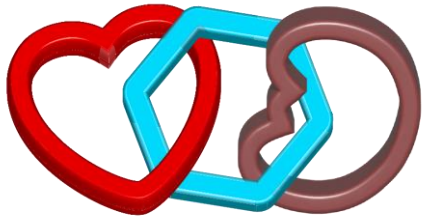


Gepersonaliseerde cardiovasculaire preventie

Prof. dr. Frank Visseren

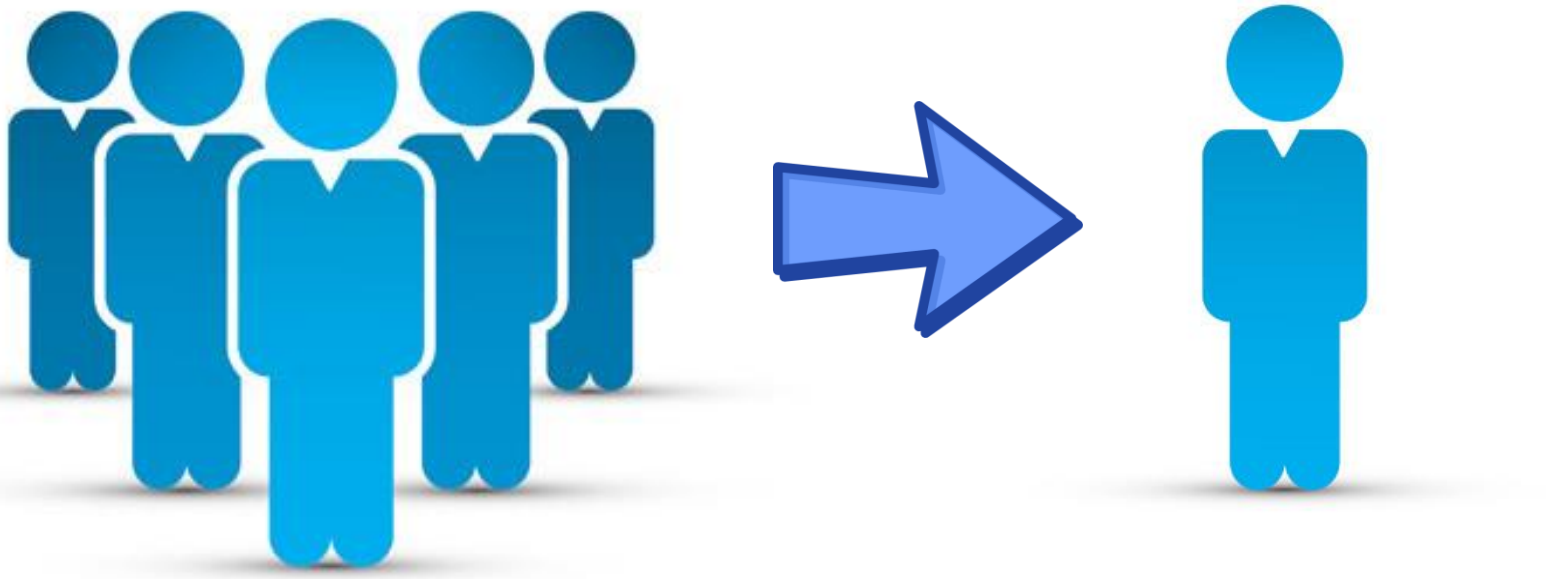
Internist-vasculair geneeskundige, UMC Utrecht

Disclosures

Research	ZonMw, Wellerdieck-de Goede fonds, Leatare foundation, Vrienden UMC Utrecht, Dutch Heart Foundation, Van Leerzem Foundation
Honoraria	None
Stocks	None
Other …	Fase II/III clinical research in the field of lipid-lowering (Sanofi, Medicines Company, Amgen, Pfizer, Eli Lilly, Merck, ISIS, Regeneron)
	Guideline committees: CV Risk Management 2019, CV Risk Management in elderly, (Genetic) lipid disorders. Chair ESC 2021 CV Prevention Guidelines.
	Scientific advisor U-Prevent. Website is based on published data, is supported by ZonMw-GGG and Dutch Heart Foundation and owned by ORTEC.

WHAT IS THE CHALLENGE IN CLINICAL PRACTICE?

How do we translate the results of group level evidence to individual patients?



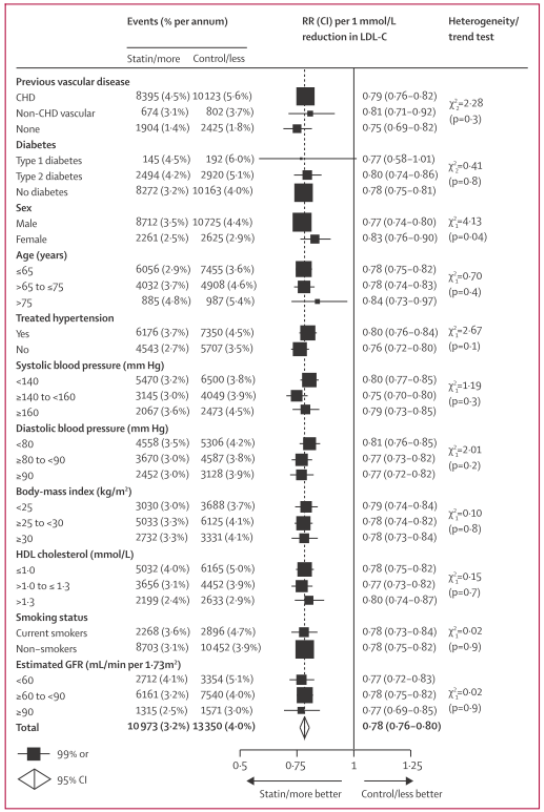
Average patient?

The CV prevention toolbox!

Risk factor	Drugs	Dose / combi	Treatment goal
Lipids	Statin Ezetimibe PCSK9-mab	Dose? Combination?	LDL-c <2.5 mmol/l LDL-c <1.8 mmol/l Even lower
Blood pressure	ACEi/ARB, Diuretics CCB, Betablocker, Spironolactone	Dose? Combination?	SBP <140 mmHg SBP <130 mmHg Elderly goal
Antithrombotics	Antiplatelet (COX, P2Y12, cAMP) DOAC	Dose? Combination?	
Diabetes	Metformin, SU,DPP-4 insulin, GLP-1ra, SGLT-2i		HbA1c <53, <58, <64 mmol/mol
Inflammation Triglycerides, Lp(a)	Colchicine, EPA		

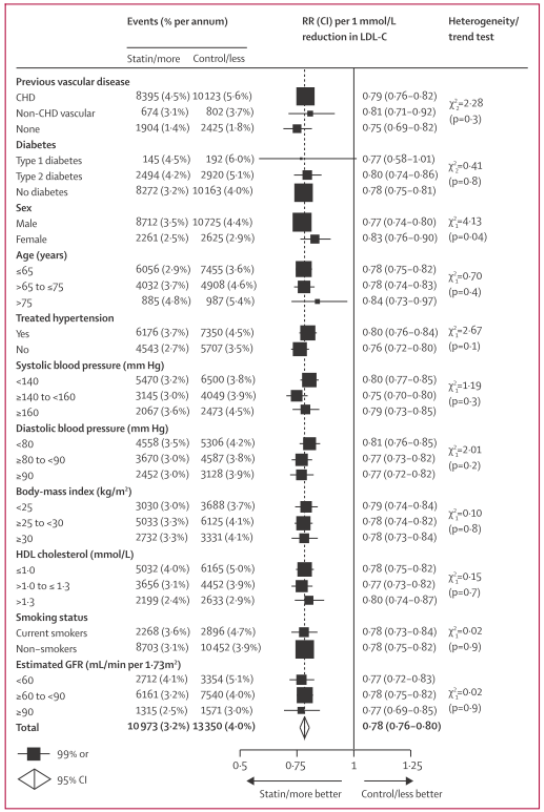
Individual Risk Reduction

Relative Risk Reduction

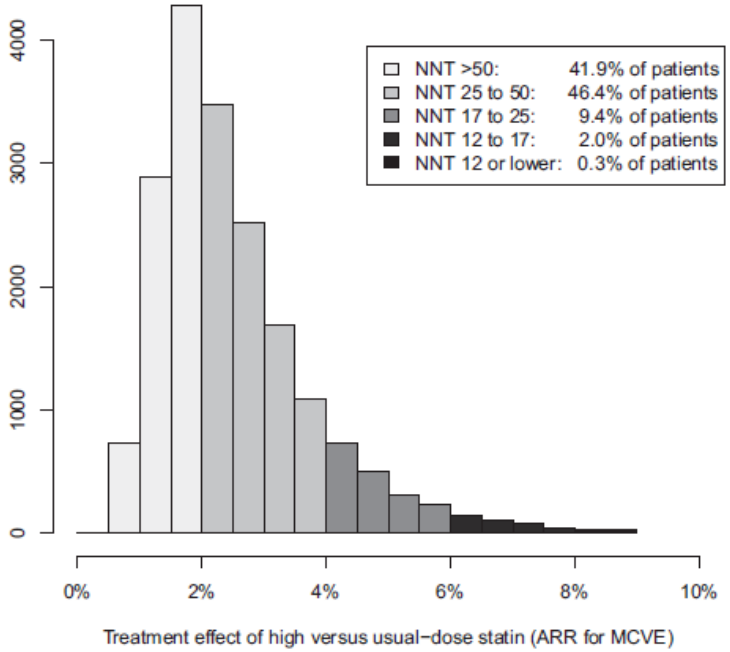


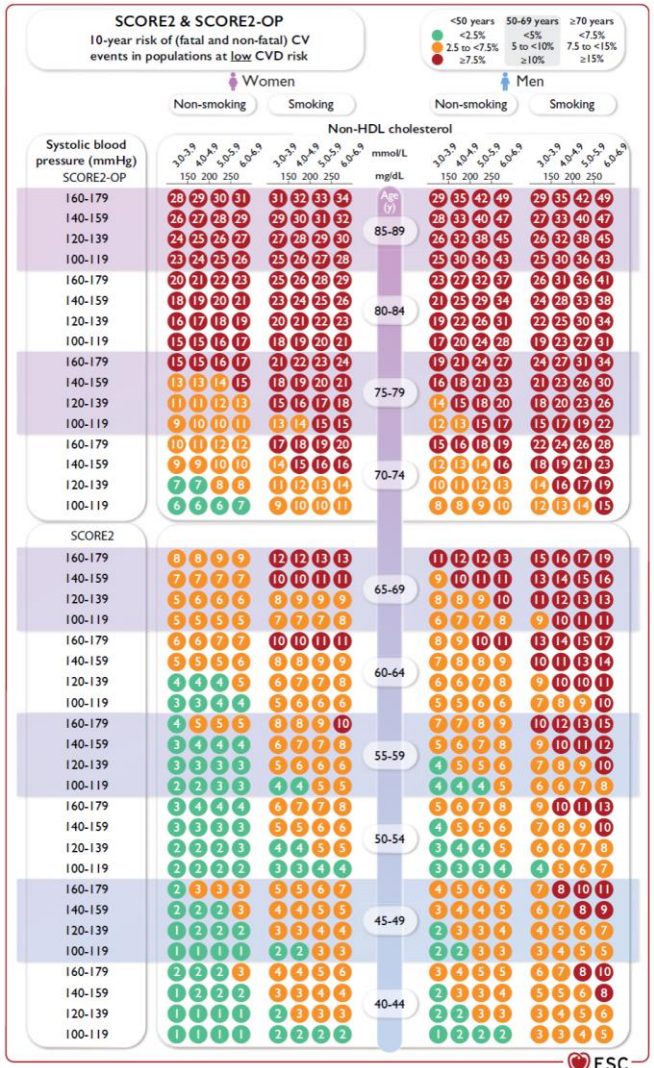
Individual Risk Reduction

Relative Risk Reduction



Absolute Risk Reduction





Individual 10-year CV risk

SCORE2																
160-179	8	8	9	9	12	12	13	13	65-69	11	12	12	13	15	16	17	19
140-159	7	7	7	7	10	10	11	11		9	10	11	11	13	14	15	16
120-139	5	6	6	6	8	9	9	9		8	8	9	10	11	12	13	13
100-119	5	5	5	5	7	7	7	8		6	7	7	8	9	10	11	11
160-179	6	6	7	7	10	10	11	11	60-64	8	9	10	11	13	14	15	17
140-159	5	5	5	6	8	8	9	9		7	8	8	9	10	11	13	14
120-139	4	4	4	5	6	7	7	8		6	6	7	8	9	10	10	11
100-119	3	3	4	4	5	6	6	6		5	5	6	6	7	8	9	10
160-179	4	5	5	5	8	8	9	10	55-59	7	7	8	9	10	12	13	15
140-159	3	4	4	4	6	7	7	8		5	6	7	8	9	10	11	12
120-139	3	3	3	3	5	6	6	6		4	5	5	6	7	8	9	10
100-119	2	2	3	3	4	4	5	5		4	4	4	5	6	6	7	8
160-179	3	4	4	4	6	7	7	8	50-54	5	6	7	8	9	10	11	13
140-159	3	3	3	3	5	5	6	6		4	5	5	6	7	8	9	10
120-139	2	2	2	3	4	4	5	5		3	4	4	5	6	6	7	8
100-119	2	2	2	2	3	3	4	4		3	3	3	4	4	5	6	7
160-179	2	3	3	3	5	5	6	7	45-49	4	5	6	6	7	8	10	11
140-159	2	2	2	3	4	4	5	5		3	4	4	5	6	7	8	9
120-139	1	2	2	2	3	3	4	4		2	3	3	4	4	5	6	7
100-119	1	1	1	1	2	2	3	3		2	2	3	3	3	4	5	5
160-179	2	2	2	3	4	4	5	6	40-44	3	4	5	5	6	7	8	10
140-159	1	2	2	2	3	3	4	4		2	3	3	4	5	5	6	8
120-139	1	1	1	1	2	3	3	3		2	2	3	3	3	4	5	6
100-119	1	1	1	1	2	2	2	2		1	2	2	2	3	3	4	5

ESC

The SMART2 risk score for vascular patients

ESC European Society of Cardiology

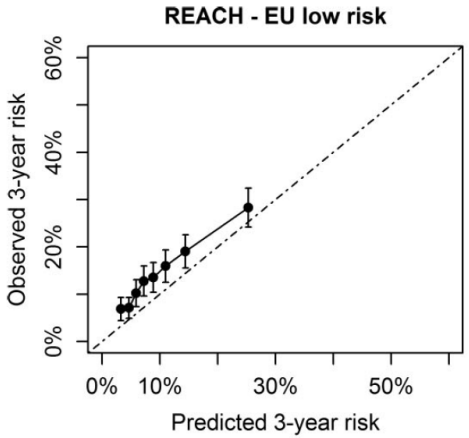
European Heart Journal (2022) **00**, 1–13
https://doi.org/10.1093/eurheartj/ehac056

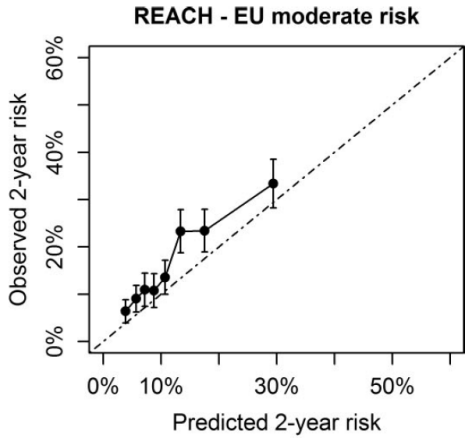
CLINICAL RESEARCH
Epidemiology and prevention

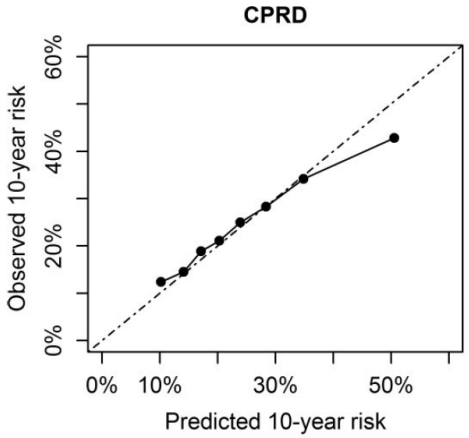
Estimation of recurrent atherosclerotic cardiovascular event risk in patients with established cardiovascular disease: the updated SMART2 algorithm

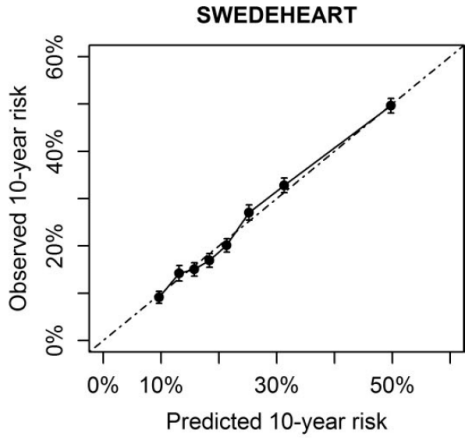
Steven H.J. Hageman [1], Ailsa J. McKay [2], Peter Ueda [3], Laura H. Gunn [2,4], Tomas Jernberg[5], Emil Hagström [6], Deepak L. Bhatt [7], Ph. Gabriel Steg[8], Kristi Läll [9], Reedik Mägi[9], Mari Nordbø Gynnild [10,11], Hanne Ellekjær[10,11], Ingvild Saltvedt [10,12], José Tuñón [13,14], Ignacio Mahíllo[15], Álvaro Aceña[13], Karol Kaminski [16], Malgorzata Chlabicz [16,17], Emilia Sawicka [16,18], Taavi Tillman [19], John W. McEvoy [20,21], Emanuele Di Angelantonio [22], Ian Graham [23], Dirk De Bacquer [24], Kausik K. Ray [2], Jannick A.N. Dorresteijn [1†], and Frank L.J. Visseren [1*†] on behalf of the UCC-SMART Study Group and the ESC Cardiovascular Risk Collaboration[‡]

Recalibrated to most global regions


REACH - EU low risk
Observed 3-year risk
0%
20%
40%
60%
0%
10%
30%
50%
Predicted 3-year risk


REACH - EU moderate risk
Observed 2-year risk
0%
20%
40%
60%
0%
10%
30%
50%
Predicted 2-year risk

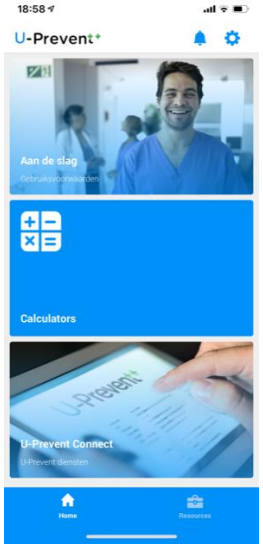

CPRD
Observed 10-year risk
0%
20%
40%
60%
0%
10%
30%
50%
Predicted 10-year risk


SWEDEHEART
Observed 10-year risk
0%
20%
40%
60%
0%
10%
30%
50%
Predicted 10-year risk

SMART2 prediction algorithm

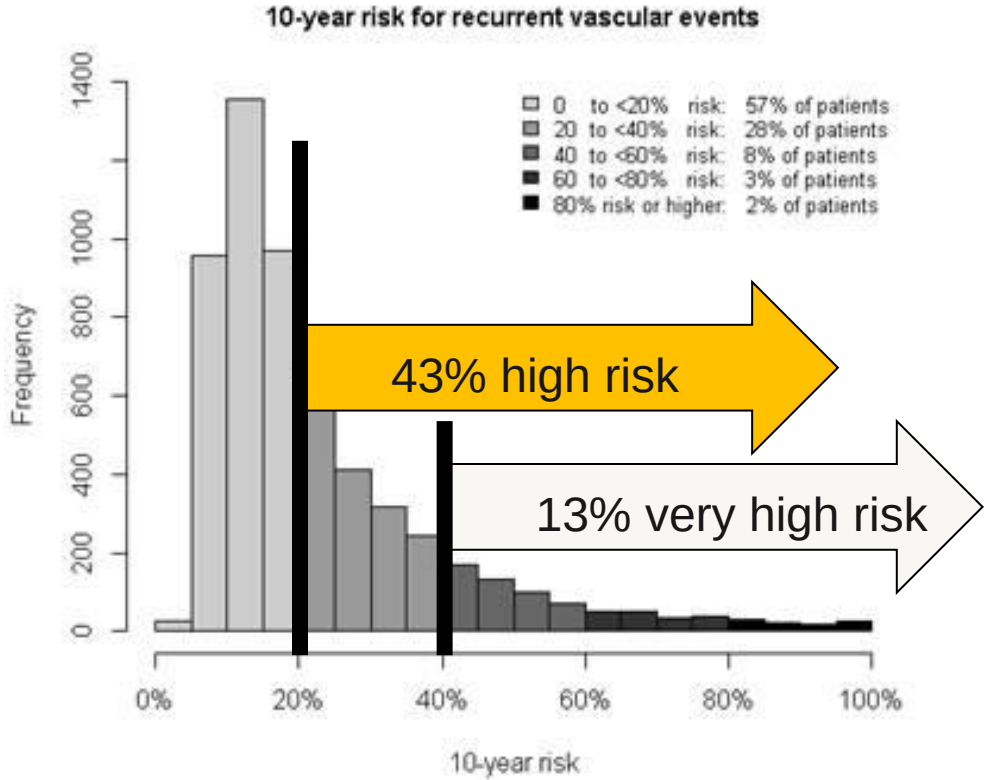
```
LP= -0.0349602236 * age +
     0.0005510715 * age^2 +
     ifelse(sex=="M", 0.2876587433, 0) +
     0.3455832714 * isSmoking +
     0.0018913154 * sbp +
     0.3181706587 * diabetesDiagnosis +
     0.2947019539 * coronaryArteryDisease +
     0.3483178604 * cerebrovascularDisease +
     0.3303566308 * aorticAneurysm +
     0.2244665798 * peripheralArteryDisease +
     0.0476995851 * yearsSinceFirstDiagnosis -
     0.0016497342 * yearsSinceFirstDiagnosis^2 +
     0.5403642493 * log(nonHdl) -
     0.0396752081 * gfr +
     0.0002186126 * gfr^2 +
     0.1517601731 * log(crp) -
     0.2107210313 * usingAnticoag

tenYearRisk <- 1 - (1-0.1658228)^exp(LP + 0.0463729 - log(ratioRegion))
```



U-Prevent
you are in control

Residual CV risk in vascular patients



Hageman et al Eur Heart J 2022;43:1715-1727
Dorresteijn et al. Heart 2013;99:866-872.

ESTIMATING LIFETIME CV RISK & LIFETIME TREATMENT BENEFIT

How to translate clinical trial results into gain in healthy life expectancy for individual patients

Jannick A N Dorresteijn,[1] Lotte Kaasenbrood,[1] Nancy R Cook,[2] Rob C M van Kruijsdijk,[1] Yolanda van der Graaf,[3] Frank L J Visseren,[1] Paul M Ridker[2]

[1]Department of Vascular Medicine, University Medical Centre Utrecht, PO Box 85500, 3508 GA Utrecht, Netherlands

[2]Harvard Medical School, Boston, MA, USA; Centre for Cardiovascular Disease Prevention, Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, MA, USA

[3]Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, Netherlands

Correspondence to: J A N Dorresteijn J.A.N.Dorresteijn2@umcutrecht.nl

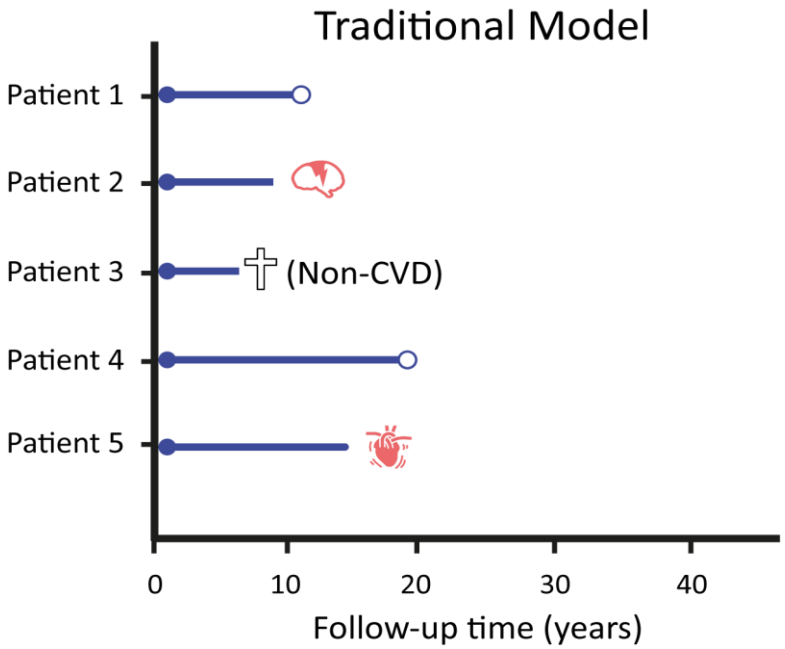
Additional material is published online only. To view please visit the journal online.

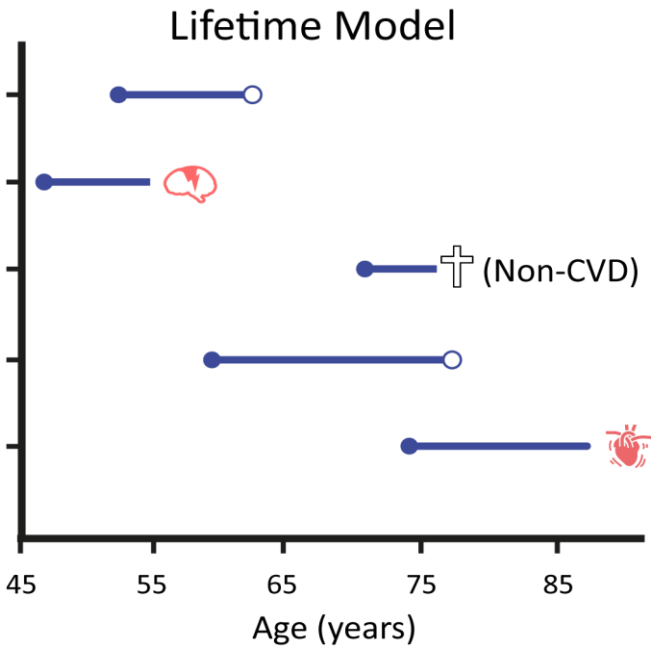
Cite this as: *BMJ* 2016;352:i1548
http://dx.doi.org/10.1136/bmj.i1548

Treatment effects from randomised trials are typically expressed as numbers needed to treat to prevent one adverse disease event during a fixed time interval (eg, five or 10 years). In the actual patient, however, many diseases are chronically progressive, despite treatment. Examples are diabetic nephropathy, some types of malignancies, osteoporosis, and atherosclerosis. In these examples, the aim of treatment is not to prevent but to delay the occurrence of symptomatic disease. Thus the actual effect of treatment is gain in disease-free life expectancy

before the end of follow-up.[5 6] Conventional statistical models can then suffice for making lifetime predictions. Usually, however, the remaining life expectancy of study participants is much longer than the follow-up duration of studies. Many participants are still healthy and alive at the end of the study. Simple extrapolation of risk predictions beyond the follow-up time of the original study is often precarious. Therefore, lifetime models compared with traditional survival models use age instead of follow-up time as the underlying timescale. A participant does not enter the study at time 0 but rather at his or her age at study entry. Similarly, the time to event or censoring is defined by the age of study exit. This is called left truncation and right censoring, respectively. Each study participant contributes data to the survival model from the age of entry until the age of censoring or disease event.[7 8] As a result, predictions of lifetime models are not limited by the follow-up time of the study but rather by the age distribution of study participants. Therefore, observations in elderly patients are essential for stable long

No extrapolation, but age as time-scale

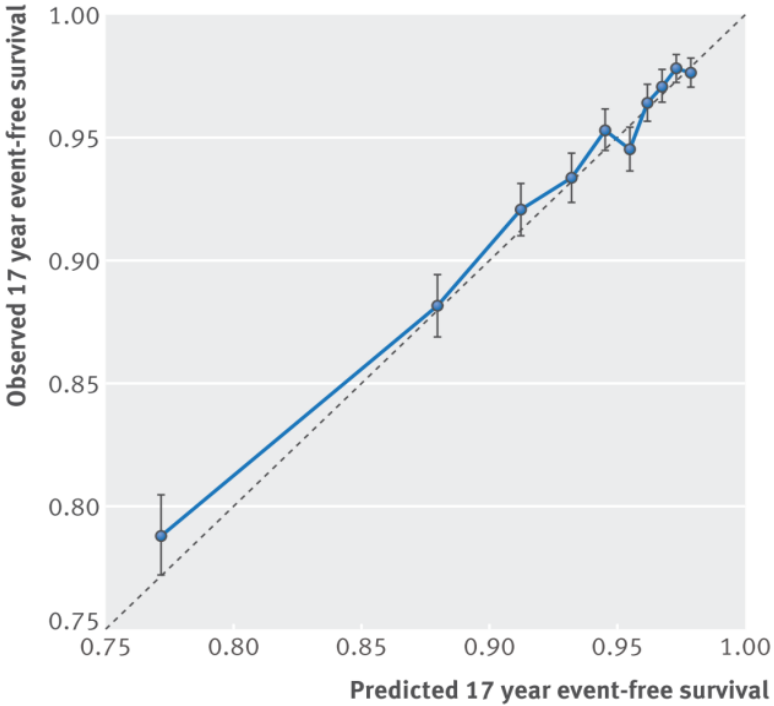




Geskus, Biometrics 2011;67:39-49

Dorresteijn ea, BMJ. 2016 Mar 30;352:i1548

Reliable predictions up to 17 year regular follow up!

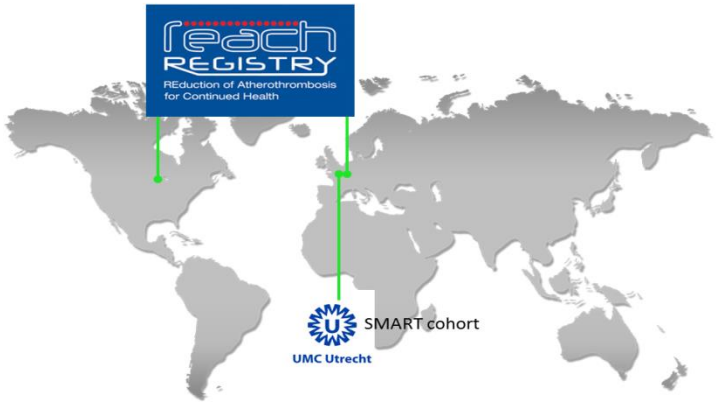


Dorresteijn ea, BMJ. 2016 Mar 30;352:i1548

Lifetimescore for vascular patients

SMART-REACH model

N = 40,388



ORIGINAL RESEARCH

American Heart Association | American Stroke Association.

Estimated Life Expectancy Without Recurrent Cardiovascular Events in Patients With Vascular Disease: The SMART-REACH Model

Lotte Kaasenbrood, MD; Deepak L. Bhatt, MD, MPH; Jannick A.N. Dorresteijn, MD, PhD; Peter W.F. Wilson, MD; Ralph B. D'Agostino Sr, PhD; Joseph M. Massaro, PhD; Yolanda van der Graaf, MD, PhD; Maarten J.M. Cramer, MD, PhD; L. Jaap Kappelle, MD, PhD; Gert J. de Borst, MD, PhD; Ph. Gabriel Steg, MD, PhD; Frank L. J. Visseren, MD, PhD

Background—In patients with vascular disease, risk models may support decision making on novel risk reducing interventions, such as proprotein convertase subtilisin/kexin type 9 inhibitors or anti-inflammatory agents. We developed and validated an innovative model to estimate life expectancy without recurrent cardiovascular events for individuals with coronary, cerebrovascular, and/or peripheral artery disease that enables estimation of preventive treatment effect in lifetime gained.

Methods and Results—Study participants originated from prospective cohort studies: the SMART (Secondary Manifestations of Arterial Disease) cohort and REACH (Reduction of Atherothrombosis for Continued Health) cohorts of 14 259 (REACH Western Europe), 19 170 (REACH North America) and 6959 (SMART, The Netherlands) patients with cardiovascular disease. The SMART-REACH model to estimate life expectancy without recurrent events was developed in REACH Western Europe as a Fine and Gray competing risk model incorporating cardiovascular risk factors. Validation was performed in REACH North America and SMART. Outcomes were (1) cardiovascular events (myocardial infarction, stroke, cardiovascular death) and (2) noncardiovascular death. Predictors were sex, smoking, diabetes mellitus, systolic blood pressure, total cholesterol, creatinine, number of cardiovascular disease locations, atrial fibrillation, and heart failure. Calibration plots showed high agreement between estimated and observed prognosis in SMART and REACH North America. C-statistics were 0.68 (95% confidence interval, 0.67–0.70) in SMART and 0.67 (95% confidence interval, 0.66–0.68) in REACH North America. Performance of the SMART-REACH model was better compared with existing risk scores and adds the possibility of estimating lifetime gained by novel therapies.

Conclusions—The externally validated SMART-REACH model could be used for estimation of anticipated improvements in life expectancy without recurrent cardiovascular events in individual patients with cardiovascular disease in Western Europe and North America. **(*J Am Heart Assoc.* 2018;7:e009217. DOI: 10.1161/JAHA.118.009217.)**

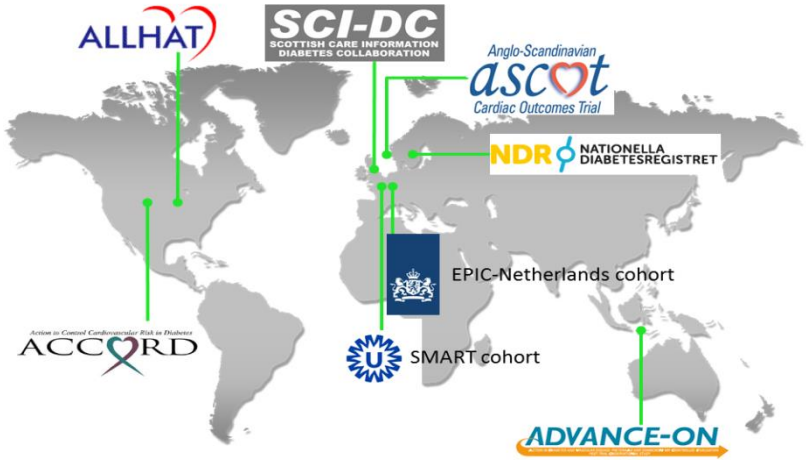
Key Words: life expectancy • prognosis • risk stratification • secondary prevention • treatment effect

Kaasenbrood e.a., JAHA 2018;7;e009217

Lifetime score for patients with DM2

DIAL2 model

N = 587,151



ESC European Society of Cardiology
European Heart Journal (2019) 0, 1–10
doi:10.1093/eurheartj/ehy839
CLINICAL RESEARCH
Prevention and epidemiology

Prediction of individual life-years gained without cardiovascular events from lipid, blood pressure, glucose, and aspirin treatment based on data of more than 500 000 patients with Type 2 diabetes mellitus

Gijs F.N. Berkelmans[1], Soffia Gudbjörnsdottir[2], Frank L.J. Visseren[1]*, Sarah H. Wild[3], Stefan Franzen[2], John Chalmers[4], Barry R. Davis[5], Neil R. Poulter[6], Annemieke M. Spijkerman[7], Mark Woodward[4,8,9], Sara L. Pressel[5], Ajay K. Gupta[6,10], Yvonne T. van der Schouw[11], Ann-Marie Svensson[2], Yolanda van der Graaf[11], Stephanie H. Read[3], Bjorn Eliasson[2], and Jannick A.N. Dorresteijn[1]

ESC European Society of Cardiology
European Journal of Preventive Cardiology (2023) 30, 61–69
https://doi.org/10.1093/eurjpc/zwac232
FULL RESEARCH PAPER
Diabetes and metabolic disorders

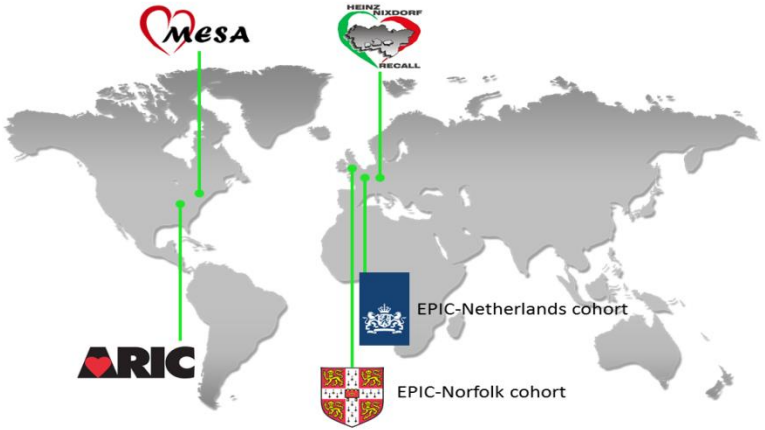
Estimating individual lifetime risk of incident cardiovascular events in adults with Type 2 diabetes: an update and geographical calibration of the DIAbetes Lifetime perspective model (DIAL2)

Helena Bleken Østergaard[1†], Steven H.J. Hageman[1†], Stephanie H. Read[2,3†], Owen Taylor[4†], Lisa Pennells[4], Stephen Kaptoge[4], Carmen Petitjean[4], Zhe Xu[4], Fanchao Shi[4], John William McEvoy[5], William Herrington[6], Frank L.J. Visseren[1], Angela Wood[4], Björn Eliasson[7†], Naveed Sattar[8†], Sarah Wild[2,3†], Emanuele Di Angelantonio[4,9†], and Jannick A.N. Dorresteijn[1*†]

Lifetime score for apparently healthy persons

LIFE-CVD model

N = 69,523



ESC European Society of Cardiology
European Heart Journal (2019) **0**, 1–10
doi:10.1093/eurheartj/ehz239

CLINICAL RESEARCH
Prevention and epidemiology

Prediction of individualized lifetime benefit from cholesterol lowering, blood pressure lowering, antithrombotic therapy, and smoking cessation in apparently healthy people

Nicole E.M. Jaspers[1], Michael J. Blaha[2], Kunihiro Matsushita[3], Yvonne T. van der Schouw[4], Nicholas J. Wareham [5], Kay-Tee Khaw[6], Marie H. Geisel[7], Nils Lehmann[7], Raimund Erbel[7], Karl-Heinz Jöckel[7] Yolanda van der Graaf[4], W.M. Monique Verschuren[4,8], Jolanda M.A. Boer[8], Vijay Nambi[9,10], Frank L.J. Visseren [1]*, and Jannick A.N. Dorresteijn[1]

Jaspers e.a., Eur Heart J 2019

European Journal of
Heart Failure

Research Article

Personalized lifetime prediction of survival and treatment benefit in patients with heart failure with reduced ejection fraction: The LIFE-HF model

Pascal M. Burger, Gianluigi Savarese, Jasper Tromp, Carly Adamson, Pardeep S. Jhund, Lina Benson, Camilla Hage, Wan Ting Tay, Scott D. Solomon, Milton Packer, Xavier Rossello, John W. McEvoy, Dirk De Bacquer, Adam Timmis, Panos Vardas, Ian M. Graham, Emanuele Di Angelantonio, Frank L.J. Visseren, John J.V. McMurray, Carolyn S.P. Lam, Lars H. Lund, Stefan Koudstaal, Jannick A.N. Dorresteijn, Arend Mosterd ✉,
in collaboration with the European Society of Cardiology's Cardiovascular Risk Collaboration (ESC CRC)
... See fewer authors

First published: 10 September 2023 | https://doi.org/10.1002/ejhf.3028

On behalf of the ASIAN-HF investigators (see online supplementary material).

Calculating lifetime treatment effect (simplified)

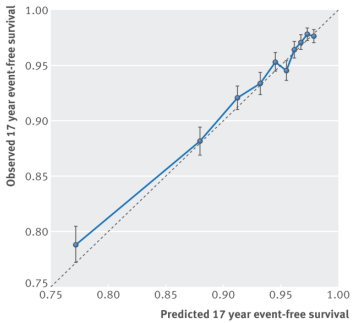
Individual lifetime risk

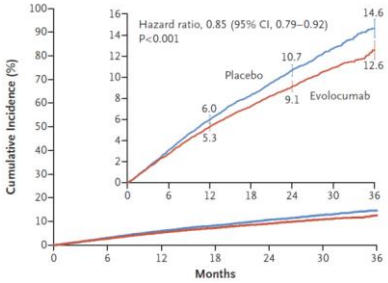
x

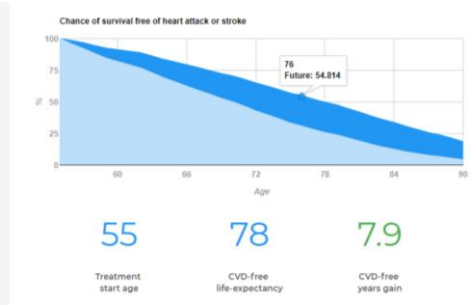
Treatment effect trial (hazard ratio)

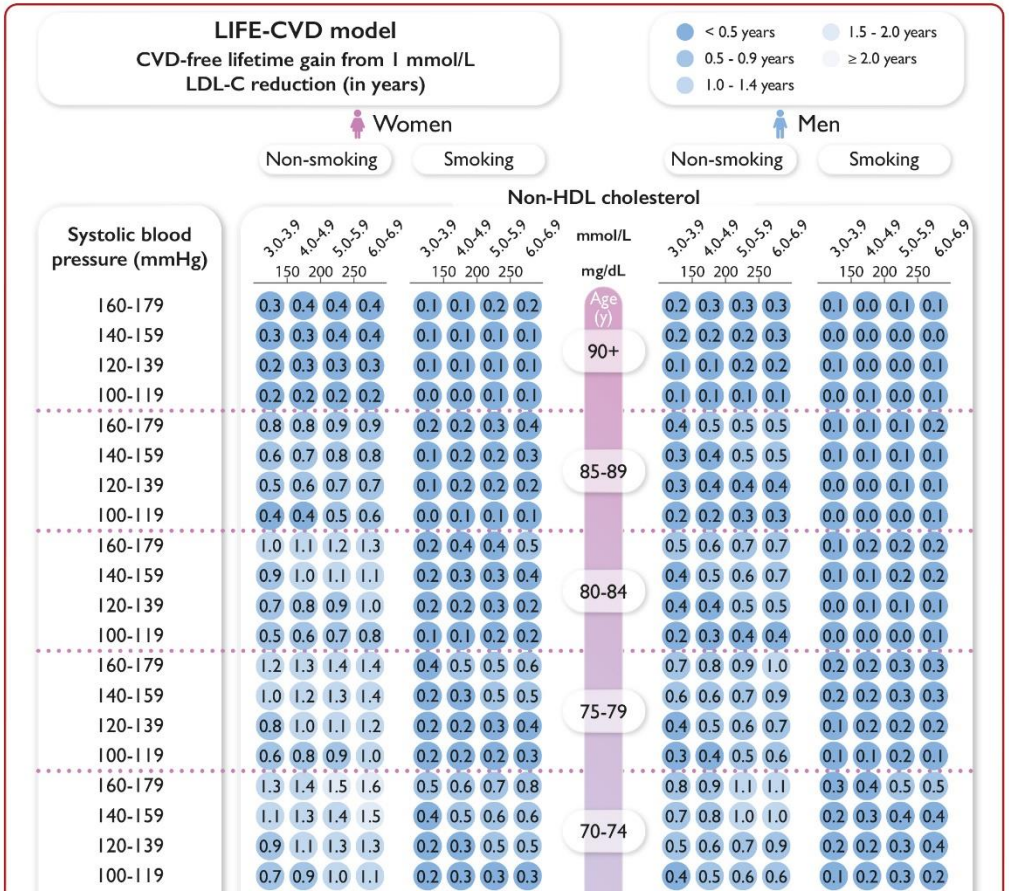
=

Individual lifetime treatment effect (gain in CVD-free life)



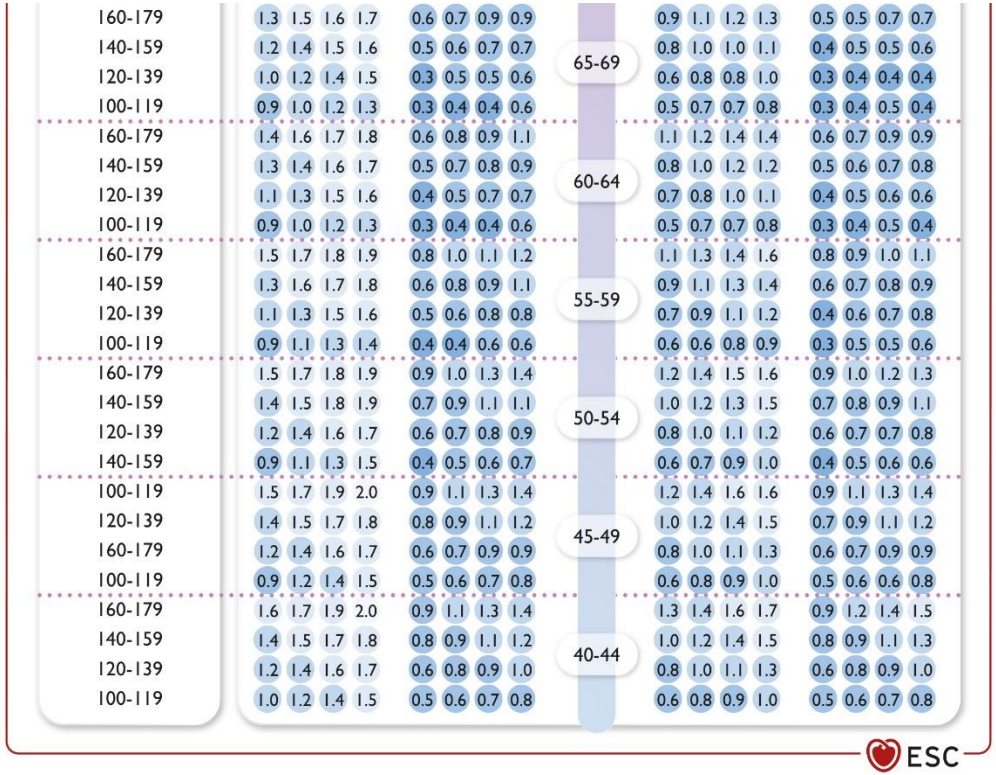






Years-free-of-cardiovascular disease gained per 1 mmol/L LDL-C reduction in apparently healthy persons (1)

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

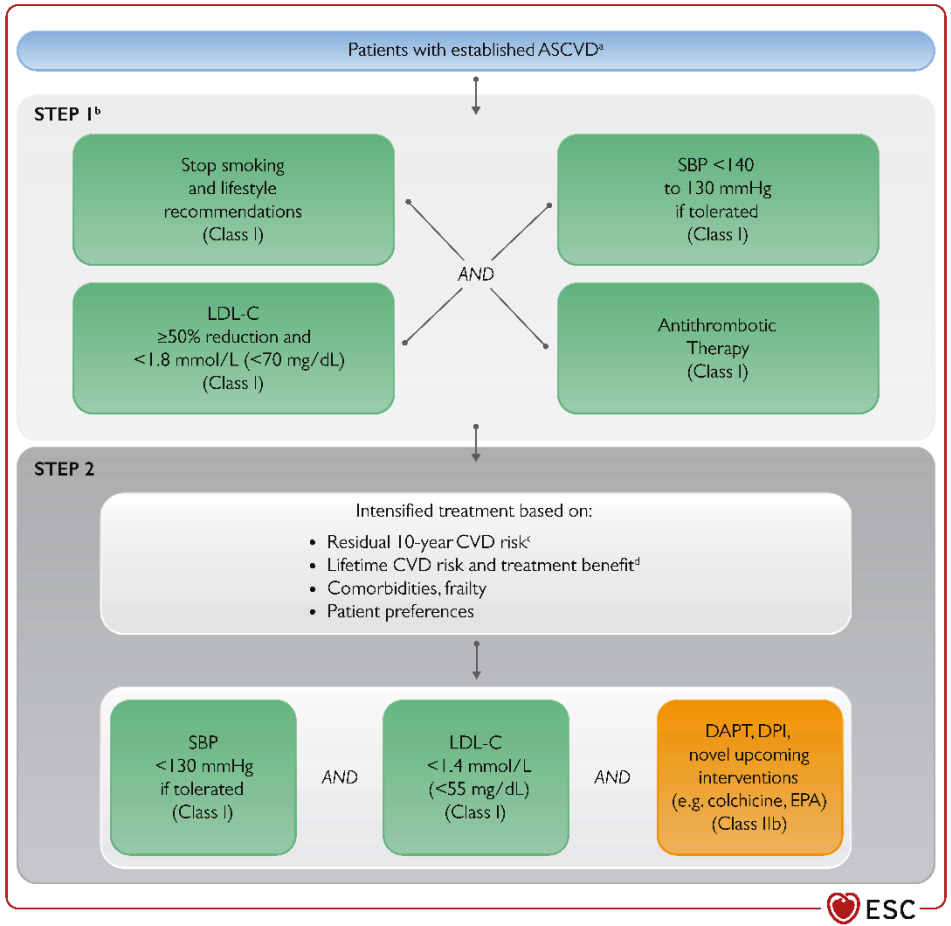


Years-free-of-cardiovascular disease gained per 1 mmol/L LDL-C reduction in apparently healthy persons (2)

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)

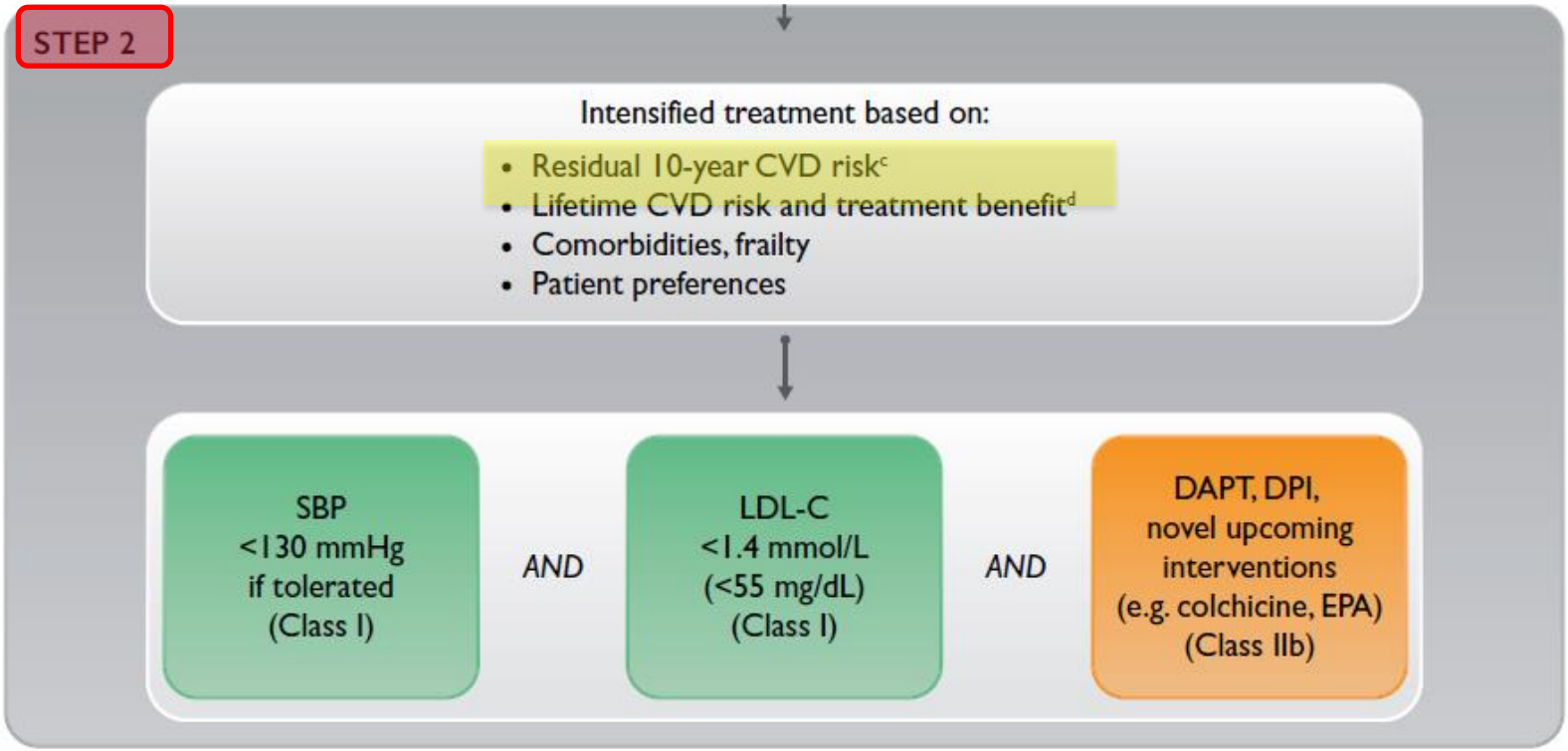
2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

ESC
European Society of Cardiology



Cardiovascular risk and risk factor treatment in patients with established cardiovascular disease

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
(European Heart Journal 2021 – doi:10.1093/eurheartj/ehab484)



2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
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European Journal of Preventive Cardiology (2023) **00**, 1–13
https://doi.org/10.1093/eurjpc/zwad221

FULL RESEARCH PAPER
Coronary artery disease

Individual lifetime benefit from low-dose colchicine in patients with chronic coronary artery disease

Pascal M. Burger [1], Jannick A.N. Dorresteijn [1†], Aernoud T.L. Fiolet[†2,3], Stefan Koudstaal [3,4], John W. Eikelboom [5], Stefan M. Nidorf [6,7], Peter L. Thompson[6,7], Jan H. Cornel [3,8], Charley A. Budgeon [9], Iris C.D. Westendorp [10], Driek P.W. Beelen[11], Fabrice M.A.C. Martens [3,12], Philippe Gabriel Steg[13], Folkert W. Asselbergs [2], Maarten J. Cramer [2], Martin Teraa [14], Deepak L. Bhatt [15‡], Frank L.J. Visseren [1‡], and Arend Mosterd [3,16*‡], for the LoDoCo2 Trial Investigators[§], UCC-SMART Study Group[§]; and REACH Registry Investigators[§]

Individual lifetime benefit from low-dose colchicine in chronic CAD

1. CVD risk prediction

ESC guideline-recommended SMART-REACH model and new lifetime model, validated in one trial (LoDoCo2) and two cohorts (UCC-SMART & REACH) (36,642 patients, 6,927 events)

Individual 10-year risk of MACE(+), and MACE(+)-free life expectancy on current therapy.

2. Treatment benefit

Combined with HRs from trials: low-dose colchicine (LoDoCo2), LDL-c and SBP reduction (meta-analyses).

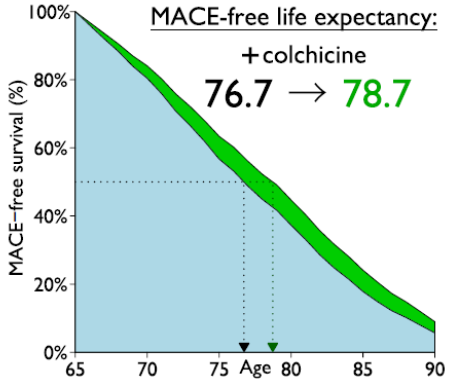
Individual 10-year ARR for MACE(+), and MACE(+)-free life-years gained, from low-dose colchicine, and intensified LDL-c and SBP reduction.

Patient example

♂, 65 years
Chronic CAD
Prior stroke
Diabetes mellitus

LDL-c 1.8 mmol/L
SBP 140 mmHg

Medication:
HI statin
2 AHT drugs
Antiplatelet

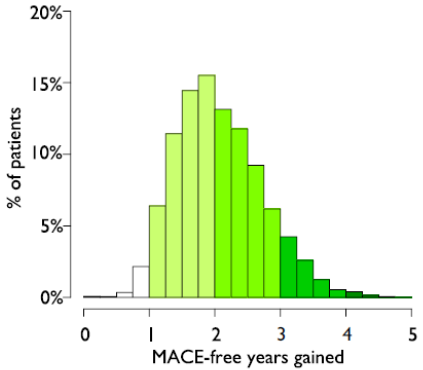


MACE-free years gained

Colchicine	2.0
LDL-c to 1.4	0.6
SBP to 130	1.3

Application to 10,830 patients from LoDoCo2 & UCC-SMART

Distribution of lifetime benefit from low-dose colchicine



Comparison with alternative ESC step 2 goals

	MACE-free years gained (median)	Most effective (% patients)
Low-dose colchicine	2.0	49%
LDL-c to 1.4	1.2	23%
SBP to 130	0.7	28%

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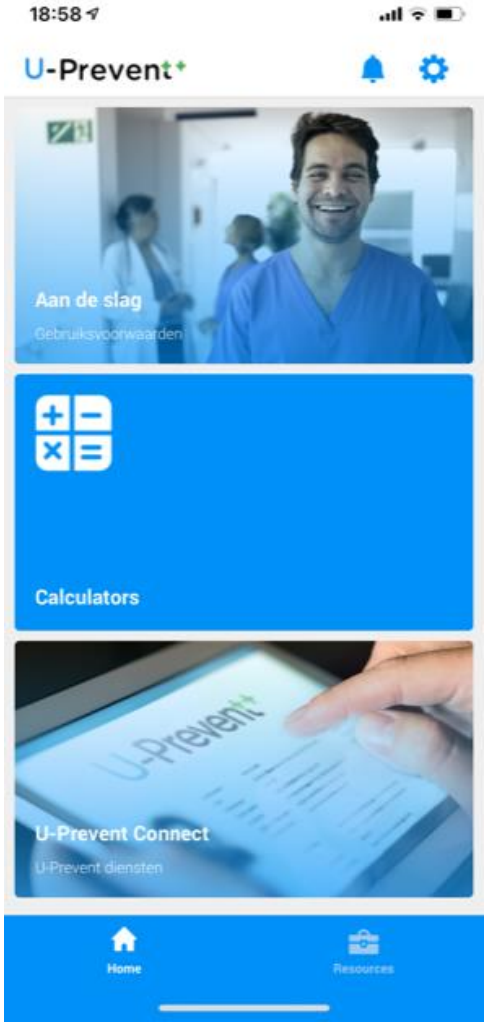
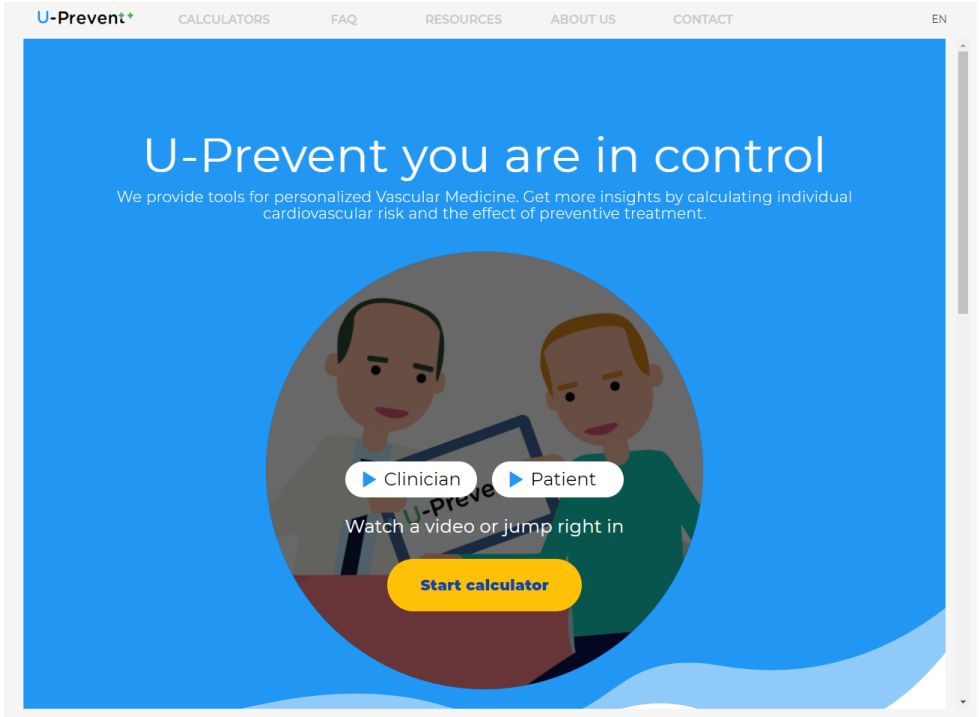
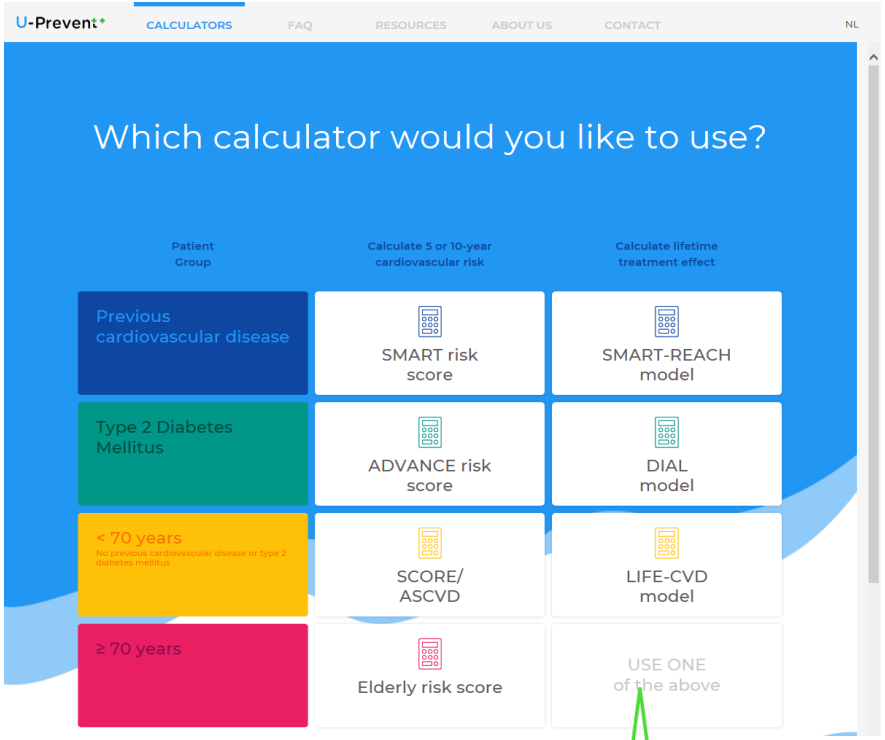


New interactive website (www.U-Prevent.nl)





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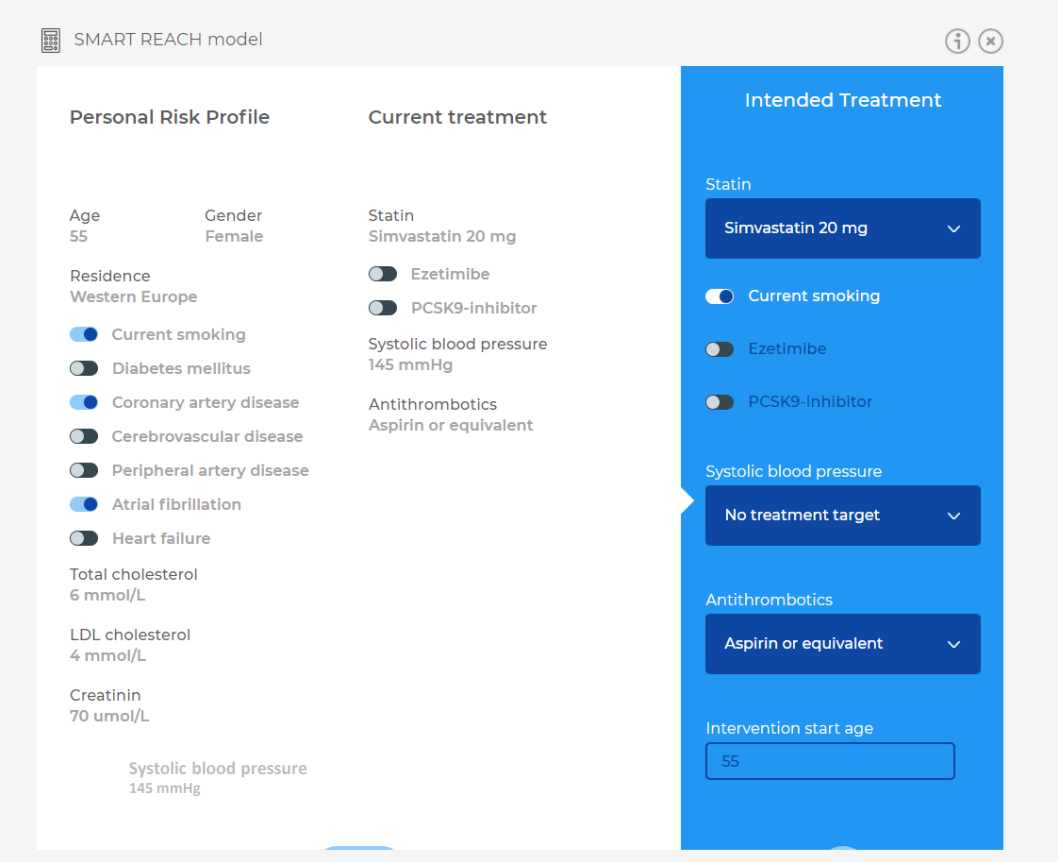
Patient example



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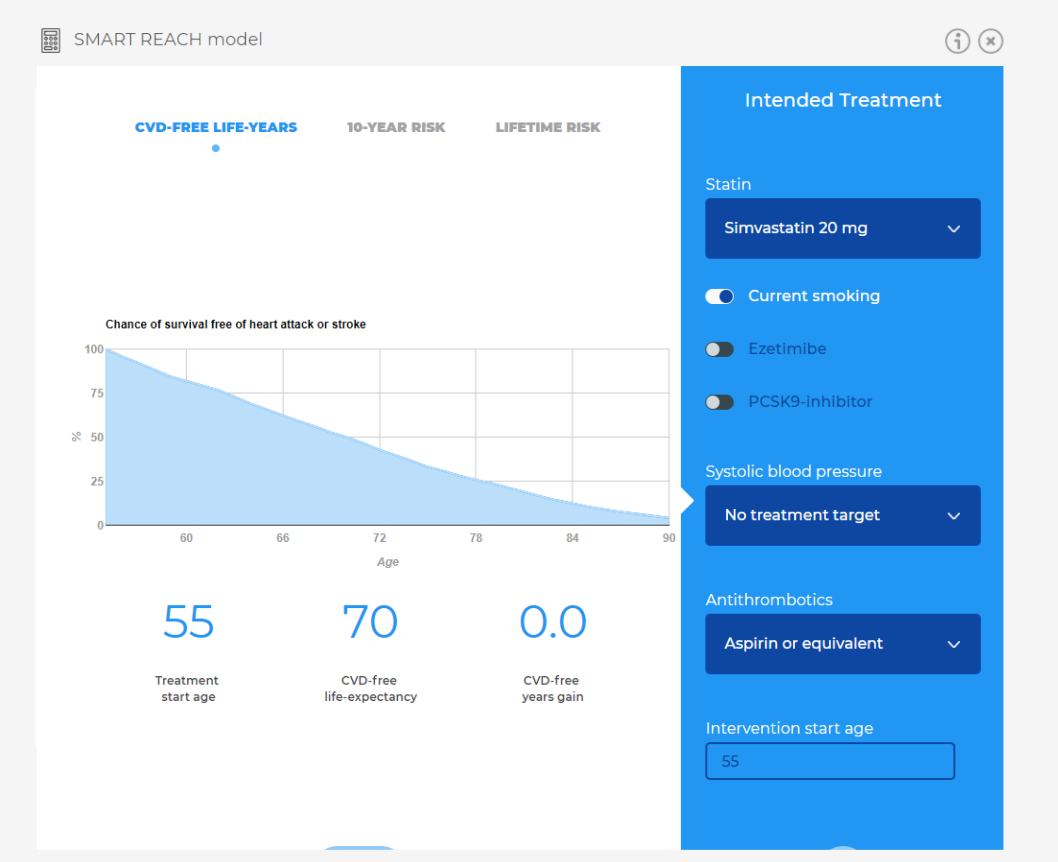
Patient example



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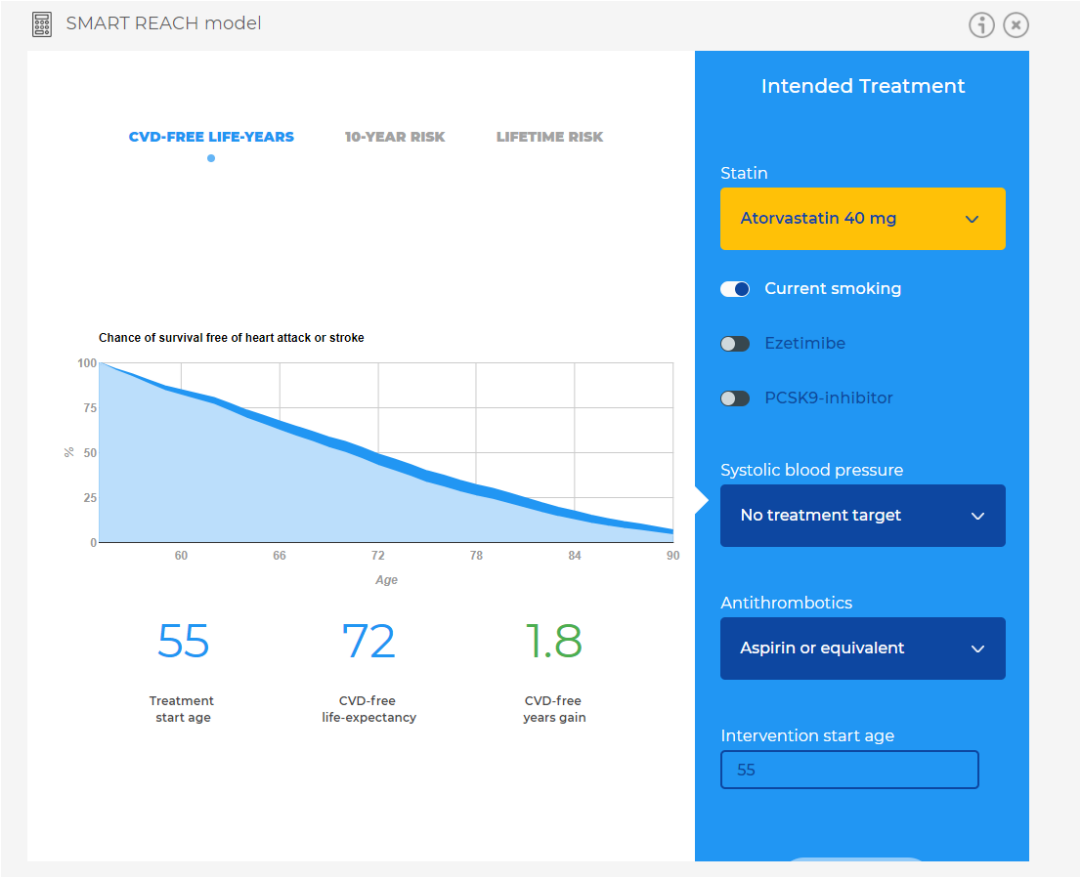
Patient example



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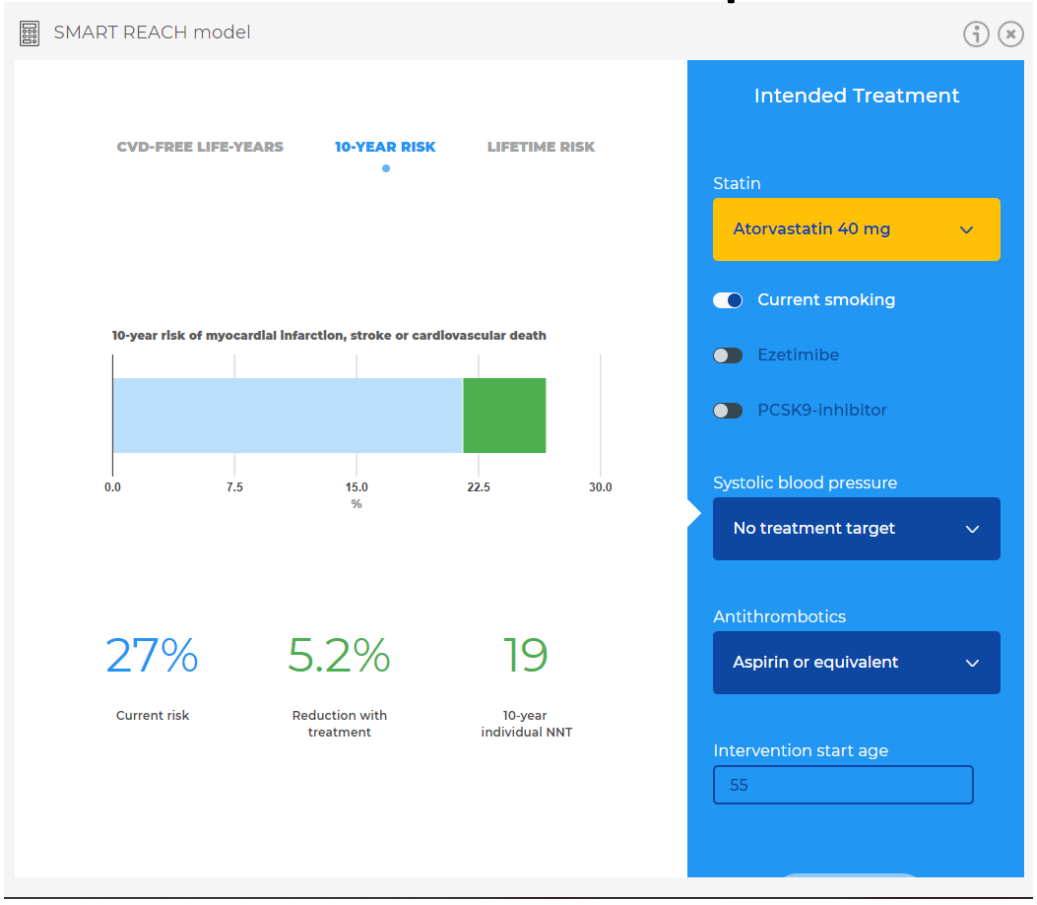
Patient example



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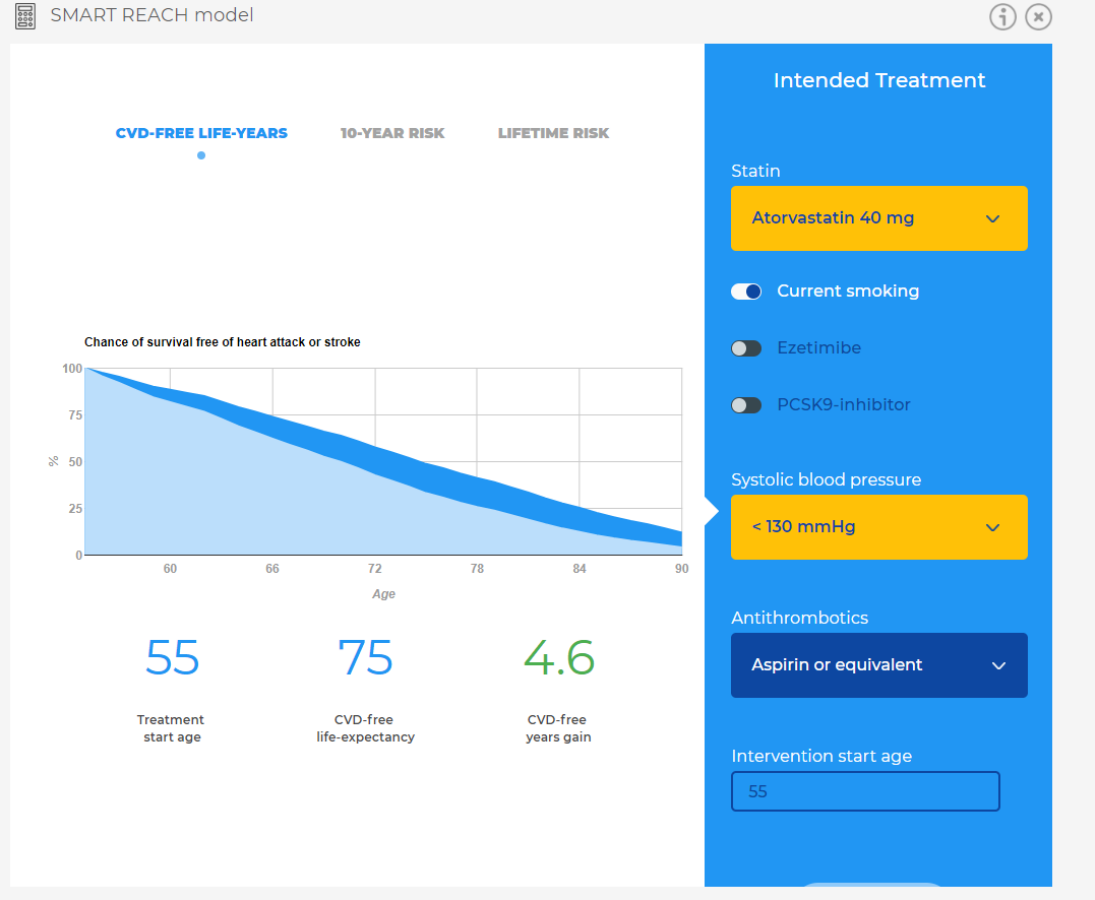
Patient example



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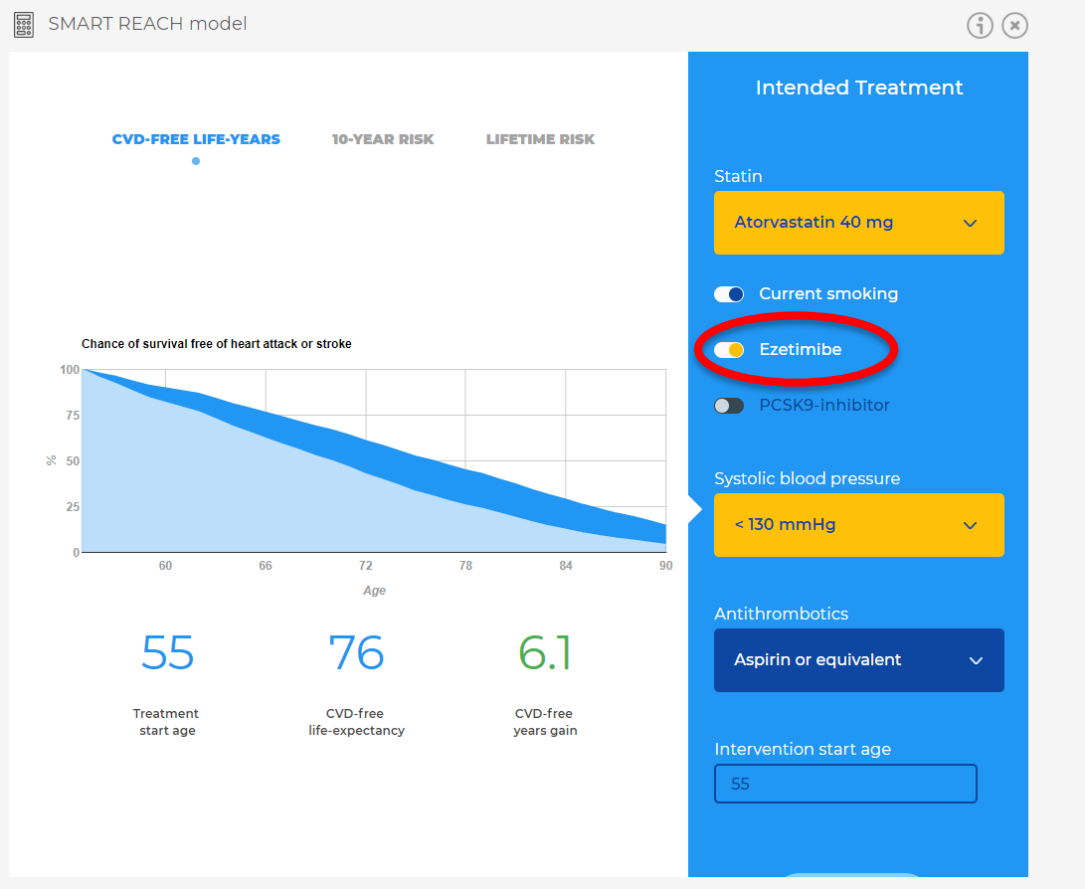
Patient example



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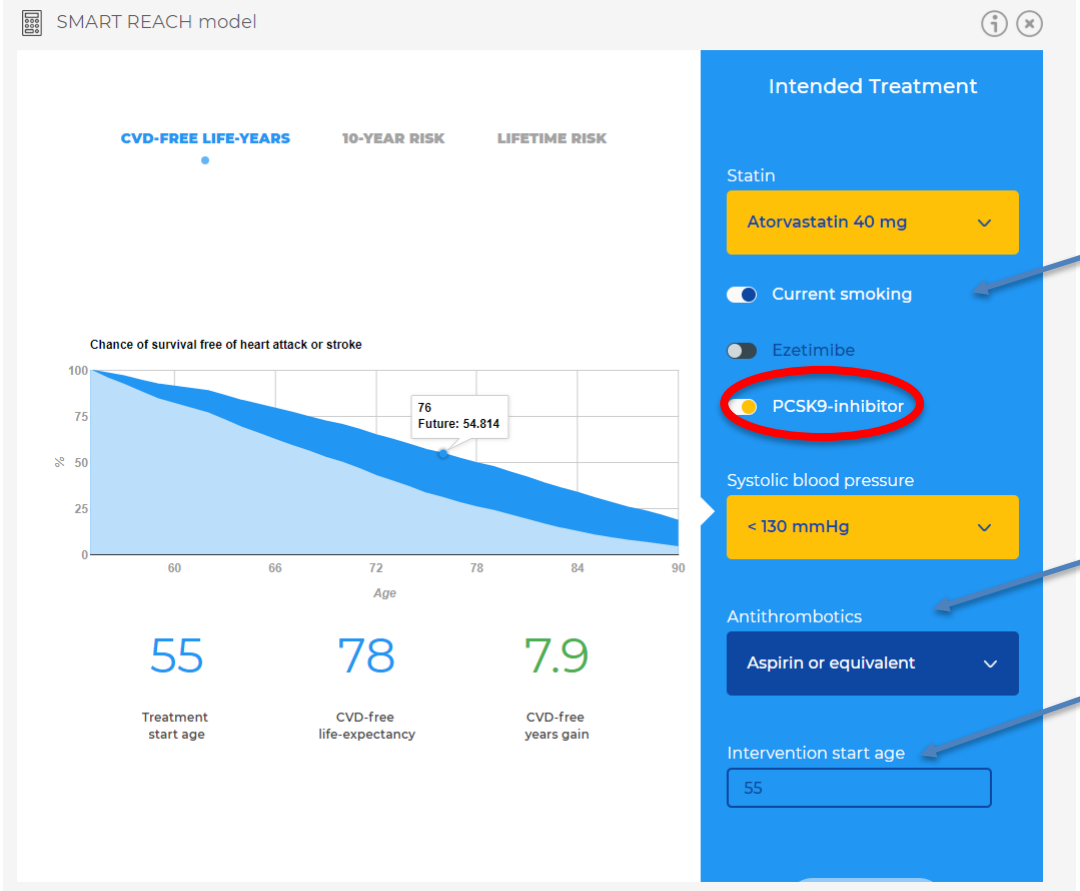
Patient example



Stop smoking

antithrombotics

Start later

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Gepersonaliseerde cardiovasculaire preventie, dat doe je samen!