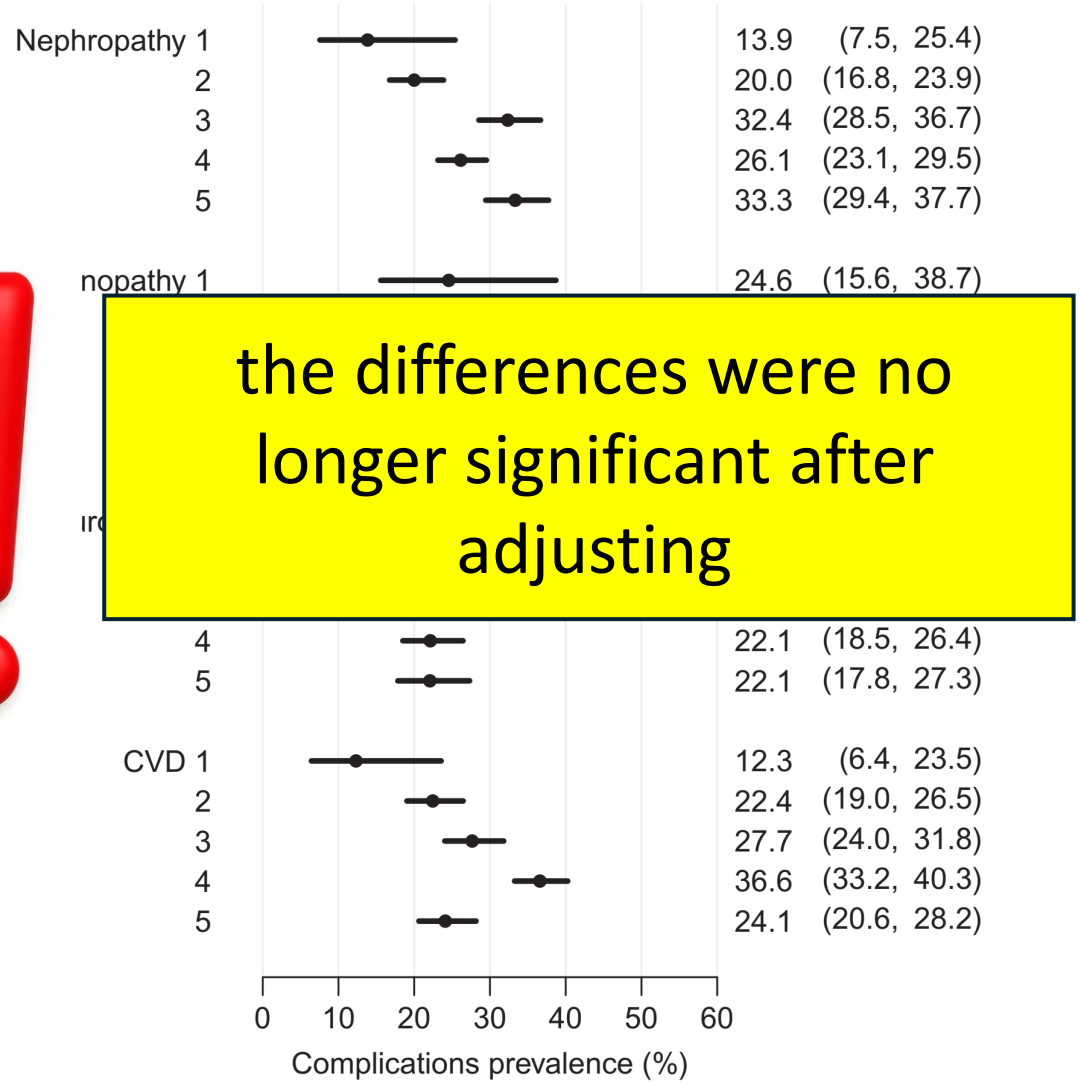
Narges Safai [a,2,*], *Ashfaq Ali* [b,2], *Peter Rossing* [c,d], *Martin Ridderstråle* [e,1]

retrospective cohort study



diabetesresearchandclinicalpractice141(2018)275–283

Diabetes complication in each of the five subgroups from the population



the differences were no longer significant after adjusting

Development and validation of optimal phenomapping methods to estimate long-term atherosclerotic cardiovascular disease risk in patients with type 2 diabetes

Matthew W. Segar[1,2], Kershaw V. Patel[1,3], Muthiah Vaduganathan[4], Melissa C. Caughey[5], Byron C. Jaeger[6], Mujeeb Basit[1], Duwayne Willett[1], Javed Butler[7], Partho P. Sengupta[8], Thomas J. Wang[1], Darren K. McGuire[1,2], Ambarish Pandey[1,2]

data from **ACCORD, Look AHEAD** and **BARI 2D trials**

Diabetologia. 2021 July ; 64(7): 1583–1594

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data from **ACCORD, Look AHEAD** and **BARI 2D trials**

Phenogroup 1: the greatest burden of comorbidities, cardiometabolic risk factors and insulin use

Phenogroup 2: the lowest burden of microvascular complications

Phenogroup 3: more favourable risk factor profile

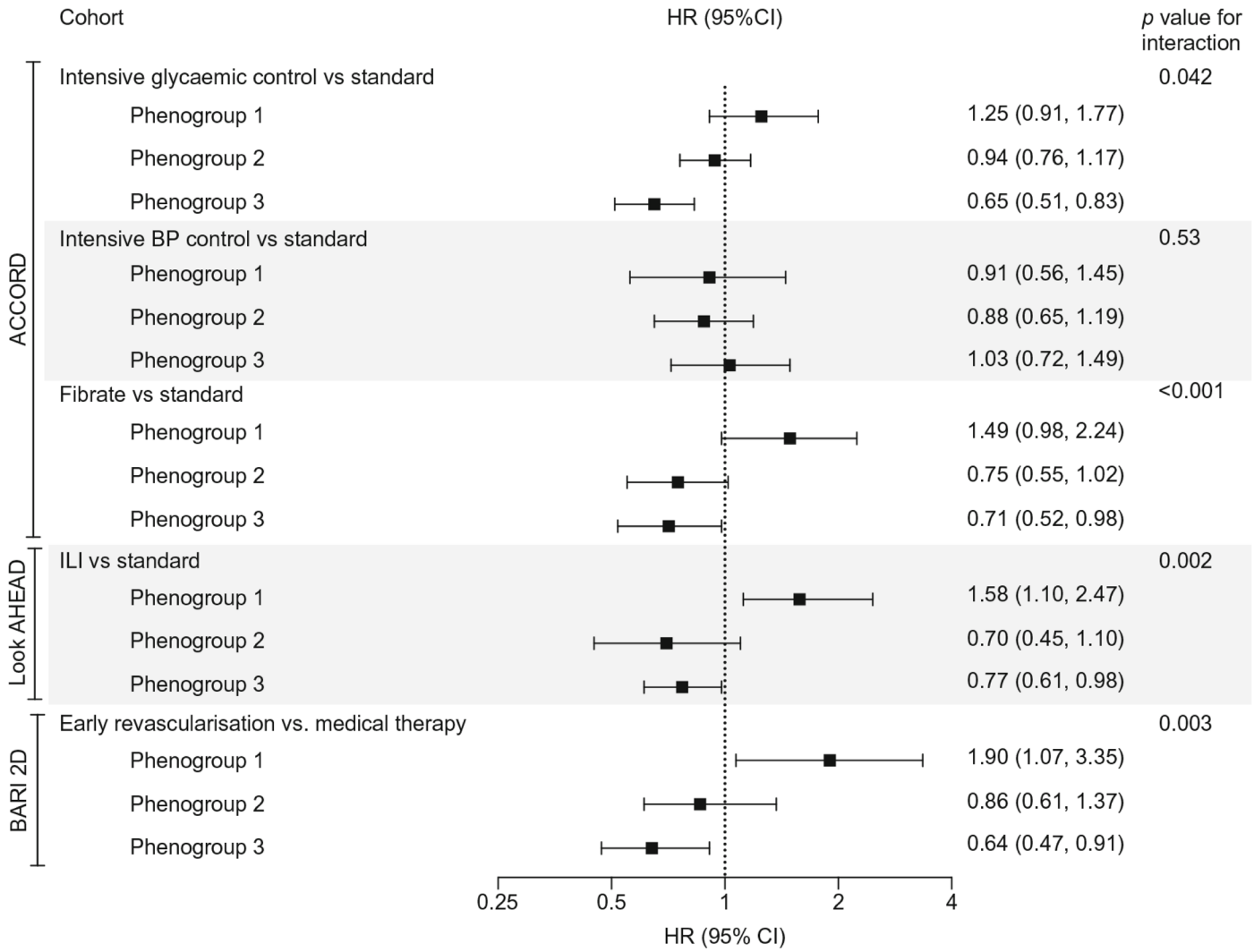
The primary outcome was a composite of fatal MI, non-fatal MI or unstable angina in the **ACCORD** trial cohort.

In the **Look AHEAD** trial cohort, the primary outcome included fatal or non-fatal MI plus hospitalisation for angina.

In **BARI 2D**, the primary outcome was a composite of fatal MI or non-fatal MI

Diabetologia. 2021 July ; 64(7): 1583–1594

Multivariable-adjusted associations of randomised treatment groups with risk of primary outcome events stratified by FMM-based phenogroups



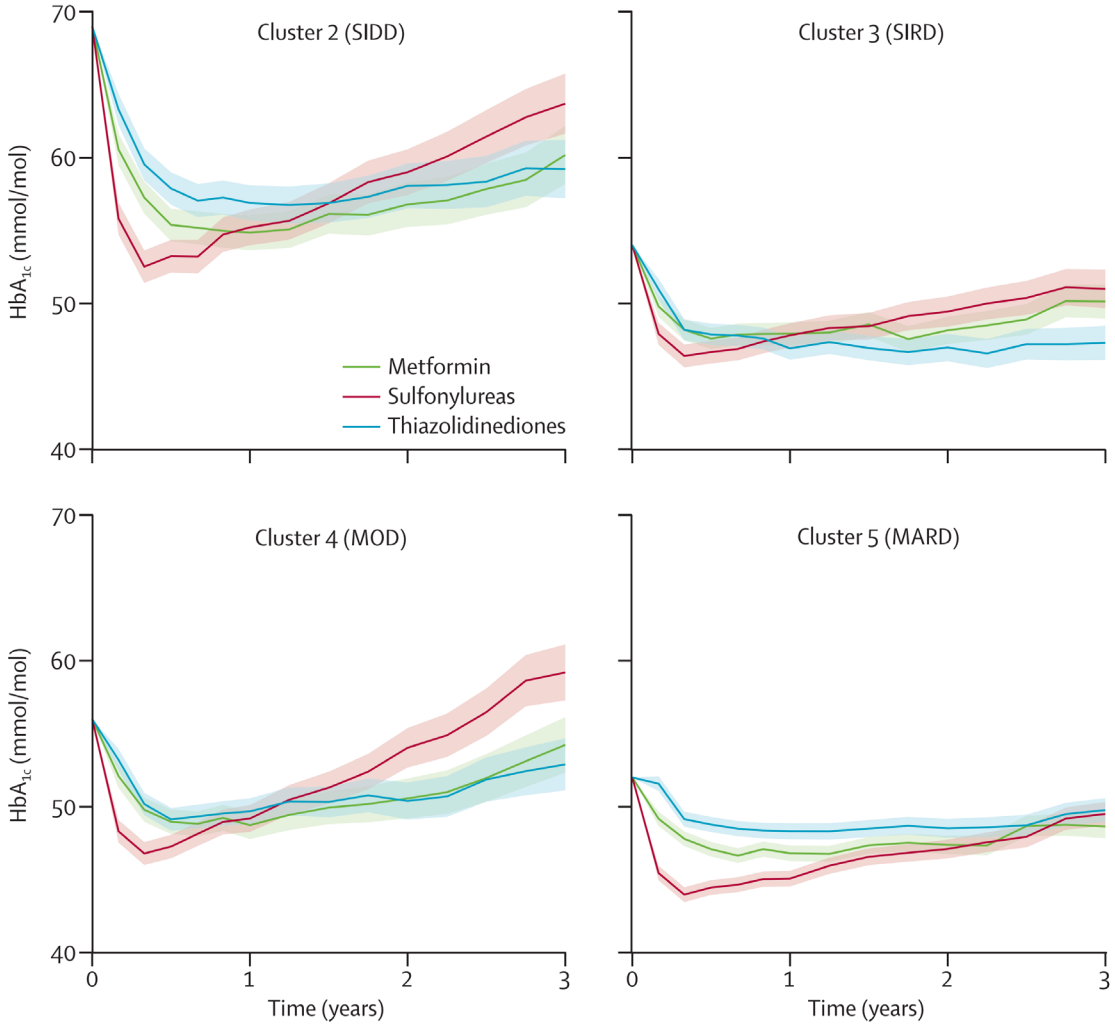
Disease progression and treatment response in data-driven subgroups of type 2 diabetes compared with models based on simple clinical features: an analysis using clinical trial data

John M Dennis, Beverley M Shields, William E Henley, Angus G Jones, Andrew T Hattersley

data from **ADOPT** and **RECORD** study

a prediction model approach combining phenotypic measures to predict specific outcomes for individual patients is likely to have greater clinical utility than is subgroup assignment

Change in HbA1c by drug for clusters in ADOPT



Lancet Diabetes Endocrinol 2019; 7: 442–51

Cluster Analysis of Cardiovascular Phenotypes in Patients With Type 2 Diabetes and Established Atherosclerotic Cardiovascular Disease: A Potential Approach to Precision Medicine

Abhinav Sharma,[1,2] Yinggan Zheng,[3] Justin A. Ezekowitz,[2,3] Cynthia M. Westerhout,[3] Jacob A. Udell,[4] Shaun G. Goodman,[3,5] Paul W. Armstrong,[3] John B. Buse,[6] Jennifer B. Green,[7] Robert G. Josse,[5] Keith D. Kaufman,[8] Darren K. McGuire,[9] Giuseppe Ambrosio,[10] Lee-Ming Chuang,[11] Renato D. Lopes,[7] Eric D. Peterson,[7] and Rury R. Holman[12]

data from **TECOS** study

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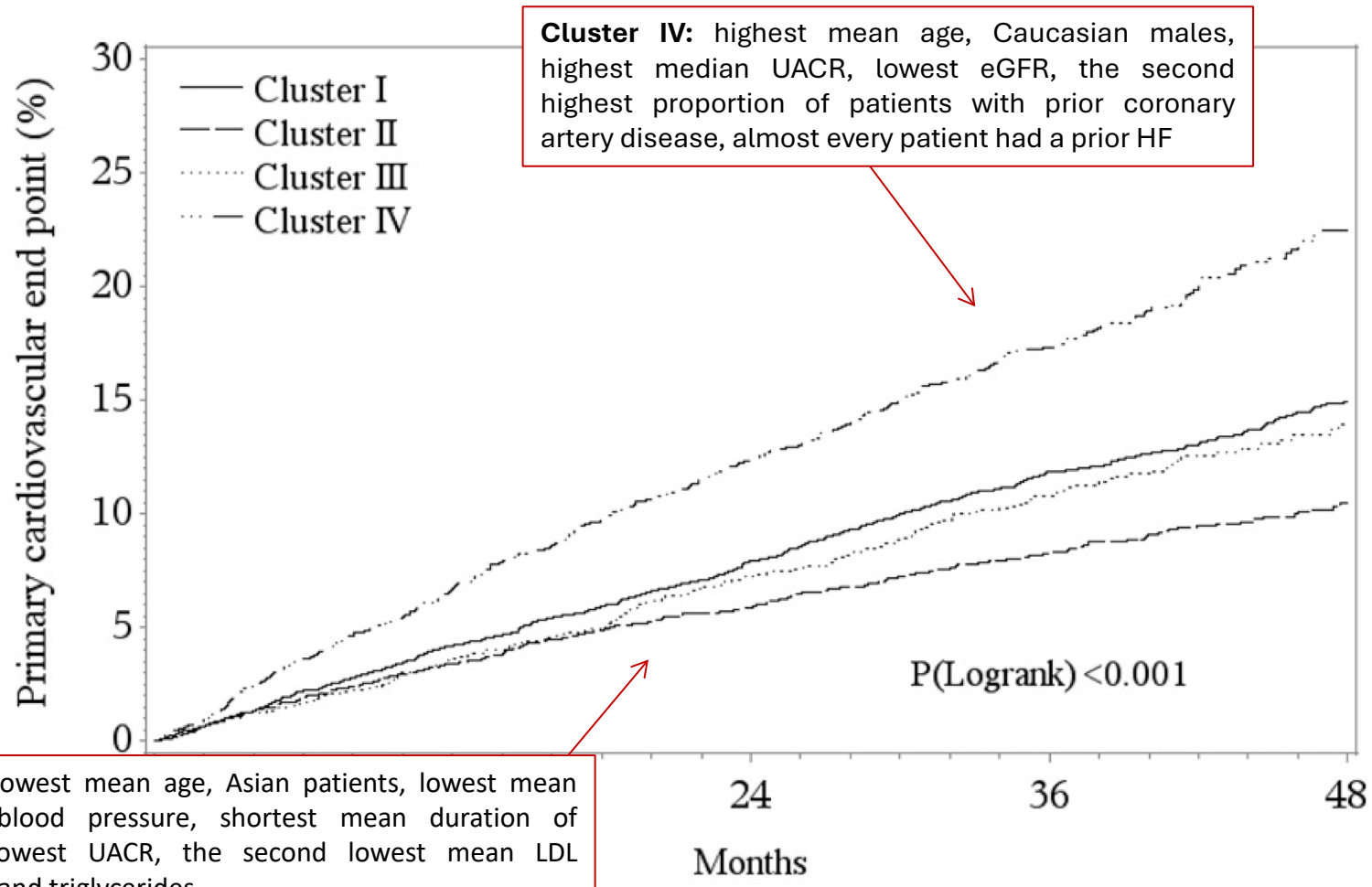
data from **TECOS** study

clustered for

Continuous variables	age, BMI, weight, systolic BP at baseline, diastolic BP at baseline, heart rate, HbA1c, hemoglobin, HDL cholesterol, triglycerides, log-transformed UACR, LDL cholesterol, duration of diabetes, and eGFR
Categorical variables	sex, Hispanic or Latino ethnicity, race, NYHA class, prior coronary artery disease, prior MI, prior percutaneous coronary intervention, prior peripheral arterial disease, prior coronary artery bypass graft prior cerebrovascular disease, heart failure, chronic obstructive pulmonary disease; chronic liver disease, cancer, hypertension, alcohol abuse, complication of amputation, foot ulcer, retinopathy, blindness, diabetic neuropathy, currently smoking, depression.

cumulative incidence of CV death, nonfatal MI, nonfatal stroke, or hospitalization for unstable angina end point by cluster

Cluster IV: highest mean age, Caucasian males, highest median UACR, lowest eGFR, the second highest proportion of patients with prior coronary artery disease, almost every patient had a prior HF



Cluster II: lowest mean age, Asian patients, lowest mean BMI and blood pressure, shortest mean duration of diabetes, lowest UACR, the second lowest mean LDL cholesterol and triglycerides

Diabetes Care 2022;45:204–212

Cluster Analysis of Cardiovascular Phenotypes in Patients With Type 2 Diabetes and Established Atherosclerotic Cardiovascular Disease: A Potential Approach to Precision Medicine

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clustered for

Continuous variables	age, BMI, weight, systolic BP at baseline, diastolic BP at baseline, heart rate, HbA1c, hemoglobin, HDL cholesterol, triglycerides, log-transformed UACR, LDL cholesterol, duration of diabetes, and eGFR
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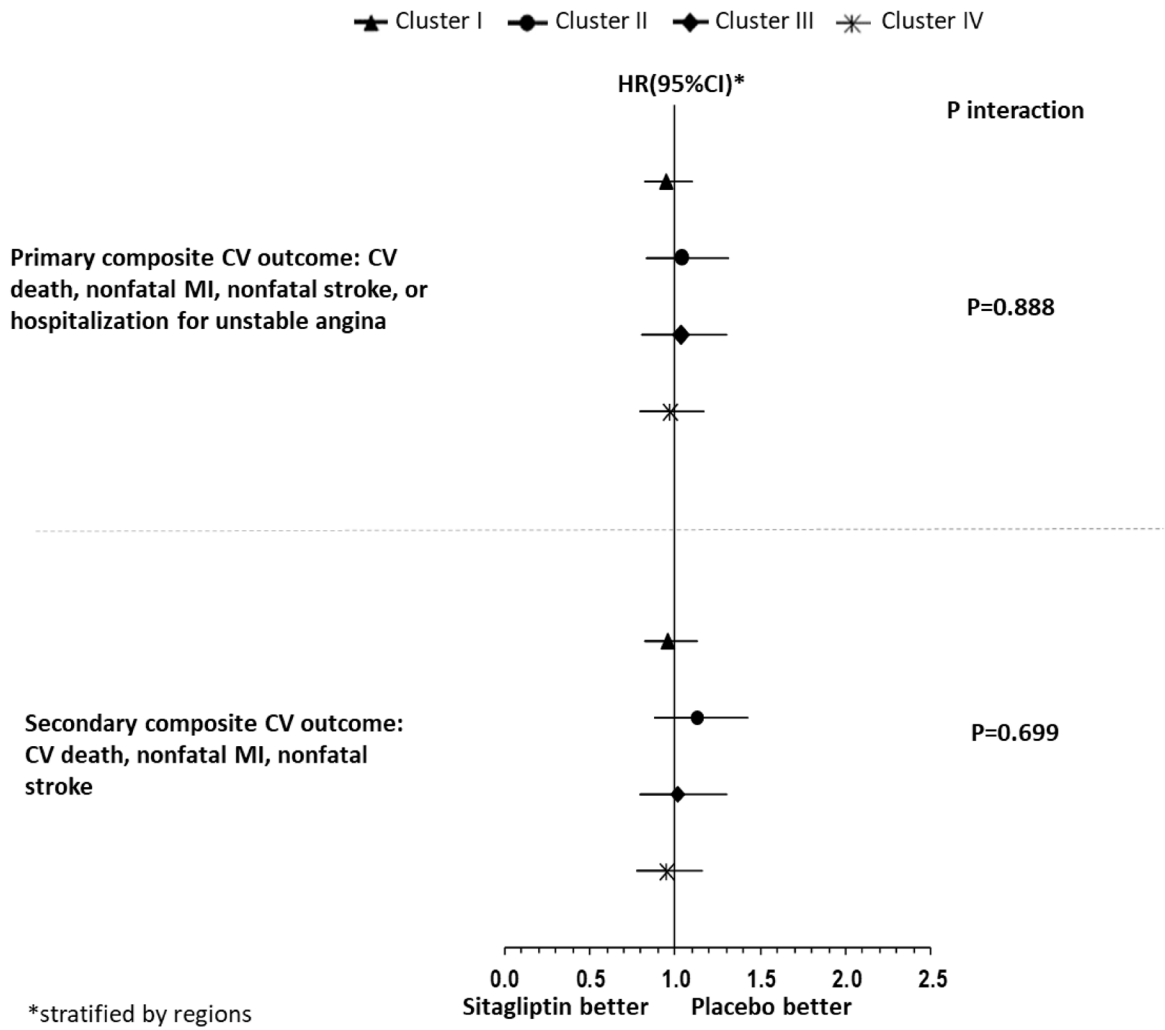
Diabetes Care 2022;45:204–212

Interaction Between Study Treatment and Cluster on Clinical Outcomes

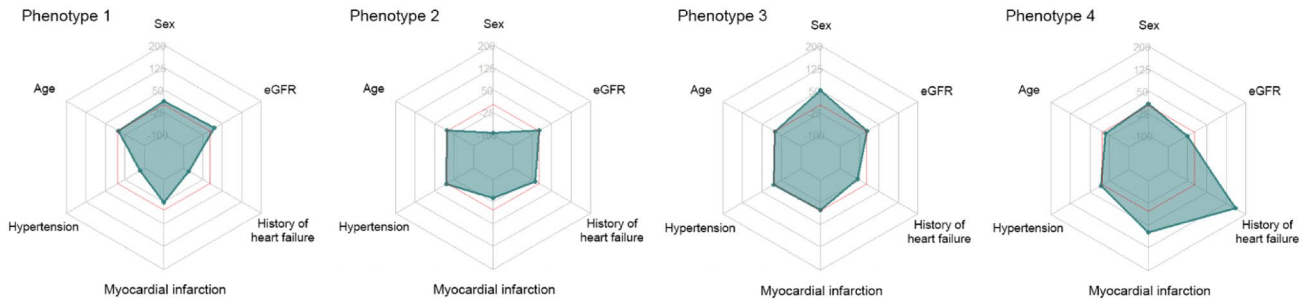


*stratified by regions

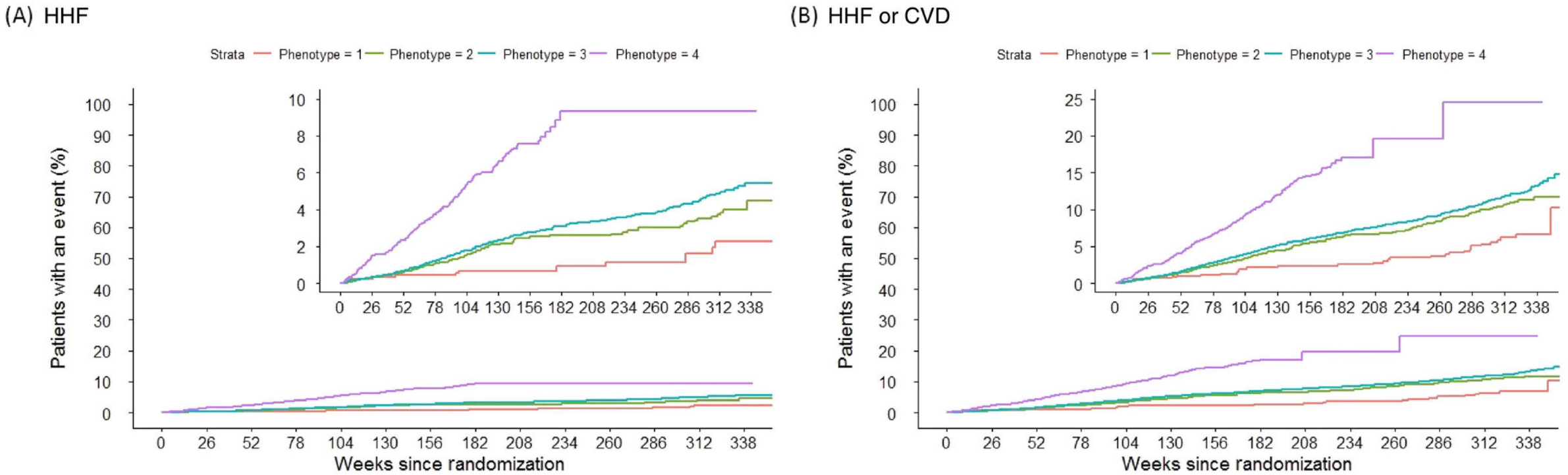
Cardiovascular phenotypes in type 2 diabetes: Latent class analysis of the CANVAS Program and CREDENCE trial

Amir Razaghizad MSc[1,2] | Jiayi Ni MSc[1] | Pedro Marques MD[3,4,5] | Thomas A. Mavrakanas MD[2,6] | Michael A. Tsoukas MD[2,7] | Elite Possik PhD[1] | Thao Huynh MD[3] | Jodi D. Edwards PhD[8,9] | Peter Liu MD[9] | Walter Swardfager PhD[10,11] | Frederic Baroz MD[1,2] | João Pedro Ferreira MD[12,13,14] | Abhinav Sharma MD[1,3]

Cardiovascular phenotypes according to major cardiovascular risk factors



Risk of the co-primary endpoints according to patient phenotype



Diabetes Obes Metab. 2024;26:5025–5035.

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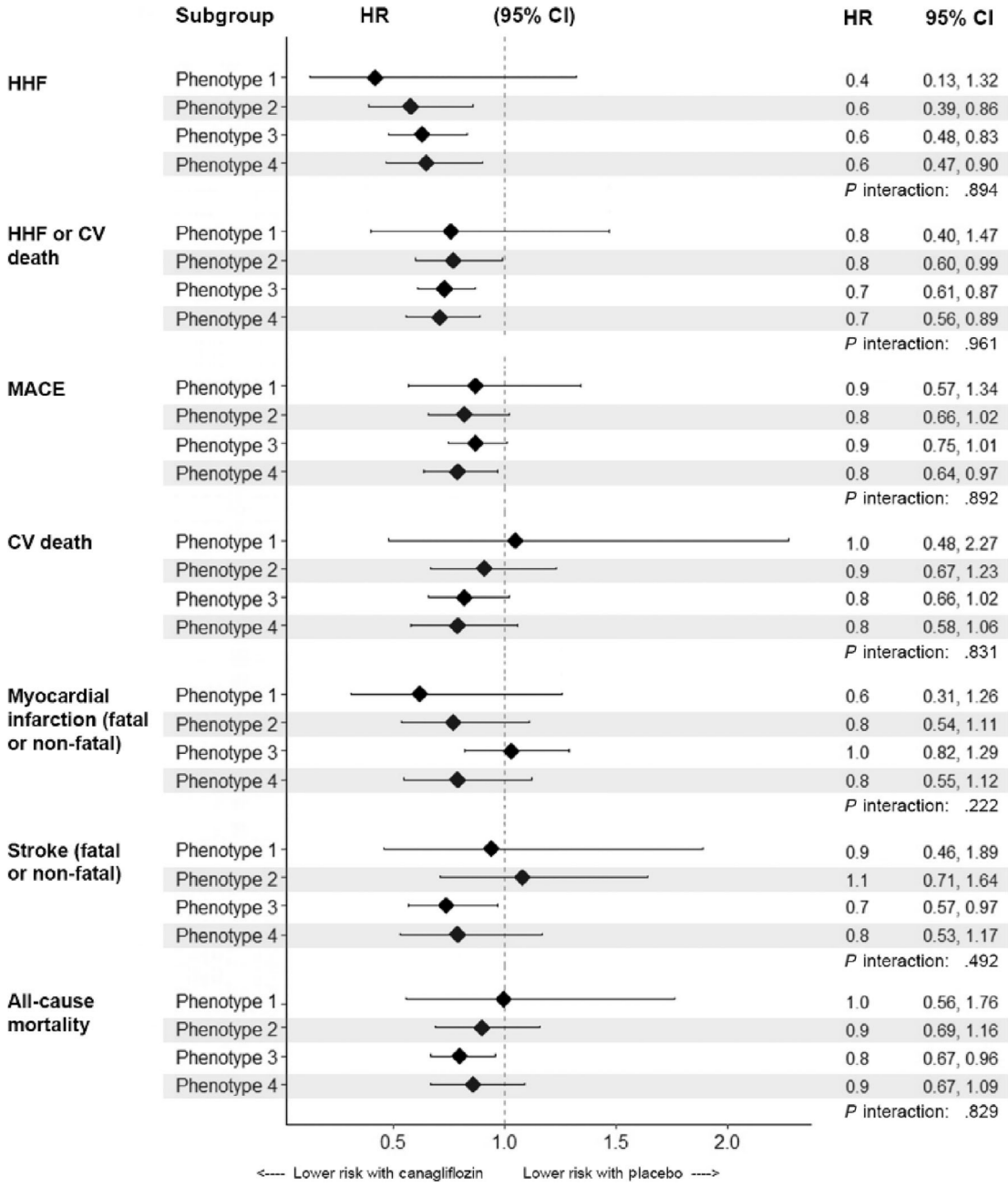
Effect of canagliflozin versus placebo on CV outcomes according to patient phenotype



Diabetes Obes Metab. 2024;26:5025–5035.

Patient Phenotypes and SGLT-2 Inhibition in Type 2 Diabetes

Insights From the EMPA-REG OUTCOME Trial

Abhinav Sharma, MD, PhD,[a] Anne Pernille Ofstad, MD, PhD,[b] Tariq Ahmad, MD, MPH,[c] Bernard Zinman, MD,[d] Isabella Zwiener, PhD,[e] David Fitchett, MD,[f] Christoph Wanner, MD, PhD,[g] Jyothis T. George, MBBS, PhD,[e] Stefan Hantel, PhD,[h] Nihar Desai, MD, MPH,[c] Robert J. Mentz, MD[i]

Group 1: Generally younger, more likely to be Asian, current smokers, had shorter T2D duration, less hypertension, higher eGFR, and higher frequency of history of MI at baseline

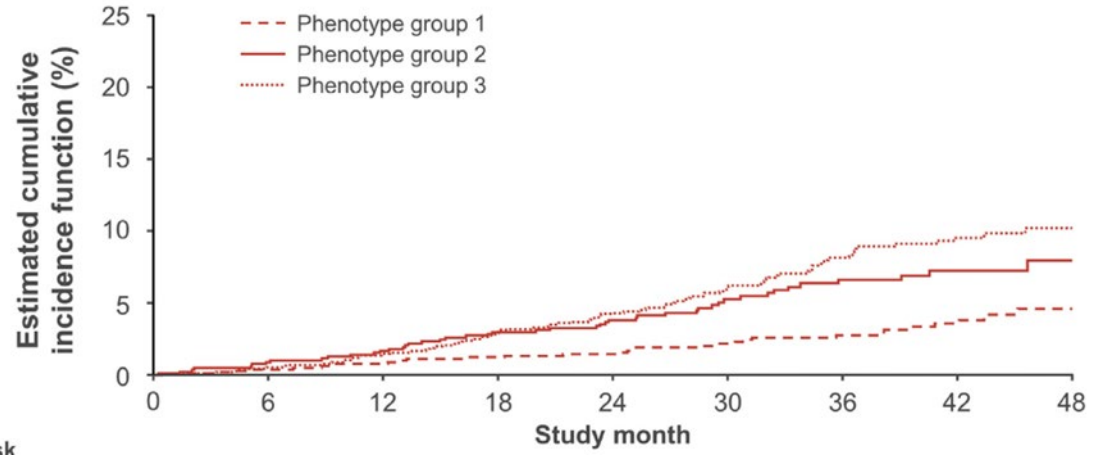
Group 2: More women and Hispanic participants with a lower frequency of CAD, and a higher likelihood of cerebrovascular and PAD at baseline

Group 3: Older participants with more advanced CAD, high prevalence of CABG, lower eGFR, lower hematocrit, and higher uric acid

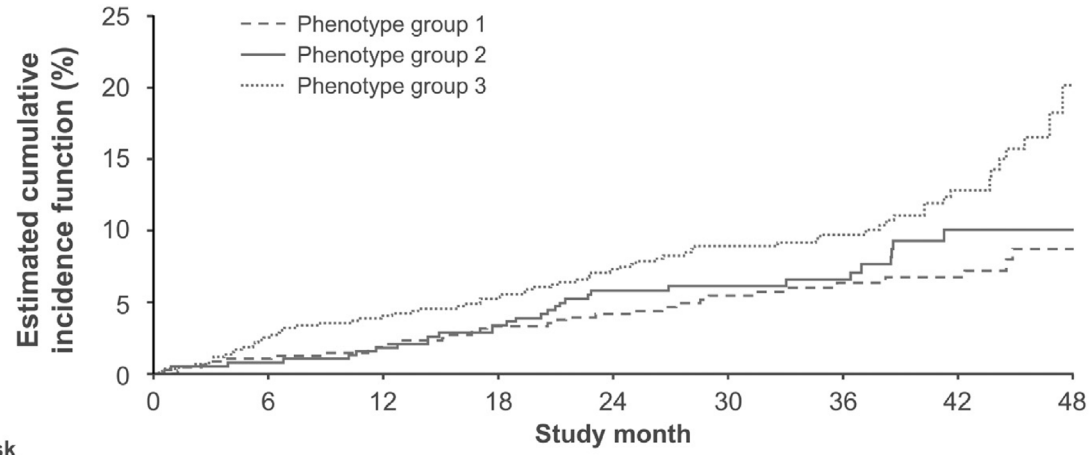
J Am Coll Cardiol HF. 2021;9(8):568–77.

Time to CV Death* or HHF by Treatment Arm Across Phenotype Groups

Patients randomized to empagliflozin



Patients randomized to placebo



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smokers, had shor
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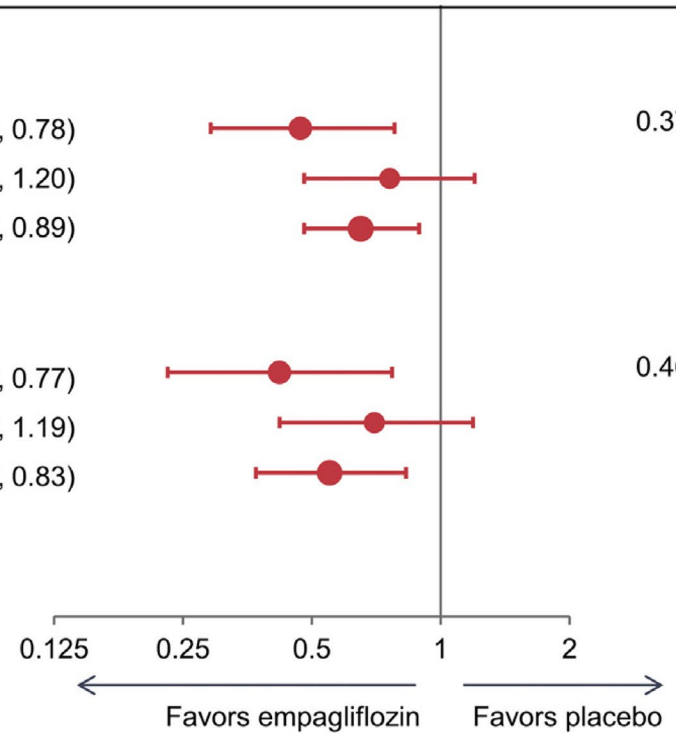
Group 2: More wo
frequency of CAD,
and PAD at baseline

Group 3: Older p
prevalence of CAB
uric acid

Treatment Effect of Empagliflozin Versus Placebo Across Phenotype Groups: Training Set

	Empagliflozin			Placebo			Hazard ratio (95% CI)	Interaction p-value
	n event/N	%	IR/1000 py	n event/N	%	IR/1000 py		
CV death* or HHF								
Phenotype group 1	31/977	3.2	10.6	32/486	6.6	22.4	0.47 (0.29, 0.78)	0.37
Phenotype group 2	46/778	5.9	21.4	30/394	7.6	28.1	0.76 (0.48, 1.20)	
Phenotype group 3	94/1187	7.9	27.6	69/598	11.5	41.8	0.65 (0.48, 0.89)	
CV death								
Phenotype group 1	20/977	2.0	6.7	23/486	4.7	15.8	0.42 (0.23, 0.77)	0.46
Phenotype group 2	34/778	4.4	15.3	24/394	6.1	21.7	0.70 (0.42, 1.19)	
Phenotype group 3	50/1187	4.2	14.2	44/598	7.4	25.5	0.55 (0.37, 0.83)	

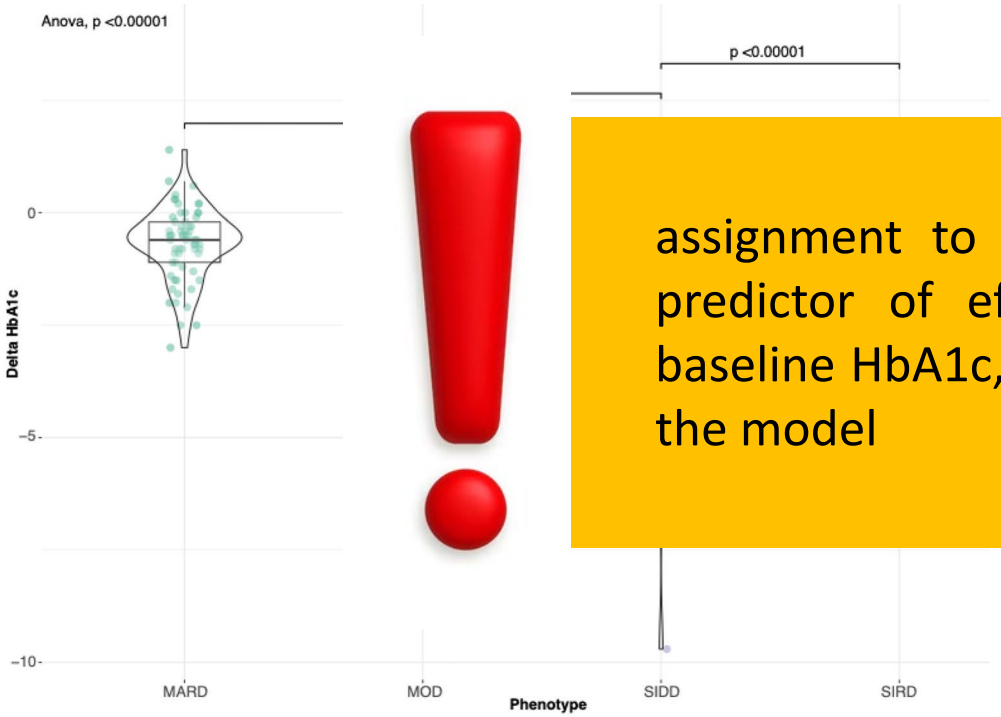


J Am Coll Cardiol HF. 20

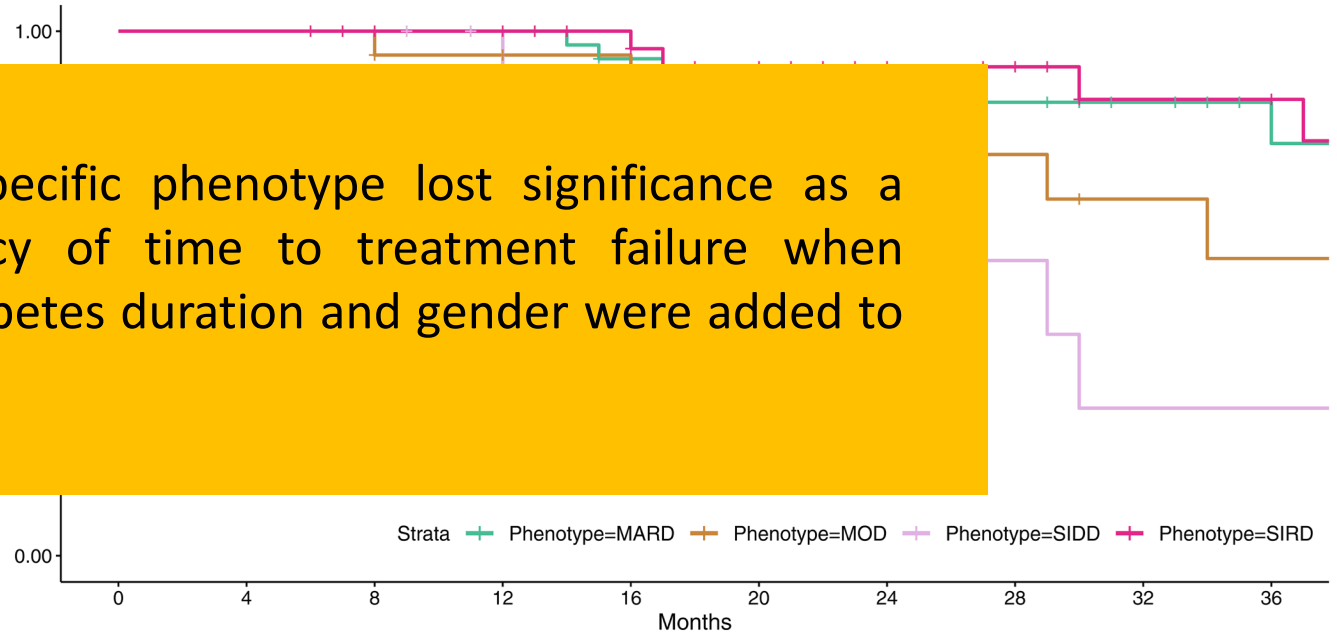
Effectiveness of GLP-1RA according to different type 2 diabetes phenotypes: A retrospective study

Irene Caruso PhD | Fiorella Giordano MD | Immacolata Ilaria Matichecchia MD | Ludovico Di Gioia MD | Sergio Di Molfetta PhD | Angelo Cignarelli PhD | Gian Pio Sorice PhD | Annalisa Natalicchio PhD | Luigi Laviola PhD | Francesco Giorgino PhD

Change from baseline in HbA1c according to diabetes phenotype



Time to treatment failure according to diabetes phenotypes



assignment to a specific phenotype lost significance as a predictor of efficacy of time to treatment failure when baseline HbA1c, diabetes duration and gender were added to the model

Diabetes Obes Metab. 2025;1–10

Phenotypic and genetic classification of diabetes

Aaron J. Deutsch[1,2,3,4] · Emma Ahlqvist[5] · Miriam S. Udler[1,2,3,4]

Strategies for identifying diabetes subtypes

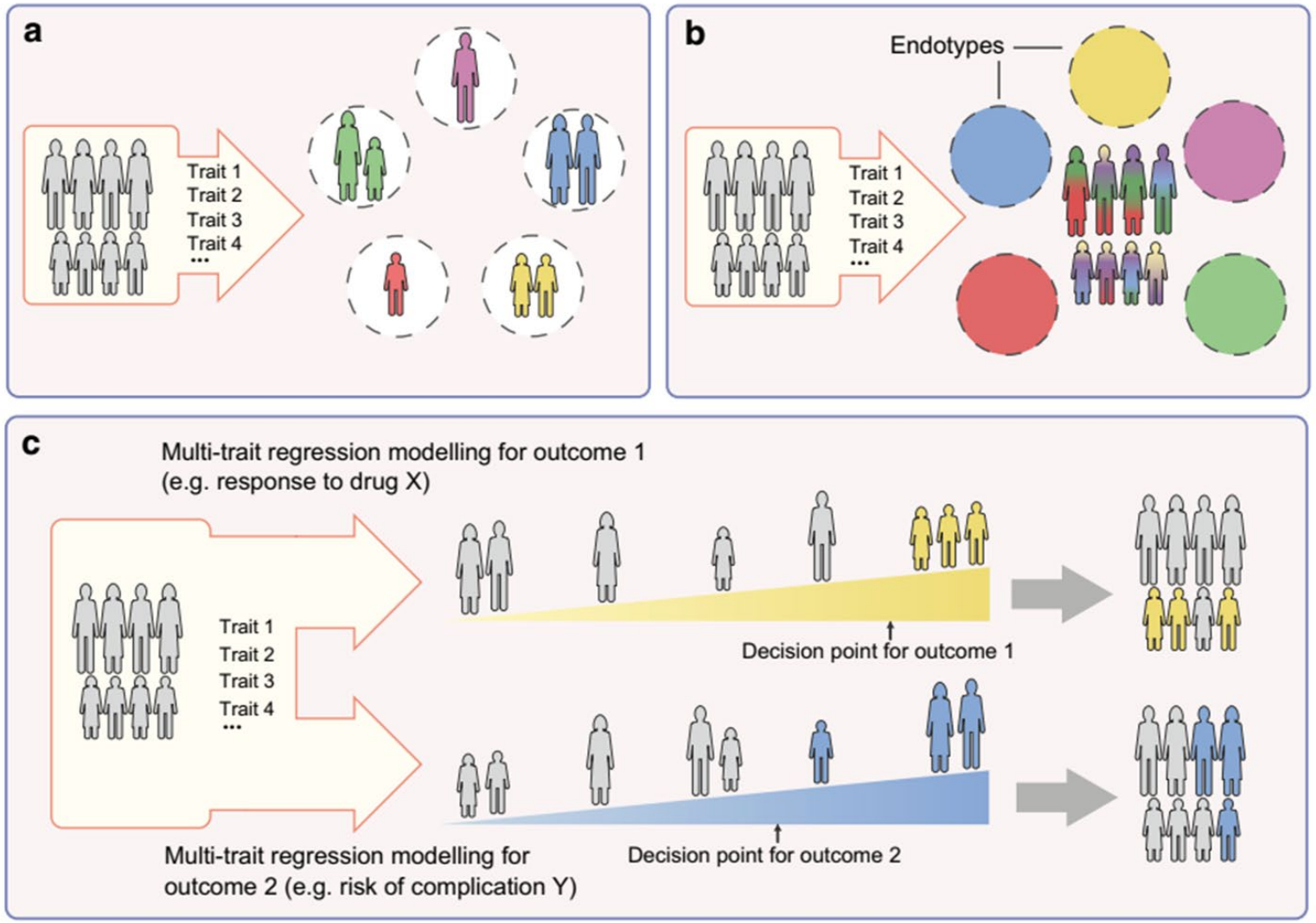


Fig. 2 Strategies for identifying diabetes subtypes. (a) Hierarchical ('hard') clustering istributes people into discrete subtypes. These clusters are defined using a series of raits, which may include phenotypic and/or genotypic criteria. (b) In a 'soft' clustering pproach, discrete subtypes are also defined using a series of traits; however, people ay have features belonging to more than one cluster. Clusters that represent a distinct athobiological mechanism may be referred to as endotypes. (c) Alternatively, clinical raits may be integrated into a regression model, yielding a continuous measurement of arious outcomes (e.g. response to a certain drug or risk of developing a certain omplication). Clinical decisions (e.g. to start a certain medication) are implemented for eople who fall above a specified threshold

Diabetologia (2022) 65:1758–1769

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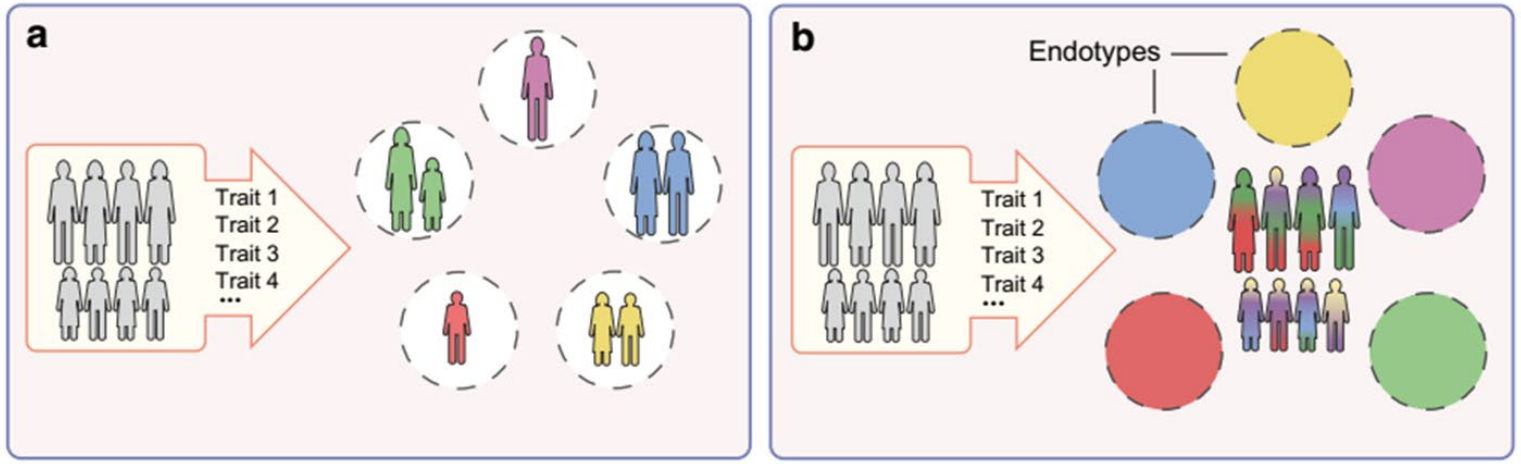

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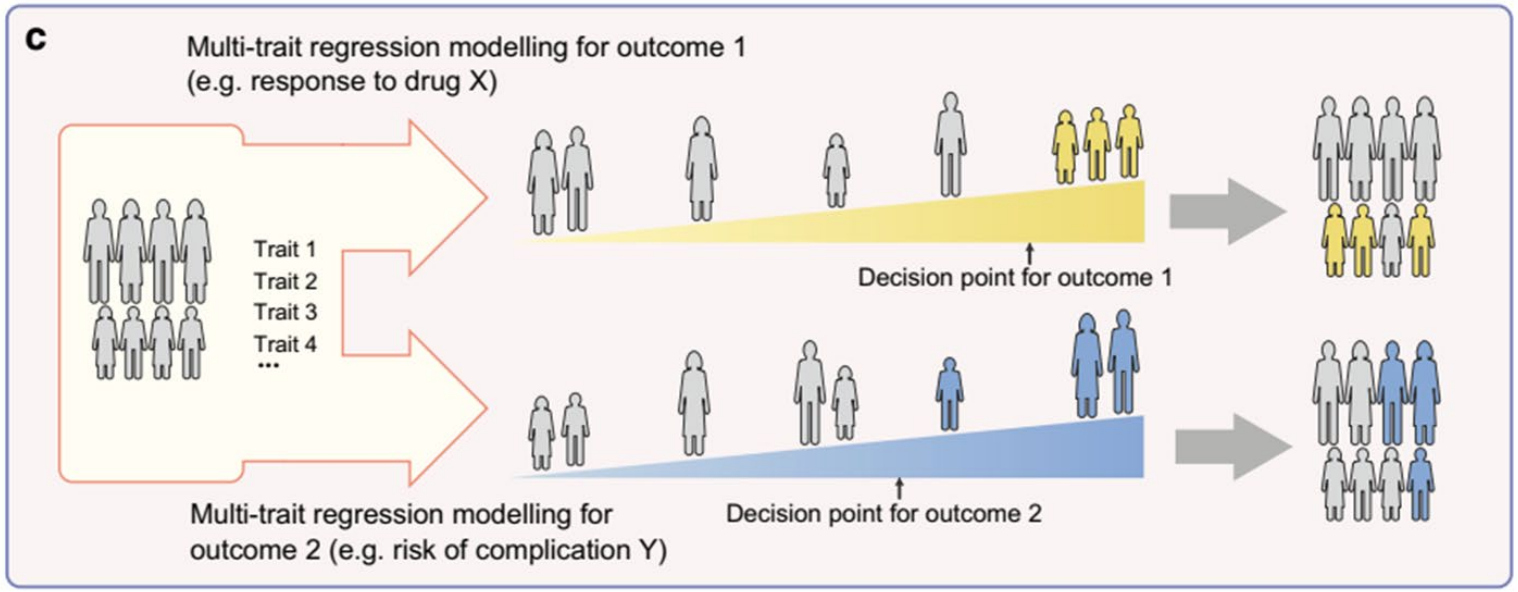

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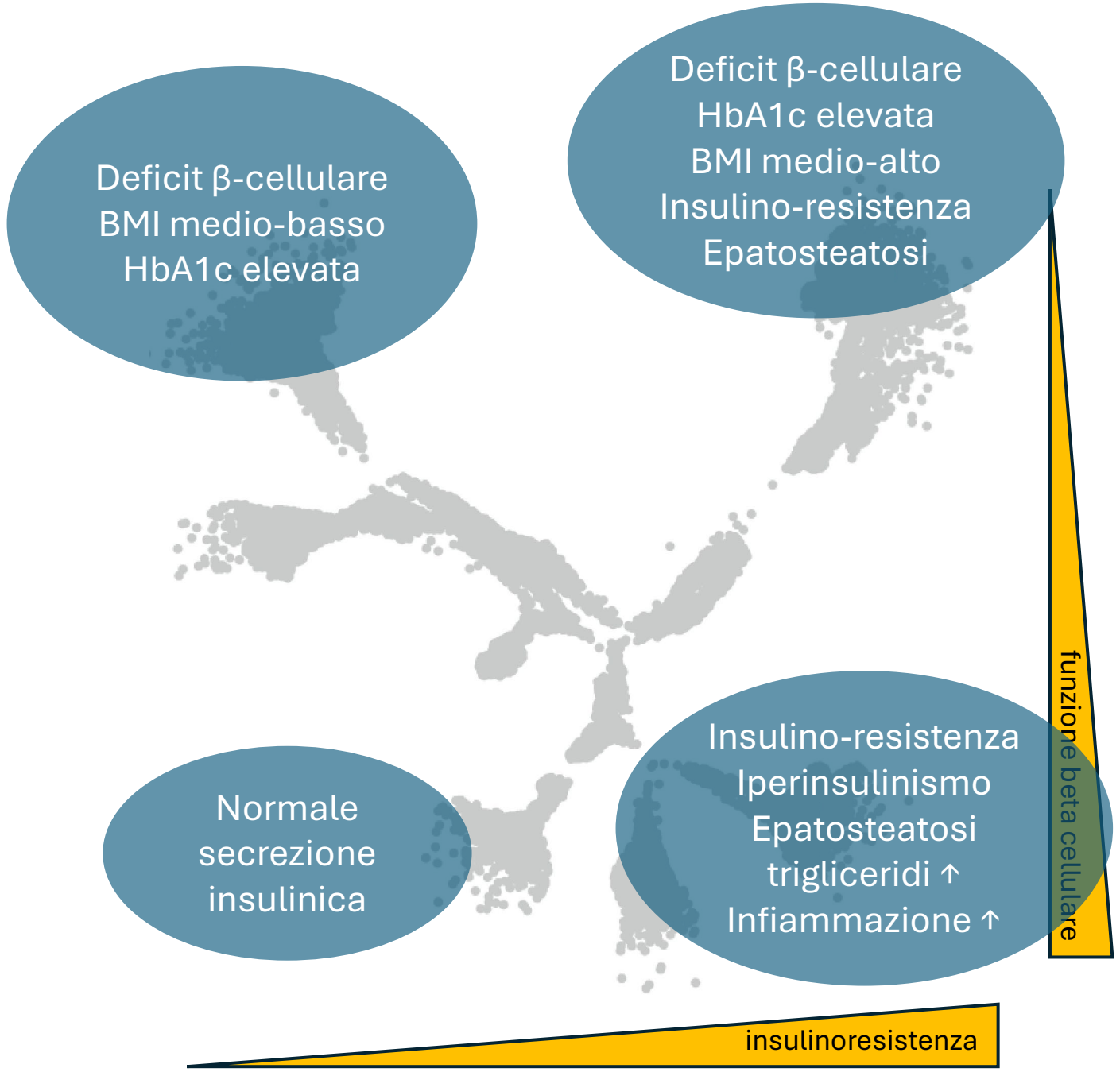
Diabetologia (2022) 65:1758–1769

Analysis of type 2 diabetes heterogeneity with a tree-like representation: insights from the prospective German Diabetes Study and the LURIC cohort

Martin Schön, Katsiaryna Prystupa, Tim Mori, Oana P Zaharia, Kálmán Bódis, Maria Bombrich, Clara Möser, Iryna Yurchenko, Yuliya Kupriyanova, Klaus Strassburger, Pavel Bobrov, Anand T N Nair, Gidon J Bönhof, Alexander Strom, Graciela E Delgado, Sema Kaya, Rainer Guthoff, Norbert Stefan, Andreas L Birkenfeld, Hans Hauner, Jochen Seissler, Andreas Pfeiffer, Matthias Blüher, Stefan Bornstein, Julia Szendroedi, Svenja Meyhöfer, Sandra Trenkamp, Volker Burkart, Vera B Schrauwen-Hinderling, Marcus E Kleber, Alexander Niessner, Christian Herder, Oliver Kuss, Winfried März, Ewan R Pearson, Michael Roden, Robert Wagner, for the German Diabetes Study Group

F

- HbA_{1c}
- BMI
- Total cholesterol
- HDL-cholesterol
- Triglycerides
- Alanine aminotransferase
- Serum creatinine
- Systolic blood pressure
- Diastolic blood pressure



Lancet Diabetes Endocrinol 2024; 12: 119–31

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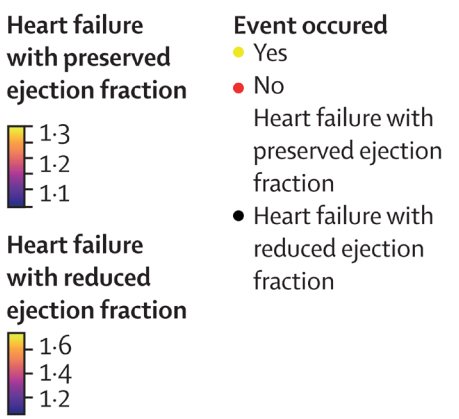
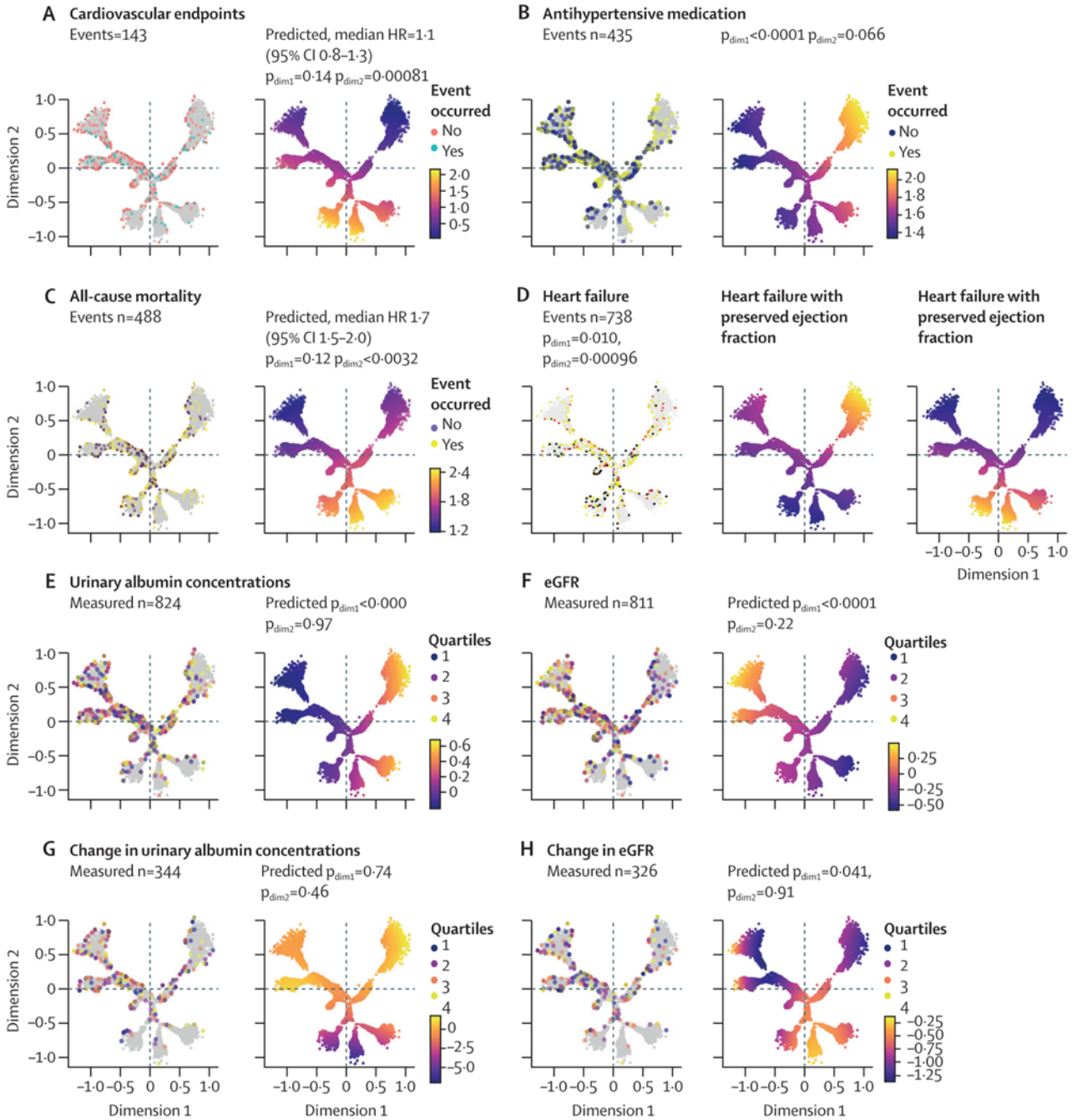
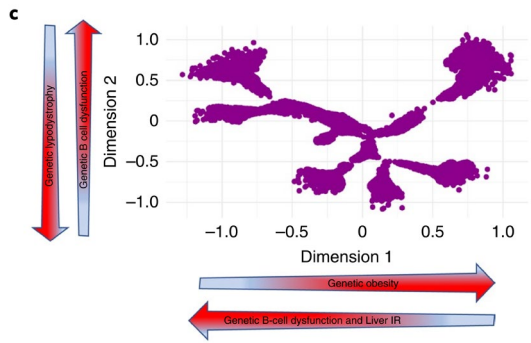




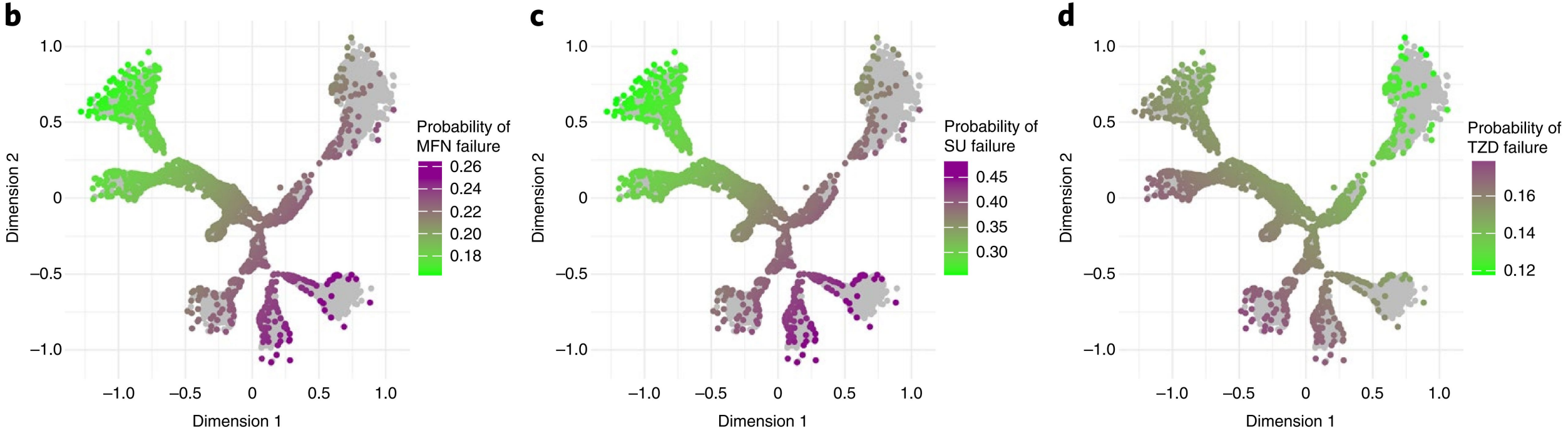
Lancet Diabetes Endocrinol 2024; 12: 119–31

Heterogeneity in phenotype, disease progression and drug response in type 2 diabetes

Anand Thakarakkattil Narayanan Nair[1], Agata Wesolowska-Andersen[2], Caroline Brorsson[3], Aravind Lathika Rajendrakumar[1], Simona Hapca[1], Sushrima Gan[1], Adem Y. Dawed[1], Louise A. Donnelly[1], Rory McCrimmon[1], Alex S. F. Doney[1], Colin N. A. Palmer[1], Viswanathan Mohan[4], Ranjit M. Anjana[4], Andrew T. Hattersley[5], John M. Dennis[5] and Ewan R. Pearson[1]✉



Visualizing the heterogeneity in anti-diabetic drug failure using ADOPT trial data

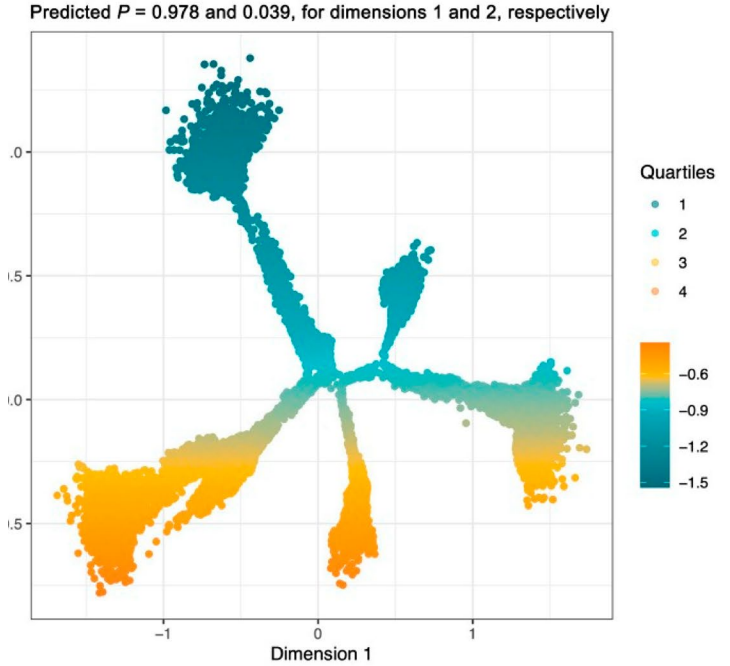


Heterogeneity in Phenotype and Early Metabolic Response to Lifestyle Interventions in Type 2 Diabetes in China Using a Tree-Like Representation

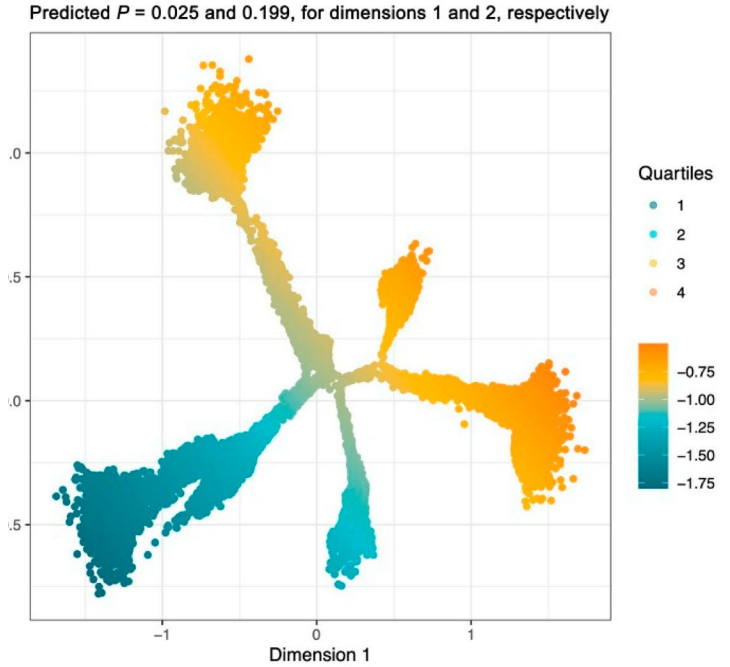
Yi Ding, Qi Zhou, Youjin Jiang, Qiuyu Cao, Xianglin Wu, Xiaoran Li, Yu Xu, Jieli Lu, Min Xu, Tiange Wang, Zhiyun Zhao, Yuhong Chen, Yan Liu, Jie Li, Guang Ning, Weiqing Wang, Yufang Bi, and Mian Li

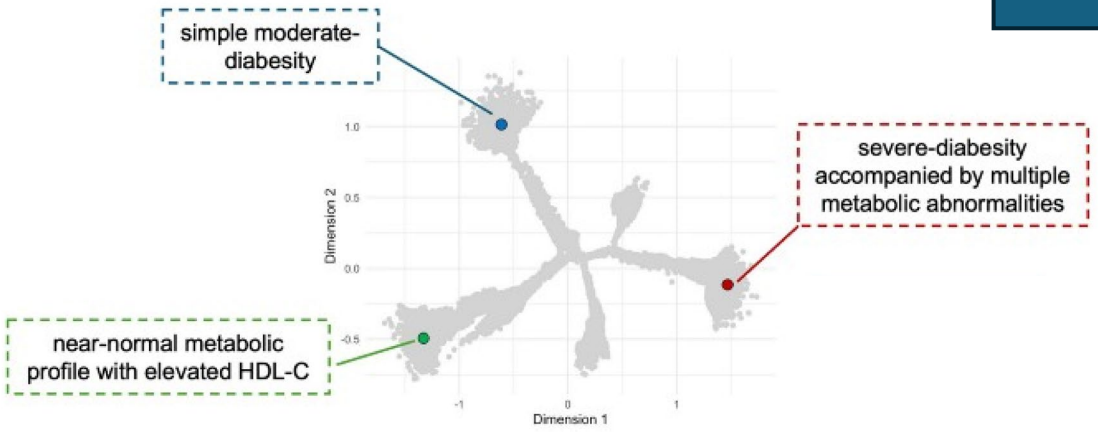
Visualization of heterogeneity in HbA1c changes after 12-week lifestyle intervention

diet



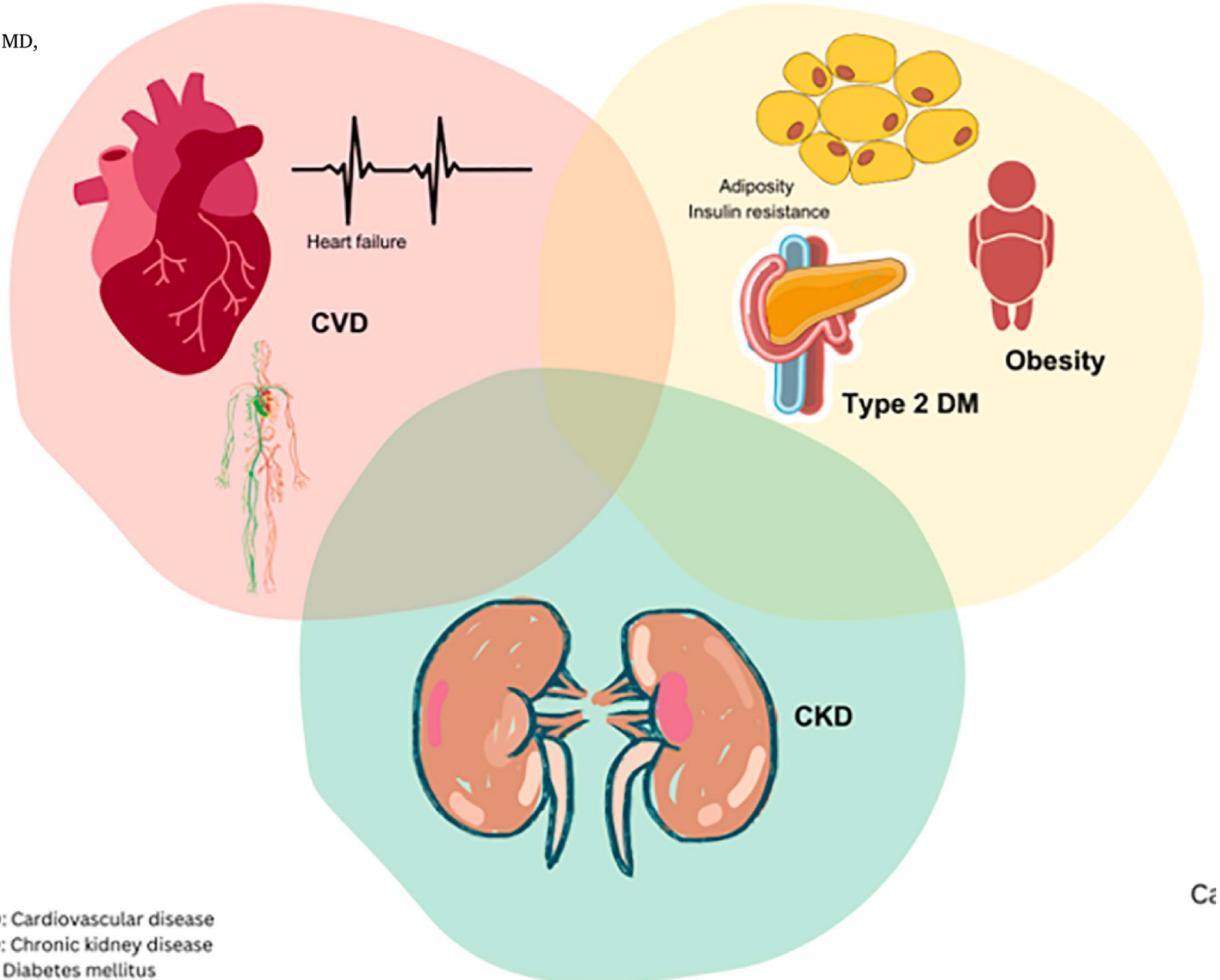
exercise





Cardiovascular-Kidney-Metabolic (CKM) syndrome: A state-of-the-art review☆

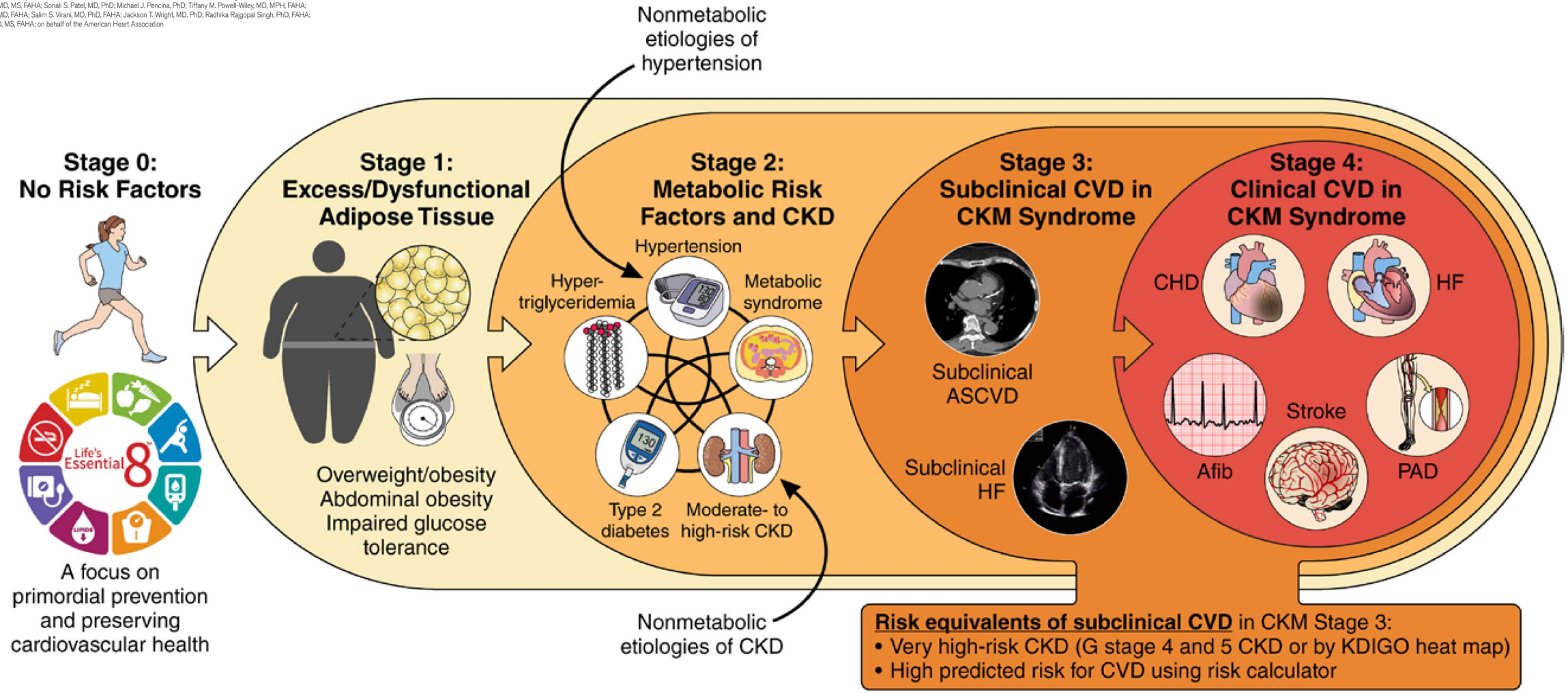
Sneha Annie Sebastian, MD [a,*], Inderbir Padda, MD, MPH [b], Gurpreet Johal, MD, FACC, FASN, FRCPC [c]



CVD: Cardiovascular disease
CKD: Chronic kidney disease
DM: Diabetes mellitus

Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association

Chiadi E. Ndumele, MD, PhD, FAHA, Chair; Janani Rangaswami, MD, FAHA, Vice Chair; Sheryl L. Chow, PharmD, FAHA, Vice Chair; Ian J. Neeland, MD, FAHA; Katherine R. Tuttle, MD; Sadiya S. Khan, MD, MSc, FAHA; Josef Coresh, MD, PhD; Roy O. Mathew, MD; Carissa M. Baker-Smith, MD, MPH, FAHA; Mercedes R. Carnethon, PhD, FAHA; Jean-Pierre Despres, PhD, FAHA; Jennifer E. Ho, MD, FAHA; Joshua J. Joseph, MD, MPH, FAHA; Walter N. Kernan, MD; Amit Khera, MD, MSc, FAHA; Mikhail N. Kosiborod, MD; Carolyn L. Lekavich, PhD; Eldrin F. Lewis, MD, MPH, FAHA; Kevin B. Lo, MD; Bige Ozkan, MD, ScM; Latha P. Palaniappan, MD, MS, FAHA; Sonali S. Patel, MD, PhD; Michael J. Pencina, PhD; Tiffany M. Powell-Wiley, MD, MPH, FAHA; Laurence S. Sperling, MD, FAHA; Salim S. Virani, MD, PhD, FAHA; Jackson T. Wright, MD, PhD; Radhika Rajgopal Singh, PhD, FAHA; Mitchell S.V. Elkind, MD, MS, FAHA; on behalf of the American Heart Association



Circulation. 2023;148:1606–1635

A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association

Chiadi E. Ndumele, MD, PhD, FAHA, Chair; Ian J. Neeland, MD, FAHA; Katherine R. Tuttle, MD; Sheryl L. Chow, PharmD, FAHA, Vice Chair; Roy O. Mathew, MD; Sadiya S. Khan, MD, MSc, FAHA; Josef Coresh, MD, PhD; Carissa M. Baker-Smith, MD, MPH, FAHA; Mercedes R. Carnethon, PhD, FAHA; Jean-Pierre Després, PhD, FAHA; Jennifer E. Ho, MD, FAHA; Joshua J. Joseph, MD, MPH, FAHA; Walter N. Kernan, MD; Amit Khera, MD, MSc, FAHA; Mikhail N. Kosiborod, MD; Carolyn L. Lekavich, PhD; Eldrin F. Lewis, MD, MPH, FAHA; Kevin B. Lo, MD; Bige Ozkan, MD, ScM; Latha P. Palaniappan, MD, MS, FAHA; Sonali S. Patel, MD, PhD; Michael J. Pencina, PhD; Tiffany M. Powell-Wiley, MD, MPH, FAHA; Laurence S. Sperling, MD, FAHA; Salim S. Virani, MD, PhD, FAHA; Jackson T. Wright, MD, PhD; Radhika Rajgopal Singh, PhD, FAHA; Mitchell S.V. Elkind MD, MS, FAHA; Janani Rangaswami, MD, FAHA, Vice Chair; on behalf of the American Heart Association

Circulation. 2023;148:1636–1664.

STAGE 0[79,86,196,197]
- Attaining and maintaining ideal CVH linked to decreased CVD and mortality
- Multilevel school-based and family-based interventions increase likelihood of ideal CVH
- Avoiding weight gain with aging decreases likelihood of developing CKM risk factors

STAGE 1[125-128,197,198]
- Nonjudgmental weight loss counseling increases the likelihood of weight loss attempts
- A comprehensive lifestyle intervention is most effective for sustained behavioral changes
- 5%–10% weight loss associated with improved BP, glycemia, and lipids
- ≥10% weight loss associated with lower CVD event rates
- Incretin analogues* induce >15% weight loss and improve metabolic risk factors
- Bariatric surgery associated with reductions in metabolic risk factors, CVD events, and mortality

STAGE 2[39,66,71,76,77,129,133,135,138,139,142,143,145,146,151,159,168]

Hypertension
- BP control reduces risk for multiple CVD outcomes; goal of <130/80 mmHg
- Pharmacotherapy for those with diabetes, CKD, age ≥65 y or ≥10% CVD risk; ACEi/ARB if CKD or diabetes with albuminuria

Hypertriglyceridemia
- Initial focus on lifestyle changes and addressing secondary causes; use statins if intermediate or higher ASCVD risk
- In those with diabetes + risk factors + triglycerides ≥135 mg/dL, icosapent ethyl lowers CVD risk

MetS
- Lifestyle changes/weight loss improve MetS components and other pathophysiologic features
- Lifestyle changes accompanied by targeted pharmacotherapy for risk factor control lowers CVD event rates

Diabetes
- Statins lower CVD event rates; ezetimibe helps achieve 50% LDL-C reduction and further lowers ASCVD risk
- SGLT2i decrease adverse kidney events, HF events, and MACE/CVD mortality
- GLP-1RA reduce weight, glycemia, MACE, and CVD mortality
- Metformin in concert with SGLT2i useful for achieving glycemic targets if HbA1c ≥7.5%

CKD
- ACEi/ARB in albuminuric CKD decrease adverse kidney and CVD events
- SGLT2i in CKD with eGFR >20 mL/min/1.73 m^2 decrease adverse kidney and CVD events
- Finerenone in CKD with diabetes with eGFR >25 mL/min/1.73 m^2 reduces adverse kidney and CVD events

STAGE 3[100,149-151,154-156]

Subclinical ASCVD
- Presence of CAC favors statin therapy in those with borderline-intermediate ASCVD risk
- CAC score ≥100 indicates greater net benefit from aspirin and other preventive therapies

Subclinical HF
- In asymptomatic LV systolic dysfunction, ACEi and β-blockers associated with less HF/CVD mortality
- In diabetes, SGLT2i decrease the risk for incident HF

STAGE 4[39,59,60,65,71,72,76,77,103,125,129,135,147,151,158,161,163,164,169,170,177,203]
- All ASCVD: Aspirin or P2Y12i + high-intensity statin indicated to reduce ASCVD events; use of additional LDL-C-lowering agents based on the presence of high risk ASCVD and LDL-C thresholds.
- All HF: 4 pillars of GDMT (β-blockers, ARNi, MRAs, SGLT2i) to improve HF outcomes/mortality, particularly for HFrEF

Obesity and CVD
- Nonjudgmental approach to weight loss discussion improves effectiveness
- Exercise training in obesity and HFpEF improves functional status
- Integrated weight management teams facilitate patient-centered approach
- Incretin analogues induce >15% weight loss, improve QOL, and reduce recurrent CVD events
- Bariatric surgery reduces recurrent CVD events and mortality

Hypertriglyceridemia and CVD
- Statin therapy modestly reduces triglycerides (10%–30%) and lowers ASCVD risk
- Icosapent ethyl reduces CVD events and mortality

Hypertension and CVD
- BP control reduces recurrent CVD events and mortality; goal <130/80 mmHg
- ACEi/ARB in CVD with CKD or diabetes; in African American patients with HFrEF, hydralazine/isosorbide after 4 pillars of GDMT

Diabetes and CVD
- Lifestyle modification improves control of glycemia/risk factors and QOL
- In HF, SGLT2i improve QOL, reduce HF hospitalizations, and reduce mortality risk
- In ASCVD, SGLT2i reduce MACE and HF hospitalizations
- In ASCVD, GLP-1RA reduce weight, glycemia, and MACE

CKD and CVD
- Statin continuation recommended for reducing recurrent ASCVD events
- ACEi/ARB reduce adverse kidney events and reduce morbidity and mortality rates in CVD
- SGLT2i in CKD with eGFR >20 mL/min/1.73 m^2 reduce adverse kidney events, HF hospitalizations, MACE, and CVD mortality
- Finerenone in CKD with diabetes with eGFR >25 mL/min/1.73 m^2 reduces adverse kidney events and CVD events
- ARNi reduces adverse kidney events, HF hospitalizations, and CV death in HF

conclusioni

Nella crescente consapevolezza della complessa eterogeneità del «Diabete Mellito tipo 2» vi sono diversi modelli di «rotte» per la personalizzazione della descrizione e della previsione di evoluzione di malattia finalizzati ad ottimizzare le strategie terapeutiche che ad oggi sono però di «limitata» applicabilità nella pratica clinica quotidiana….

… senza dimenticare che….

Heterogeneity in the development of diabetes-related complications: narrative review of the roles of ancestry and geographical determinants

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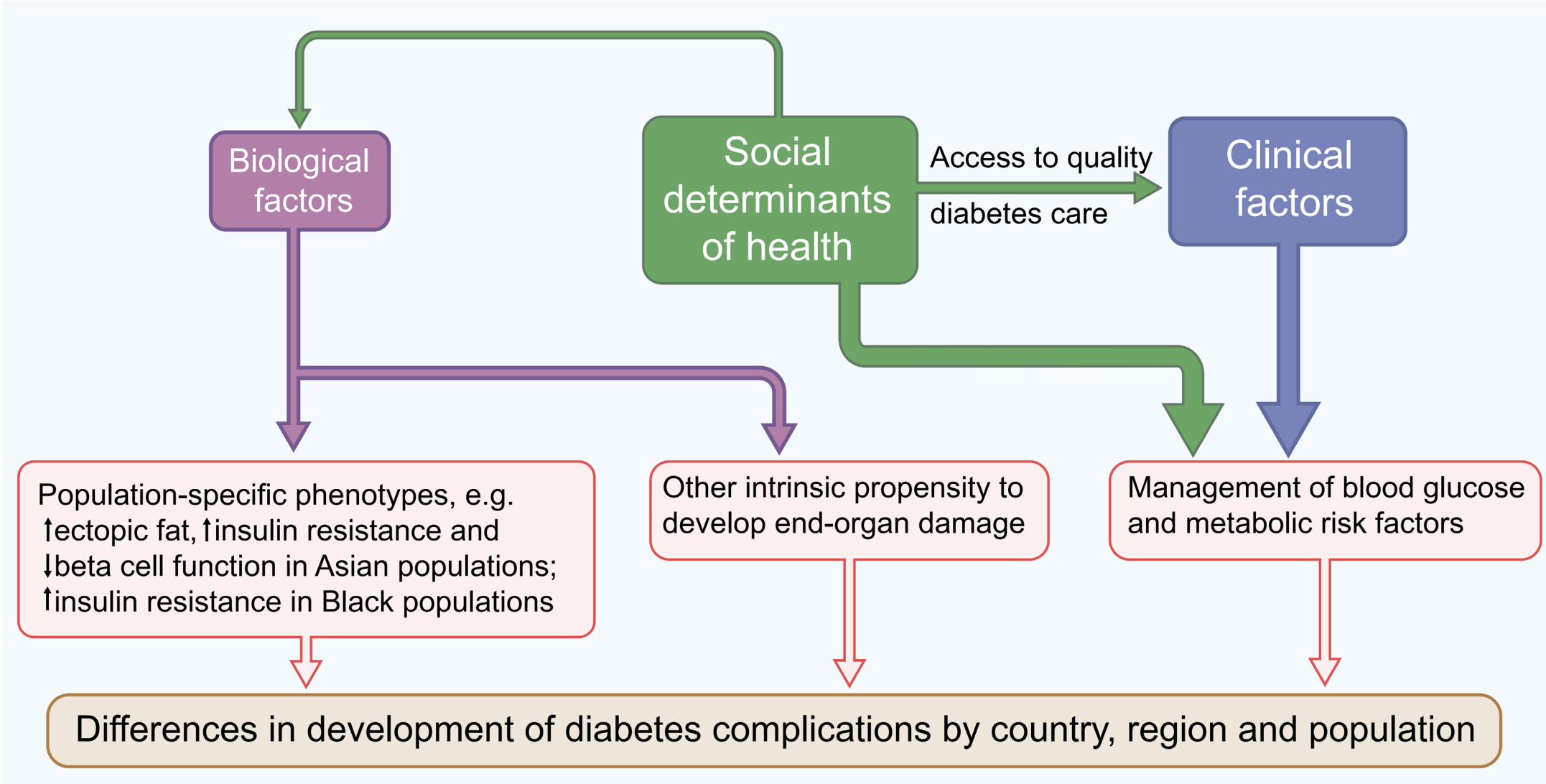

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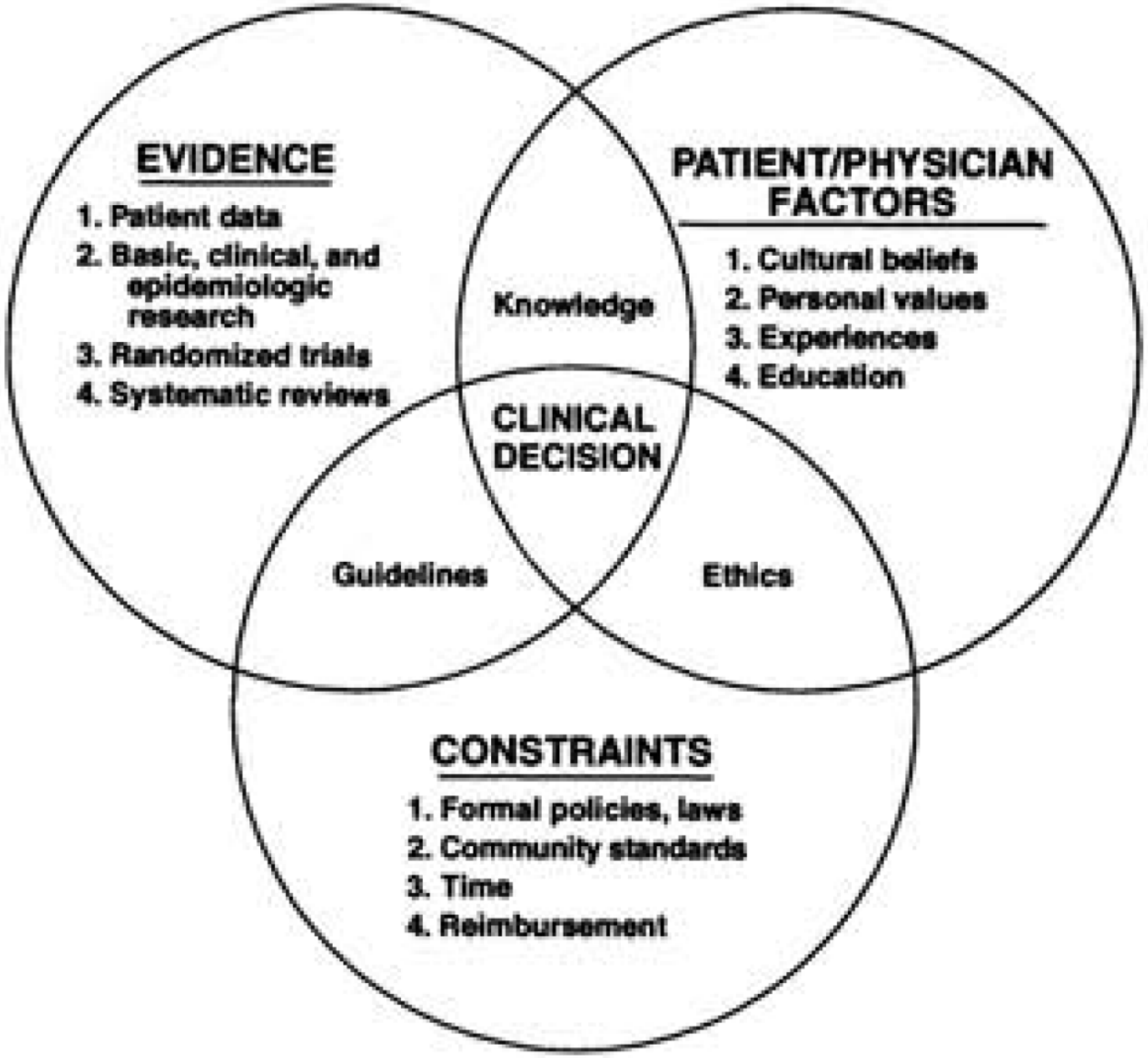
Systematic Reviews: Critical Links in the Great Chain of Evidence



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