Wat is het CV risico bij asymptomatische vliegers en na een CV event ?

dr. Jeroen J.J. Bucx, cardioloog
partner CardioExpert Bunnik
2e Luchtvaart Cardiologie Symposium 25.04.25
Centrum voor Mens en Luchtvaart, Soesterberg

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Potentiële belangenverstrengeling	Geen
Voor bijeenkomst mogelijk relevante relaties met bedrijven	n.v.t.
Sponsoring of onderzoeksgeld Honorarium of andere (financiële) vergoeding Aandeelhouder Andere relatie, namelijk …	Geen vermeldingen

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Agenda

- Risk is relative
- CAD: major determinant of risk
- Evaluation of risk
- Utility of risk calculators
- Overview of risk calculators
- How to calculate CVD risk
- Presence or absence of CAD / DM
- Take Home Messages

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Acceptable risk acute incapacitation/yr

Risk of incapac./year	0 % %	1 %	2 %	3 %	4 %	5 %	6 %	7 %	8 %	9 %	10
Class 1 or 3											
Restricted class 1 or 3											
Class 2											
Restricted class 2											
LAPL											
Restricted LAPL											

Acceptable level of risk for incapacitation due to acute pain attacks or similar medical incidents (grade 1 incapacitation)

Acceptable level of risk for incapacitation due to syncope or similar medical incidents (grade 2 incapacitation)

Acceptable level of risk for incapacitation due to epileptic seizures or similar medical incidents (grade 3 incapacitation)

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Guidance material for CAA-NO aeromedical examiners. 1178/2011 Part-MED & 2015/340 Part-ATCO.MED. VERSION 4.

Age Related Risk Score

Risico	< 50 jaar	50 - 69 jaar	≥ 70 jaar
laag	< 2,5%	< 5%	-
matig verhoogd	≥ 2,5% - < 7,5%	≥ 5% - < 10%	< 15%
hoog	≥ 7,5%	≥ 10%	≥ 15%

Laag risico: aanbieden van medicamenteuze behandeling doorgaans niet aangewezen

Matig verhoogd risico: aanbieden van medicamenteuze behandeling doorgaans niet aangewezen
Speciale aandacht is gewenst bij jonge mensen in verband met het lifetimerisico

Hoog risico: overweeg medicamenteuze behandeling aan te bieden

De groepen met een zeer hoog risico vallen buiten deze tabel, zie daarvoor **tabel 1**

NHG-Standaard Cardiovasculair risicomanagement (M84) Versie 4.1, september 2024

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Classification Cardiovascular risk

Very high Risk:	Subjects with any of the following: ▪ CVD ▪ Type 2 diabetes, or type 1 diabetes & target organ damage ▪ Patients with moderate to severe CKD (GFR <60mL/min/1.73m^2) ▪ SCORE ≥10%
High Risk:	Subjects with: ▪ Markedly elevated single risk factors such as: - Familial dyslipidaemias - Severe hypertension. ▪ SCORE ≥ 5% and <10%
Moderate Risk:	SCORE is ≥1 and <5% at 10 years, further modulated by: ▪ family history of premature CAD ▪ abdominal obesity ▪ physical activity pattern ▪ HDL-C ▪ TG ▪ hsCRP ▪ social class
Low Risk:	SCORE less than 1% and free of qualifiers

SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. SCORE2 working group and ESC Cardiovascular risk collaboration *EHJ*, Volume 42, 1 July 2021, Page 2439

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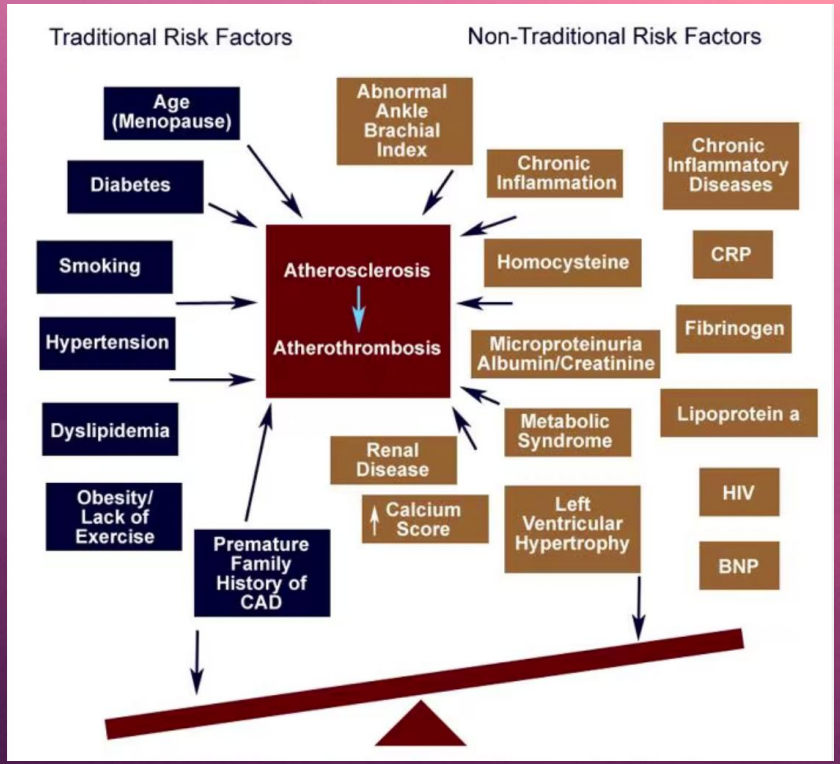
Risk factors and Coronary Artery Disease



-Age (men ≥ 45 years; women ≥ 55 years)
-Family history of premature coronary artery disease (CAD in male first-degree relative < 65 years)
-Hypertension (BP > 140/90 mmHg or on antihypertensive medications)
-Cigarette Smoking
-Diabetes
-Hypercholesterolemia
-Low HDL cholesterol (< 40 mg/dl)
-Hypertriglyceridemia (> 200 mg/dl)
-Obesity

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Guideline for evaluation of CVD risk

The American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA): Guidelines for the procedures of detection, management, or prevention of cardiovascular disease.

In **asymptomatic** adults, **global risk scoring** should be performed and a **family history of cardiovascular disease** should be obtained for cardiovascular risk assessment. **The following tests and measures** could be used as well:

- Measurement of lipid parameters beyond a standard fasting lipid profile
- Brachial/peripheral arterial flow-mediated dilation studies
- Specific measures of arterial stiffness
- Coronary CT angiography
- MRI for detection of vascular plaque

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Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: ACC/AHA Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140:e563–e595.

Evaluation of CVD risk (cntd)

- **ECG** may be considered in asymptomatic adults without hypertension or DM.
- **Exercise ECG** may be considered in intermediate-risk asymptomatic adults, particularly when attention is paid to non-ECG markers such as exercise capacity.
- **Transthoracic echocardiography** is not recommended in asymptomatic adults without hypertension.
- **Stress echocardiography** is not indicated for low- or intermediate-risk asymptomatic adults.

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Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: ACC/AHA Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140:e563–e595.

Evaluation of CVD risk (cntd)

- **Coronary artery calcium (CAC) measurement** is reasonable in asymptomatic intermediate-risk adults, but not in persons at low risk; it may be reasonable when the patient's risk falls between low and intermediate.
- For cardiovascular risk assessment in asymptomatic adults with **diabetes mellitus**, measurement of CAC is reasonable (patients 40 years and older). Stress myocardial perfusion scan (MPS) may be considered.
- **Cardiac MRI** among asymptomatic individuals with regional myocardial dysfunction (RMD).
- In postmenopausal women with **hormone replacement therapy** sudden cardiac death comprised most cardiac deaths. Independent predictors of sudden cardiac death included myocardial infarction, congestive heart failure, decreased eGFR, atrial fibrillation, physical inactivity, and diabetes.

Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardio-vascular disease: ACC/AHA Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140:e563–e595.

Nontraditional/novel risk factors 1/2

- C-reactive protein
- Lipoprotein(a)
- Homocysteine
- Tissue plasminogen activator
- Small, dense LDL
- Fibrinogen

Nontraditional/novel risk factors 2/2

- End-stage renal disease (ESRD), chronic inflammatory diseases affecting connective tissues (eg, lupus, rheumatoid arthritis), HIV infection/AIDS, highly active antiretroviral therapy [HAART]), and other markers of inflammation.
- Low serum testosterone levels and/or presence of erectile dysfunction.
- Woman aged 50 years or younger following hysterectomy.
- Too little sleep (≤5-6 h per night) or too much sleep (>8-9 h per night).
- Birth weight.
- Xanthelasmata (but not arcus corneae).
- Vitamin D deficiency.

Limitations risk score calculators

- Incomplete risk stratification
  - DM: HbA1c, UACR (urine albumin creatinine ratio), and eGFR
- Exclusion of relevant risk factors
  - Recognized risk enhancing factors
    - Family history of premature ASCVD
    - Kidney disease
    - Inflammatory disorders
    - Metabolic syndrome
    - Lipids / biomarkers
  - Coronary artery calcification
- Timeframe considerations
  - Estimation of 10 yr or 30 yr risk, lifetime risk
  - Effect of therapeutic interventions
- Requirements for updating

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Utility of CVD risk calculators

- Ease of use
  - Availability and performance (www, integration in EPD)
  - Required data easily measurable and available
- Accuracy
  - External validation to determine accuracy and utility
- Applicability
  - Major clinical endpoints for individual and population
- Major society endorsement
  - Recommendations of professional society and health organization guidelines

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CVD risk assessment calculator

Name (acronym) and discription of the calculator

- Derivation dataset (interval)
- External validation dataset (interval)
- (Risk Region)
- Risk factors
- Clinical endpoints

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Often applied CVD risk calculators

PREVENT (AHA) (Predicting Risk of CVD calculator) (USA), age 30-79;

ASCVD Risk Estimator Plus (2018) (USA), age 20-79;

SCORE-2 (**S**ystematic **CO**ronary **R**isk **E**valuation), ESC (2012) (EUROPE), age 40-69;

SCORE2-OP (**S**ystematic **CO**ronary **R**isk **E**valuation **O**lder **P**ersons), ESC (2012), age > 70;

QRISK3-2018 and **QRISK-lifetime calculator**, to estimate ASCVD risk for adults aged 25-84 (including DM2) without CVD (UK);

CHINA-PAR Risk Estimator (2016) for Chinese individuals, age not specified (CHINA);

The **World Health Organization (WHO) CVD updated risk charts** (2019) for 21 worldwide regions, age not specified (WHO);

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Online calculators of CVC risk (1/2)

TOOL	Patient categories	Geographical region	Prediction outcomes	Additional features
SCORE www.heartscore.org	Healthy people	Europe high and low risk regions	10-year CVD risk	Personal health advice based on ESC-Guidelines Available in 17 languages Print option for patient handout Patient history and progress Calibrated versions
QRISK3 www.qrisk.org/three	Healthy people	United Kingdom	10-year CVD risk Relative risk Heart age	Infographics for patient communication
JBS-3 risk calculator www.jbs3risk.com	Healthy people	United Kingdom	10-year CVD risk Lifetime CVD risk Heart age CVD-free life-expectancy	Effect of risk factor optimisation Infographics for patient communication
ASSIGN score www.assign-score.com	Healthy people	Scotland	10-year CVD risk	Missing data filled in by population average/median Print option for patient handout
PROCAM score Various websites	Healthy people	Germany	10-year coronary event risk	
CUORE www.cuore.iss.it/sopra/calc-rischio_en.asp	Healthy people	Italy	10-year CVD risk	Also available in Italian language
ASCVD risk-estimator plus http://tools.acc.org/ASCVD-Risk-Estimator-Plus	Healthy people	United States	10-year CVD risk Lifetime CVD risk	Effect of risk factor optimisation Personal health advice based on ACC/AHA guidelines Print option for patient handout
Framingham risk score www.framinghamheartstudy.org	Healthy people	United States	10-year CVD risk 30-year CVD risk Heart age	Additional calculators for other vascular disease outcomes

EAPC European Association of Preventive Cardiology

ACCA Acute Cardiovascular Care Association

ACNAP Association of Cardiovascular Nursing & Allied Professions

The ESC Prevention of Cardiovascular Disease Programme is led by the European Association of Preventive Cardiology (EAPC) in collaboration with the Acute Cardiovascular Care Association (ACCA) and the Association of Cardiovascular Nursing and Allied Professions (ACNAP).
This programme is supported by Amgen, AstraZeneca, Ferrer, and Sanofi and Regeneron in the form of educational grants.

ESC European Society of Cardiology

Online calculators of CVC risk (2/2)

TOOL	Patient categories	Geographical region	Prediction outcomes	Additional features
Reynolds risk score www.reynoldsriskscore.org	Healthy people	United States	10-year CVD risk Relative risk	Effect of risk factor optimisation Projection of risk increase with advancing age Print option for patient handout
Globorisk www.globorisk.org	Healthy people	Worldwide	10-year CVD risk	Country adjusted risk charts available
UKPDS risk engine V2 www.dtu.ox.ac.uk/riskengine	Type 2 diabetes	United Kingdom	Fatal and non-fatal CVD risk for any risk interval	Print option for patient handout
ADVANCE risk engine www.advanceriskengine.com	Type 2 diabetes	Europe, Asia, Australasia and North America	4-year CVD risk	Missing data filled in by population average/median Additional calculator for kidney disease outcomes
SMART risk score www.escardio.org/Education/ESC-Prevention-of-CVD-Programme/Risk-assessment/SMART-Risk-Score	Vascular patients	Europe and United States	10-year CVD risk	Missing data filled in by population average/median
MAGGIC risk calculator www.heartfailurerisk.org	Heart failure patients	Worldwide	1 and 3-year mortality risk	
Seattle Heart Failure model www.SeattleHeartFailureModel.org	Heart failure patients	Northern-America	1, 2 and 5-year mortality risk	Effect of specific treatment options
U-Prevent www.U-prevent.com	Healthy people Type 2 diabetes patients Vascular patients Elderly	Europe and Northern-America	10-year CVD risk Lifetime CVD risk CVD free life expectancy	Also available in Dutch Effect of specific treatment options Effect of deferred treatment Infographics for patient communication Print option for patient handout Missing data filled in by population average/median Calculator selection aid

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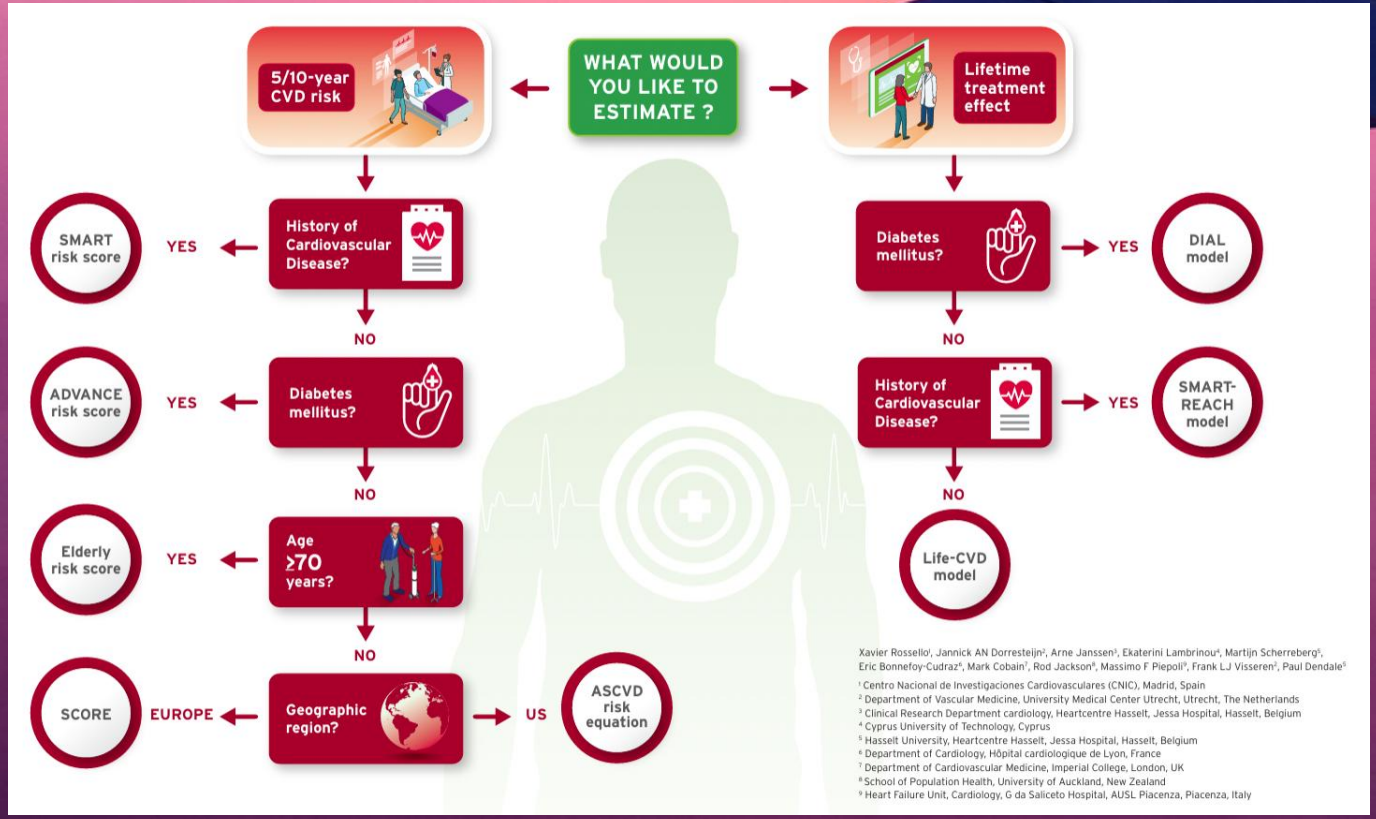
Approach to CVD risk calculation



Xavier Rossello[1], Jannick AN Dorresteijn[2], Arne Janssen[3], Ekaterini Lambrinou[4], Martijn Scherreberg[5], Eric Bonnefoy-Cudraz[6], Mark Cobain[7], Rod Jackson[8], Massimo F Piepoli[9], Frank LJ Visseren[2], Paul Dendale[5]

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No actual or previous CVD events

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U-Prevent (EUR and USA)

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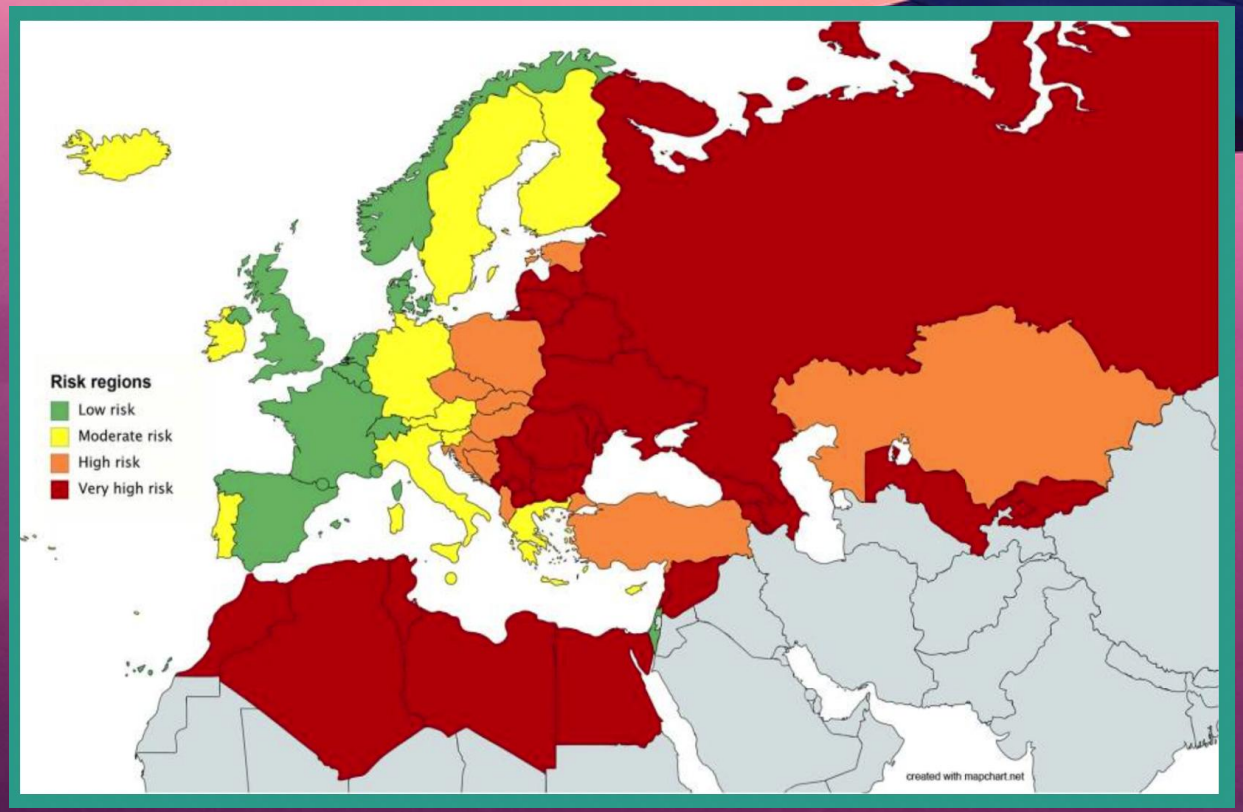
U-Prevent: Determine Risk Region



SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. EHJ (2021) 42, 2439–2454

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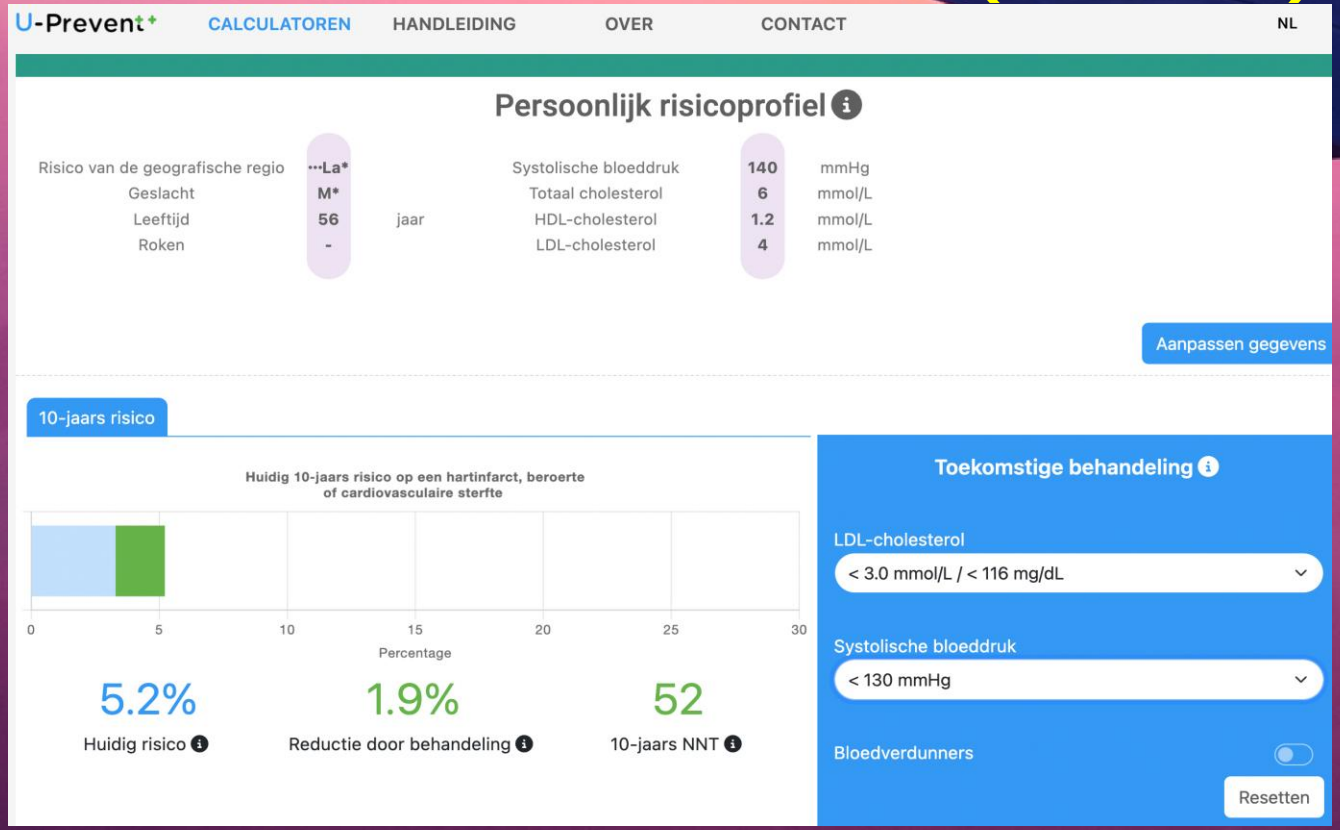
Risk calculator: Score2 (CVD-)



SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. EHJ (2021) 42, 2439–2454

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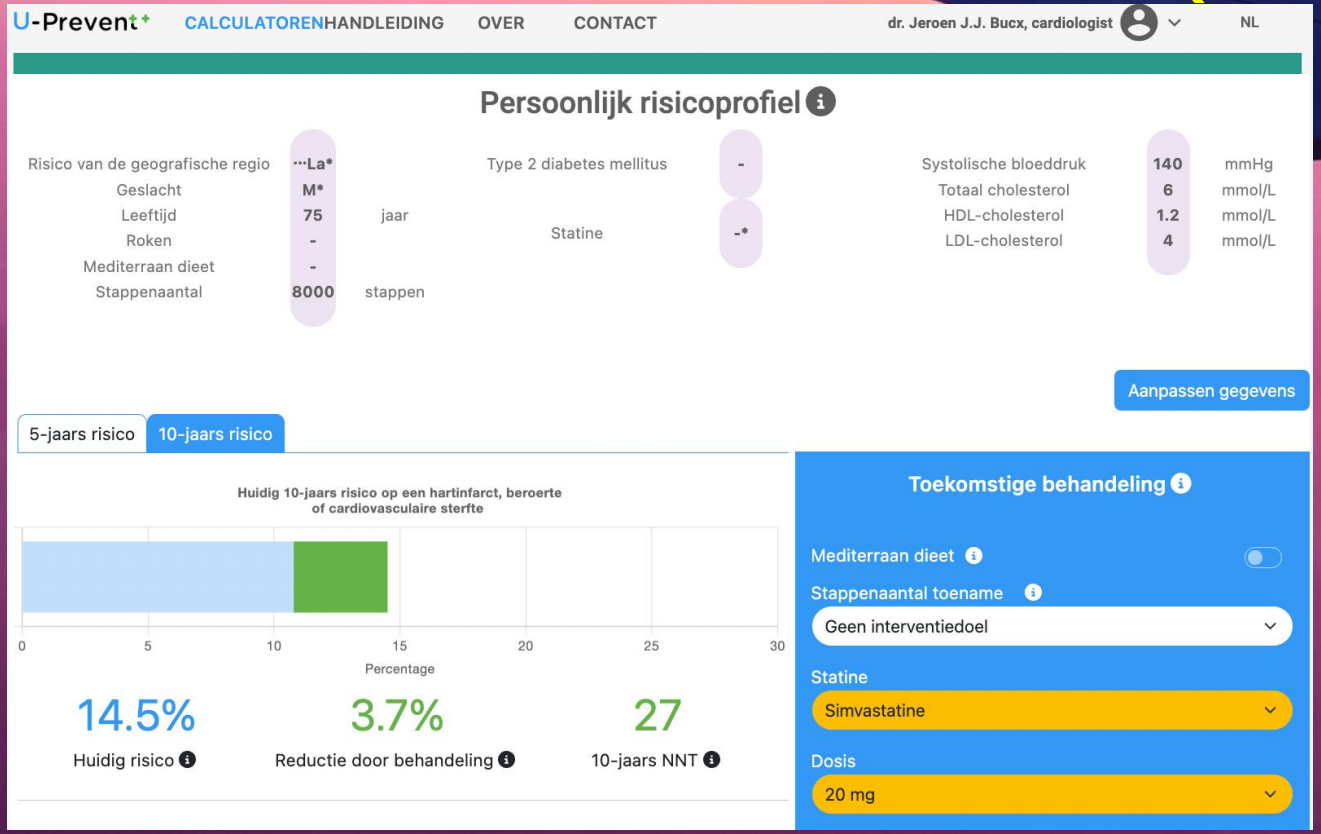
Risk calculator: Score2-OP (CVD-)



SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. EHJ (2021) 42, 2439–2454

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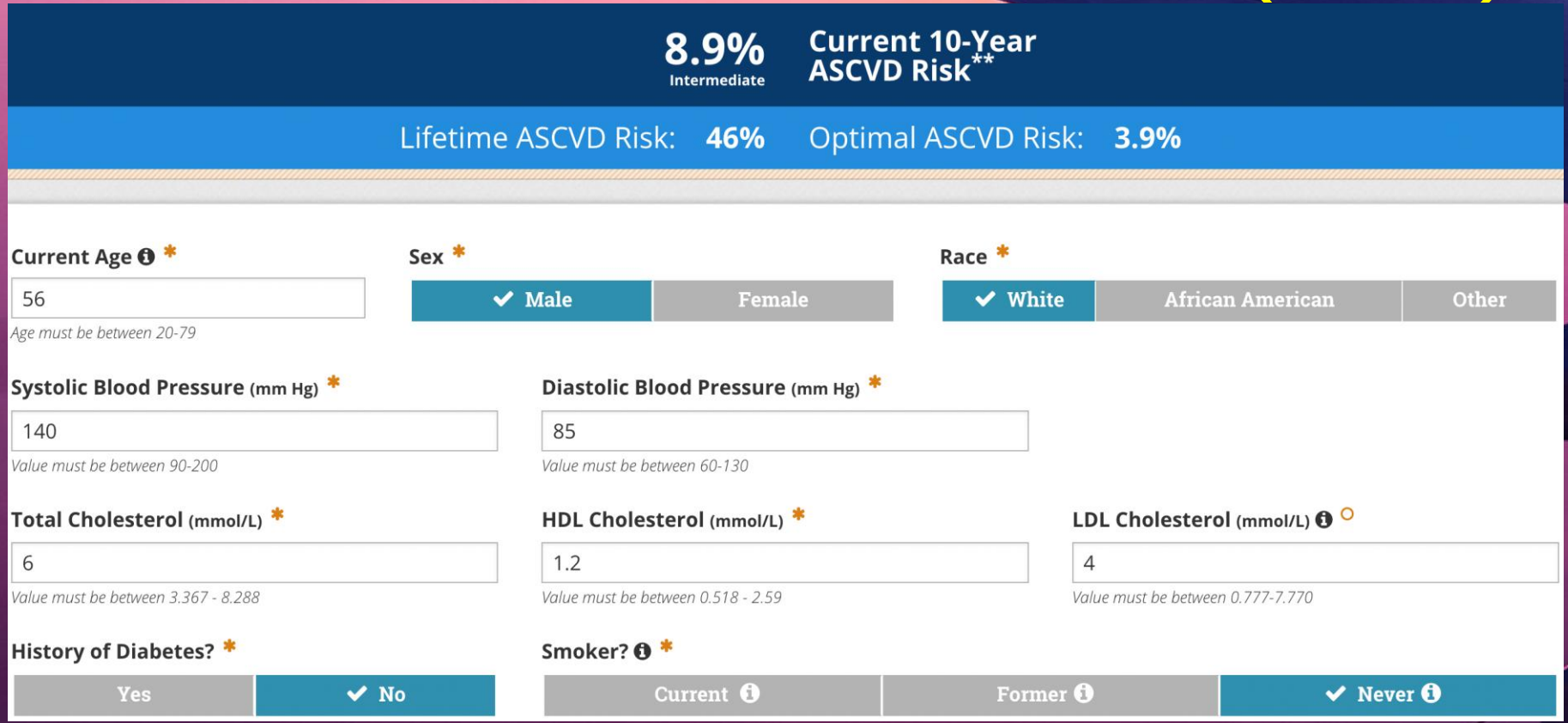
ASCVD Risk Estimator Plus (USA)



Lloyd-Jones DM, Braun LT, Ndumele CE et al. Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease: JACC Nov 2018, 25711

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Risk calculator: QRISK®3 (UK) (CVD-)

ClinRisk

Welcome to QRISK®3-lifetime cardiovascular risk calculator: https://qrisk.org/lifetime

This calculator is only valid if you do not already have a diagnosis of coronary heart disease (including angina or heart attack) or stroke/transient ischaemic attack.

Reset | UKCA

About you

Age (25-84): 56

Sex: (•) Male ( ) Female

Ethnicity: White or not stated

UK postcode: leave blank if unknown

Postcode:

Clinical information

Diabetes status: none

Angina or heart attack in a 1st degree relative < 60? ☐

Chronic kidney disease (stage 3, 4 or 5)? ☐

Atrial fibrillation? ☐

On blood pressure treatment? ☐

Do you have migraines? ☐

Rheumatoid arthritis? ☐

Systemic lupus erythematosus (SLE)? ☐

Severe mental illness? (this includes schizophrenia, bipolar disorder and moderate/severe depression) ☐

On atypical antipsychotic medication? ☐

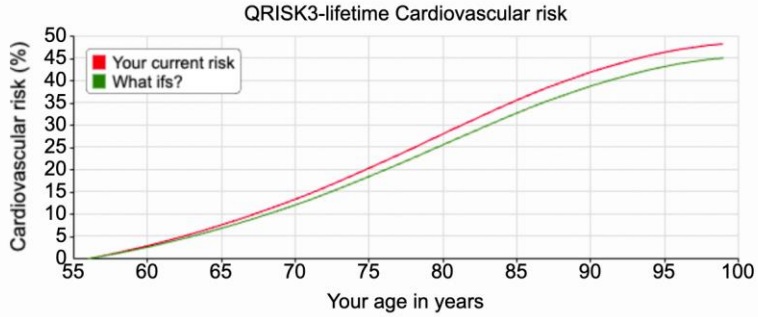
Are you on regular steroid tablets? ☐

A diagnosis of or treatment for erectile disfunction? ☐

Your results

Your QRISK3-lifetime score

	Current	What if?
Your lifetime risk (i.e. by the time you are 99)	48.2%	45.1%



In other words, in a crowd of 100 people like you,

- 48 will develop heart disease or have a stroke/TIA by the time they reach 99.

Your score has been calculated using estimated data, as some information was left blank.

Hippisley-Cox J, Coupland C, and Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. BMJ 2017; 357

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Reynolds Risk Score (> 45 yrs USA)

Age	50	years
Systolic BP	140	mm Hg
Diabetes mellitus	**No**	Yes
Current smoker	**No**	Yes
HDL cholesterol	1.5	mmol/L ⇋
Total cholesterol	5	mmol/L ⇋
hsCRP	3	mg/L ⇋
Parent with MI before age 60 years	No	**Yes**

1.9 %

10 year risk of MI or stroke
Recommendation: Unclear evidence for statin therapy

Copy Results | Next Steps

» Next Steps | Evidence | Creator Insights

FACTS & FIGURES

Interpretation:

Risk classification	Recommendation
<5%	Unclear evidence for statin therapy
5% to <10%	Minimal benefit of statin therapy compared to risk and cost of therapy in preventing a cardiovascular event in the next ten years
10% to <20%	• Discussion of lifestyle modification and initiation of statin therapy • U.S. treatment guidelines recommend initiation of treatment with 10-year risk estimates >10% • Understanding patient preference and motivation and frank discussion with patients about the risks and benefits of statin therapy in reducing cardiovascular events such as stroke, MI, and CVA in female patients over the next ten years
≥20%	Strongly recommend statin therapy in conjunction with lifestyle modification

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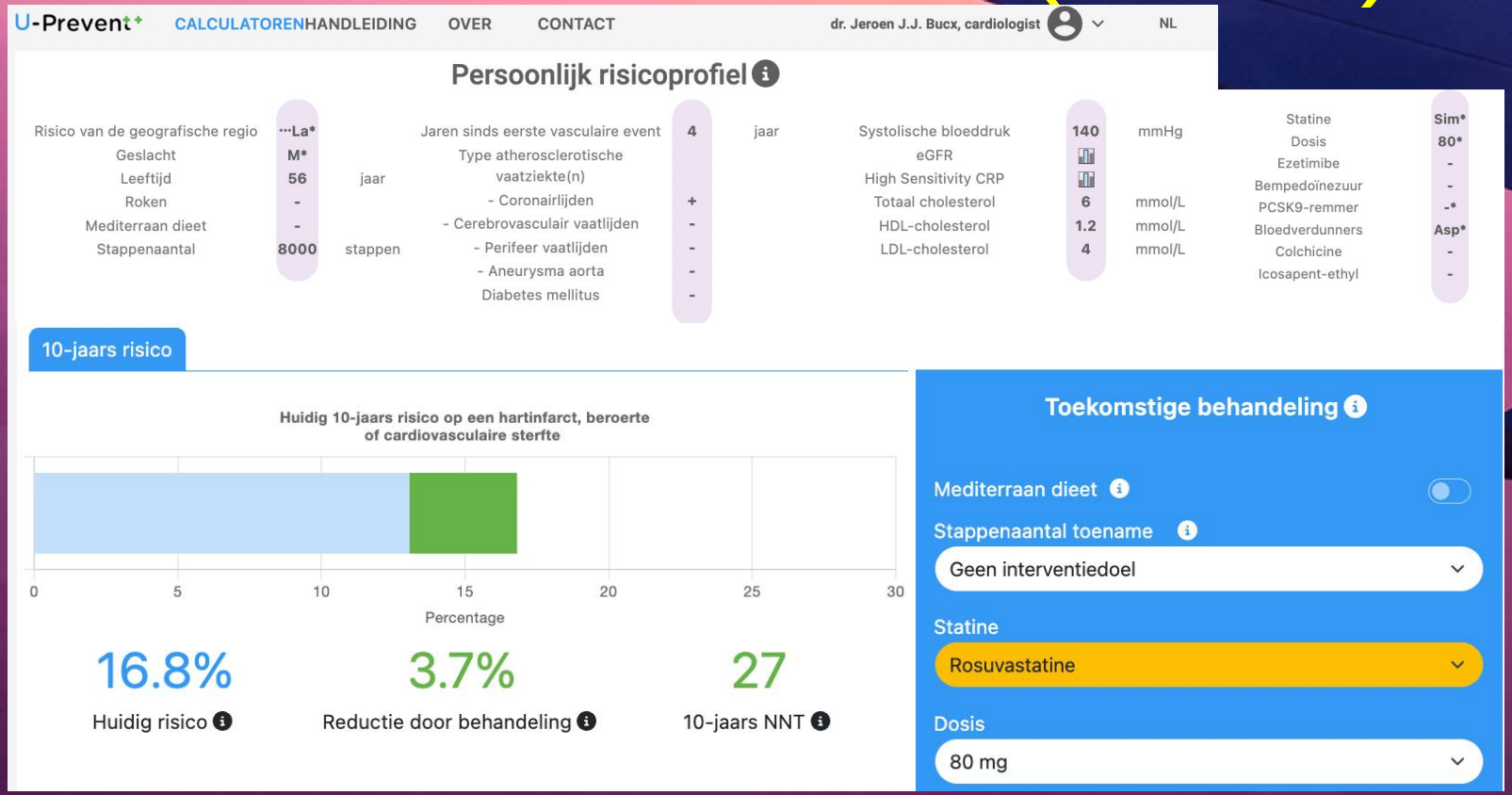
Ridkers PM, Buring JE, Rifai N et al. Development and Validation of Improved Algorithms for the Assessment of Global Cardiovascular Risk in Women. The Reynolds Risk Score. JAMA. 2007;297:611-619

Actual/previous CVD events / DM

Risk calculator: Smart2 (CVD+)



SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. EHJ (2021) 42, 2439–2454

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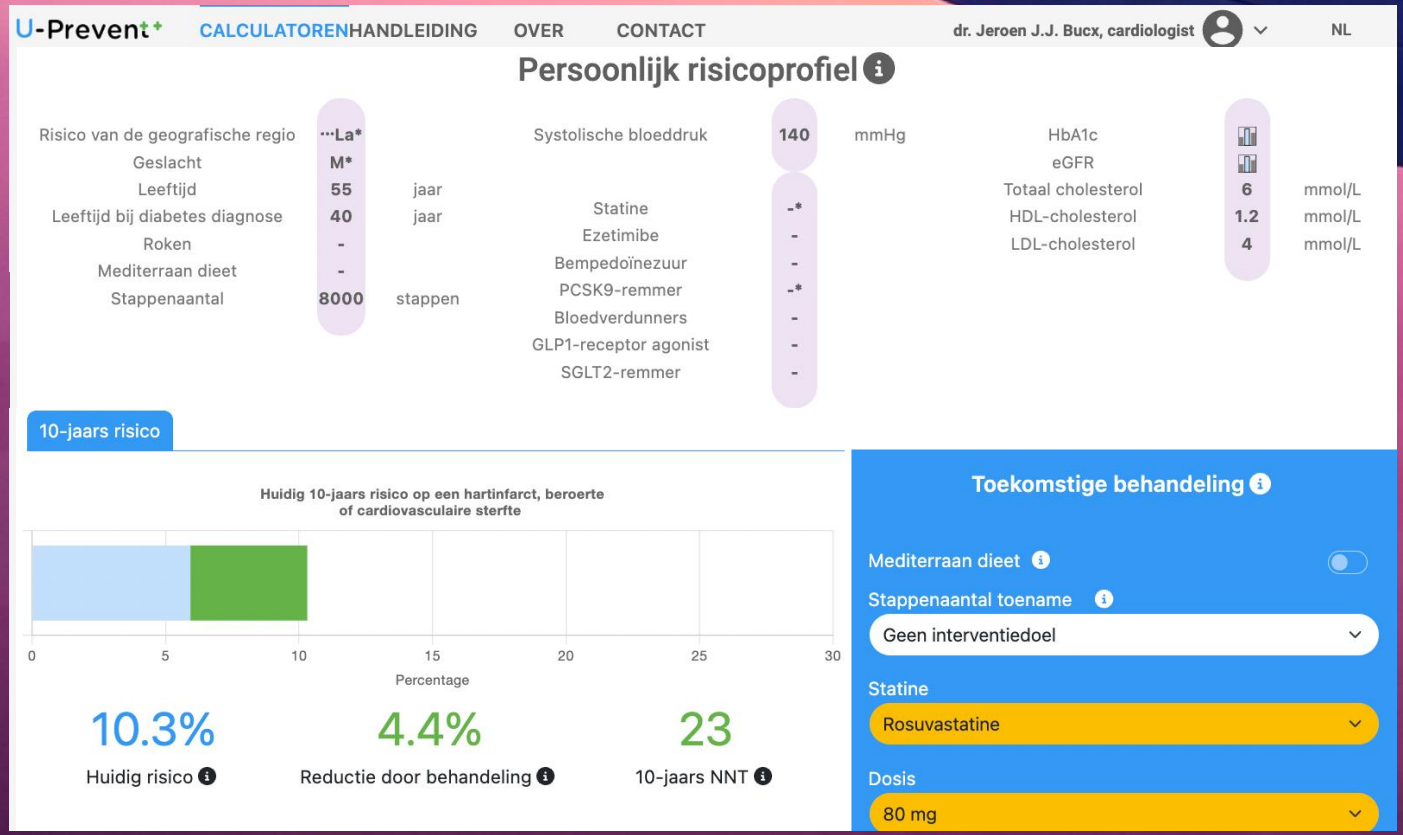
Risk calculator: Score2-DM



SCORE2 working group and ESC Cardiovascular risk collaboration. SCORE2 risk prediction algorithms: new models to estimate 10-year risk of cardiovascular disease in Europe. EHJ (2021) 42, 2439–2454

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Risk calculator: ADVANCE (DM) / 4yrs

Step 1

Age at diagnosis (years)	Points
29–34	0
35–39	1
40–44	2
45–50	3
51–56	4
57–62	5
63–68	6
69–74	7
75–80	8
81–86	9

Step 2

Known duration (years)	Points
0	0
1–5	1
6–10	2
11–15	3
16–20	4
21–25	5
26–30	6
31–35	7
36+	8

Step 3

Gender	Points
Men	0
Women	–1

Step 4

Atrial fibrillation	Points
No	0
Old or present	2

Step 5

Retinopathy	Points
No	0
Yes	1

Step 6

Treated hypertension	Points
No	0
Yes	1

Step 7

Pulse pressure, mmHg	Points
< 50	0
50–110	1
111 +	2

Step 8

HbA_{1c} (%)	Points
< 6	0
6 – < 9	1
9 +	2

Step 9

Albuminuria	Points
Normoalbuminuria	0
Microalbuminuria	2
Macroalbuminuria	3

Step 10

Non HDL-C (mmol/l)	Points
< 3	0
3 – < 6	1
6 – < 9	2
9 +	5

Step 11

Sum-up points from steps 1 to 10

Look up predicted four-year risk of major CVD in the table

Predicted four-year risk of major CVD

Total points	Four-year risk (%)
5 or less	< 0.5
6	0.5
7	0.7
8	1.0
9	1.4
10	2.1
11	3.0
12	4.3
13	6.2
14	8.9
15	12.6
16	17.8
17	24.7
18	33.7
19	41.9
20	57.8
21	71.4
22	Above 83

AP Kengne.
The ADVANCE cardiovascular risk model and current strategies for cardiovascular disease risk evaluation in people with diabetes.
Cardiovasc J Afr
2013 Nov;24(9):376

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Take Home Messages

- Individual CVD risk may vary considerably by age, risk factors, previous CVD, DM and other conditions;
- The flight license of a pilot is associated with an acceptable risk for airborn incapacitation;
- There is a number of risk calculators available to calculate CVD risk (see also website CardioExpert);
- EASA CVD risk may deviate from clinical CVD risk;
- By showing the effects of risk reduction by therapy, a CVD risk calculator may motivate the pilot to adhere to therapy;

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Thanks for your attention
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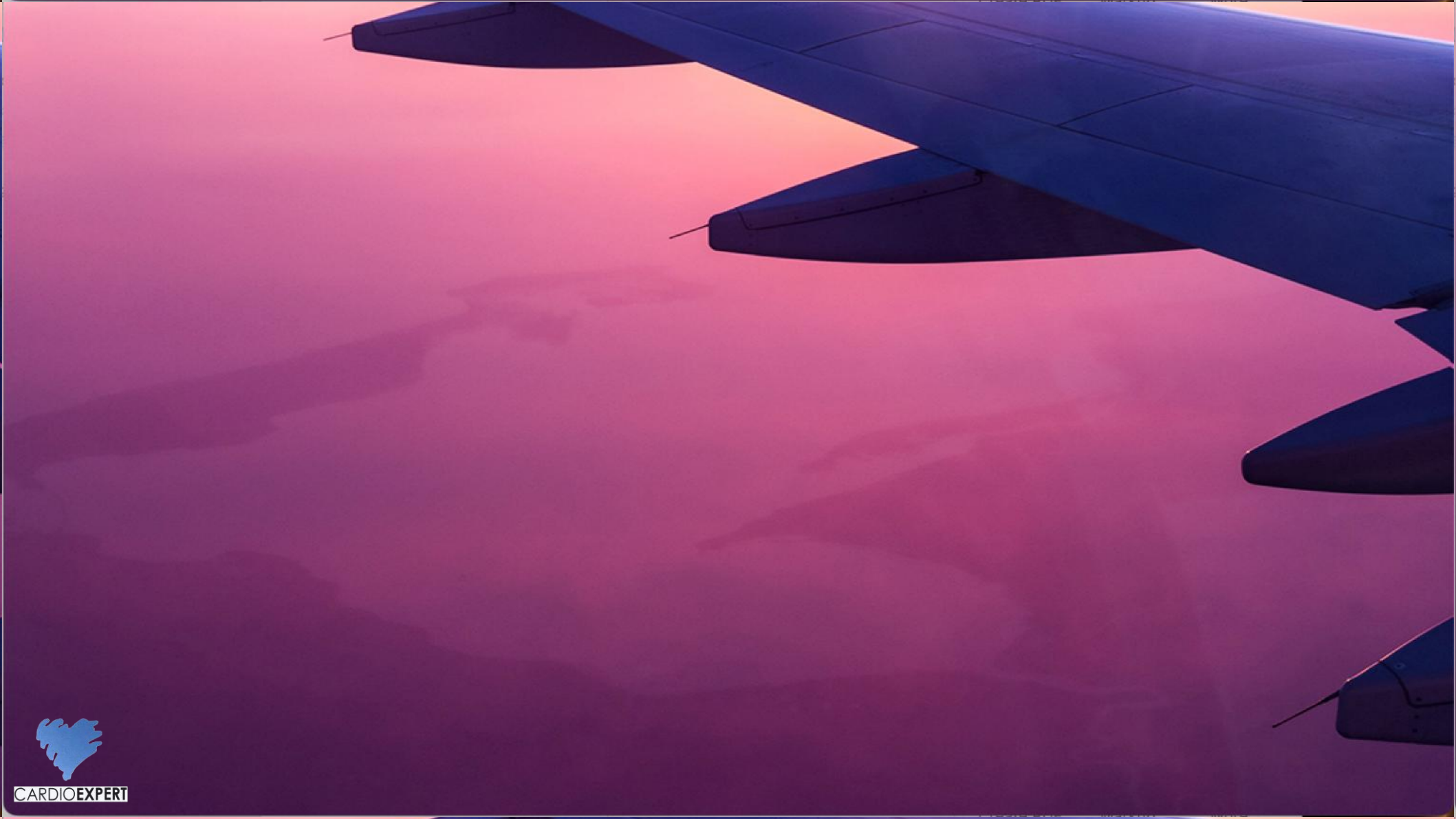
QUESTIONS
ANSWERS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