

Further Development of the Programme on Preventive Health Check-Ups in Austria



Risk Scores for Cardiovascular Disease: A Systematic Review

Final report

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GmbH

Further Development of the Programme on Preventive Health Check-Ups in Austria

Risk Scores for Cardiovascular Disease:
A Systematic Review

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List of abbreviations

ACA.....	Austrian Court of Auditors
ACS	Acute coronary syndromes
AGREE II	Appraisal of Guidelines for Research and Evaluation II
AJ.....	Applicability judgement
AMSTAR	A MeaSurement Tool to Assess Systematic Reviews
ARRIBA.....	Aufgabe gemeinsam definieren, Risiko subjektiv, Risiko objektiv, Information über Präventionsmöglichkeiten, Bewertung der Präventionsmöglichkeiten und Absprache über weiteres Vorgehen (<i>engl: Define the task together, assess risk subjectively and objectively, provide information on prevention options, evaluate these options, and agree on the next step</i>)

ASCVD	Atherosclerotic cardiovascular disease
AUC	Area under the curve
BMI	Body mass Index
BP	Blood pressure
CAC.....	Coronary artery calcium
CDN	Canada
CH.....	Switzerland
CHD	Coronary heart disease
CI.....	Confidence interval
CKD	Chronic kidney disease
CPRD.....	Clinical Practice Research Datalink
CRP	C-reactive protein
CT.....	Computer tomography
CV.....	Cardiovascular
CVD	Cardiovascular disease
CVRM	Cardiovascular, renal, and metabolism
DDPOS	Diabetes Prevention Program Outcomes Study
DEGAM.....	Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin
DIAL2	DIABetes Lifetime-perspective prediction (version 2)
E	Spain
ERS-RA.....	Expanded Risk Score in Rheumatoid Arthritis
ESC	European Society of Cardiology
FH	Familial hypercholesterolemia
FRS	Framingham Risk Score
FRS ATP-III....	Framingham Risk Score Adult Treatment Panel III
Gamma-GT.....	Gamma-glutamyl transferase
GCP.....	Good Clinical Practice
GIN	Guidelines International Network
GR	Greece
HbA1c	Hemoglobin A1c
HDL	High-Density-Lipoprotein
HF	Heart failure
HIV.....	Human immunodeficiency virus
HKE	Herz-Kreislauf-Erkrankung
H-L	Hosmer-Lemeshow
IT	Italy
IQWiG.....	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
LDL.....	Low-Density-Lipoprotein
LP(a)	Lipoprotein(a)
MEX.....	Mexico
MI.....	Myocardial infarctions
N.....	Norway
N.A	not available
NB	Net Benefit

NCD	Non-communicable disease
NDR.....	National Diabetes Register
NHG.....	Nederlands Huisartsen Genootschap (<i>engl.: Dutch College of General Practitioners</i>)
NICE.....	National Institute for Health and Care Excellence
NL	Netherlands
NRI.....	Net reclassification Index
O:E	Observed to expected events
PAD.....	Peripheral arterial disease
PCE	Pooled Cohort Equations
PGS	polygenic risk scores
PMCU	preventive medical check-up
PVD.....	peripheral vascular disease (
PICO	Population Intervention Comparison Outcome
ROBAST	Prediction model Risk of Bias Assessment Tool)
PROCAM.....	Prospective Cardiovascular Münster Study
PS	Primary study
RA.....	Rheumatoid arthritis
RCT.....	Randomised controlled trials
RJ.....	Risk of Bias Judgement
RoB.....	Risk of Bias
ROBIS	Risk of Bias in Systematic Reviews
RPM	Risk prediction models
RQ	Research question
S	Sweden
SCID	Scottish Care Information – Diabetes
SCORE2.....	Systematic Coronary Risk Evaluation 2
SCORE2-OP	Systematic Coronary Risk Evaluation 2 – Older Persons
SHHEC	Scottish Heart Health Extended Cohort
SHIP.....	Study of Health in Pomerania
SIGN	Scottish Intercollegiate Guidelines Network
SMART	Second Manifestations of ARTerial disease
SR.....	Systematic review
TIA	Transient ischemic attack
TRA.....	Total risk assessment
T1DM.....	Type 1 diabetes
T2DM.....	Type 2 diabetes
UA	Unstable angina
UK.....	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study
USA.....	United States of America
VS	Validation study
VU	Vorsorgeuntersuchung
WHO	World Health Organization
ZA.....	South Africa

Inhaltliche Weiterentwicklung der österreichischen Vorsorgeuntersuchung

SCORES ZUR PROGNOSE VON HERZ-KREISLAUF-ERKRANKUNGEN



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Forschungsfragen



- FF1:** Wie vergleichen sich kardiovaskuläre Risikoprognosemodelle (z. B. ARRIBA, SCORE2, SCORE2-OP und SCORE2-Diabetes) und wie unterscheiden sie sich hinsichtlich ihrer Evidenz, Vorhersagevalidität, der Nutzen-Schaden Bilanz und ihrer Implementierbarkeit im Rahmen österreichischer Vorsorgeuntersuchungen?
- FF2:** Inwiefern führt die Anwendung kardiovaskulärer Risikoprognosemodelle zu einem langfristigen gesundheitlichen Nutzen, sowie zu Veränderungen im Gesundheitsverhalten der Patient:innen?
- FF3:** Welche Parameter werden bereits standardmäßig in Vorsorgeuntersuchungen erhoben, welche zusätzlichen Untersuchungen sind für eine optimale Implementierung der Risikoscores erforderlich, und welche organisatorischen, zeitlichen und personellen Ressourcen werden hierfür benötigt?

Hintergrund



- HKE: weltweit häufige nicht übertragbare Krankheiten und Todesursache
- Jährliche HKE-Kosten EU: ca. 282 Mrd. €
- Risikofaktoren umfassen u.a. modifizierbare (z. B. Blutdruck, Cholesterin) & nicht modifizierbare (z. B. Alter, Geschlecht) Faktoren
- Internationale Präventionsprogramme (z.B. Ö VU): Frühzeitige Erkennung und Minimierung von HKE-Risikofaktoren
- Kardiovaskuläre Risikoscores: mathematische Modelle für 5-10- Jahres-Ereigniswahrscheinlichkeit
- Ziel: Frühzeitige individuelle Prävention (Lebensstil, Medikation)
- In Ö bisher teilweise eingesetzt: ARRIBA – Tool

Methodik



Limitationen

- Evidenzqualität überwiegend niedrig bis moderat
- Keine SR berichten über Implementierungsaspekte
- Keine RCTs zu langfristigem Nutzen
- Einschränkungen durch SR-Fokus - eingeschränkte Information zu patient:innenrelevanten Outcomes
- Keine Evidenz zu national relevanten Scores (PROCAM, ARRIBA)

Ergebnisse

SR & VS

Statistische Performance von Scores

- Leistungsfähigkeit der Scores variiert stark je nach Population, Modell und Zielgruppe
- Keine perfekte Vorhersagbarkeit: FRS, SCORE, QRISK, PCE haben moderate Diskriminierung mit jeweiligen Stärken/Schwächen in Subgruppen
- Die meisten Scores tendieren zur Über- oder Unterschätzung von Risiken
- Bessere Diskriminierung bei Frauen > Männer
- Spezifische Krankheitspopulationen: Schlechtere Performance bei Diabetes, Rheumatoide Arthritis, chronischen Erkrankungen

Implementierbarkeit

- Technisch: Benötigung spezieller Software mit regionalen Anpassungen
- Personell: Schulung des medizinischen Personals erforderlich
- Organisatorisch: Verschiedene Scores für unterschiedliche Patientenpopulationen nötig
- Regelmäßige Neubewertung aufgrund von Populationsunterschieden notwendig
- Relevante Parameter für die meisten Scores bereits in VU erhoben
- Klare leitlinienbasierte Standards für Nachsorge nötig

Leitlinienempfehlungen (5 Leitlinien)

- Risikobewertung: Gesamteuropäische Leitlinie ESC und nationale Leitlinien empfehlen regelmäßige kardiovaskuläre Risikoabschätzung bei Erwachsenen
- Modelle: ESC nutzt SCORE2 (<70 J.) und SCORE2-OP (≥70 J.); national z. B. ARRIBA, QRISK3, ASSIGN, SCORE2-basiert
- Diabetes: Bei Typ 2 teils allgemeine, teils spezifische Modelle; Typ 1 meist ausgeschlossen
- Primäre Interventionsstrategie: Lebensstilmodifikationen, medikamentöse Therapie bei Risikoschwellen von 10-20%
- Ausschluss von Hochrisikopatient:innen mit manifesten Erkrankungen, Niereninsuffizienz oder genetischen Lipidstörungen
- Alle Leitlinien betonen individuelle Beratung und gemeinsame Entscheidungsfindung mit unterschiedlichen Alters- und Score-Ansätze

Diskussion

- Potenzielle Über- oder Unterbehandlung bestimmter Patient:innengruppen
- Evidenz beschränkt auf Surrogatendpunkte statt Morbidität und Mortalität
- Ethische Aspekte: Informierte Zustimmung nötig, Patient:innenakzeptanz variabel, Equity-Bedenken bei diversen Populationen
- Keine Nachweise für verbesserte Langzeit-Gesundheitsergebnisse
- Risikoscores können interaktiv zeigen, wie sich Risiken durch Lebensstil und medikamentöse Interventionen verändern können
- Notwendigkeit individueller Risikobewertung
- Kontinuierliche Modellverbesserungen erforderlich
- Begrenzte Übertragbarkeit auf nicht getestete Bevölkerungsgruppen
- Kein Score in Ö validiert

Conclusio



Keine Nachweise und Langzeitstudien für verbesserte Gesundheitsergebnisse



Insgesamt unzureichende Evidenz um einen Score klar zu empfehlen oder abzulehnen



Fehlende Validierung in österreichischen Populationen



Multidisziplinärer Implementierungsprozess erforderlich



Potenzielle Scores für Österreich: SCORE2 mit europäischer Kalibrierung und ARRIBA als alternative Option



Vor Implementierung Pilotierung mit umfassender Evaluierung empfohlen

Abkürzungen: EU: Europäische Union; FRS: Framingham Risk Score; HKE: Herz-Kreislauf-Erkrankungen; PCE: Pooled Cohort Equations; SCORE: Systemic Coronary Risk Estimation; SR: Systematisches Review VS: Validierungs Studie; VU: Vorsorgeuntersuchung; Ö: Österreich

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Summary

Background

Cardiovascular diseases (CVDs) are among the most common non-communicable diseases and remain a leading cause of death globally. Within the European Union, their annual economic burden is estimated at approximately €282 billion, reflecting not only the high prevalence but also the long-term societal and healthcare impact of these conditions. The development of CVD is driven by a combination of modifiable risk factors – such as elevated blood pressure, dyslipidaemia, smoking, and unhealthy lifestyle habits – and non-modifiable determinants, including age, sex, and genetic predisposition.

To address these challenges, international prevention programmes, including the Austrian preventive medical check-up, have been established to detect cardiovascular risk factors early and reduce their impact through timely intervention. A key component of such preventive strategies is the use of cardiovascular risk scores – mathematical models that estimate the likelihood of a cardiovascular event occurring within a 5- to 10-year period. These tools support clinicians in stratifying patients according to their individual risk and in recommending targeted preventive measures, ranging from lifestyle modification and behavioural counselling to pharmacological therapy, before disease onset. In Austria, the ARRIBA tool currently serves as the standard instrument for cardiovascular risk assessment. It has been adapted to the Central European population and is already widely used by general practitioners, although it has not been officially recommended for use during preventive medical check-ups (PMCU).

CVD as a leading cause of death worldwide

high economic burden in the EU

various risk factors

targeted prevention through risk stratification

scores as an individual risk prediction tool

ARRIBA as the current standard instrument in Austria

Research question and project aim

The umbrella organisation of Austrian social insurance institutions is considering introducing a cardiovascular (CV) risk assessment as part of the national preventive medical check-up. Various models are used internationally for CV risk prediction, including FRS, SCORE2, QRISK3, PROCAM, PCE, ARRIBA, and UKPDS.

This project systematically reviewed and compared the most relevant risk prediction models applicable to Western Europe, focusing on SCORE2, SCORE2-OP, SCORE2-Diabetes, ARRIBA, and PROCAM, to evaluate their predictive performance, potential benefits and harms, and feasibility for implementation within the Austrian PMCU.

RQ1: How do CV risk prediction models compare, and how do they differ in terms of their evidence, predictive validity, benefit-harm balance and their implementability within the framework of Austrian PMCU?

RQ2: To what extent does the application of CV risk prediction models lead to long-term health benefits, as well as to changes in the health behaviour of patients?

RQ3: Which parameters are already standardly collected in preventive health check-ups, which additional examinations are required for an optimal implementation of the risk scores, and which organisational, time and personnel resources are needed for this?

aim: assessment of benefits, risks and feasibility

research questions

Methods

This report followed a structured, pre-registered methodology, combining evidence from systematic reviews (SRs), one validation study (VS), and relevant clinical guidelines. A comprehensive literature search for publications from 2015-2025 was conducted across Medline, Embase, and the Cochrane Library, focusing on SRs and validation studies of CV risk scores in Western European populations. A total of seven SRs, one VS and five guidelines (identified through manual search) were identified for the report. Study selection, data extraction, and quality assessment were performed independently by multiple reviewers using ROBIS, PROBAST, and AGREE-II tools. Results were synthesised narratively, with a focus on predictive validity, feasibility, and implementation aspects of cardiovascular risk models within the context of the Austrian preventive medical check-up (PMCU).

Results

The included data revealed a complex picture of predictive accuracy in different patient populations. In the general population, scores such as the Framingham Risk Score and the Pooled Cohort Equations show moderate discriminatory power, with results often varying depending on the population and risks sometimes being over- or underestimated. In patients with rheumatoid arthritis, scores such as Framingham and SCORE tend to underestimate risk, highlighting the need for specific adjustments systematically. In the field of diabetes, the results vary depending on the type of diabetes. For type 1 diabetes, UKPDS and FRS show limited calibration, whereas for type 2 diabetes, the RECODE score provides promising moderate to good discrimination results. Despite these differentiated findings, the overall evidence for clinical benefit remains limited, and researchers repeatedly emphasise the need for further validation studies to improve the implementation of risk scores in various medical contexts. Regarding implementation in a PMCU context, the evidence highlighted several practical challenges. Different risk scores may be required depending on the population group of the PMCU participant, adding complexity to implementation. Although all necessary clinical parameters are already collected within the PMCU, additional implementation challenges remain, including the need for specialised software with regional calibration, training requirements for healthcare professionals, and organisational differences between health systems. Regular recalibration of models was deemed necessary to maintain accuracy due to population-level differences.

European guidelines consistently recommend risk assessment in apparently healthy adults as part of cardiovascular health management, though this does not imply a population wide screening approach and recommendations differ in tools, age thresholds, and reassessment intervals. The ESC endorses SCORE2 (<70 years) and SCORE2-OP (≥70 years) with regional calibration. In national guidelines, ARRIBA (Germany), QRISK3 (UK), ASSIGN (Scotland), and SCORE2-based models (Netherlands) are preferred.

Some guidelines apply general scores to patients with type 2 diabetes, while others recommend diabetes-specific models. Patients with type 1 diabetes, established cardiovascular disease, significant kidney impairment, familial or severe hyperlipidaemia, very high blood pressure, or other conditions conferring high baseline risk are typically excluded from standard risk assessment.

Treatment thresholds differ yet all guidelines emphasise individualised counselling and shared decision-making.

systematic search for systematic reviews (SR) and evidence-based guidelines; hand search; quality assessment using ROBIS, PROBAST and AGREE-II

SRs: heterogeneous prediction accuracy between populations

moderate discrimination in the general population

underestimation of risk in cases of specific pre-existing conditions

limited clinical benefit demonstrated to date

various implementation requirements are needed

guidelines: recommend CV risk assessment; differ in tools, age thresholds & intervals.

patients with pre-existing CVD or other specific conditions are excluded from standard risk assessment

different scores have different thresholds

Discussion

The evidence synthesis revealed no clear proof that the use of cardiovascular risk scores leads to improved long-term health outcomes. Several reviews highlighted the potential for both over- and undertreatment in specific patient groups, and the limited generalisability of most models to populations beyond the validation cohorts. None of the included systematic reviews provided detailed insights into practical implementation aspects. The available evidence was largely confined to surrogate endpoints – such as changes in risk factors – rather than hard outcomes like morbidity or mortality. Nonetheless, risk scores can serve as valuable interactive tools to illustrate how lifestyle modifications or pharmacological interventions may influence cardiovascular risk. The findings underline the need for personalised risk assessment, continuous model refinement, and regular recalibration, resulting in substantial practical implementation challenges in the PMCU context. All reviewed guidelines consistently recommend cardiovascular risk assessment for healthy adults, though age ranges and preferred scoring models differ between recommendations.

**no clear evidence
of long-term benefit**

**risk of over- or
undertreatment**

**surrogate endpoints rather
than hard outcomes**

**personalised assessment
and regular recalibration**

Conclusion

There is currently no evidence from long-term studies demonstrating improved health outcomes, and overall, the available data are insufficient to clearly recommend or reject the use of a specific risk score. Furthermore, none of the existing scores has been validated in Austrian populations. Implementing any risk score would require a multidisciplinary approach, sufficient training and defined care pathways following risk assessment. Based on our results, SCORE2 with European calibration appears most suitable for Austria, with ARriba as an alternative. Additional evaluation and further evidence are needed to support widespread adoption.

**no validation in
Austrian populations**

**implementation requires
multidisciplinary approach**

**further evaluation needed
before adoption**

1 Introduction/Background

1.1 Medical check-ups

The preventive medical check-up program was introduced in Austria in 1974 [1]. In the national context, preventive medical check-ups (PMCU) aim to avoid health risk factors (primary prevention) and detect diseases early (secondary prevention). Particular emphasis is placed on cardiovascular diseases (CVD) and cancer, which are among the most common causes of death in Austria [2]. To sustainably improve the health of the population, the program targets all individuals aged 18 and over whose primary residence is in Austria [2, 3]. The program is mainly carried out by general practitioners and specialists in internal medicine and is offered once a year, free of charge. In a two-step process, medical examinations are performed, and laboratory parameters are collected, followed by a consultation to review and discuss the results. The basis of the annual health check consists of the following for all age groups and genders [4]:

Table 1-1: PMCU categories

Component	Purpose/Details
Medical history	record family history, medications, lifestyle habits, risk factors
Blood & Urine Tests	Blood: sugar, cholesterol, triglycerides, gamma-GT, haemoglobin Urine: leucocytes, protein, glucose, nitrites, urobilinogen, blood
Physical Examination	comprehensive physical assessment of the skin, neck (including the thyroid gland), heart, lymph nodes, lungs, abdomen, joints, spine, and blood circulation, as well as measurements of blood pressure and BMI
Periodontal Examination	
Discussion of findings and counselling	Review findings and provide advice on health and prevention strategies at a follow-up appointment, which is scheduled after completion of the initial health check-ups

Abbreviation: BMI ... Body-Mass-Index; gamma-GT ... gamma-glutamyl transferase

Depending on age and gender, further examinations are recommended, including a cervical smear, mammogram, prostate examination, colonoscopy, as well as hearing and vision tests [4, 5], which will not be discussed further here. People who attend the PMCU do so on average every three years [5].

In 2023, 17.5% of the Austrian population took advantage of a PMCU, representing a 14.9% increase compared to the previous year [6]. There was a gender-specific difference: women (18.3%) used the service more frequently than men (16.6%) [3].

Public expenditure on general preventive measures totalled €1,877 million in 2023, which corresponds to 4.64% of the annual public health expenditure [7]. The costs for the PMCU health screening amounted to approximately €201 million, which represents 10.71% of the total costs in health prevention [3].

gratis
Vorsorgeuntersuchung
in Österreich:
jährlich für alle Personen
ab 18 Jahren

VU umfasst Anamnese,
Blut- & Urintest,
körperliche und
parodontale
Untersuchung, sowie
Befundbesprechung
und Beratung

weitere alters- &
geschlechtspezifische
Untersuchungen

steigende
Inanspruchnahme;
mehr Frauen

Präventivkosten
gesamt €1,8 Mrd.;
VU: €201 Mio.

The last update of the screening program took place in 2005 [8], and the Federation of Social Insurances is currently in the process of revising the included screening services. Although a scientific revision was conducted in 2020, it was not implemented [9, 10]. In 2023, the Austrian Court of Audit (ACA) assessed the PMCU as a fundamentally effective tool for the early detection of diseases and identification of risk groups. However, criticism was expressed at the low participation rate and the inadequate quality of documentation, which prevents evidence-based management and further development of preventive measures [11]. The report also referred to a university study which showed that participants appreciated the PMCU for early detection and health maintenance but criticised the lack of standardisation and the lack of individualised examinations [11].

The most recent evidence-based recommendations for revising the PMCU [12] date from 2022 and are based on guidelines from renowned international institutions in the United Kingdom, Canada and the United States. In accordance with these international guidelines, the current recommendations for revising the Austrian PMCU comprise 26 interventions for 20 target diseases or risk factors. As outlined in the Appendix, the recommendations include a range of interventions for CVD.

To further increase the participation rate, the social insurance system relies on improved communication measures, such as a targeted invitation system and risk group-specific screening programs [5].

**Update notwendig;
VU laut Rechnungshof
effektiv, aber
verbesserungswürdig**

**evidenzbasierte
Empfehlungen basieren
auf internationalen
Richtlinien;
VU umfasst
26 Interventionen für
20 Zielkrankheiten**

**bessere Kommunikation
zu Vorsorge-Steigerung**

1.2 Cardiovascular disease

CVDs are among the most common non-communicable diseases (NCDs) and causes of death worldwide [13, 14]. They include conditions such as coronary heart disease, cerebrovascular disease, and peripheral arterial disease. These disorders arise primarily from atherosclerosis, a process in which fatty deposits accumulate in the arteries, restricting blood flow, reducing arterial wall elasticity, and predisposing vessels to rupture. Such changes can trigger acute events like heart attacks or strokes [15, 16]. CVD can usually be prevented or delayed through targeted prevention (lifestyle changes and medication) [17].

The outlook for the coming years is particularly concerning: while approximately 17.3 million people currently die each year due to CVD (as of 2018), it is predicted that this number will rise to about 23.6 million by 2030, despite ongoing progress in cardiac medicine [18]. Mortality from CVDs varies greatly across regions: 45% of all deaths occur in Western countries compared to 25% in developing nations [19]. In addition to a considerable burden of disease, CVD also causes high costs for healthcare systems. The annual costs of CVD in the European Union (EU) are estimated at around €282 billion. Around €155 billion (55%) is attributable to allocated healthcare costs and long-term care, while a further €48 billion (17%) is due to productivity losses. The remaining approximately €79 billion (28%) is due to the time and effort of informal carers [20].

**HKE häufigste nicht
übertragbare Krankheiten
weltweit**

**durch gezielte Prävention
verhinder- oder
verzögerbar**

**globale Tendenz:
steigende HKE-Todesfälle**

**Mortalität variiert nach
Regionen**

**jährliche Kosten von HKE
in der EU auf ca. € 282 Mrd.
geschätzt**

Austrian statistics illustrate this global health problem: of the 31,129 people who died from CVD in 2023, 22,510 were aged 80 or over – a significant proportion of the total mortality in this age group [21]. Overall, these deaths represented 34.7% of all mortality cases in Austria during the same year [22].

Ö:
**HKE = Haupttodesursache
im Alter**

1.2.1 Risk factors

CVDs occur with varying frequencies in different regions of the world. This is due to a variety of factors, including individual lifestyle, dietary habits and exercise patterns, genetic differences, and environmental conditions [19]. A complex interplay of different risk factors influences the development and progression of CVD. They can be divided into modifiable (e.g., hypertension, cholesterol, lifestyle) and non-modifiable (e.g., sex, gender, ethnicity) categories, a distinction that is useful for prevention and treatment [14]. Some risk factors, such as psychosocial or socioeconomic factors, fall outside this binary classification.

**regionale Unterschiede
bei Risikofaktoren und
Präventionsansätzen**

**Unterscheidung
in modifizierbare und
nicht modifizierbare
Risikofaktoren**

Beyond this traditional classification, CVD risk can also be conceptualised across four dimensions; physical, psychological, cultural/social and lifestyle-related factors, reflecting a multidimensional concept of risk.[14, 23].

**multidimensionales
HKE-Risikokzept**

Non-modifiable risk factors

Age and biological sex/gender

The risk of CVD increases significantly with age [24].

**Alter und Geschlecht
als nicht modifizierbare
Risikofaktoren**

While men tend to develop CVD 7-10 years earlier than women and exhibit risk factors such as higher levels of dyslipidaemia, women display distinct patterns characterised by elevated systolic blood pressure. In Europe, the non-age-adjusted mortality rate from CVD is higher among women than men (45% vs. 39%), despite nearly identical lifetime risk. These sex-specific nuances highlight the necessity for a tailored medical approach [25]. Furthermore, other sex-specific factors such as premature menopause, polycystic ovary syndrome, and preeclampsia are also recognised as important risk enhancers [26, 27].

Family history of CVD

Family history of CVD reflects both genetic predisposition and shared environmental and lifestyle factors [26, 27].

**familiäre Vorbelastung
als nicht modifizierbarer
Risikofaktor**

Ethnic background

Compared with individuals of European origin, CVD risk is higher among people of South Asian and sub-Saharan African descent, while it is generally lower among South American or Chinese populations[26, 27].

**ethnische Unterschiede
beim HKE-Risiko**

Genetic risk

Genetic risk factors play an important role in the development of cardiovascular disease. Single gene mutations, such as those in LDLR, APOB, or PCSK9, can cause familial hypercholesterolaemia and significantly increase the risk of early coronary artery disease. Additionally, many smaller genetic variants, summarised in polygenic risk scores (PGS), influence an individual's risk by affecting pathways like lipid metabolism, blood pressure regulation, and inflammation. Despite this genetic predisposition, maintaining a healthy lifestyle can greatly reduce the overall risk of developing cardiovascular disease [28].

**unterschiedliche
genetische Risikofaktoren
beeinflussen HKE
Entwicklungen**

Modifiable risk factors

Cholesterol

LDL cholesterol and non-HDL cholesterol, are major contributors to CVD [19]. Over 50% of the population in industrialised countries suffers from elevated cholesterol levels. Familial hypercholesterolemia (FH), affecting about 1 in 500 people, leads to very high cholesterol levels, which can cause heart attacks even at a young age. Statins, ezetimibe, and PCSK9 inhibitors effectively reduce LDL cholesterol and have been shown to prevent CV events, but more than half of patients still fail to achieve recommended target levels. [19]. With increasing age, the correlation between non-HDL cholesterol and CVD weakens – a pattern also observed for blood pressure, smoking and diabetes. However, this only applies to CVD, as these factors continue to influence the overall mortality risk [29].

erhöhtes LDL- und non-HDL-Cholesterin: zentrale CVD-Risikofaktoren

Lipoprotein(a)

Lipoprotein(a) (Lp(a)) is an LDL-like particle characterised by the attachment of apolipoprotein(a) and contributes to cardiovascular disease through pro-inflammatory, atherogenic, calcifying, and prothrombotic mechanisms. Around 20-25% of the population have elevated Lp(a) levels (≥ 50 mg/dL), which are associated with a significantly increased risk of atherosclerotic events. Even with optimal control of traditional risk factors such as LDL cholesterol, a so-called “residual risk” remains, largely driven by high Lp(a) concentrations [30].

erhöhte Lp(a) Werte fördern HKE-Risiko

Smoking

Tobacco consumption represents one of the leading preventable causes of CVD worldwide. On average, smokers lose about a decade of life expectancy. Nicotine exposure during adolescence can cause long-term vascular damage and even passive smoking increases the risk of CVDs [31].

Rauchen als vermeidbarer HKE-Risikofaktor

Obesity

Excess weight is a significant risk factor for CVD. In Europe, each 5 kg/m² increase in Body-Mass-Index (BMI) is associated with a 39% increase in mortality, thus underscoring the importance of prevention through lifestyle changes [19].

Adipositas als HKE-Risikofaktor

Physical inactivity

Insufficient physical activity doubles the risk of coronary heart disease [32]. Physical activity is a crucial protective factor against CVD, enhancing metabolic function and substantially lowering the risk for CVD [19, 32].

körperliche Inaktivität erhöht HKE-Risiko

Diet

Diet plays a crucial role in CV health. A balanced nutritional approach can considerably lower the risk of CVD. Conversely, diets high in saturated fats, added sugars, and sodium has been shown to increase mortality from CVDs [24, 33].

Ernährung als wichtiger Präventionsfaktor

Alcohol consumption

Excessive alcohol consumption elevates blood pressure and triglyceride levels, thereby increasing the risk of CVD [26].

exzessiver Alkoholkonsum erhöht HKE-Risiko

Other, less common determinants may also contribute, but as they are not typically included in established risk scores, they are not discussed further here.

Socioeconomic risk factors

Low socioeconomic status and social isolation increase the risk of CVD. Mortality from CVD is estimated to be up to three times higher among individuals living in the most deprived communities compared with those in the wealthiest. A lack of social support increases the risk for coronary artery disease (CAD) and worsens its prognosis [26, 27].

HKE-Risiko auch von sozioökonomischen und sozialen Faktoren beeinflusst

However, these socioeconomic and social factors are only partly modifiable, as they are strongly influenced by broader structural, political, and societal conditions. Individual lifestyle changes alone are often insufficient to overcome the disadvantages associated with low socioeconomic status, highlighting the need for targeted policy and community-level interventions [34].

Comorbidities that increase the risk of developing CVD

Arterial hypertension

Hypertension is recognised as one of the primary modifiable risk factors contributing to CVD worldwide [23, 35]. A reduction in systolic blood pressure by just 10 mm Hg lowers the risk of CV events by approximately 20% and decreases overall mortality by 13% [35].

Hypertonie als zentraler, modifizierbarer HKE-Risikofaktor

Diabetes

Diabetes, particularly type 2 diabetes (T2DM), significantly increases the risk of CVD through complex interactions such as hyperglycaemia, insulin resistance, inflammation, obesity, hypertension, and diabetes-related comorbidities. Early comprehensive monitoring and intervention are crucial to reducing the CV risk associated with diabetes [36].

Diabetes und komorbide Erkrankungen verstärken das HKE-Risiko

Other comorbidities associated with an increased risk of developing CVD include chronic kidney disease, atrial fibrillation, autoimmune and inflammatory disorders (e.g. rheumatoid arthritis, systemic lupus erythematosus), as well as conditions like serious psychiatric illnesses, periodontitis, and a history of influenza infection [26, 27].

Mental Health

Subjective well-being encompasses positive mental states, including life satisfaction, purpose, and psychological well-being, which have been linked to protective effects against mortality and CVD. Research suggests that positive psychological traits and affects can reduce the risk of CV events through stress-buffering mechanisms, potentially improving physiological regulation and promoting healthier behaviours. Conversely, negative affect has been associated with increased CV risk, highlighting the complex relationship between mental states and physical health [37].

psychische Gesundheit und Wohlbefinden als HKE-Risikofaktoren

Risk prevention

In addition to risk prediction, risk prevention is another important factor in preventing CVD. This will only be explained briefly here, as preventive measures are relevant in cases of increased CVD risk.

Risikoprävention neben Risikovorhersage ebenfalls relevant

CVD prevention requires a comprehensive and layered approach that distinguishes between general population-wide risk reduction and targeted interventions for high-risk groups, focusing on a holistic view of risk factors throughout the entire life course [38].

By implementing suitable preventive measures, it is possible to delay CVD onset and premature deaths, thereby enhancing healthy life expectancy [23]:

- **Primary prevention:** Avoidance and reduction of known risk factors. The promotion of a healthy lifestyle is paramount here before any disease occurs.
- **Secondary prevention:** Early detection of diseases and risks, enabling timely intervention.
- **Tertiary prevention:** Prevention of disease progression and possible secondary diseases.

The overarching aim is to identify risk factors early and intervene in a targeted manner before severe disease develops, not only reducing CVD risk but also improving quality of life and promoting long-term health [23, 38].

3 Ebenen der Prävention:
primäre sekundäre und
tertiäre Prävention

**Früherkennung und
gezielte Intervention
zur nachhaltigen
Risikoreduktion**

1.3 Cardiovascular risk prediction

Risk prediction in preventive cardiology employs a comprehensive approach that evaluates a patient's overall CV risk rather than analysing individual risk factors in isolation. This approach allows for an estimation of the probability of CV events over a defined time horizon, typically 5-10 years, depending on the risk tool used, and subsequent classification into risk groups such as low, moderate, and high [38]. It is essential to recognise that risk assessments have no immediate clinical value on their own, health improvements only occur through subsequent risk-targeted interventions [39].

Risikovorhersage:
wesentlicher Bestandteil
der präventiven
Kardiologie

Over the past two decades, numerous prediction models have been developed, which mathematically combine multiple predictors to estimate the risk of developing CVD. These models are typically derived from longitudinal cohort studies and most often use Cox proportional hazards regression, accelerated failure time analysis, or logistic regression [40]. Their construction involves identifying and weighing risk factors. Common predictors include age, smoking status, blood pressure, and cholesterol levels [40]. Central to mathematical modelling is the consideration of events per included variable to avoid overfitting. Statistical performance is often evaluated using measures such as discriminatory power (C-statistic) and calibration (chapter 1.4) [40, 41].

**Entwicklung verschiedener
mathematischer Modelle
zur HKE-Risikovorhersage**

When applying a risk score, it is essential to note that the risk assessment depends not only on the measured risk factors (Table 1-3) of a person, but also on the average risk of a population (incidence or mortality) and the relative risks associated with different levels of each predictor [42].

Risikobewertung:
individuell und
populationsbezogen

The longest epidemiological study to identify key risk factors for CVDs was the Framingham Heart Study. It has provided essential insights into the development of the disease since its inception in 1948 [43]. It provided the foundation for the Framingham Risk Score, one of the earliest and most well-used multivariable risk prediction models.

**längste epidemiologische
Studie:
Framingham-Herz-Studie**

Treatment decisions should be guided by overall CV risk rather than by individual factors alone. Established risk algorithms, based on a limited number of key variables (chapter 1.2), enable reliable risk categorisation and help prevent underestimation of risk [44].

**Therapieentscheidungen
basieren auf Gesamt-
HKE-Risiko**

1.3.1 Risk scores for cardiovascular diseases

Risk score types

The data used in the respective CVD risk prediction models, on which the risk assessment is based, are derived from multiple cohort studies that differ geographically and demographically, and vary in size and scope [45].

Table 1-2 presents a comprehensive overview of various CV risk prediction models relevant to this review. The models cover diverse populations across different countries, primarily focusing on predicting 10-year CVD risk, with variations in specific outcomes, risk factors, and methodological approaches. It provides a systematic comparison of these risk prediction tools, offering researchers and clinicians a comprehensive overview of their characteristics and potential applications.

Table 1-3 provides an overview of the included variables in the risk models considered in this review, ranging from routinely available parameters such as age and blood pressure to more specialised measurements chronic kidney diseases (CKD) and Rheumatoid arthritis (RA)

**Modell-Datenquellen
vielfältig bzgl. Kohorten
und Demographie**

**Übersicht und Vergleich
bestehender CVD-
Risikovorhersagemodelle**

**Übersicht der in
die CVD-Risikomodelle
einbezogenen Variablen**

Table 1-2: CVD risk prediction model selection adapted from [42]

Risk scores	Derivation cohort	Outcomes and timeframe	Statistical model	Internal validation	External validation	Country-specific versions
ARRIBA [46]	a longitudinal analysis; 1,973 subjects (mean age 51 ± 13 years, 48% men) from the Study of Health in Pomerania (SHIP), aged 30-80 years without prior CV events; baseline study (1997-2002); located in Germany	10-year overall risk for fatal and non-fatal CV events	Cox proportional hazards model (implied by the use of risk prediction instruments)	✓	✓ (with the SHIP in Germany)	developed and validated in Germany, based on the Arriba instrument, which was adapted from the Framingham risk score for European data
ASSIGN [47]	SHHEC prospective cohort study with 6540 men and 6757 women aged 30-70 years, baseline survey conducted in period 1984-87; located in Scotland	10-year risk of fatal and non-fatal CVD	Cox survival models	✓	X (not validated in non-Scottish population)	for the population of Scotland
DIAL2^a [48]	prospective registry-based derivation 467,856 individuals with type 2 diabetes without prior CVD from the Swedish NDR, aged 30-85 years with T2DM; located in Europe	CVD-free life expectancy and lifetime CVD risk for people with T2DM without previous CVD	two cause-specific Cox proportional-hazard models (one for CVD events, one for non-CVD mortality)	✓	✓ 218 267 individuals in the UK (CPRD) and Scotland (SCID) without prior CVD	recalibrated for the European low- and moderate-risk regions
Framingham Risk Score [49]	prospective cohort studies; 8,491 participants; age range 30-75 years; baseline survey; located in the USA	10-year risk of developing all atherosclerotic CVD or specific components of CVD, i.e., coronary heart disease, stroke, peripheral vascular disease, or heart failure	Cox survival models (Sex-specific Cox proportional-hazards regression)	✓	✓ (validations are transportable -with calibration- to culturally diverse populations in Europe, the Mediterranean region, and Asia)	American calculator, adaptations mentioned for European Mediterranean areas
PCE [50]	four prospective cohort studies (ARIC, CHS, CARDIA, Framingham Original and Offspring cohort); 24,626 individuals; baseline survey conducted in period 1984-93; located in the USA	10-year risk of developing a first ASCVD event	Cox survival models (sex- and race-specific proportional-hazards models)	✓	✓ ARIC study, Cardiovascular Health Study, CARDIA study, and Framingham Original and Offspring Study cohorts	N.A
PROCAM [51, 52]	18,460 men and 8,515 women (coronary risk score), 5,905 men and 2,225 women (stroke score), aged 35-65 years for stroke score recruited between 1979 and 1985; suitable for patients aged 20 to 75 years; baseline survey located in Germany	10-year risk of acute coronary events (fatal or nonfatal MI or sudden coronary death)	Cox proportional hazards models	✓	N.A	developed based on the PROCAM (Prospective Cardiovascular Münster) study in Germany
QRISK3 [53]	prospective open cohort study; QResearch with over 7.89 million patients aged 25-84 years; baseline survey; located in the UK	10 year risk of CVD in women and men	Cox proportional hazards models	✓	QRISK3 no extra external validation; Previous models (QRISK 1 and 2) validated in several cohorts	for the population of the UK

Risk scores	Derivation cohort	Outcomes and timeframe	Statistical model	Internal validation	External validation	Country-specific versions
RECODE^a [54]	based on 3 RCTs (ACCORD, DPPPOS; Look AHEAD) 15,413 participants, ACCORD study: 2001-2009 DPPPOS study: 1996-2001 Look AHEAD study: 2001-2012; baseline survey; located in the USA	10-year risk of microvascular and CV events and all-cause mortality	Cox proportional hazards models	✓ (with the ACCORD study)	✓ (with the DDPOS and Look AHEAD study)	for the US population
SCORE2 [55]	45 prospective cohorts with 677,684 individuals and 30,121 CDE participant age: 40-69 years; baseline survey conducted in period 1990-2009; located in Europe	10-year fatal and non-fatal CVD risk	Fine and Gray competing risk-adjusted models stratified by cohort	✓	✓ (using data from 25 additional cohorts in 15 European countries)	risk charts for grouped European countries. country grouping in: low-risk, moderate-risk, high-risk, and very high-risk
SCORE - DIABETES [56]	Pooled individual-participant data from 4 large datasets comprising 229,460 persons with T2DM without prior CV, located in Europe	10-year risk of fatal and non-fatal CVD	sex-specific competing risk-adjusted models	✓	✓ (included 217 036 further individuals in 4 European countries)	risk charts for grouped European countries. country grouping in: low-risk, moderate-risk, high-risk, and very high-risk
SCORE2-OP [57]	(Norwegian) prospective cohort (28,503 individuals, 10,089 CVD events); individuals aged over 65 without pre-existing atherosclerotic CVD, baseline survey; located in Europe	5- and 10-year risk of CVD (>70 years in four geographical risk regions)	fine and gray proportional subdistribution hazards models	✓	✓ (using data from six additional European study populations)	risk charts for grouped European countries. country grouping in: low-risk, moderate-risk, high-risk, and very high-risk
UKPDS^a [58]	prospective diabetes study; 4,540 individuals; aged 25-65 years at diabetes diagnosis; baseline study; located in the UK	10-year risk of a fatal or non-fatal CHD event (MI or sudden death)	Cox proportional-hazards regression	✓ (cross-validation methods)	✓ (UK intern)	for the population of the UK

Abbreviation: ASCVD ... Atherosclerotic Cardiovascular Disease; ARRIBA ... Aufgabe gemeinsam definieren, Risiko subjektiv, Risiko objektiv, Information über Präventionsmöglichkeiten, Bewertung der Präventionsmöglichkeiten und Absprache über weiteres Vorgehen (engl. Shared Decision Making); CHD ... Coronary heart disease; CPRD ... Clinical Practice Research Datalink; CVD ... Cardiovascular Disease; CV ... Cardiovascular; DDPOS ... Diabetes Prevention Program Outcomes Study; FRS ATP-III ... Framingham Risk Score Adult Treatment Panel III; MI ... myocardial infarction; NDR ... National Diabetes Register; N.A ... not available; PCE ... Pooled Cohort equations; PROCAM ... Prospective Cardiovascular Münster Study; SCID ... Scottish Care Information – Diabetes; SCORE2 ... Systematic Coronary Risk Evaluation 2; SCORE2-OP ... Systematic Coronary Risk Evaluation 2 – older persons; SHHEC ... Scottish Heart Health Extended Cohort; SHIP ... Study of Health in Pomerania; T2DM ... type 2 diabetes; UK ... United Kingdom; UKPDS ... United Kingdom Prospective Diabetes Study; USA ... United state of America

^a CVD Risk scores for diabetes patients

Table 1-3: Predictor variables included in CVD risk prediction scores

Risk Score	Age	Sex	Ethnicity	Country of residence	BMI	Total cholesterol	LDL-cholesterol	HDL-cholesterol	Triglycerides	Systolic blood pressure	Blood pressure medication	Atrial fibrillation	atherosclerosis	Diabetes	Smoking	Family history of CVD	Chronic Kidney Disease	Rheumatoid arthritis	severe mental illness	migraines	antipsychotic medication	regular steroid tablets	erectile disfunction	Systemic lupus erythematosus
ARRIBA [59]	X	X				X		X		X	X		X	X	X	X								
ASSIGN[60]	X	X		X		X		X		X				X	X	X								
DIAL2 ^a [48]	X	X				X		X		X			X	X*										
Framingham Risk Score [61]	X	X				X		X		X	X			X	X	X								
FRS ATP-III [62]	X	X				X		X		X					X									
PCE [63]	X	X	X			X		X		X	X			X	X									
PROCAM [64]	X	X					X	X	X	X				X	X	X								
QRISK3 [65]	X	X	X		X	X		X		X	X	X		X	X	X	X	X	X	X	X	X	X	X
RECODE ^a [54]	X	X	X			X	X	X		X	X			X*	X	X								
SCORE2 [66]	X	X		X		X		X		X				X	X							X		
SCORE2-DIABETES[67]	X	X		X		X		X		X				X*										
SCORE2-OP [66]	X	X		X		X		X		X				X	X									
UKPDS ^a [68]	X	X	X			X		X		X		X		X*	X									

The parameters marked in blue are already collected in the regular PMCu.

Abbreviations: ARRIBA ... Aufgabe gemeinsam definieren, Risiko subjektiv, Risiko objektiv, Information über Präventionsmöglichkeiten, Bewertung der Präventionsmöglichkeiten und Absprache über weiteres Vorgehen (engl. Shared Decision Making); CVD ... Cardiovascular Disease; FRS ATP-III ... Framingham Risk Score Adult Treatment Panel III; PCE ... Pooled Cohort equations; PROCAM ... Prospective Cardiovascular Münster Study; SCORE2 ... Systematic Coronary Risk Evaluation 2; SCORE2-OP ... Systematic Coronary Risk Evaluation 2 – older persons; UKPDS ... United Kingdom Prospective Diabetes Study

* incl. duration of diabetes and HbA1c, a CVD Risk score for diabetes patients

^a extended model: predictors as mentioned above and diabetes specific risk factors (albuminuria, BMI, retinopathy and insulin use)

CV risk prediction models differ in their construction and the variables they include, but five core predictors are universally included across scores: age, sex, total cholesterol, systolic blood pressure, and smoking status. Variations are evident in the depth of analysis and the additional risk factors considered. While some models concentrate on a few key factors, others, like QRISK3, adopt a more comprehensive approach.

The Framingham Risk Score (FRS) laid the foundation by incorporating basic predictors such as age, gender, blood pressure, and cholesterol levels and is based on the Framingham Heart Study. Over time, these models became increasingly accurate and comprehensive [43]. The PCE score differs from the FRS in that it takes into account not only age and sex but also origin, but not family history [63]. It was developed from pooled data of four large US cohorts, broadly representing the American population [42].

The ARRIBA model considers factors such as diabetes (if applicable), blood pressure, and cholesterol in its calculations. If required, it can also consider atherosclerosis, although this parameter is not mandatory. Compared to other models, it uses a smaller set of predictors but emphasises those most relevant [59]. It was developed based on the FRS, and the data for this model are derived from the SHIP (Study of Health in Pomerania) cohort study, which represents parts of the German population [46]. PROCAM, which is also based on the German population, focuses more on the analysis of the lipid profile. It includes LDL cholesterol and triglycerides, which are not consistently considered in other models [64]. Like the ARRIBA model, the PROCAM score is based on a study conducted in Germany, the PROCAM study of the same name, and is therefore also based on the German population [69].

The SCORE2 model was developed from 45 prospective European cohort studies of middle-aged adults (40-69 years), whilst SCORE2-OP was derived from a large Norwegian cohort and is specifically designed for adults aged 65 years and older without preexisting CVD. Both models incorporate a geographical component by categorising European countries into low-to-moderate, high, or very high-risk regions, and share a similar parameter structure, differing mainly in the age range of the target population [42]. This enables a differentiated risk prognosis between younger and older patients [66].

The QRISK3 model was developed from a large prospective open cohort study using the UK-based QResearch database and incorporates a broad range of predictors. In addition to the classic parameters, it also includes factors such as ethnicity, mental illness, and comorbidities, including rheumatoid arthritis and kidney disease. [65].

Unlike other scores, the DIAL2, SCORE2-Diabetes, UKPDS and RECODE scores were specifically designed for patients with type 2 diabetes. The SCORE2-Diabetes and UKPDS risk engine incorporates information such as HbA1c levels and diabetes duration [67, 68]. In addition to the parameters listed above, RECODE includes variables such as the use of anticoagulants, serum creatinine and urine albumin-to creatinine-ratio in the risk calculation [54]. DIAL2 includes additional parameters beyond those mentioned above: albuminuria, BMI, retinopathy, and insulin use. Furthermore, it calculates CVD-free life expectancy and lifetime CVD risk for people with T2DM, whereas all other scores calculate the 10-year risk of a CVD/CHD event [48].

The 2020 recommendations for preventive medical check-ups in Austria state that the ARRIBA tool is recommended for counselling on CVD risk, as it has been validated with German cohorts, among others, which are more ap-

Kernparameter der Risikobewertung:
Alter, Geschlecht, Gesamtcholesterin, systolischer Blutdruck und Raucherstatus

US Scores:
FRS und PCE

deutsche Risikomodelle:
ARRIBA- und PROCAM-Score

europäische Risikomodelle:
SCORE2 und SCORE2-OP

britischer Risikoscore:
QRISK3

Diabetes-spezifische CVD-Risikomodelle:
DIAL2, SCORE2-Diabetes, UKPDS und RECODE

ARRIBA-Tool als Empfehlung für HKE Beratung in Österreich

plicable to the Austrian population [70]. It is based on a further development of the FRS and the PROCAM score. It was specifically developed and adapted for the German primary care context [46].

1.3.2 Risk categories

CV risk is typically stratified into three to four categories: low (to) moderate, high and very high risk. The threshold used to defined these categories vary across age groups, with the aim of ensuring balanced treatment, avoiding under-treatment in younger patients while preventing overtreatment in older individuals [71].

The risk categories do not automatically imply pharmacological therapy; other individual factors must be considered when making treatment decisions [71]:

- Specific risk modifiers
- Lifetime risk of CVD
- Potential treatment benefits
- Existing comorbidities
- Frailty
- Personal preferences of the patient

The division into age groups enables a differentiated and personalised assessment of health risk [71].

The exact cut-off values for defining the risk categories differ between prediction models, reflecting variation in derivation cohort, outcomes, and calibration strategies. The following section outlines the thresholds applied in the respective risk scores relevant to this review.

Klassifizierung des CVD-Risikos nach Schweregrad (leicht, moderat, hoch und sehr hoch)

individuelle Faktoren bei Therapieentscheidungen berücksichtigen

Modelle haben unterschiedliche Risikoschwellenwerte

Table 1-4: Risk categories ARRIBA, FRS, PROCAM and QRISK3 [46, 72-74]

Risk categories	Risk
Low to moderate risk	< 10 %
High risk	10% to 19%
Very high risk	≥ 20 %

Table 1-5: Risk categories SCORE2/SCORE2-OP [75]

Risk categories	< 50 years	50-69 years	≥ 70 years
Low to moderate risk	< 2.5%	< 5%	< 7.5%
High risk	2.5% to 7.5%	5% to < 10%	7.5% to 50 %
Very high risk	≥ 7.5%	≥ 10%	≥ 15%

Table 1-6: Risk categories UKPDS score [76]

Risk categories	Risk
Low risk	< 10 %
moderate risk	10% to 20%
High risk	20% to 30%
Very high risk	≥ 30 %

Table 1-7: Risk categories PCE score [77]

Risk categories	Risk
Low risk	< 5 %
Borderline risk	5% to 7.5%
intermediate risk	7.5% to 20%
high risk	≥ 20 %

Based on this individual baseline risk evaluation, clinicians can make guideline-directed, targeted decisions regarding the initiation of preventive measures – such as lifestyle modifications or pharmacological therapy – once a defined risk threshold is reached [38, 39, 43].

**gezielte
Präventionsentscheidung
basierend auf
individuellem Risiko**

1.4 Performance metrics of risk prediction models

Evaluating risk prediction models is an essential step to determine how well they predict outcomes and differentiate between individuals with varying risk levels. Models are typically assessed using population-based statistical measures of calibration and discrimination [78]. To assess the accuracy of a risk model's predictive ability, the C-statistic, also known as the area under the curve (AUC), can be computed. The C-statistic is a comprehensive measure of a risk prediction model's discriminatory power, reflecting the likelihood that the model correctly distinguishes between two randomly chosen individuals based on their probability of experiencing an event. The C-statistic ranges from 0.5 (no better than chance) to 1 (perfect discriminatory ability). The closer the value is to 1, the stronger the predictive power [41]. The interpretation can be divided into [41, 79, 80]:

- ≤ 0,5: no discrimination
- 0.6-0.7: Poor discrimination
- 0.7-0.8: Modest discrimination
- 0.8-0.9.: Good discrimination
- ≥ 0.9: Excellent discrimination

When data are available, the C-statistic should always be complemented with additional measures such as positive/negative predictive values, sensitivity, specificity, and clinical context to enable comprehensive model evaluation [41].

In addition to discrimination ability, calibration is another key aspect of model performance. It assesses whether the predicted probabilities correspond to the events observed. For example, in a well-calibrated model, a group of 100 individuals with a predicted risk of 5% would be expected to experience five events [81].

The O:E ratio (observed-to-expected ratio) evaluates an instrument's calibration by comparing actual events to predicted events [82]. A ratio near 1 indicates accurate prediction, with values above 1 suggesting risk underestimation and below 1 indicating risk overestimation.

**Bewertung der
Genauigkeit der Modelle
mithilfe der C-Statistik**

**AUC von
>0,8 = gute
Diskriminierung**

**C-Statistik allein
unzureichend zur
Modellbewertung**

**Kalibrierung weiterer
wichtiger Aspekt**

**E/O Ratio 1 = exakte
Vorhersage;
>1 = Unterschätzung;
<1 = Überschätzung**

Calibration can be further assessed through the intercept and slope analysis. The intercept (ideally 0) indicates systematic over- or underestimation of risks, while the slope (ideally 1) assesses the strength of the association between predicted and observed risks [81]. Deviations from these benchmark values indicate that the model may not fully capture risk complexities.

Advanced reclassification methods, such as the Net Reclassification Index (NRI), assess predictive accuracy by indicating how correctly individuals are assigned to risk groups. The Net Benefit (NB) extends this evaluation by considering the consequences of misclassification and assessing a model's clinical utility [81].

**Kalibrierung:
Intercept- und
Slope-Analyse**

**erweiterte
Bewertungsmethoden:
NRI und Net Benefit**

2 Research question and project aim

2.1 Project aim

The umbrella organisation of social insurance institutions is considering the implementation of a cardiovascular (CV) risk assessment as part of the annual preventive medical check-up, which includes screening for cardiovascular diseases (CVD).

As presented in chapter 1.3.1 various models and tools for risk assessment exist in different settings, such as online self-assessments (FRS, SCORE2, QRISK3, PROCAM, PCE, UKPDS) or evaluations by healthcare professionals (ARRIBA, RECODE).

This report systematically reviews the main instruments for CV risk prediction used in Europe, with a focus on SCORE2, SCORE2-OP, SCORE2-Diabetes, ARRIBA, and PROCAM, aiming to compare the most described risk prediction models applicable to the Western European population and evaluate their feasibility for implementation within the Austrian PMCU. Consideration is given to the prerequisites needed for implementing these tools and how the results of risk scores influence subsequent health examinations, with a focus on uniform application across Austria.

The scope is limited to risk prognosis scores whose parameters can be assessed during a standard PMCU, without the need for additional investigations. This excludes models requiring specialist assessments, such as genetic risk scores or imaging-based approaches like the Coronary Artery Calcium score (CAC-Score), which uses cardiac computed tomography (CT) to measure calcium deposits in the coronary arteries [83].

Berichtziel:
Bewertung von relevanten
HKE-Risikomodellen für
Einsatz im Rahmen der
Vorsorgeuntersuchung

2.2 Research questions

RQ1: How do CV risk prediction models compare, and how do they differ in terms of their evidence, predictive validity, benefit-harm balance and their implementability within the framework of Austrian PMCU?

RQ2: To what extent does the application of CV risk prediction models lead to long-term health benefits, as well as to changes in the health behaviour of patients?

RQ3: Which parameters are already standardly collected in preventive health check-ups, which additional examinations are required for an optimal implementation of the risk scores, and which organisational, time and personnel resources are needed for this?

Forschungsfragen

3 Methods

To answer the research questions RQ1 to RQ3, we conducted a literature triangulation encompassing guidelines, systematic reviews (SRs), and a validation study (VS). This research project was pre-registered on the Open Science Framework platform. The literature search was restricted to SRs and validation studies. This is a deviation from the protocol, which a search for primary studies (RCTs). This change was justified because sufficient high-quality SRs were available. It only became clear later in the process, after drafting the protocol, that these reviews already critically appraised and synthesised relevant RCTs, providing a comprehensive and reliable evidence base. In addition, a guideline synopsis was conducted.

**methodisches Vorgehen
und Quellenbasis**

**Fokus auf Sekundär- statt
Primärstudien**

**Ergänzung durch
Leitliniensynopse**

3.1 PICO

The population-intervention-comparison-outcome (PICO) scheme was used to define the research questions and guide the final selection of the literature. Table 3-1 shows the PICO that was defined for this assessment.

PICO

Table 3-1: PICO

Population	Addressees of cardiovascular risk prediction (PMCU users) Keywords: Arriba, SCORE2, Procam, cardiovascular risk prediction, cardiovascular disease, cardiovascular disease, screening, ARRIBA score, Framingham Risk Score
Intervention	Risk prediction models for cardiovascular diseases (e.g. SCORE2, PROCAM, ARRIBA)
Comparison	Comparison of the various risk models with each other and, if necessary, with standard care without structured risk assessment. Current prevention programme without extended risk scores.
Outcomes	Predictive validity of the risk models Long-term effects on cardiovascular event rates and mortality Quality of life Practical feasibility Additional resources required (time, personnel, structures) Acceptance by physicians and patients
Study Design	High-quality systematic reviews and comparative studies of risk prediction models Guidelines on cardiovascular risk prediction
Countries	Western Europe, Austria
Languages	English, German

Abbreviations: PICO ... Population, Intervention, Comparison, Outcomes; SCORE2 ... Systematic Coronary Risk Evaluation 2; PMCU ... Preventive medical check-up; PROCAM ... Prospective Cardiovascular Münster Score; RCT ... randomised controlled trial

Inclusion criteria were intentionally stringent, targeting SRs and comparative studies published between 2015 and 2025 in English or German, with a particular focus on Western European populations. Guidelines underwent a similarly strict selection, requiring origin from reputable institutes and at least five citations in scientific literature.

**Beschränkung auf
systematische Reviews und
komparative Studien**

3.2 Literature search

Systematic reviews and validation studies

A comprehensive literature search was conducted in May 2025 by an information specialist (TM). The following databases were searched: Medline via Ovid, Embase, and The Cochrane Library. The search was restricted to articles published between 2015 and 2025 in English or German. This limitation was applied because older score models are considered outdated, and the scores have been updated within the past 10 years. Additionally, conference abstracts in Embase and study records from study registries in the Cochrane Library were excluded. After removing duplicates, 1019 citations remained. We manually examined the reference lists of included studies and some potentially relevant hits to identify additional reviews.

The full search strategy is provided in the appendix.

**systematische
Literatursuche in
3 Datenbanken**

Guidelines

Relevant guidelines were identified through a manual search conducted on GIN (Guidelines International Network), TRIPS, and Google Scholar. One guideline, originally in Dutch, was included and translated due to its contemporary relevance and Western European context, despite deviating from the initial language restrictions.

**Handsuche nach Leitlinien
in Datenbanken und auf
Websites verschiedener
Institutionen**

3.3 Literature selection

Systematic reviews and comparative studies

We systematically screened the literature for studies relevant to our research question. Studies were included if they met the predefined eligibility criteria defined in the PICO. We identified seven SRs and one additional validation study. No comparative studies were found.

The literature selection adhered to the four-eyes principle to ensure unbiased screening. Two researchers (LG and JP) independently reviewed titles, abstracts, and full texts, with a third reviewer (VH) consulted to resolve any potential disagreements.

Our data analysis systematically evaluated cardiovascular (CV) risk prediction models by first identifying frequently reported tools from SRs. We then critically examined their predictive accuracy and potential health benefits within the European and Austrian context, with a specific focus on practical implementation aspects such as required parameters and additional resource needs.

**Selektion und
Qualitätsbewertung
der Studien und
Leitliniendokumente
nach 4-Augen-Prinzip**

Guidelines

For the guideline search, we conducted a manual search following the same methodological steps used for SRs. Literature selection, quality assessment, and data extraction were performed using the dual control principle, ensuring systematic and thorough evaluation of the guidelines.

3.4 Quality assessment

Methodological quality was carefully evaluated using established, specialised tools:

- ROBIS (Risk of Bias in Systematic Reviews) for SRs [84]
- PROBAST (Prediction Model Risk of Bias Assessment Tool) for validation studies [85]
- AGREE-II (Appraisal of Guidelines for Research & Evaluation) for clinical practice guidelines [86]. Following the IQWiG methods for guideline synopses [87], the assessment was restricted to three of the six AGREE II domains:
 - Domain 2: Stakeholder Involvement,
 - Domain 3: Rigour of Development
 - Domain 6: Editorial Independence.

Two authors (LG and JP or LG and DG) independently assessed each study's quality, with any discrepancies resolved through collaborative discussion or consultation with a third reviewer (VH).

Because we incorporated data from primary studies (PSs) cited within the SRs, we considered it important to report the respective RoB assessments. This information was added where relevant in the Score statistic extraction table. More detailed information on the RoB of the PSs is provided in Table 4-3 (RoB assessment method) and in the Appendix.

**Qualitätsbewertung:
ROBIS (SRs), PROBAST (VS)
und AGREE-II (Leitlinien)**

**Berücksichtigung
der RoB Bewertung der
Primärstudien in den SRs**

3.5 Study selection

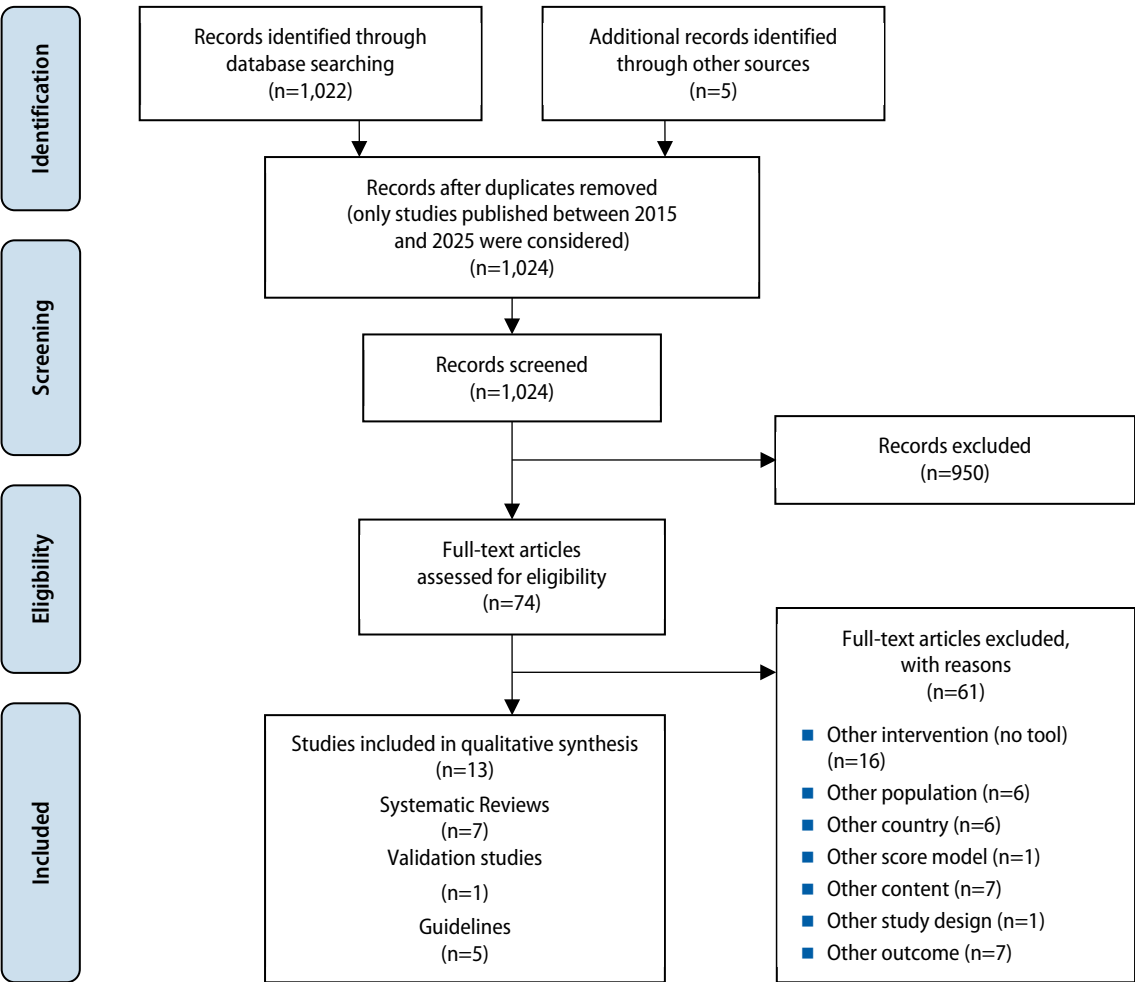


Figure 3-1: Presentation of the selection process (PRISMA flow diagram)

3.6 Data extraction and synthesis

To manage the extensive landscape of CV risk prediction scores, we applied stringent selection criteria focusing on model currency, Western European applicability, alignment with guideline recommendations, and practical parameter availability. Given the aggregated nature of SRs, we supplemented review-level information with data from primary studies (PSs) reported within the included reviews (including supplementary materials), to provide a comprehensive evidence synthesis.

Data extraction was performed using carefully designed pre-structured tables (see Appendix). One author (LG) initially extracted the data, with independent verification by a second author (JP/DG). A third author (VH) was consulted in cases of uncertainty or ambiguity. Results were summarised through a narrative synthesis and supplemented with tables and graphs.

**strenge Auswahl nach
Relevanz und strukturierte
Datensynthese von
CV-Risikoscores**

4 Results

4.1 Systematic reviews and validation study

We identified seven systematic reviews (SRs) and one validation study (VS).

4.1.1 Risk of bias and study characteristics

We identified four SRs as “Low Risk,” two as “High Risk”, and one as “unclear” (Table 4-1 and Figure 4-1)

**RoB Bewertung
der SRs**

Table 4-1: Risk of Bias Overview SR

Review ID [Reference]	Phase 2				Phase 3
	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias in the review
Karmali et al 2017	☺	☺	☺	☺	☺
Colaco et al 2020	☹ ^a	? ^b	? ^c	☹ ^d	☹ ^e
Studziński, et al. 2019	☺	☺	☺	☺	☺
Damen et al. 2019	☺	? ^f	☺	☺	☺
Lucaroni et al. 2019	☹ ^g	? ^h	☺	☺	☹ ^e
Erqou et al. 2025	☺	? ⁱ	? ^{c,j}	☺	? ^e
Buchan et al. 2021	☺	☺	? ^k	☺	☺

Legend: ☺ = low risk; ☹ = high risk; ? = unclear risk

Rationale:

^a Pre-registration is not mentioned, and the protocol is not available; eligibility criteria and outcome measures are not specified.

^b no additional literature search and unjustified language/date restrictions, but extensive systematic search, dual reviewers, and detailed search strategy provided methodological rigour

^c No information about how many reviewers did the Risk of Bias assessment

^d Absence of protocol; synthesis not explained

^e Concerns of the review were not addressed in the interpretation of findings

^f Abstract screening was only performed by one reviewer

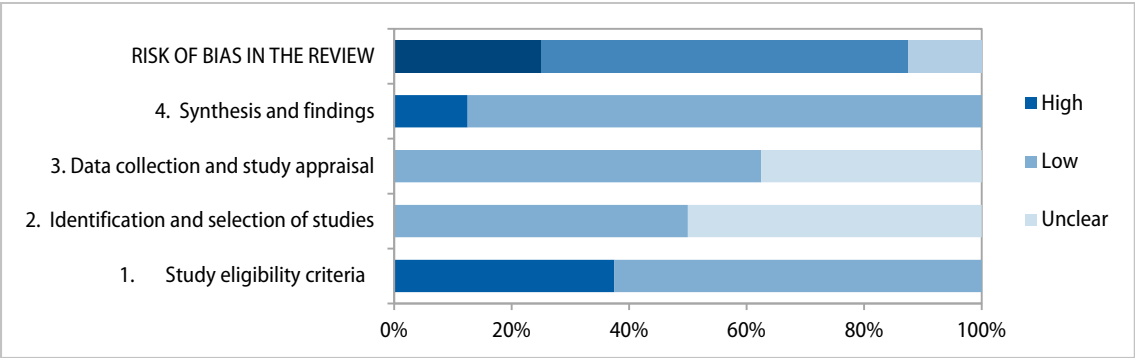
^g Only publications with available abstracts

^h No search of EMBASE; no specific information on full text screening

ⁱ No information about the whole screening process

^j No specific information about the whole data extraction process.

^k Missing information on the data extraction process regarding number of reviewers



Darker colours indicate overall ROB rating; lighter colours concern judgments

Figure 4-1: Risk of Bias chart SR

The VS was assessed using the PROBAST (Prediction Model Risk of Bias Assessment Tool). A low risk of bias was identified across all four evaluation domains – participants, predictors, outcome, and analysis. However, regarding the overall applicability of the study, the transferability was rated as unclear (see Table 4-2).

**RoB Bewertung
der VS**

Table 4-2: RoB VS: PROBAST

Review	Domain 1: Participants		Domain 2: Predictors		Domain 3: Overall		Domain 4: Analysis	Overall	
	RJ	AJ	RJ	AJ	RJ	AJ	RJ	RJ	AJ
Zhang et al 2024	Low	Low	Unclear	Low	Low	Low	Low	Unclear	Low

Abbreviations: AJ ... applicability judgement; RJ ... Risk of Bias judgement; RoB ... Risk of Bias; VS ... validation study; PROBAST ... Prediction study Risk Of Bias Assessment Tool

Our data extraction is based on seven systematic reviews (SRs) published between 2017 and 2025: one umbrella review, one review of reviews, three with meta-analyses and two narrative reviews. The SRs were predominantly based on observational cohort studies evaluating cardiovascular (CV) risk prediction models and their internal or external validation. One review (Cochrane) focused on the effect of using CVD risk models on clinical outcomes rather than model accuracy and included RCTs. The studies primarily originate from well-developed healthcare systems in North America and Europe, particularly the United States (US), Canada, the Netherlands, Poland, and Italy, with additional contributions from China and the United Kingdom, reflecting international collaboration in this field (see Table 4-3).

**Grundlage der
Datenerhebung:
7 systematische Reviews
zu CV-Risikomodellen und
eine Validierungsstudie
(2017-2025)**

The reviews cover a broad range of topics: from general primary prevention in the population to the evaluation of risk scores commonly used in the USA and Europe to specialised applications for specific patient groups, such as patients with type 1 diabetes (T1DM) and type 2 diabetes (T2DM), and inflammatory rheumatic diseases, who are particularly susceptible to cardiovascular disease (CVD). Notably, none of the reviews identified head-to-head comparison trials between risk scores.

**Reviews untersuchten
allgemeine und
spezialisierte Risikoscores
ohne direkte
Vergleichsstudien**

Table 4-3: SR characteristics

Author, year [Reference]	Country	Included study designs (number)	Population of the included studies	Types of intervention	RoB assessment method
Karmali et al. 2017 [88]	N.A	41 RCTs	adults (≥ 18 years) in outpatient settings free of clinical CVD. Participants with diabetes mellitus or elevated risk factors, as well as those already on background preventive medications, were eligible for inclusion.	systematic provision of a multivariable CVD risk score by a clinician, healthcare professional, or healthcare system versus usual care in primary CVD prevention	criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions
Colaco et al. 2020 [89]	Canada	11 cohort studies	Patients with rheumatoid arthritis, systemic lupus erythematosus, psoriatic arthritis	N.A	Newcastle-Ottawa Scale
Studziński et al. 2019 [90]	Poland	10 SRs (66 unique PSs)	adult participants (≥ 19 years) and free of clinical CVD	CVD risk assessment with use of total risk assessment (TRA)	AMSTAR
Damen et al. 2019 [91]	Netherlands	38 studies (112 external validations)	Adult participants free of clinical CVD	N.A	CHARMS checklist and preliminary version of Cochrane PROBAST
Lucaroni et al. 2019 [92]	Italy	16 SRs (8 on diabetes, 6 on CVDs, 2 on hypertension)	aged 18-65 with no major illness	Comparison of different risk prediction models	e ROBIS tool, AMSTAR tool
Erqou et al. 2025 [93]	USA, UK	11 observational studies	Individuals with T1DM	comparison of different CVD risk prediction models	TRIPOD checklist, Newcastle-Ottawa Quality Assessment Scale
Buchan et al. 2021 [94]	Canada	15 observational studies	adults with T2DM	N.A	PROBAST

Abbreviations: AMSTAR ... A Measurement Tool to Assess systematic Reviews; CVD ... cardiovascular disease; e- ROBIS ... Risk Of Bias In Systematic reviews; N.A ... not available; PROBAST ... Prediction Model Risk of Bias Assessment Tool; PSs ... Primary studies RCT ... randomised controlled trials; SRs ... systematic reviews; T1DM ... type 1 diabetes; T2DM ... type 2 diabetes; UK ... United Kingdom; USA ... United States of America

The additionally identified validation study was conducted in China and examined the performance of various CV risk scores for T2DM.

Table 4-4: Validation Study characteristics

Author, year [Reference]	Country	Included study designs (number)	Population of the included studies	Sample size	RoB assessment method
Zhang et al. 2024 [95]	China, Hong Kong	7 models consisted of 17 unique risk equations	Adults with T2DM	23,685 adults	PROBAST

Abbreviations: PROBAST ... Prediction Model Risk of Bias Assessment Tool; T2DM ... type 2 diabetes

4.1.2 Research question 1: Performance of risk prediction models

The aim of research question 1 was the comparison of Cardiovascular Risk Prediction Models in terms of evidence, predictive validity, benefit–harm balance, and implementability within the Austrian preventive medical check-up (PMCU).

Across the included SRs, reporting formats varied widely. Because most reviews evaluated a broad range of risk scores, data specific to the models of interest for this report were often fragmented or located in appendices. As a result, we extracted and synthesised the information as presented in the SRs, which in some cases included pooled estimates, and in others only individual study-level findings or descriptive summaries.

Discrimination was consistently reported using the C-statistic, although the level of detail varied across reviews. Calibration was reported less consistently and with substantial methodological heterogeneity, including ratio of observed to expected events (O:E ratio), Hosmer-Lemeshow tests (L-H), calibration slopes, and graphical plots. For the risk of bias (RoB) of the primary studies (PSs), we relied on the assessments provided within the SRs rather than conducting new evaluations.

Risk scores in general populations

Overall, only one SR [91] evaluated examined CV risk scores in the general population, considering their applicability, predictive accuracy, and benefit–harm balance across models.

Framingham models (FRS)

A total of 15 PSs published between 2001 and 2014 evaluated the Wilson FRS, assessing both the total cholesterol and LDL cholesterol versions. Cohort sizes range from fewer than 1,000 [96] to over 250,000 [97]. Most were conducted in the USA (8 studies), followed by Spain (2 studies) and one study each from Italy, France, South Korea, Czechia, the United Kingdom (UK), and Japan. Most studies used the Wilson version of the FRS, which included total cholesterol, while one study [98] tested the LDL cholesterol variant. All studies validated the FRS score for the prediction of fatal or non-fatal coronary heart disease (CHD) and examined both gender-specific and combined versions of the model. Follow-up times were not reported.

RoB assessments indicated concerns in most cases, with 13 rated as high risk and two at of unclear risk.

Discriminatory performance showed variation among studies. In male populations, C-statistic values ranged from 0.58 [99] to 0.75 [100], with most values falling within the range of 0.63 to 0.72. The pooled performance for male populations yielded a C-statistic of 0.68 with a 95% confidence interval (CI) of 0.66–0.69, indicating moderate discriminatory ability of the model. The C-statistics for the female population ranged from 0.58 [99] to 0.83 [100], but no pooled estimate was available. In general, C-statistics were similar or higher in women compared with men.

**Daten heterogen,
uneinheitliche
Ergebnisberichte**

**C-Statistik konsistent,
Kalibrierung seltener und
methodisch heterogen
berichtet.**

**1 SR zu
CV-Risikomodellen in der
Allgemeinbevölkerung**

**15 Primärstudien
(2001–2014) zur
Validierung von
Wilson-FRS**

überwiegend hohes RoB

**moderate Diskriminierung,
tendenziell höher bei
Frauen**

Calibration, measured by the O:E ratio, showed evidence of systematic over- or underestimation of risk in different populations. European cohorts consistently indicated overestimation of risk, with ratios of 0.37 in Italy [101], 0.22 in Czechia [102], and 0.40-0.67 in Spain [103, 104]. In contrast, some US studies showed O:E ratios above 1.0, such as Rodondi with values of 1.08 for men and 2.05 for women, indicating an underestimation of risk [99]. Calibration results also differed by sex within some cohorts. In Spain, Buitrago reported O:E ratios of 0.42 in women compared with 0.67 in men, and Empana reported 0.42 in women versus 0.76 in men [98, 104]. In contrast, in the USA, Rodondi found O:E ratios of 2.05 in women and 1.08 in men, and Vaidya reported 1.14 in women compared with 1.70 in men [96, 99].

The pooled O:E ratio for men was 0.58 with a wide prediction interval of 0.19-1.77, indicating heterogeneity of calibration across populations. For women, no pooled O:E ratio was available.

Pooled Cohort Equations (PCE)

16 PSs published between 2014 and 2017 validated the PCE across external populations. Sample sizes ranged from 922 participants [105] to 192,605 participants [106]. Studies were conducted across 13 different countries and regions, including the US, Germany, Malaysia, South Korea, the Netherlands, Iran, China, Denmark, and others. All studies validated the PCE for predicting fatal or non-fatal CVD and examined both gender-specific and combined versions of the model. Follow-up times were not reported.

RoB assessments indicated concerns in most cases, with 13 studies rated as high risk, one as unclear risk [107], and one receiving a mixed rating [108].

Discriminatory performance showed variation among studies. In male populations, C-statistic values ranged from 0.55 [105] to 0.77 in Chinese cohorts [109], with most American studies reporting values within the moderate range of 0.63 to 0.72. The pooled performance for male populations yielded a C-statistic of 0.70 (95% CI of 0.68-0.72), indicating moderate discriminatory ability of the model. The C-statistics for the female population ranged from 0.61 [105] to 0.82 [110], with the pooled estimate showing a C-statistic of 0.74 (95% CI: 0.72-0.76).

Calibration, measured by O:E ratio, showed over- or underestimation of risk in different populations. Most American studies consistently indicated overestimation of risk, with ratios between 0.41 and 0.84. German studies [108] reported O:E ratios between 0.62 and 0.70, also indicating overestimation. In contrast, some Chinese cohorts showed O:E ratios above 1.0, with values between 1.10 and 1.44, indicating underestimation of risk.

The pooled O:E ratio for men was 0.66 (95% CI of 0.59-0.73). For women, the pooled O:E ratio was 0.76 (95% CI: 0.65-0.88).

Framingham Adult Treatment Panel III (FRS ATP III)

Four PSs published between 2005 and 2014 evaluated the FRS ATP III. Cohort sizes ranged from 3,407 participants [107] to 9,249 participants [111]. Most were conducted in the Netherlands (two studies) followed by the USA and the UK. All studies validated the FRS score for the prediction of fatal or non-fatal CHD and examined both gender-specific and combined versions of the model. Follow up times were not reported.

RoB assessment indicated lack of information as three were reported with unclear risk and one with high risk.

Kalibrierung:
Überschätzung
in europäischen,
Unterschätzung
in US-Populationen;
geschlechtsspezifische
Unterschiede

16 Primärstudien
(2014-2017) zur externen
Validierung von PCE

überwiegend hohes
Verzerrungsrisiko (RoB)

moderate Diskriminierung,
tendenziell höher bei
Frauen
gepoolte C-Statistik
(M: 0,7, F: 0,74)

Kalibrierung:
Überschätzung des
Risikos in westlichen,
Unterschätzung in
chinesischen Populationen
und bei Männern > Frauen

4 Primärstudien
(2005-2014) zur
Validierung des FRS ATP III

begrenzte RoB-Daten:
3 unklar, 1 hohes Risiko

Discriminatory performance showed moderate variation among studies. In male populations, C-statistic values ranged from 0.60 [111] to 0.71 [112]. The pooled performance for male populations yielded a C-statistic of 0.64 9(95% CI: 0.59-0.68), indicating moderate discriminatory ability of the model. The C-statistics for the female population consistently showed higher values, with the highest value reported at 0.69 [107]. The pooled C-statistic for women was 0.66 (95% CI: 0.65-0.67).

**moderate Diskriminierung,
bessere Werte bei Frauen**

Calibration, measured by the O:E ratio, showed systematic overestimation of risk across all studied populations, with all reported values below 1.0. Among men, O:E ratios ranged from 0.39 [112] to 0.47 [113], and the pooled estimate was 0.58 (95% CI: 0.37-0.79; prediction interval: 0.16-2.13). For women, O:E ratios ranged from 0.57 [107] to 0.69 [112], with a pooled estimate of 0.79 (95% CI: 0.60-0.97).

**Kalibrierung:
systematische
Überschätzung des Risikos,
Männer > Frauen**

Risk scores in disease-specific populations

Inflammatory Rheumatic Diseases

Overall, one SR [89] examined the applicability/statistical accuracy of cardiac scores in patients with Inflammatory Rheumatic Diseases/Rheumatoid Arthritis (RA).

**1 SR zu kardiologischen
Scores bei rheumatischen
Erkrankungen**

Framingham models

A total of eight PSs, published between 2012 and 2018, evaluated the Framingham Risk Score in RA populations. Cohort sizes ranged from 118 participants [114] to 12,747 participants [115]. Studies were conducted across various countries including Western Europe (UK, NL, CH, IT), the USA and Canada, as well as two multinational studies. All studies validated the FRS for the prediction of myocardial infarctions (MI), strokes, CHD and CV-related deaths. One study [114] examined various extensions of the original score. Follow-up periods ranged from 5.8 years [116] to 9 years [114], with some studies not providing precise time frames.

**8 Primärstudien
(2012-2018) zur
Validierung von FRS
bei RA-Patient:innen**

RoB assessments showed mixed results, with one study rated as low risk, five as moderate risk, and two as high risk.

**gemischte RoB-Bewertung:
1 niedrig, 5 moderat, 2 hoch**

Discriminatory performance varied, with C-statistic values ranging from 0.50 (FRS intermediate risk) to 0.81 (FRS + anti-apoA-I), mostly in the moderate range. No pooled estimates or gender specific data were available.

**C-Statistik 0,50-0,81;
überwiegend moderate
Diskriminierung**

Calibration consistently revealed systematic underestimation of CV risk. The Framingham Risk Score (FRS) tends to underestimate CV risk across RA populations. Urowitz demonstrated that applying a multiplication factor of 2 increased sensitivity from 13.0% to 31.5% but reduced specificity from 98.2% to 80.9%, highlighting the trade-off between risk detection and classification precision [117]. Several studies evaluated the impact of additional biomarkers on model performance. The addition of extra biomarkers such as C-reactive protein (CRP), multipliers, or other laboratory parameters did not lead to improvement in the predictive performance of the FRS.

**Kalibrierung:
systematische
Risikounterschätzung**

The SR concludes that the FRS systematically underestimates CV risk, with discriminatory ability varying across populations, in patients with RA. Furthermore, there are varying results due to differences in model assessment. Some studies found no improvement with additional markers (MACE or CRP), others showed slight changes in risk evaluation (Application of a multiplication factor of 2 lead to the FRS more accurately). Differences in predictive accuracy among different risk groups were particularly notable.

**Zusatzmarker
ohne klaren Mehrwert**

SCORE models

A total of four PSs validated the SCORE model in RA populations. Cohort sizes ranged from 155 participants [118] to 5,638 participants [116]. Studies were conducted across the Netherlands, the UK, Italy, and multinational settings (UK, N, NL, USA, S; GR; ZA, E, CDN, MEX)¹. Studies evaluated the SCORE model for prediction of CV outcomes, with one study [119] restricting endpoints to nonfatal events only, while others used composite outcomes including both fatal and nonfatal CVD encompassing acute coronary syndromes (ACS, unstable angina (UA), MI), chronic ischemic heart disease, coronary revascularization, cerebrovascular events (stroke, transient ischemic attack (TIA)), peripheral vascular disease (PVD), and heart failure (HF). Model variants included the recalibrated SCORE model and the adapted SCORE model, with one study incorporating EULAR modifications [118]. Follow-up time was reported at 5.8 years in one study only [116].

RoB assessment classified one study as high risk, while the remaining three were judged to be of moderate risk.

Predictive ability was consistently reported using the C-statistic, while calibration was not formally assessed; conclusions regarding under- or overestimation were based on comparisons between predicted and observed incidence rates. No gender specific data was available.

Discriminatory performance showed variation among studies. C-statistic values ranged from 0.70 to 0.80, with most studies reporting values around 0.78, indicating moderate discriminatory ability of the model. Variants, such as the recalibrated SCORE model (0.78) and the adapted SCORE model, demonstrated minimal differences in performance. A modified version incorporating EULAR did not significantly alter the C-statistic [118].

Calibration revealed systematic underestimation of CV risk in most cohorts. The Arts study was an exception, showing risk overestimation in low and moderate risk groups both in the original score and the modifications [119].

In summary, the authors conclude that the SCORE model tends to underestimate cardiovascular risk in low- and moderate-risk groups while overestimating it in high-risk groups. Adapted versions of SCORE did not improve overall risk estimation.

QRISK

A total of five PSs published between 2015 and 2018 validated QRISK2 in RA populations. Sample sizes ranged from 155 participants [118] to 12,747 participants [115]. Studies were conducted in the UK, the Netherlands, Italy, Sweden, and two multinational studies (UK, N, NL, USA, S; GR; ZA, E, CDN, MEX)². All studies validated QRISK2 for prediction of composite CV endpoints, including nonfatal events such as MI, UA or other ACS, ischemic stroke, TIA, and PVD, with some also incorporating CV mortality, coronary revascularisation, and HF. Some studies tested QRISK2 with the addition of CRP and the EULAR multiplier. Follow-up periods ranged from 5.8 [116] to 6.9 [120] years, although several studies did not report follow-up duration.

RoB assessments indicated three studies as moderate risk and two as high risk.

4 Primärstudien zur Validierung des SCORE-Modells bei RA-Patient:innen

RoB:
1 hoch, 3 moderat

moderate Diskriminierung (C-Statistik $\approx$ 0,78); Varianten ohne Mehrwert

Kalibrierung: überwiegend Unterschätzung des CV-Risikos

SCORE unterschätzt Risiko bei niedrigen/mittleren und überschätzt bei Hochrisikogruppen

5 Primärstudien (2015-2018) zur Validierung von QRISK2 bei RA-Patient:innen

RoB-Bewertung:
3 moderat, 2 hoch

¹ United Kingdom, Norway, Netherlands, United States of America, Sweden, Greece, South Africa, Spain, Canada Mexico

Discrimination was reported consistently with C-statistic values ranging from 0.72 to 0.87, indicating moderate to good performance overall.

Alemao reported C-statistics of 0.76 and 0.77 with the addition of CRP for MI, CHD, stroke, and TIA [115]. Arts reported a C-statistic of 0.79 for a broad composite including ACS, angina, CVA, TIA, PVD and HF [119]. Crowson analysed broad CV events in two cohorts, both reporting C-statistics of 0.72 [116, 120]. Navarini achieved the highest discrimination with a C-statistic of 0.87 for CV death, CAD, CVA, TIA, PAD and HF. No gender specific data was available [118].

Calibration was rarely reported formally, with most studies judging over- or underestimation by comparing predicted and observed incidence rates. Calibration results were inconsistent across studies. Alemao and Navarini reported that QRISK2 underestimated CV risk, whereas Arts (2015) and both Crowson studies found overestimation of risk [115, 116, 118-120].

A consistent finding was lower QRISK2 discrimination in RA populations compared to the general population. CRP addition did not significantly improve risk classification, and RA-specific calculators performed no better than traditional scores like PCE or FRS. The EULAR multiplier failed to improve discrimination or calibration.

PCE & FRS ATP III

Two PSs [116, 120] comprising two cohorts validated the PCE and FRS-ATP models. Cohort sizes ranged from 1,796 to 5,638 participants. The studies were conducted in multinational settings (UK, N, NL, USA, S; GR; ZA, E, CDN, MEX). All studies validated the models for prediction of composite CV outcomes including ACS, chronic ischaemic heart disease, coronary revascularisation, coronary death, other CV death, cerebrovascular events, and PVD. Follow-up periods ranged from 5.8 to 6.9 years.

All studies were rated as high risk of bias.

Discriminatory performance showed variation between cohorts and models. In the larger cohort (5,638 participants), PCE reported a C-statistic of 0.72 for a broad composite including ACS, chronic ischaemic heart disease, coronary revascularisation, coronary death, other CV death, cerebrovascular events, and PVD. In the smaller cohort (1,796 participants) restricted to MI, ischemic stroke and CV death, C-statistics were 0.75 for FRS-ATP and 0.72 for PCE. Neither model showed improved discrimination after application of the EULAR multiplier. No gender specific data was available [116, 120].

Calibration was not formally assessed but judged indirectly through comparing predicted and observed incidence rates. Results for PCE were inconsistent, with one study reporting underestimation of risk and another overestimation. FRS-ATP underestimated risk in the highest risk groups.

Overall, the authors concluded that FRS-ATP III underestimated risk in the highest-risk groups, while the PCE both underestimated and overestimated risk depending on the group.

Diabetes

Overall, two SRs [93, 94] and one VS [95] examined the applicability/ statistical accuracy of the scores to Diabetes patients. Gender-specific discrimination and calibration data for diabetes-specific scores are omitted due to space limitations; detailed information is provided in the appendix.

**moderate bis gute
Diskriminierung
(C-Statistik 0,72-0,87)**

**Kalibrierung:
widersprüchliche
Ergebnisse mit Über- und
Unterschätzung des
CV-Risikos**

**konsistent schlechtere
Diskriminierung von
QRISK2 bei RA**

**2 Primärstudien zur
Validierung von PCE
und FRS-ATP III bei RA**

hohes RoB

**moderate Diskriminierung
(C-Statistik 0,72-0,75)**

**Kalibrierung:
PCE variabel,
FRS-ATP unterschätzt
Risiko bei
Hochrisikogruppen**

**Bewertung von
CV-Risikoscores bei
Diabetes in 2 SRs, 1 VS**

T1DM

UKPDS models

A total of four PSs published between 2005 and 2017 validated the UKPDS risk engine in T1DM populations. Sample sizes ranged from 84 participants [121] to 4,306 participants [122]. Studies were conducted in Western European countries and the USA and validated the UKPDS models for prediction of CV outcomes including fatal CHD, nonfatal MI, silent MI, CHD, cerebrovascular disease, PVD, and HF. Follow-up periods ranged from 6.6 [122] to 11.2 [123] years.

RoB assessments indicated that two studies were judged to have a moderate risk of bias while the remaining two were rated as lower risk.

Discriminatory performance showed variation across studies, with C-statistics ranging from 0.56 to 0.77. Zgibor reported a C-statistic of 0.76 for fatal CHD and nonfatal MI [123]. Llauradó found lower discrimination (C = 0.56) for silent MI. Vistisen reported C-statistics of 0.77 and 0.74 in two cohorts for a broad composite of CV outcomes [121].

Calibration was consistently poor when reported. Zgibor found systematic overestimation (O:E > 1; H-L $\chi^2 = 324.1$, $p < 0.0001$), and Vistisen reported miscalibration in both cohorts (H-L $p < 0.001$) [122, 123]. The SR concluded that the UKPDS Risk Engines were poorly calibrated for T1DM and made recommendations against using scores developed for T2DM or the general population.

FRS

Two PSs, published between 2006 and 2017, validated CV risk models in T1DM populations. Sample sizes ranged from 84 participants [121] to 573 participants [123]. Studies were conducted in Spain and the USA and validated the models for prediction of silent MI via perfusion stress and fatal CHD, nonfatal MI/Q waves. Follow-up period was 11.2 years [123]. RoB was rated 4/7 in a modified Newcastle-Ottawa Scale ranking.²

Zgibor reported sex-specific C-statistics of 0.77 in men and 0.87 in women, indicating acceptable to good discrimination, while Llauradó reported a more modest C-statistic of 0.69 for silent MI [121, 123]. Calibration was only reported in Zgibor, showing poor model fit with H-L values of 310.3 ($p < 0.0001$) for men and 6,873.9 ($p < 0.0001$) for women. No calibration was reported for the other study [123].

QRISK

QRISK3 was applied in a T1DM population by one PSs [124] published in 2021. The study comprised 60,710 participants from the UK and Sweden and validated QRISK3 for prediction of a broad CV composite excluding death (MI, stroke, UA, TIA, PVD, CAD, CVD, PAD, ACS). Follow-up period was 10 years. RoB was rated 6/7 in a modified Newcastle-Ottawa Scale ranking².

The study demonstrated a C-statistic of 0.75 for the combined CV composite. Calibration was assessed using the O:E ratio, which was 0.72, indicating overestimation of CV risk.

Typ 1 DM

4 Primärstudien (2005-2017) zur Validierung von UKPDS Risk Engine bei T1DM

**RoB-Bewertung:
2 moderat, 2 niedrig**

**Diskriminierung
niedrig bis moderat
(C-Statistik 0,56-0,77)**

**Kalibrierung konsequent
unzureichend;
UKPDS überschätzt**

2 Primärstudien (2006 & 2017) zur Validierung von FRS bei T1DM

RoB moderat

**geschlechtsspezifische
Diskriminierung
unterschiedlich,
Frauen > Männer**

**Kalibrierung schwach
oder nicht berichtet**

**1 Primärstudie (2021)
zur Validierung des QRISK3
bei T1DM**

ROB: niedrig

**Moderate Diskriminierung
(C=0,75) und Risiko-
überschätzung (O:E: 0,72)**

² No information in the SR about the risk classifications (low, moderate, high) – just the sum and the total score

T2DM

UKPDS models

A total of eleven PSs published between 2009 and 2024 validated the UKPDS risk engine in T2DM populations. Sample sizes ranged from 125 [125] to 79,946 participants [126]. Studies were conducted across various geographical regions including Western European countries, Asian countries, Australia, and the USA and validated the UKPDS Outcome Model 1 and 2 for prediction of CV mortality, stroke, MI, all-cause mortality, HF, and ischaemic heart disease. Follow-up periods ranged from 4.2 [126] to 12 [95] years.

RoB assessments were heterogeneous with some studies classified as high risk, low risk, or receiving endpoint-specific risk ratings ranging from high to low.

Discriminatory performance showed considerable variation across endpoints. C-statistics for CV mortality ranged from 0.64 [127, 128] to 0.72 [125], between 0.57 and 0.86 for stroke, and 0.57 [127, 128] to 0.86 [129] for MI. Zhang (2024) reported additional endpoints including all-cause mortality (0.67) and HF (0.58) [95]. Model performance showed minimal sex differences, with slightly better performance observed in younger age groups (40-59 years) and among non-white ethnicities.

Pooled results showed UKPDS Model 1 achieved a C-statistic of 0.70 (95% CI 0.58-0.81) for CV mortality and 0.70 (95% CI 0.66-0.74) for stroke, but overestimated risk. UKPDS Model 2 showed lower C-statistics of 0.68 (95% CI 0.61-0.75) for CV mortality, 0.60 (95% CI 0.50-0.61) for stroke, and 0.64 (95% CI 0.58-0.70) for MI.

Numerical calibration data were largely not reported in detail in the SRs. The studies included used variable and often inconsistent approaches to calibration, which limited direct comparison across validation cohorts. As formal calibration statistics were frequently absent, the SR authors relied on visual inspection of calibration plots where available and provided descriptive summaries rather than numerical estimates. Calibration of the UKPDS Outcomes Models 1 and 2 tended to overestimate risk – particularly for CV mortality, stroke, and MI – though Model 2 appeared better calibrated for CV mortality in low-risk patients. Zhang reported calibration slopes ranging from 0.268 to 0.690, with all values below 1.0., with good calibration for CV mortality in low-risk patients but overestimation in high-risk patients[95].

RECODE model

A total of four studies (three PSs and one validation study) published between 2017 and 2024 validated RECODE in T2DM populations. Sample sizes ranged from 1,082 [130] to 9,635 participants [54]. Studies were conducted in the US, Italy, and the UK and validated RECODE for prediction of all-cause mortality, CV mortality, MI, stroke, and HF across different cohorts and outcomes. Follow-up periods ranged from 4.7 (ACCORD cohort) to 10.6 years (Look AHEAD cohort) [54]. RoB assessments were outcome-specific, with most outcomes (12) rated as low risk and four as high risk.

Discriminatory performance showed variation among studies and outcomes. C-statistics for all-cause mortality ranged from 0.67 [95] to 0.81 [131], for CV mortality from 0.74 to 0.87, for MI from 0.67 to 0.74, and for stroke from 0.65 to 0.75. The pooled performance yielded C-statistics of 0.75 (95% CI 0.70-0.80) for all-cause mortality, 0.79 (95% CI 0.75-0.84) for CV mortality, 0.72 (95% CI 0.69-0.74) for MI, and 0.71 (95% CI 0.68-0.74) for stroke, indicating moderate

Typ 2 DM

11 Primärstudien (2009-2024) zur Validierung von UKPDS bei T2DM

RoB: unterschiedlich nach Outcome

moderate bis gute Diskriminierung (je nach Endpunkt: 0,57-0,86)

gepoolte Statistik: Model 2 schlechtere Diskriminierung als Model 1

Kalibrierung nicht im Detail berichtet

UKPDS Modelle überschätzen Risiko

bessere Kalibrierung bei Niedrigrisikopatient:innen

3 Primärstudien & 1 VS (2017-2024) zur Validierung von RECODE bei T2DM

RoB: 12 niedrig, 4 hoch

Diskriminierung moderat bis gut (0,67-0,87) je nach Endpunkt

to good discriminatory ability of the model. Zhang reported similar performance across sexes, with slightly better performance in younger patients [95].

Calibration was assessed using calibration plots in most studies, with results varying across outcomes. RECODE demonstrated perfect calibration in low-risk patients for all-cause mortality, CV mortality, and MI, while stroke tended to be underestimated. Zhang reported that RECODE showed the best calibration performance across all comparable outcomes (CV mortality, HF, MI, stroke), except for all-cause mortality [95].

Overall, the SR authors concluded that this data indicates that RECODE demonstrates moderate to good discriminatory performance across various CV outcomes in T2DM populations, with generally good calibration, particularly in low-risk patients, though stroke risk tends to be underestimated.

FRS

Four PSs and one VS published between 2009 and 2024 evaluated CV risk models in T2DM populations. Sample sizes ranged from 125 [125] to 18,160 participants [95]. Studies were conducted in the USA, UK, and the Netherlands and validated the models for prediction of CV mortality, congestive HF, and stroke. Follow-up periods ranged from 4 years [95] to 10.4 years [132]. All were judged to be at high risk of bias.

Discrimination for CV mortality was assessed in three studies, with C-statistics ranging from 0.61 [125] to 0.76 [132]; the pooled estimate was 0.73 (95% CI 0.67-0.78). Zhang additionally reported discrimination for HF (0.62) and stroke (0.63) [95].

Calibration analyses suggested that the model underestimated risk in low-risk patients and may have overestimated it in high-risk patients. Zhang reported calibration slopes of 0.839 for HF and 0.288 for stroke [95].

SCORE

A total of two PSs and one VS published between 2007 and 2024 validated CV risk models in T2DM populations. Sample sizes ranged from 125 participants [125] to 20,527 participants [95]. Studies were conducted in the United Kingdom and the Netherlands and validated the models for prediction of CV mortality exclusively. Follow-up periods ranged from 10 [95, 125] to 10.4 years [132]. RoB assessments indicated high risk of bias for both PSs.

Discriminatory performance showed a wide variation, with C-statistics ranging from 0.63 [95] to 0.77 [132]. The pooled effect yielded a C-statistic of 0.77 (95% CI 0.76-0.78). Zhang reported negligible sex-specific differences with C-statistics of 0.61 for women and 0.60 for men, and slightly better model performance in younger age groups and non-white ethnicities [95].

Calibration was only reported in Zhang, who reported a slope of 0.331, indicating poor calibration with overprediction of observed risk [95].

A comprehensive list of statistical results and study characteristics of all scores above is provided in the Appendix.

Implementability

Beyond statistical accuracy, the implementability of risk prediction models is crucial for their potential use in Austrian preventive healthcare. Therefore, this section will identify the implementation prerequisites from the SRs and validation studies.

Kalibrierung variabel je Endpunkt

perfekt kalibriert bei Niedrigrisiko für CV-Mortalität, Herzinfarkt und Gesamtmortalität

aber Schlaganfallrisiko unterschätzt

4 Primärstudien & 1 VS (2009-2024) zur Validierung von FRS bei T2DM

RoB: hoch

Diskriminierung niedrig bis moderat (0,61-0,76); gepoolte C-Statistik 0,73

Unterschätzung bei Niedrig-, Überschätzung bei Hoch-Risiko möglich

2 Primärstudien & 1 VS (2007-2024) zur Validierung von SCORE bei T2DM

RoB: hoch

Diskriminierung niedrig bis moderat (0,63 -0,77); gepoolte C-Statistik: 0,77

Risikoüberschätzung, schwache Kalibrierung

praktische Anwendbarkeit für Implementierung relevant

Table 4-5: Implementability

Author, Year	System requirements	Required resources	Acceptance by doctors and patients
Karmali et al. 2017 [88]	N.A	N.A	N.A
Colaco et al. 2020 [89]	N.A	N.A	N.A
Studziński et al. 2019 [90]	Funders and policymakers ought to be aware that spending resources on adopting TRA into practice may be against current evidence which is not strong.	N.A	N.A
Damen et al. 2019 [91]	N.A	N.A	although excessive risk estimates could stimulate patients to adopt a healthier lifestyle (similarly to patients with more risk factors), it could also cause unnecessary anxiety for future CV events
Lucaroni et al. 2019 [92]	risk models can be very important and should be regularly implemented in medical settings to support the activity of general practitioners and public health authorities involved in monitoring and evaluation of patients	N.A	N.A
Erqou et al. 2025[93]	score results have important clinical implications as the risk of CVD among T1DM is generally understated or overlooked. The findings of a good performance of the T1DM-specific risks score suggest that these models may be used to guide clinicians and health policy makers in assessing CVD risk in people with T1DM	N.A	N.A
Buchan et al. 2021 [94]	N.A	N.A	N.A
Zhang et al. 2024 [95]	Independent external validations of CVD risk prediction models are crucial to assess their applicability to support clinical decision-making and healthcare planning for people with T2DM	N.A	N.A

Abbreviations: BMI ... Body Mass Index; BP ... blood pressure; CRP:c-reactive protein; CV ... cardiovascular; CVD ... Cardiovascular disease; Hb1Ac ... hemoglobin A1c; LDL ... Low Density Lipoprotein; N.A ... not available; T1DM ... type 1 diabetes; T2DM ... type 2 diabetes; TRA ... total risk assessment

The synthesis on the implementability of risk models reveals a complex landscape in medical risk assessment. Data extraction shows a range of consistent predictors, including demographic factors such as age, gender, and ethnicity, as well as clinical parameters like blood pressure, cholesterol levels, and smoking status. More detailed models also include laboratory values, medication histories, and disease-specific markers, especially in specialised approaches like human immunodeficiency virus (HIV) risk models.

Key implementation aspects were seldom addressed in the SRs or their included PSs. Evidence about practical feasibility, resource requirements, and acceptance by physicians and patients was largely absent. Limited findings suggest that the possible psychological effects of risk assessments can either motivate or induce anxiety.

One review highlights that risk models are considered important, particularly for specific patient groups such as those with diabetes, but are often overlooked [93]. They could support clinicians and health policymakers in risk assessment, as CV risk is often underestimated in this group.

Some reviews suggest regularly integrating risk models into medical facilities to aid healthcare professionals in patient monitoring and assessment. Meanwhile, the need for further research is highlighted, especially to validate the models in various settings and to evaluate their overall feasibility for implementation.

komplexes Zusammenspiel zwischen Risikofaktoren und Gesundheit

Implementierungs-voraussetzungen kaum untersucht; psychologische Effekte wenig belegt

CV-Risiko bei Risikogruppen oft zu wenig beachtet

Integration von Risikomodellen in Praxis befürwortet, aber Valdierungs-Forschung erforderlich

4.1.3 Research question 2: Long-term outcomes

The aim of research question two was to evaluate the long-term benefits and changes in the health behaviour after assessing the CV risk.

Table 4-6: Long term benefits

Author, Year	Quality of-life	Health benefits	SR conclusion/recommendation for risk scores
Karmali et al. 2017 [88]	providing CVD risk scores may have little to no effect on medication adherence or health-related quality of life.	- providing CVD risk scores may reduce CVD risk factor levels by a small amount compared with usual care (total cholesterol, SBP, and multivariable CVD risk) - may increase prescriptions for new or intensified lipid-lowering medications, antihypertensive medications, and new aspirin therapy in higher-risk people, may increase healthier lifestyle	uncertainty about the optimal implementation of CVD risk scores in clinical practice to improve CV health outcomes. further research necessary
Colaco et al. 2020 [89]	N.A	N.A	further validation and recalibration of the ERS-RA to target populations is needed
Studziński et al. 2019 [90]	N.A in SR In PS: <i>adverse events physical:</i> health-related quality of life: no difference (n=1) <i>harmful specified:</i> decrease in the quality of life; adverse physical, psychological or social outcomes (n=2)	- impact of TRA on global CVD risk and individual risk factors is ambiguous; tendency towards slight reduction of BP, TC, and smoking levels, especially in high risk patients group, was observed. - TRA had no influence on lifestyle behaviour.	demonstration of benefits of using SCORE is still lacking no effect on fatal and non-fatal CV events compared with conventional care further research is still necessary
Damen et al. 2019 [91]	N.A	N.A	future studies should investigate reasons for overprediction and that guidelines offer advice how to make better use of existing models and subsequently tailor or recalibrate them
Lucaroni et al. 2019 [92]	N.A	- no evidence in the scientific literature for the evaluation of the effectiveness of RPMs on - long-term patient outcomes.	benefits could be further improved by supplementing existing models with information on lifestyle, personal habits and family history, social network relationships, income, education and employment history.
Erqou et al. 2025[93]	N.A	N.A	further studies are required that address whether implementing these models into clinical care improves the quality of care and delays or prevents CVD
Buchan et al. 2021 [94]	N.A	N.A	future studies that aim to develop novel risk models or validate existing models should apply robust analytical methods to mitigate these sources of bias.
Zhang et al. 2024 [95]	N.A	N.A	to account for cases where people with T2DM experience composite CVD events, future validation studies specifically on missing/not validated outcomes are recommended

Abbreviations: CV ... cardiovascular; CVD ... Cardiovascular disease; ERS-RA ... Expanded Risk Score in Rheumatoid Arthritis; N.A ... not available; PS ... primary study; RPMs ... risk prediction models; TRA ... Total risk assessment; T2DM ... type 2 diabetes

Evidence on health benefits and potential harms of CV risk scores was limited. None of the included SRs identified trials reporting direct patient-relevant outcomes such as CV morbidity and mortality. Karmali et al. (2017) found that provision of risk scores may have little to no effect on medication

**Langzeitergebnisse unklar;
gesundheitlicher Nutzen
für Patient:innen
größtenteils nicht belegt**

adherence or health-related quality of life [88]. They reported small reductions in total cholesterol, systolic blood pressure, and multivariable CV risk, alongside increased prescribing of lipid-lowering drugs, antihypertensives, and aspirin in higher-risk individuals, and some evidence for healthier lifestyle changes. Studziński et al. (2019) described ambiguous effects on global CVD risk and individual risk factors, with a slight reduction in blood pressure, cholesterol, and smoking in high-risk groups, but no overall influence on lifestyle behaviour [90]. They also noted one study showing no difference in health-related quality of life, while another reported a decrease due to adverse physical, psychological, or social outcomes. Lucaroni et al. (2019) concluded that there is no evidence in the scientific literature for the effectiveness of risk prediction models on long-term patient outcomes [92].

In summary, most SRs highlight limitations of current CV risk prediction models, including potential overprediction of risk, lack of clear evidence for improving fatal and non-fatal CV events, and insufficient validation across diverse populations. Few reviews identified studies demonstrating clear clinical benefits and emphasised the need for studies that demonstrate the actual clinical benefits of implementing these risk models.

**Überschätzung des Risikos,
begrenzte Evidenz für
klinischen Nutzen und
fehlende Validierung**

4.1.4 Research question 3: Applicability during medical check-ups

The objective of research question three was to evaluate which parameters relevant to CV risk assessment are already collected within the PMCU, to identify additional parameters required, and to assess the organisational, staffing, and time resources needed for integrating CV risk assessment.

Parameter

The analysis of risk scores (Table 1-3, Table 1-4) in relation to parameters currently collected during the PMCU (Table 1-1) shows which scores can readily be calculated without the need for the collection of additional medical parameters.

**Großteil der Risikomodelle
sind mit den erhobenen
Vorsorgeparametern
weitgehend kompatibel**

Some risk scores, such as PCE, SCORE2/SCORE-OP; PROCAM and the FRS models already largely correspond to the parameters collected in the preventive examination.

The UKPDS, a score explicitly developed for diabetes patients, requires some parameters not included in the PMCU assessment. However, these values are typically already collected in specialised diabetes examinations.

**UKPDS mit ergänzenden
Diabetesparametern
berechenbar**

The ARRIBA score, currently the standard of care model in Austria, is based on PROCAM and FRS and can therefore also be calculated using the parameters included in the PMCU. Additional markers of atherosclerosis or diabetes can be incorporated to refine risk assessment, but they are optional and not required for routine use.

**ARRIBA nutzt bereits
vorhandene Daten;
durch weitere Parameter
ergänzen**

The QRISK3 CV risk assessment tool requires additional parameters beyond those currently collected in the PMCU. It demands information on various medical conditions and treatments, including chronic kidney disease, rheumatoid arthritis, severe mental illness, migraine, antipsychotic use, regular steroid use, erectile dysfunction, and systemic lupus erythematosus.

**QRISK3 benötigt
zusätzliche, derzeit
nicht erfasste Parameter**

Organisational, time and personnel resources

The SRs did not report specific information on organisational or time resources for the application of CV risk scores. However, it is emphasised that these scores require special training and targeted instruction to ensure correct interpretation, interpret, adequate communication and them appropriate action.

Most CV risk scores are accessible via online calculators. These tools can be applied during the consultation or retrospectively if the relevant parameters are available. ARRIBA, DIAL2 and RECODe represent exceptions, as they require dedicated software modules rather than freely accessible online tools. The ARRIBA and DIAL2 software is free for General Practitioners [133, 134]. For RECODe no information was available.

In addition to risk calculation, ARRIBA offers the possibility of mapping the effects of treatment options, which requires a specific tool [46].

Organisation und
Zeitbedarf unklar,
Schulung erforderlich

Modelle zumeist online
verfügbar, andere durch
Gratissoftware

ARRIBA visualisiert
Therapieeffekte,
spezielles Tool nötig

4.2 Guidelines

4.2.1 Risk of bias: AGREE II

During the quality appraisal, the percentages for the individual domains were calculated, showing that the guidelines are predominantly above 50%. Overall, the ESC guideline performed worst in the respective categories. Not all the necessary materials and supplements were provided.

The guidelines demonstrate varying performance across the three evaluated domains (Stakeholder Involvement, Rigour of Development, Editorial Independence). While all guidelines scored over 60% in Domain 2 (Stakeholder Involvement), there was significant variation in Domain 3 (Rigour of Development), with scores ranging from around 27% to 77%. The Editorial Independence domain (Domain 6) showed more consistent and the highest scores across guidelines, with most results falling between 70% and 90%.

Leitlinienqualitäts-Score
meist >50 %,
ESC schlechter bewertet

Leitlinienqualität:
Stärken in Unabhängigkeit,
Schwächen in Entwicklung

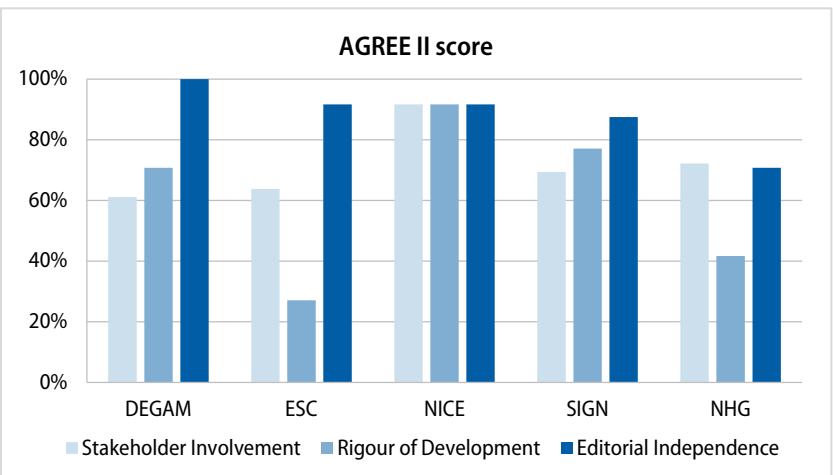


Figure 4-2: Total AGREE II score

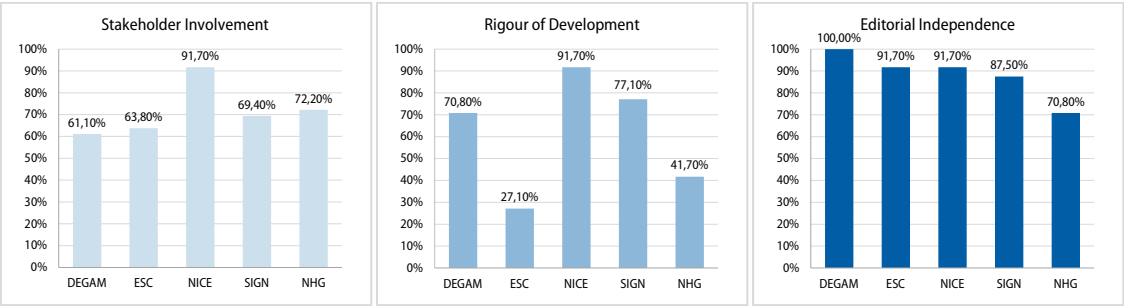


Figure 4-3: AGREE II score Domains two, three and six

4.2.2 Guideline synopsis

Characteristics of the identified guidelines

We identified five guidelines that fulfil the specified criteria for the guideline synopsis.

The guidelines all originate from European countries (Germany, the UK, the Netherlands, the EU, and Scotland) and were published between 2017 and 2024. The guidelines are primarily aimed at general practitioners, family doctors, and healthcare professionals in the field of internal medicine, with the aim of creating an evidence-based foundation for the prevention of CVD. The focus is on individuals without manifest CVD, considering both primary and secondary prevention. The guidelines concentrate on risk classification, risk management, and the prevention of atherosclerotic CVD in adults with increased CV risk (see Table 4-7).

5 europäische Leitlinien für CVD-Prävention inkludiert

Table 4-7: Guideline characteristics

Institute	Author, Year	Title	Country	Target Population	Guideline Topic
DEGAM	Ludt et al. 2017 [135]	Hausärztliche Risikoberatung zur kardiovaskulären Prävention*	Germany	general practitioners and family doctors specialising in internal medicine	to set out the evidence base for this care problem and make recommendations for people who do not yet have manifest CVD.
ESC	Visseren et al 2021 [13]	2021 ESC Guidelines on cardiovascular disease prevention in clinical practice	Europe	healthcare professionals	CVD prevention mainly focused on risk factors, risk classification, and ASCVD prevention.
NICE	N.A 2023 [136]	CVD: risk assessment and reduction, including lipid modification	UK	healthcare professionals and adults who are at risk of CVD or who have CVD	CVD risk prediction and primary care
SIGN	N.A 2017 [137]	Risk estimation and the prevention of CVD: A national clinical guideline	Scotland	healthcare professionals involved in the management of patients with CVD	addresses the management of cardiovascular risk in both primary prevention (intervention before disease manifests) and secondary prevention (intervention after a cardiovascular event)
NHG	N.A 2024 [138]	cardiovascular risk management	Netherlands	Dutch general practitioners and healthcare providers involved in CVRM and persons without known CVD	CV risk management; CVD risk assessment and categorisation

* Degam published the updated version of the guideline in 8/2025, after the completion of our literature search. As a result, it was not incorporated into the results, but changes are addressed in the discussion

Abbreviations: ASCVD ... Atherosclerotic Cardiovascular Disease; CV ... cardiovascular; CVD ... cardiovascular disease; CVRM ... Cardiovascular, Renal, and Metabolism; DEGAM ... Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin; ESC ... European Society of Cardiology Task Force for CVD prevention; N.A. ... not available; NHG ... Nederlands Huisartsen Genootschap; NICE ... National Institute for Health and Care Excellence; SIGN ... Scottish Intercollegiate Guidelines Network

Risk factors addressed

All guidelines address various aspects of risk prevention and prediction in detail. In many respects, the recommendations do not solely refer to prognosis scores but cover the entire scope of CVD prevention.

The next section will concentrate on the specific recommendations and details about the proposed risk score models, rather than on general CVD prevention (see Table 4-8).

Fokus auf Risikofaktoren und Score-Modelle

Table 4-8: Guideline recommendations on cardiac risk scores

Guideline	Risk calculation	Specific score	when/with whom	Grade of recommendation/ Level of evidence	Suggested Benefits and Harms
DEGAM [135]	✓	✓ ARRIBA	apparently healthy adults without established ASCVD, familial hypercholesterolaemia, very high cholesterol (>8 mmol/L), or severe hypertension (≥180/110 mmHg) in the context of PMCU: Women > 60 years, men > 55 years in routine primary care: - adults with one or more new risk factors (smoking, hypertension, dyslipidaemia, type 2 diabetes, positive family history, or central obesity/obesity). - individuals 35+ with high psychosocial stress or low education/social status - at patient request reassessment every 1-2 years in high-risk groups	risk assessment: A/IA ¹ Score: B/GCP ²	+ supports counselling & shared decision-making, provides clear information on prognosis & therapy effects, enables tracking of risk changes – errors remain possible (though more transparent), difficult/uncertain representation of intervention effects, especially in combinations
ESC [13]	✓	✓ SCORE2 SCORE-OP SCORE-Diabetes	apparently healthy people without established ASCVD, diabetes, CKD, genetic/rare lipid/BP disorders and pregnant women: - SCORE2: <70 years - SCORE-OP: >70 years both calibrated to WHO country risk region (low, moderate, high, very high-risk) patients with T2DM without established ASCVD, organ damage, CKD, genetic/rare lipid/BP disorders and pregnant women: - SCORE-Diabetes: 40-69 yrs sex- and age-specific SCORE2-Diabetes charts, calibrated to WHO country risk regions (low–very high).	Risk assessment + score: SCORE/OP: Class I/B ³	+ stratifies CVD prevention strategies, avoids undertreatment in younger people, considers lifetime benefit – may overestimate risk if competing mortality risks are present
NICE [136]	✓	✓ QRISK 34	apparently healthy adults aged 25-84 years without established CVD, CKD, type 1 diabetes, or familial/ inherited lipid disorders patients with T2DM prioritise risk assessment using EHR-recorded parameters; perform full formal assessment only if estimated 10-yr risk ≥10%. reassess regularly ⁵	N.A.	+ – – may underestimate risk in certain groups (HIV, ex smokers, severe mental illness, ...)

Guideline	Risk calculation	Specific score	when/with whom	Grade of recommendation/ Level of evidence	Suggested Benefits and Harms
SIGN [137]	✓	No specific recommendation ⁶	adults ≥40 yrs , without established CVD, familial hypercholesterolaemia, CKD, diabetes or existing BP/lipid treatment (Re)assessment min. every 5 years	strong recommendation ⁷	+ identifies high-risk individuals for targeted interventions, helps assess/estimate risk and prioritise treatment equitably – under- or overestimation in some ethnic minorities (not validated) true CVD risk may be higher for some groups (ethnic groups, atrial fibrillation, premature menopause)
NHG [138]	✓	✓ SCORE2 SCORE-OP for people with known CVD: SMART2/SMART-REACH T2DM: DIAL2	assess whether the patient falls into one of the patient groups for which a risk category can be identified immediately (moderate – very high) ⁸ in adults without established CVD and not yet on BP/lipid treatment (or with risk factors stable for several years) ■ 40-70 years: SCORE2 ■ > 70 years: SCORE-OP ⁹ (multiply the risk score by 1.5 in rheumatoid arthritis) consider DIAL2 in diabetes	N.A	+ estimates 10-year risk of both fatal and non-fatal CVD, provides more comprehensive risk assessment than mortality-only scores – may underestimate risk in younger people due to low 10-year risk lifetime risk tools recommended for younger populations

Abbreviation: ASCVD ... atherosclerotic cardiovascular disease; BP ... blood pressure; CKD ... chronic kidney disease; CVD ... cardiovascular disease; DEGAM ... Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin (engl: Society for General Practice and Family Medicine); DIAL2 ... DIAbetes Lifetime-perspective prediction (version 2); EHR ... electronic health record; ESC ... European Society of Cardiology; GCP ... Good Clinical Practice; HIV ... human immunodeficiency; NHG ... Nederlands Huisartsen Genootschap (engl: Dutch College of General Practitioners); NICE ... National Institute for Health and Care Excellence; PMCU ... preventive medical check-up; QRISK ... cardiovascular disease risk algorithm; SCORE ... Systematic Coronary Risk Estimation; SCORE-OP ... Systematic Coronary Risk Estimation – Older Persons; SIGN ... Scottish Intercollegiate Guidelines Network; SMART ... Second Manifestations of ARterial disease; T2DM ... type 2 diabetes mellitus; WHO ... World Health Organization; yrs ... years

¹ A/IA: grade of recommendation A/IA/Highest level of evidence, supported by meta-analyses or systematic reviews of randomised controlled trials.

² B/GCP: grade of recommendation B/Good Clinical Practice; Expert consensus

³ Class I/B: Is recommended or is indicated/Data derived from a single randomised clinical trial

⁴ Based on randomised controlled trials or large non-randomised studies.

⁵ No specific time interval provided

⁶ ASSIGN score has been developed and used in Scotland to identify individuals at highest risk of CVD

⁷ We could not identify the base of the strong recommendation in terms of evidence level

⁸ A specific table is provided in the guideline

⁹ ≥80 yrs generally considered very high risk

Overview guideline recommendations

All examined guidelines recommend CV risk assessment in apparently healthy adults, though they vary in age thresholds, reassessment intervals, specific risk scores endorsed and the strength of their recommendations or level of evidence provided.

DEGAM strongly advises the use of validated risk score algorithms (Grade A, Level IA) and, by expert consensus, recommends the ARRIBA calculator for use in German primary care (Grade B, Level GCP). This is the only guideline that explicitly discusses CV risk assessment in the context of a preventive health screening, suggesting that in this setting, women over 60 and men over 55 years of age should be screened. In routine primary care, risk assessment should be applied to adults with newly identified risk factors such as smoking, hypertension, dyslipidaemia, type 2 diabetes, positive family history, or central/overall obesity³. For individuals with high psychosocial stress or low educational or social status, DEGAM advises starting risk assessment from the age of 35 years.

NICE recommends CV risk assessment using the QRISK3 in apparently healthy adults aged 25-84 years without established CVD, CKD, type 1 diabetes or familial/hereditary lipid disorders. Patients with T2DM are included in the target population and can also be assessed with the same score. The guideline emphasises the pragmatic use of existing electronic health record data to generate an initial risk estimate; a full formal calculation is only required if the estimated 10-year risk is $\geq 10\%$. Risk assessment should be repeated regularly, although NICE does not specify a fixed interval. A specific recommendation grade or evidence level is not provided.

SIGN gives a strong recommendation for CV risk assessment in adults over 40 years of age without established CVD, CKD, familial hypercholesterolaemia or who are already receiving treatment for hypertension or dyslipidaemia. Reassessment is advised at least every five years. Individuals with a 10-year risk $\geq 20\%$ are classified as high risk, warranting targeted lifestyle and pharmacological interventions. In Scotland, the ASSIGN score is used, although without a formal grading of recommendation.

NHG recommends SCORE2 in adults aged 40-70 years and SCORE-OP in those over 70 years, provided they do not have established CVD and are not receiving treatment for hypertension or dyslipidaemia. Risk calculation may be deferred if risk factors are existent but have remained stable for several years. For patients with RA a multiplier of 1.5 is suggested. For patients with established CVD, NHG recommends the use of DIAL2 for those with T2DM. A specific grade of recommendation or level of evidence is not provided. No formal evaluations on these tools were identified in the reviewed literature, likely reflecting their recent introduction.

At the European level, the ESC guideline (2021) gives a class I recommendation for CV risk assessment using SCORE2 for adults < 70 years and SCORE2-OP for those ≥ 70 years who are apparently healthy and without established ASCVD, diabetes, chronic kidney disease, genetic or rare lipid and blood pressure disorders, or pregnancy. Both tools are calibrated to World Health Organization (WHO) country-specific risk regions (low, moderate, high, and very high-risk).

**Risikobewertung
bei asymptomatischen
Erwachsenen empfohlen**

**DEGAM: validierte
Risikoscores (ARRIBA)
für hausärztliche Praxis;
einzige Leitlinie,
die Anwendung im
Vorsorgekontext empfiehlt
(Frauen > 60 J und
Männern > 55 J);
bei Risikofaktoren oder
psychosozialer Belastung
ab 35 J.**

**NICE: QRISK3 für
Erwachsene 25-84 J,
T2DM eingeschlossen**

**Nutzung von Routinedaten
für Erstschtzung, formale
Berechnung ab
 $\geq 10\%$ Risiko**

**SIGN empfiehlt ASSIGN ab
40 J. im 5-Jahres-Intervall**

**NHG: SCORE2 für 40-70 J,
SCORE-OP für > 70 J und
DIAL2 für T2DM
Patient:innen**

**ESC empfiehlt
SCORE2/OP alters- und
regionsspezifisch**

³ No specific age range was described

For patients with T2DM who do not have established ASCVD, organ damage, or CKD, the guideline recommends the use of SCORE-Diabetes in adults 40-69 years of age, using sex and age-specific charts calibrated to the WHO risk regions.

**SCORE-Diabetes für
T2DM-Patienten 40-69J**

Score-specific recommendations

The synopsis shows country-specific differences in preferred risk scores. Germany favours ARRIBA, the UK QRISK, Scotland ASSIGN and the Netherlands SCORE2 with subtools. At the European level, SCORE2 and SCORE-OP are endorsed. While QRISK3 and ASSIGN are based on national population data and are therefore only partially transferable to other countries, SCORE2 was explicitly developed from large European cohorts and offers region-specific calibration, making it more broadly applicable within European contexts.

**Deutschland: ARRIBA,
UK: QRISK,
Scotland: ASSIGN,
SCORE2 europaweit
anwendbar**

Age groups

The guidelines specify different age groups for applying risk scores. While the QRISK3 can be used for people aged between 25 and 85, the age range for the SCORE2 is much lower at 40-70, although the SCORE-OP can be used from the age of 70. No specific age range was specified for the two other risk prediction models.

**QRISK3 25-85,
SCORE2 40-70,
SCORE-OP ≥70**

The ESC deliberately excludes patients under 50 years without risk factors from the risk prognosis. As with SCORE2, specific models for the alternative calculations (SCORE2-OP) were developed for people over 70 years of age, considering the changed physiological parameters.

**ESC: Risikoabschätzung
erst ab 50 Jahren**

Recommendations on treatment

Current guidelines generally recommend lifestyle modifications as the first-line approach for individuals with lower cardiovascular risk, reserving pharmacological intervention for those at higher risk. DEGAM suggests drug therapy for patients with a $\geq 20\%$ 10-year cardiovascular risk, including statins and antiplatelet therapy (ASS 75-100mg). Similarly, ESC guidelines advocate treatment for very high-risk individuals (SCORE2 ≥ 7.5 -15% depending on age), while QRISK and ASSIGN suggest intervention at $\geq 10\%$ and $\geq 20\%$ 10-year risk thresholds, respectively. NHG uses age-specific thresholds ($\geq 7.5\%$ for >50 years, $\geq 10\%$ for 50-69 years, and $\geq 15\%$ for ≥ 70 years), emphasising that treatment decisions should be personalised and discussed with patients. ASSIGN and NHG did not make specific recommendations.

**Lebensstilberatung
zuerst, Medikamente bei
höherem Risiko**

**individuelle Behandlung
je nach Score und Alter**

**Risikoschwellenwerte je
nach Score unterschiedlich**

Exclusion of existing diseases

Standard risk assessments cannot be applied to patients with established CVD, advanced CKD, or severe metabolic and structural risk factors. Across guidelines, consistent exclusions include familial hypercholesterolemia, very high LDL levels (>8 mmol/L), severe hypertension ($\geq 180/110$ mmHg), and pregnancy. NICE, SIGN, and NHG also exclude patients with diabetes once complications or long duration are present, while ESC and NHG provide dedicated tools for selected patients with type 2 diabetes. In all cases, such groups are considered high-risk by default and require targeted management rather than population-based scoring.

**Ausschlusskriterien:
Hochrisikopatient:innen,
etablierte HKE, familiäre
Hypercholesterinämie,
schwere Hypertonie,
Schwangerschaft**

Expected benefits of using scores

Guidelines view risk prediction models as an opportunity to assess and minimise the 10-year risk of CV events and to intervene in time with medication or lifestyle interventions if necessary. SIGN emphasises that using scores can help assess or estimate risk and prioritise treatment on an equitable basis. ESC also points out that they can be used to avoid under-treatment in younger patients and thus minimise risk at earlier stages. DEGAM additionally frames risk scores such as ARRIBA as counselling and decision-support instruments that strengthen shared decision-making, making prognostic and therapeutic options more transparent for patients.

Vorteile:
Risikomodelle unterstützen Prävention und gezielte Therapie, Vermeidung von Unterbehandlung, Transparenz für Patienten

Risks of using Scores

The ESC, NHG and DEGAM emphasise that classic risk prediction models tend to overestimate the risk of an event if other competing mortality risks are present but not considered.

Risiken:
Risikomodelle können über- oder unterschätzen

Furthermore, NICE points out that the risk in certain patient groups (e.g. pregnant women, other ethnicities) is systematically underestimated. These include HIV patients, people on medication that affects CV risk factors, recent smoking cessation, patients on medication that causes dyslipidaemia, individuals with severe mental illness and people with autoimmune diseases. In addition, SIGN notes that there may be ethnic and gender-specific limitations, leading to misclassifications.

bestimmte Gruppen systematisch unterschätzt

The SCORE2 model demonstrates a significant limitation: for younger people, the risk is underestimated due to the low 10-year risk, although the lifetime risk is potentially high. Alternative risk assessment tools are recommended for this group.

bei jungen Menschen Lebenszeitrisko oft höher als 10-Jahres-Prognose

Tools and requirements

The Guidelines reported that the technological requirements of CV risk prediction models are evolving from statistical calculation tools to adaptive, software-supported systems. Computer-based tools such as QRISK3 and SCORE2 require technical infrastructure (software/hardware) and methodologically trained medical personnel. The system requires region-specific adjustments for mortality rates (SCORE2 and QRISK); these scores mandate particular software and hardware to determine risk. Additionally, there are associated implementation expenses as healthcare workers become accustomed to new information.

technische Infrastruktur und Schulung für Scores nötig

Einarbeitung des Personals verursacht zusätzliche Kosten

5 Discussion

5.1 Summary of findings

SR evidence

This review synthesised findings from systematic reviews (SRs) and validation studies of cardiovascular (CV) risk scores in general and disease-specific populations. Because only a limited body of validation evidence was available for the general population, we also included results from scores tested in or developed for populations with common non-communicable diseases (NCDs), such as diabetes and inflammatory rheumatic diseases.

SRs und VS zu kardiovaskulären Risikoscores in Allgemein- und spezifischen Krankheitspopulationen

General population

In the general population, the most extensively studied models were the Framingham Risk Score (FRS), the Pooled Cohort Equations (PCE), and Adult Treatment Panel III (ATP-III) – all predicting fatal or nonfatal CVD or CHD as outcomes.

Allgemeinbevölkerung

**FRS, PCE, ATP-III:
geringe bis moderate
Diskriminierung**

All scores showed low to moderate discrimination, and none predicted events accurately, with systematic over- or underestimation across populations. PCE performed slightly better overall. All three scores discriminated better in women than men. Geographically, discrimination was highest in Chinese cohorts, moderate in American studies, and variable in European populations. Risk was typically overestimated in European populations and underestimated in some Asian cohorts, with mixed results in US populations.

Frauen > Männer

**Überschätzung Europa,
Unterschätzung Asien**

Rheumatoid arthritis (RA)

In RA populations, the most extensively validated models were the FRS, SCORE, and QRISK2. Across studies, discrimination ranged from poor to good but all models performed worse than in the general population cohorts. Calibration was rarely reported formally, though most studies showed systematic underestimation of CV risk with FRS and SCORE, while QRISK2 produced mixed results. Simple adjustments such as applying the EULAR multiplier or adding CRP did not meaningfully improve performance. Overall, existing scores showed only moderate utility in RA populations, with systematic miscalibration limiting clinical applicability.

Rheumatoide Arthritis

**FRS, SCORE, QRISK2:
geringe bis moderate
Diskriminierung**

**systematische
Unterschätzung des
CV-Risikos**

Diabetes

Type 1 diabetes (T1DM)

In T1DM, only a few studies evaluated UKPDS, FRS and QRISK3. UKPDS showed poor to moderate discrimination, performing better for fatal CHD and broad CV composites but poorly for silent myocardial infarctions (MI). The FRS achieved moderate to good discrimination. QRISK3 demonstrated moderate discrimination, based on evidence from only one large study. Calibration was consistently poor across models, with systematic overestimation where reported. Overall, tools derived from T2DM or general cohorts show only moderate predictive utility in T1DM.

T1DM:

**UKPDS, FRS, QRISK3
moderat Diskriminierung,
schlechte Kalibrierung –
Risiko meist überschätzt**

Type 2 diabetes (T2DM)

In T2DM populations, four main models have been validated: UKPDS, RECODE, FRS, and SCORE. The UKPDS Risk Engine was specifically developed for diabetes and remains the most extensively evaluated, showing moderate discrimination for CV mortality and stroke but poor performance for MI and heart failure (HF). RECODE performed best overall, with moderate to good discrimination. FRS and SCORE showed poor to moderate discrimination in most cohorts, with some studies reporting good performance up to 0.86 for stroke or MI.

Calibration was consistently problematic: UKPDS and SCORE tended to overpredict, while FRS underestimated risk in low-risk patients but overestimated in high-risk groups. RECODE again showed the most consistent calibration, particularly for CV mortality in low-risk patients, though stroke risk was often underestimated.

T2DM:

**RECODE zeigt insgesamt beste Diskriminierung und Kalibrierung;
UKPDS spezifisch für T2DM, aber ungenau;
FRS und Score variabel je nach Endpunkt**

konsistente Über- und Unterschätzung des Risikos

Health benefits and harms

Evidence on the health benefits and harms of CV risk scores was sparse. None of the trials reported direct patient-relevant outcomes such as morbidity or mortality. Findings were limited to small reductions in risk factors, some changes in prescribing, and minimal or no effects on quality of life.

**Nutzen/Schaden:
begrenzte Evidenz, kaum patient:innenrelevante Effekte**

Implementation aspects

No SR reported implementation aspects explicitly, though several reviews emphasised the importance of training and support to ensure correct interpretation and communication of results.

Most established risk scores (FRS, PCE, SCORE2, PROCAM, ARRIBA) can be calculated with parameters routinely collected in the Austrian preventive medical check-up (PMCU), while UKPDS requires data from diabetes care and QRISK3 demands additional information. Furthermore, it was developed using data from the British population, which calls into question its generalisability to the Austrian population.

**Implementierung
kaum untersucht,
Anwenderschulungen wichtig**

Großteil der Scores mit PMCU-Parameter berechenbar

Guideline recommendations

Across Europe, all major guidelines recommend CV risk assessment in apparently healthy adults using validated prediction models, but they differ in age thresholds, reassessment intervals and the specific tools endorsed. Germany (DEGAM) recommends the Framingham-derived ARRIBA calculator for use in primary care, while in the UK QRISK3 is endorsed, Scotland applies ASSIGN, and the Netherlands recommends SCORE2 and related instruments (e.g. DIAL2). At the European level, the ESC guideline gives SCORE2 (<70 years) and SCORE2-OP (≥70 years) a Class I recommendation with region-specific calibration, making them broadly applicable across different European populations. Despite these national differences, the guidelines share important exclusion criteria: patients with established CVD, advanced CKD, familial hypercholesterolaemia or other rare lipid disorders, very high LDL (>8 mmol/L), severe hypertension, and (in some cases) pregnancy are not candidates for general population scores and should be managed as high-risk.

europaweit validierte Scores empfohlen, aber nur in D im Vorsorgekontext, Details variieren

SCORE2/OP europaweit empfohlen, altersabhängig

ARRIBA, QRISK3, ASSIGN, national etabliert

Diabetes is treated differently across guidelines. NICE and DEGAM include T2DM in the general risk score population, while ESC and NHG provide dedicated tools for patients with T2DM. Type 1 diabetes was excluded consistently.

Age thresholds for initiating risk assessment differ across guidelines: NICE begins at 25 years, DEGAM at 35 years in socially vulnerable groups and at 55/60 years in the context of statutory health checks, SIGN from 40 years, and ESC/NHG from 40-70 years with SCORE2 or ≥ 70 years with SCORE-OP. Recommended reassessment intervals also vary, ranging from every 1-2 years in high-risk individuals (DEGAM) to every 5 years in lower-risk adults (SIGN), with other guidelines advising regular but unspecified intervals.

Treatment thresholds vary considerably across guidelines, ranging from $\geq 10\%$ (QRISK) to $\geq 20\%$ (DEGAM, ASSIGN) 10-year cardiovascular risk, with ESC and NHG employing age-stratified approaches. NHG and ASSIGN emphasise the importance of personalised risk assessment and shared decision-making in clinical practice.

While finalising our report, DEGAM released a new update on cardiovascular risk counselling. The guideline now recommends offering risk assessment irrespective of known risk factors from age 50, and once between 18-35 years in individuals with strong familial or genetic risk. Repeated assessments are advised when new or changing risk factors, chronic conditions, or preventive interventions are present. For the general population without established CVD, DEGAM lists ARRIBA, ESC charts⁴, and PROCAM as examples of validated tools, while for people with T2DM, it advises using models that integrate diabetes-specific factors such as HbA1c, age at diagnosis, and kidney function (e.g., ARRIBA with HbA1c module or SCORE2-Diabetes).

T2DM teils integriert, teils eigene Tools empfohlen; T1DM ausgeschlossen

Altersgruppe für Risikobewertung je nach Leitlinie unterschiedlich

Intervalle: 1-2 Jahre bis 5 Jahre empfohlen

Behandlungsgrenzen unterschiedlich, personalisierte und gemeinsame Entscheidungsfindung betont

DEGAM (neu): Risikobewertung ab 50 J, einmalig 18-35 J bei familiärem Risiko; Kombination aus ARRIBA, SCORE2 und PROCAM empfohlen

5.2 Critical reflection

Despite their widespread use in preventive cardiology, CV risk scores face important methodological and clinical limitations. Most models are primarily evaluated for discrimination – their ability to distinguish between individuals who will and will not develop events – whereas calibration, the alignment between predicted absolute risks and observed outcomes, is less frequently assessed. This distinction has direct treatment implications: for example, if a model systematically overestimates absolute risk, more patients may cross the threshold for pharmacological therapy, leading to potential overtreatment. Conversely, underestimation of risk may result in undertreatment of individuals who would benefit most

Strikingly, while these scores are widely recommended in guidelines, there is little evidence that their use improves health outcomes such as CV events or mortality. Validation studies demonstrate various levels of predictive performance, but no conclusions can be drawn about their effectiveness within a screening program. Given their probabilistic nature and the variability between different models, uncritical use may lead to inappropriate treatment decisions.

methodische Grenzen und Risiken von CV-Scores

Ungenauigkeiten können Über- oder Untertherapie fördern

fehlende Evidenz für Nutzen im Screening-Kontext

⁴ ESC charts originate from the European Society of Cardiology and are based on the SCORE2 data. They can be applied according to the country's risk classification.

At the same time, it is important to acknowledge that risk scores have made a substantial contribution to preventive cardiology. They provide a standardised framework and offer clinicians a practical tool for initiating conversations about prevention. Despite their limitations, these models remain useful for identifying higher-risk groups at a population level and have driven ongoing refinements, such as SCORE2 or newer versions of QRISK. So, while their limitations should not be ignored, they continue to serve as a starting point for more individualised approaches. Moreover, most established risk models incorporate modifiable risk factors such as smoking, blood pressure, and lipid levels. This allows clinicians to use these tools interactively with patients, illustrating how risk can change with lifestyle modification or pharmacological intervention – for instance, smoking cessation or a 50% reduction in LDL cholesterol through statin therapy. Such visualisation of risk reduction can support shared decision-making and enhance motivation for preventive measures.

Whilst evidence suggests that communicating cardiovascular disease (CVD) risk to patients may lead to improvements in risk perception and potentially motivate behaviour change, there is currently no robust evidence that this translates into reductions in hard clinical endpoints, such as CVD events or mortality [139]. This is consistent with the findings of the systematic reviews included in this report, which consistently noted that most available studies assess only surrogate outcomes rather than long-term clinical benefits.

These considerations need to be weighed when discussing the implementation of a standardised tool within the Austrian PMCU, as applying a score in individual clinical practice differs from using a single risk score at the population level as part of a screening. Currently, the PMCU follows a standardised scheme based only on age and sex, without considering individual risk profiles. Moving to a risk-based approach would therefore represent a major change towards more personalised prevention. Yet the evidence shows that no single model is appropriate for all groups. Scores such as SCORE2 or ARRIBA may be suitable in the general Austrian population, but they have been shown to underestimate or misclassify risk in patients with diabetes, chronic kidney disease, or inflammatory conditions. This shows the conflict between the idea of using one national tool for every participant and the fact that risk prediction is more complex and differs between groups. The updated DEGAM guideline reflects this by deliberately avoiding a recommendation for one specific tool and instead naming several validated options (e.g., ARRIBA, ESC charts, PROCAM), while highlighting the need for diabetes-specific models such as ARRIBA with HbA1c module or SCORE2-Diabetes.

In practice, several different scores may need to be applied within the Austrian PMCU to ensure comprehensive patient assessment. This increases complexity and places additional demands on physicians in terms of time, skills, and training. The use of different scores for different populations would also imply varying treatment thresholds as various models define “high risk” differently. This inconsistency complicates clinical decision making, communication with patients, and the development of national guidelines for preventive action, potentially resulting in inconsistent or inappropriate patient management. Although clinical guidelines provide recommendations on score-based treatment thresholds, the interpretation of risk estimates and translation into action remains complex. Different scores can yield divergent risk estimates for the same individual, resulting in inconsistent treatment decisions. It should be noted that this report focused on the performance and applicability of risk scores. Treatment strategies and cardiovascular management

**trotz Limitationen
wertvolles Instrument
in der Prävention:**

**Orientierung für Praktiker,
nützliches Werkzeug für
Risikokommunikation
und Motivation**

**verbesserte
Risikowahrnehmung,
aber kein Nachweis
klinischer Vorteile**

**Herausforderung:
einheitliche Anwendung
bei heterogenen Gruppen**

**Risikofehleinschätzung
bei Vorerkrankungen**

**kein Score für
Gesamtpopulation
empfehlbar**

**Ö: mehrere Scores
in der Praxis anwenden**

**verschiedene Scores
haben verschiedene
Risikoschwellenwerte**

**Herausforderungen bei
der Implementierung von
Risikomodellen**

**klare Leitlinien nötig um
adäquate Nachsorge zu
gewährleisten**

pathways were beyond its scope. To ensure the meaningful use of any model in practice, it is essential to determine how risk estimation informs subsequent action, supported by clear guideline-based standards to ensure consistent and appropriate follow-up.

A further issue is that some patients attending the PMCU will not require risk assessment, as they would automatically be classified as high risk, including those with established CVD. Guidelines suggest such individuals should bypass prediction models and move directly to more comprehensive risk management. Within a standardised setting such as the PMCU, questions arise on how these patients should be identified and addressed. There is a risk of overlap or duplication, where high-risk patients might be unnecessarily assessed with general population scores or excluded from preventive counselling.

Since risk scores provide estimates of probability rather than certainties, they are often misunderstood by patients. Effective shared decision-making therefore requires sound clinical judgement, and strong skills in risk communication. Within the structured PMCU setting, it remains uncertain whether sufficient time is available for the correct application of risk tools and the detailed discussion of results – factors that may undermine the quality of shared decision-making and limit the benefit of risk-based prevention.

In addition to clinical and operational challenges, the introduction of a CV risk score raises ethical considerations. Some individuals may prefer not to know their estimated risk of a CV event, and communication of such knowledge may be distressing. It is crucial that participants are fully aware of the meaning and limitations of the score. The use of such a tool must be based on informed consent, voluntary participation and a right to decline. Patient acceptance is another key factor, as differing results between models could confuse patients, undermine trust in the program and weaken its role in motivating preventive behaviour. Furthermore, equity concerns arise as many CV risk scores were developed in predominantly white European populations and may perform differently across diverse demographic and ethnic groups. The reliance on non-modifiable risk factors such as age and sex may lead to systematic over- or under-treatment of certain patient populations, potentially widening existing health disparities and raising questions about fairness in resource allocation and access to preventive interventions.

An important limitation is that none of the established CV risk scores have been validated in Austrian populations. This means that any implementation would rely on extrapolation from external cohorts, which may not accurately reflect local epidemiology or risk factor distributions.

From a feasibility perspective, the fact that most required parameters are already collected in the Austrian PMCU means that implementation would not require substantial structural changes. Additional clinical variables like HbA1c or eGFR would only be needed if disease-specific models were used alongside general population scores, adding complexity.

However, beyond score selection, successful implementation in the Austrian PMCU would also depend on appropriate digital infrastructure and adequate time resources. Automated calculation based on existing data could reduce workload and errors, but doctors would still require training in both technical application and risk communication.

**Identifikation und
Management von
Hochrisikogruppen**

**spezielles
Risikomanagement
empfohlen**

**Risikobewertung
erfordert klinisches Urteil
und Kommunikation**

**ethische Aspekte
der Risikobewertung**

**Patient:innen:
Akzeptanz und informierte
Entscheidung relevant**

**Ethik, Diversität und
Zugänglichkeit
berücksichtigen**

**begrenzte Übertragbarkeit
extern validierter
Risikoscores**

**bezüglich nötiger
Parameter Umsetzbarkeit
im PMCU weitgehend
gegeben**

**jedoch technische
Infrastruktur, Schulung
für Anwendung und
Risikokommunikation
erforderlich**

Finally, when discussing implementation, it is important to acknowledge that evidence on the actual benefits of CV risk scores in terms of hard outcomes such as morbidity or mortality is lacking. Implementing such tools would therefore require considerable effort and resources, without robust proof that they improve long-term health outcomes.

**begrenzte Evidenz für
gesundheitlichen Nutzen**

5.3 Limitations

Limitations of the evidence base

Despite most of the included reviews being judged at low risk of bias, the underlying primary studies were predominantly rated as moderate to high risk by the authors and displayed heterogeneity in design, outcomes and populations. Evidence for the general population was predominantly graded as low certainty, while studies in rheumatoid arthritis and diabetes populations showed mixed quality, ranging from moderate to high RoB. As a result, the certainty of the overall evidence is considered low to moderate, limiting confidence in the reliability and generalisability of the reported results.

**Evidenzqualität
überwiegend niedrig
bis moderat**

The evidence base on CV risk prediction models shows several important limitations.

At present, it relies almost exclusively on validation studies, rather than randomised controlled trials (RCTs) aimed at assessing the benefit–harm balance of risk-based prevention strategies. Reviews such as Karmali et al. (2017) and Studziński et al. (2019) explicitly sought such evidence but found only studies reporting intermediate outcomes, including changes in cholesterol, blood pressure, prescribing, or quality of life [88, 90]. Similarly, Lucaroni et al. (2019) concluded that no evidence exists in the scientific literature on the long-term effectiveness of risk prediction models, underscoring the lack of randomised trials evaluating whether score-guided prevention improves patient outcomes [92].

**fehlende RCTs zu
langfristigem Nutzen**

**nur Zwischenziele
untersucht,
kein Langzeitnachweis**

Most reviews focused on predictive validity, especially discrimination, while calibration was often underreported or inconsistently assessed.

**Kalibrierung
unterrepräsentiert**

The C-statistic (AUC) only reflects discrimination; it does not indicate absolute risk accuracy, may overestimate performance, and can be misleading in unbalanced datasets. When calibration was reported, methodological heterogeneity limited direct comparison.

**methodische Unterschiede
erschweren Vergleich**

The included studies were heterogeneous in design, outcomes, and reporting quality. Calibration was not always assessed with formal statistical methods: while some studies reported formal Observed to Expected (O:E) ratios or calibration slopes, others relied only on indirect comparisons of predicted and observed event rates to judge over- and underestimation.

**unterschiedliche Designs,
Ergebnisse und
Berichtsqualität**

Outcome definitions also varied considerably. Some studies focused on hard endpoints such as MI, stroke, or CV death, while others applied much broader composites that included unstable angina (UA), transient ischemic attack (TIA), peripheral vascular disease (PVD), revascularisation, or HF. These broader definitions capture disease burden more comprehensively but also introduce heterogeneity, as not all event types are equally predicted by conventional risk factors. This heterogeneity may in part explain the lower and more variable discrimination observed across studies.

**unterschiedliche
Endpunkte der Studien**

**Diskriminierung variiert
je nach Endpunkt**

Additionally, most of the widely validated scores are based on historical cohorts from the US or Europe. While partially relevant for European populations, they may not capture current risk factor patterns or treatment effects, particularly in the Austrian context. No SR evidence was identified for PROCAM and ARRIBA, even though these risk score tools are widely used in Austria and Germany and are therefore particularly relevant to the national context.

keine Reviews zu national relevanten Scores (PROCAM, ARRIBA) verfügbar

A further limitation is that the follow-up duration was not always aligned with the 10-year horizons of most models. Shorter follow-up can make models appear to overestimate risk, while longer follow-up can exaggerate underestimation. Together, these factors limit comparability across studies and models.

Follow-up in Studien nicht modellgerecht

Limitations of this review

Our review was based on SRs and one validation study (VS) thus our synthesis is constrained by the scope and reporting of the included publications. Consequently, relevant primary evidence on individual models may not have been captured. Most SRs were not primarily designed to evaluate patient-relevant outcomes such as morbidity, mortality, or harms, and thus only a few reported on intermediate outcomes like prescribing behaviour, risk factor changes, or quality of life. As we did not conduct a dedicated search for primary studies (PSs), we may have missed more recent individual trials, although the SRs suggest that such evidence is not available. Fragmented reporting across PS also meant that some results were only available in appendices or descriptive form, restricting the possibility of pooled synthesis. Furthermore, newer models such as QRISK3, SCORE2, and some tools only encountered during the guideline reviews, are only emerging in the literature, which limited the extent to which their performance could be assessed in this review.

Einschränkungen durch begrenzte Evidenz und SR-Fokus, daher eingeschränkte Information zu patient:innenrelevanten Endpunkten

neue Risikomodelle wenig in Literatur bewertet

Implementation data was largely drawn from SRs, whose primary focus was on predictive performance. A targeted search for studies addressing implementation aspects was not feasible due to capacity and time constraints, hence real-world and resource considerations may be underrepresented, although they remain relevant in the context of the application within the PMCU.

Vorhersageleistung dominiert, praktische Anwendung weniger untersucht

6 Conclusion

The primary aim of cardiovascular (CV) risk prediction is to provide a comprehensive assessment of an individual's overall risk of experiencing a CV event, rather than focusing on isolated risk factors. By estimating the probability of events over a defined time horizon, usually 5-10 years, depending on the tool, patients can be stratified into risk categories such as low, moderate, or high. This classification supports tailored prevention strategies based on risk thresholds, aligning intervention intensity with the predicted level of risk.

However, risk scores possess significant limitations that must be critically considered. Available tools rely on population-based data and may not accurately reflect individual patient nuances, particularly for diverse populations or those with complex medical histories. Key limitations include:

- *Moderate discriminatory performance*, with C-statistics typically ranging from 0.70 to 0.80, indicating substantial predictive uncertainty
- *Calibration challenges*, often due to missing data, resulting in frequent under- or overestimation of events across different demographic groups or ethnicities, limiting generalisability and clinical reliability
- *Limited transferability* between populations with varying genetic and geographical or healthcare characteristics
- *Inability to capture emerging or complex risk factors*

The use of CV risk scores has been proposed as a possibility to guide more personalised prevention, which makes them potentially attractive for screening. Given that most required parameters are already collected within the Austrian preventive medical check-up (PMCU), integration would be technically feasible.

Based on our guideline synopsis and the available SR evidence, SCORE2 (with European calibration) appears to be the most promising candidate for use in Austria. ARRIBA may also be considered, given its validation in German cohorts that are likely more comparable to the Austrian population. However, compared to other scores, there is little information on its accuracy available.

Several important limitations would challenge potential implementation into the Austrian PMCU:

- No single score is appropriate across all screening participants, and using multiple risk scores would add complexity through differing thresholds and management pathways. Clear national guidance is therefore essential, and such detail may be difficult to implement within the PMCU setting.
- Most of the scores have been validated for Western and Central Europe, but none specifically for Austria. As a result, they may not specifically capture the epidemiological and demographic characteristics of the Austrian population.
- A high risk for misclassification persists, with inaccurate prediction of events and a risk of subsequent under- or overtreatment of patients.

Score-Ziel:
ganzheitliche Einschätzung
des individuellen
5-10 Jahres CV-Risikos

Limitationen:
Eingeschränkte
Diskriminierung und
Kalibration,
begrenzte Übertragbarkeit
auf andere Populationen,
komplexe und neue
Risikofaktoren nicht erfasst

Risikoscores prinzipiell
zur personalisierten
Prävention im VU-Setting
geeignet

SCORE 2 als potenzielle
Option für Ö,
ARRIBA möglich,
jedoch Evidenz begrenzt

**Limitationen für
Implementierung:**
keine universelle
Score-Lösung für alle

fehlende Validierung
in Österreich

Risiko von
Fehlklassifikation und
falscher Behandlung

- Evidence points to a potential improvement in patient behaviour and risk awareness following CVD risk counselling; however, robust evidence demonstrating an impact on hard clinical outcomes, including CVD events and mortality, is lacking. Implementation would require additional resources, including staff time, digital infrastructure, and training in both technical use and risk communication in line with ethical standards
- The probabilistic nature of the tools requires time for individual clinical judgment and shared decision making, ensuring the patients understand their results, implications and available options before preventive actions are initiated

Overall, further evaluation and piloting may be needed before integrating a risk prediction score into the Austrian PMCU. Implementation decisions should be based on a structured, multi-stakeholder process involving clinicians, researchers, policymakers, and patient representatives, to ensure that the multidisciplinary nature of this topic is appropriately reflected.

begrenzte Evidenz für harte klinische Endpunkte, zusätzliche Ressourcen und Schulungen notwendig

Scores erfordern klinisches Urteil und sorgfältige Kommunikation

vor Implementierung Pilotierung und Evaluierung erforderlich

7 References

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Appendix

Preventive medical check-up recommendations

Table A-1: Recommended preventive medical check-ups [12]

Erkrankung/ Risiko-faktor	Population	Klassifizierung	Untersuchung/Beratung	Klassifizierung	Screening-Intervall	Klassifizierung	Möglicher Änderungsbedarf
Kardiovaskuläre Erkrankungen und Risikofaktoren							
Abdominales Aortenaneurysma	Männer zwischen 65 und 75 Jahren	✓✓	Abdominale Sonographie	✓✓	Screening-Intervall: Einmalig	✓✓	Nein
Alkoholkonsum	Erwachsene ≥ 18 Jahre	◇	AUDIT-C-Fragebogen zum Selbstauffüllen, einzelne Frage	◇	Bei jeder Vorsorgeuntersuchung	○	Nein
			Entwöhnungsberatung, Überweisung zu einer spezialisierten Behandlung für Alkoholkrankheiten	✓			
Körperliche Aktivität	Erwachsene ≥ 18 Jahre	✓	Beratungsgespräch, um zu regelmäßiger körperlicher Bewegung im Alltag zu motivieren (5 ES)	✓	Screening-Intervall: Bei jeder Vorsorgeuntersuchung	○	Nein
Diabetes mellitus Typ 2	Erwachsene ≥ 18 Jahre	◇	Feststellung des Diabetesrisikos mittels FINDRISK	✓	3 Jahre (Bestimmung Nüchtern- Blutzucker, HbA1C)	✓ (3-5 Jahre)	Nein
			HbA1C, Glukose-Toleranztest	✓✓			
Hypertonie	Erwachsene ≥ 18 Jahre	✓✓	Blutdruckmessung	✓✓	Individuell abgestimmt	✓✓	Nein
Lipidstoffwechsel- störung	Erwachsene ≥ 18 Jahre	~	Gesamtcholesterin, HDL, LDL-Cholesterin Quotient, Triglyzeridbestimmung	✖	5 Jahre (ohne erhöhtes Risiko), individuell abgestimmt (mit erhöhtem Risiko)	○	Ja
Nikotin-/ Tabakkonsum	Erwachsene ≥ 18 Jahre	✓	Erhebung des Rauchstatus mittels Fünf Es-Befragung	✓	Screening-Intervall: Bei jeder Vorsorgeuntersuchung	○	Nein
			Entwöhnungsberatung (Fünf Es; Motivationsanstöße, Zuweisung zu spezialisierter Entwöhnungseinrichtung)	✓			
Übergewicht/ Adipositas	Erwachsene ≥ 18 Jahre	✓	BMI und/oder Taillenumfang als Teil der physikalischen Statuserhebung	✓/○	Bei jeder Vorsorgeuntersuchung (BMI und/oder Taillen- umfang)/Jährlich (Beratung von BMI >25 kg/ m ² mit Komorbiditäten bzw. >30 kg/m ²)	✓/○	Nein
			9 BMI >25 kg/m ² mit Komorbiditäten bzw. >30 kg/m ² : Gewichtsreduktion unterstützen (Ernährungsempfehlung, Beratung zu körperlicher Aktivität unterstützt durch verhaltenstherapeutische Techniken)	✓			

Erkrankung/ Risiko-faktor	Population	Klassifizierung	Untersuchung/Beratung	Klassifizierung	Screening-Intervall	Klassifizierung	Möglicher Änderungsbedarf
Krebserkrankungen							
Kolorektales Karzinom	Erwachsene ≥ 50 Jahre	✓✓	Test auf fäkal okkultes Blut (FOBT)	✓✓	Screening-Intervall: Bei jeder Vorsorge- untersuchung (FOBT)	✓✓	Nein
			Überweisung zu einer Fachärz-tin/einem Facharzt mit Berech-tigung zur Durchführung der Vorsorgekoloskopie	◇	10 Jahre (Koloskopie)	✓	
Hautkrebs	Erwachsene ≥ 18 Jahre	✓	Beratung zur Prävention von Hautkrebs	✓	Screening-Intervall: Einmalig	○	Nein
Senium							
Altersbedingte Sehschwäche	Erwachsene ≥ 65 Jahre	✖	Gezielte Frage zu Frage nach Sehverschlechterung, optional Sehüberprüfung mittels Sehtafeln	~	Screening-Intervall: 2 Jahre	○	Ja
			Weiterführende Abklärung durch die Vorsorgeärztin/den Vorsorgearzt oder Veranlassung fachärztlicher Untersuchung	○			
Hörminderung/ Hörverlust	Erwachsene ≥ 65 Jahre	✖	Frage zu Hörverlust	~	Screening-Intervall: 2 Jahre	○	Ja
Osteoporotisches Frakturrisiko	Erwachsene ≥ 50 Jahre	~ für Männer ◇ für Frauen	FRAX Risikorechner	○	Screening-Intervall: 10 Jahre (FRAX)	○	Ja
			Personen mit erhöhtem Risiko ≥20 % weitere Abklärung durch DXA	✓			
			Beratung zur Vermeidung des Sturzrisikos	○			
Andere Erkrankungen							
Chronische Nierenerkrankungen	Erwachsene ≥ 40 Jahre mit mind. einem Risikofaktor (arterielle Hypertonie, Diabetes mellitus, Adipositas (BMI > 30 kg/m ²) oder terminale Niereninsuf- fizienz in der Familie)	✓	Albumin-/Kreatinin-Quotient aus dem Spontanharn und auf Serum-Kreatinin/eGFR aus dem Blut	✓	Screening-Intervall: 2 Jahre	○	Nein
Parodontal- erkrankungen	Erwachsene ≥ 18 Jahre	○	Gezielte Frage zu Parodontalerkrankungen Weiterführende Abklärung durch Vorsorgearzt/-ärztin oder Zuweisung parodontologisch orientierte Zahnarzt/-ärztin	○	Screening-Intervall: 3 Jahre (18-39 Jahre) 2 Jahre (≥40 Jahre)	○	Ja

Abbreviations: ✓✓... Klare Empfehlung für Maßnahme; ✖✖... Klare Empfehlung gegen Maßnahme; ✓... Schwache Empfehlung für Maßnahme; ✖... Schwache Empfehlung gegen Maßnahme;
◇... Gegensätzliche Empfehlungen der Institutionen; ~ Unklare Empfehlungen; ○... Keine Empfehlungen

Score characteristics and statistics

Table A-2: Framingham characteristics and statistics

FRAMINGHAM Risk score										
SR ref- erence	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration, E/O Ratio	Outcomes	Mean FU (yrs.)	Major findings	PS ROB
Colaco et al. 2020 [89]	Alemao 2017 [115]	UK	FRS	12,747	0.75	N.A	MI, stroke, HF, aortic aneurysm, TIA, unstable angina, IC;	6	FRS underestimates CV risk Discrimination was lower in the RA population compared to the general population. addition of CRP did not significantly improve reclassification of CV risk	moderate Risk
			FRS + CRP		0.77	NRI = 3.2% CI95% -2.8, 5.7				
	Arts 2015 [119]	NL	FRS	1,157	0.80	N.A	ACS, angina, CVA, TIA, PVD, HF	N.A	FRS underestimated risk of future CV events	moderate risk
	Crowson 2012 [140]	USA	FRS (overall)	525	0.79	N.A	MI, CV death, angina, stroke, IC, HF	8.4	FRS significantly underestimated CV risk	low risk
			FRS (low risk)		0.56					
			FRS (intermediate risk)		0.50					
	Crowson 2017 [116]	UK, N, NL, USA, S; GR; ZA, E, CDN, MEX	FRS	5,638	0.71	N.A	ACS, chronic ischemic heart disease, coronary revascularization, coronary death, other CV death, cerebrovascular events, peripheral vascular events	5.8	FRS underestimated the CV risk in the highest risk groups	high risk
	Crowson 2017 [120]	UK, N, NL, USA, ZA, CDN, MEX	FRS-ATP	1,796	0.75	N.A	MI, ischemic stroke, CV death	6.9	FRS significantly overestimated CV risk RA specific calculators did not predict CV disease more accurately than general population risk calculators.	high rik
			FRS-ATP +EULAR multiplier		0.75					
	Finckh 2012 [114]	CH	FRS + CRP	118	0.73	N.A	ACS, stroke	9	NT prob BNP was moderately predictive of subsequent MACE, but did not improve the predictive ability of traditional risk factors.	moderate risk
			FRS + RF		0.73					
			FRS + anti-CCP		0.76					
			FRS + ox-LDL		0.73					
			FRS + NT-proBNP		0.76					
			FRS + anti-apoA-I		0.81					

FRAMINGHAM Risk score										
SR ref- erence	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration, E/O Ratio	Outcomes	Mean FU (yrs.)	Major findings	PS ROB
Colaco et al. 2020 [89] <i>(continuation)</i>	Navarini 2018 [118]	IT	FRS	155	0.76	N.A	CV death, CAD (stable and unstable angina, MI), Stroke TIA, PAD, HF	N.A	FRS underestimated CV risk	moderate risk
			FRS + EULAR multiplier		0.76					
	Urowitz 2016 [117]	CDN	FRS	1,013	N.A	sensitivity: 13.0, specificity: 98.2	CAD=MI, angina, sudden death	9	application of a multiplication factor of 2 lead to the FRS more accurately identified patients and moderate to high risk of CAD and more accurately predicts subsequent CAD.	moderate risk
			1.5 FRS			sensitivity: 19.7, specificity: 89,4				
			2 FRS			sensitivity: 31.5, specificity: 80.9				
			3FRS			sensitivity: 45.5, specificity: 72.0				
			4FRS			sensitivity: 46.1, specificity: 68.8				
	Damen et al. 2019 [91]	D'Agostino 2001 [100]	USA	FRS (Wilson men Total cholesterol)	4,705 (ARIC study)	0.75	0.93 (0.80; 1.09)	fatal or nonfatal CHD	N.A	pooled performance: male population: c-Statistic: 0.68 (0.66;0.69) prediction interval: 0.68 (0.61;0.73) O:E ratio: Pooled performance + CI 0.58 (0.43;0.739 prediction Interval 0.58 (0.19;1.77) female population: C-statistic: N.A predictive interval: N.A O:E ratio: N.A prediction interval: N.A
1,428 (ARIC study)					0.67	0.90 (0.68; 1.18)				
901 (Physicians Health Study)					0.63 (0.58; 0.67)	NR				
2,755 (Honolulu Heart Program)					0.72 (0.66; 0.77)	0.47 (0.38; 0.58)				
8,713 (Puerto Rico Hart Health Program)					0.69 (0.64; 0.74)	0.35 (0.29; 0.42)				
1,527 (Strong Heart Study)					0.69 (0.61; 0.76)	0.70 (0.53; 0.92)				
956 (Cardiovascu- lar Health Study)					0.63 (0.56; 0.69)	NR				
D'Agostino 2001 [100]		USA	FRS (Wilson women Total cholesterol)	5,712 (ARIC Study)	0.83	0.82 (0.63; 1.06)	fatal or nonfatal CHD	N.A		
				2,333 (ARIC Study)	0.79	1.07 (0.79; 1.44)				
				2,255 (Strong Heart Study)	0.75	0.43 (0.29; 0.62)				
				1,601 (Cardiovascu- lar Heart Study)	0.66 (0.57; 0.74)	NR				

FRAMINGHAM Risk score										
SR ref- erence	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration, E/O Ratio	Outcomes	Mean FU (yrs.)	Major findings	PS ROB
Damen et al. 2019 [91] <i>(continuation)</i>	Buitrago 2011 [104]	ES	FRS (Wilson total cholesterol)	m: 201	0.63 (0.51; 0.74)	0.67 (0.45; 1.00)	fatal or nonfatal CHD	N.A		high Risk
				f: 246	0.65 (0.42; 0.83)	0.42 (0.22; 0.83)				
	Empana 2003 [98]	NI	FRS (Wilson men LDL cholesterol)	2,399	0.66 (0.61; 0.71)	0.76 (0.64; 0.91)	fatal or nonfatal CHD	N.A		high risk
		F		7,359	0.68 (0.64; 0.72)	0.42 (0.37; 0.49)				
	Ferrario 2005 [101]	IT	FRS (Wilson men Total cholesterol)	6,865	0.72 (0.66; 0.77)	0.37 (0.34; 0.41)	fatal or nonfatal CHD	N.A		high risk
	Jee 2014 [97]	ROK	FRS (Wilson total cholesterol)	m: 164,005	N.A	N.A	fatal or nonfatal CHD	N.A		high risk
				f: 104,310						
	Lloyd-Jones 2004 [141]	N.A	FRS (Wilson total cholesterol)	m: 2,716	N.A	N.A	fatal or nonfatal CHD	N.A		unclear risk
				f: 3,500						
	Mainous 2007 [142]	USA	FRS (Wilson total cholesterol)	m: 6,239	0.69 (0.67; 0.71)	N.A	fatal or nonfatal CHD	N.A		Unclear risk
				f: 8,104	0.81 (0.79; 0.82)					
	Marrugat 2007 [103]	ES	FRS (Wilson total cholesterol)	m: 2,447	0.68 (0.63; 0.72)	0.41 (0.34; 0.49)	fatal or nonfatal CHD	N.A		high risk
				f: 3,285	0.73 (0.67; 0.78)	0.40 (0.30; 0.51)				
	Reissigova 2007 [102]	CZ	FRS (Wilson men Total cholesterol)	646	0.64 (0.58; 0.69)	0.22 (0.18; 0.26)	fatal or nonfatal CHD	N.A		high risk
	Rodondi 2012 [99]	USA	FRS (Wilson total cholesterol)	m: 981	0.58 (0.54; 0.63)	1.08 (0.96; 1.22)	fatal or nonfatal CHD	N.A		high risk
				f: 1,212	0.58 (0.52; 0.63)	2.05 (1.75; 2.40)				
	Ryckman 2015 [143]	USA	FRS (Wilson)	N.A	N.A	N.A	fatal or nonfatal CHD	N.A		high risk
	Simmons 2008 [144]	UK	FRS (Wilson total cholesterol)	m: 4,513	0.71 (0.69; 0.73)	0.55 (0.50; 0.60)	fatal or nonfatal CHD	N.A		high risk
				f: 5,782	0.71 (0.68; 0.74)	0.56 (0.49; 0.63)				
	Suka 2001 [145]	J	FRS (Wilson men Total cholesterol)	5,611	0.71 (0.65; 0.76)	N.A	fatal or nonfatal CHD	N.A		high risk
	Vaidya 2007 [96]	USA	FRS (Wilson total cholesterol)	m: 404	0.70 (0.64; 0.75)	1.70 (1.40; 2.07)	fatal or nonfatal CHD	N.A		high risk
				F: 380	0.79 (0.70; 0.85)	1.14 (0.79; 1.64)				

FRAMINGHAM Risk score											
SR reference	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size		C – Statistic	Calibration, E/O Ratio	Outcomes	Mean FU (yrs.)	Major findings	PS ROB
Erquo et al. 2025 [93]	Llaurado 2017 [121]	E	FRS	N=84	N=10	0.69 (0.55; 0.83)	N.A	SMI via perfusion stress	N.A	NA	4/7
	Zigbor 2006 [123]	USA	FRS	N=573	m	0.77 (0.63; 0.91)	H-L 310.3 (P < 0.0001)	fatal CHD, nonfatal MI, Q waves	11.2	N.A	4/7
					f	0.87 (0.73; 1,00)	H-L 6,873.9 (P < 0.0001)				
Buchan et al. 2021 [94]	Coleman et al. 2007 [132]	UK	FRS	3,898		0.76 (0.75; 0.77)	N.A	CV mortality	10.4	total pooled effect: 0.73 (0.67,0.78) model underestimates risk for low-risk patients and may overestimate for high risk patients (Argarwal; Coleman)	high risk
	Van der Heijen et al. 2009 [125]	NL	FRS	125		0.61 (0.37; 0.85)	N.A	CV mortality	10	N.A	high risk
	Agarwal et al. 2013 [146]	USA	FRS	1,123		0.70 (0.67; 0.73)	N.A	CV mortality	7.4	model underestimates risk for low-risk patients and may overestimate risk for high-risk patients	high risk
Zhang et al. 2024 [95]		UK	FRS	3,711		0.62 (0.58; 0.68)	slope: 0.839 (0.011)	congestive HF	4	showed overprediction of observed risk	N.A
		UK	FRS	18,160		0.63 (0.61; 0.65)	slope: 0.288 (0.011)	stroke	10		N.A

Abbreviations: ACS ... Acute Coronary Syndrome; anti-apoA-I ... Anti-Apolipoprotein A-I; anti-CCP ... Anti-Cyclic Citrullinated Peptide; ARIC ... Atherosclerosis Risk in Communities; ATP ... Adult Treatment Panel; CAD ... Coronary Artery Disease; CDN ... Canada; CH ... Switzerland; CHD ... Coronary Heart Disease; CI ... Confidence Interval; CRP ... C-Reactive Protein; CV ... Cardiovascular; CVA ... Cerebrovascular Accident; CVD ... Cardiovascular Disease; CZ ... Czech Republic; E ... Spain; eGFR ... Estimated Glomerular Filtration Rate; E/O ... Expected/Observed; ES ... Spain; ESC ... European Society of Cardiology; EULAR ... European League Against Rheumatism; F ... Female; FRS ... Framingham Risk Score; FU ... Follow-Up; GR ... Greece; HbA1c ... Hemoglobin A1c; HF ... Heart Failure; H-L ... Hosmer-Lemeshow; IC ... Intermittent Claudication; IT ... Italy; J ... Japan; LDL ... Low-Density Lipoprotein; M ... Male; MACE ... Major Adverse Cardiac Events; MEX ... Mexico; MI ... Myocardial Infarction; N ... Norway; N.A ... Not Available; NHG ... Nederlands Huisartsen Genootschap; NI ... Northern Ireland; NL ... Netherlands; NR ... Not Reported; NRI ... Net Reclassification Improvement; NT-proBNP ... N-Terminal Pro-B-Type Natriuretic Peptide; ox-LDL ... Oxidized Low-Density Lipoprotein; PAD ... Peripheral Arterial Disease; PCE ... Pooled Cohort Equations; PMCU ... Preventive Medical Check-Up; PS ... Primary Study; PVD ... Peripheral Vascular Disease; RA ... Rheumatoid Arthritis; RECODE ... Risk Estimation for Cardiovascular Disease in Diabetes; RF ... Risk Factors; ROB ... Risk of Bias; ROK ... Republic of Korea; S ... Sweden; SIGN ... Scottish Intercollegiate Guidelines Network; SMI ... Silent Myocardial Infarction; SR ... Systematic Review; T1DM ... Type 1 Diabetes Mellitus; T2DM ... Type 2 Diabetes Mellitus; TIA ... Transient Ischemic Attack; UK ... United Kingdom; UKPDS ... United Kingdom Prospective Diabetes Study; USA ... United States of America; VS ... Validation Study; W ... Women; yrs ... Years; ZA ... South Africa

Table A-3: SCORE characteristics and statistics

SCORE										
SR reference	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration: expected/ observed	Outcomes	Mean FU (yrs)	Major findings	PS RoB
Colaco et al. 2020 [89]	Arts 2015 [119]	NL	SCORE	1,157	0.78	NR.	ACS, angina, CVA, TIA, PVD, HF	N.A	SCORE underestimated the risk of future CV risk	moderate Risk
	Arts 2016 [147]	NL	SCORE	1,016	0.78	NR	ACS, CVA, HF, CV death	N.A	original and adapted SCORE underestimated risk in low and moderate risk groups, and overestimated the risk in high risk groups. No improvement in risk estimates in adapted SCORE	moderate Risk
					0.78					
					0.80					
	Crowson 2017 [116]	UK, N, NL, USA, S; GR; ZA, E, CDN, MEX	SCORE	5,638	0.70	NR	ACS, chronic ischemic heart disease, coronary revascularization, coronary death, other CV death, cerebrovascular events, peripheral vascular events	5.8	SCORE overestimated CV risk	high risk
	Navarini 2018 [118]	IT	SCORE SCORE + EULAR	155	0.77 0.77	N.A	CV death, CAD (stable and unstable angina, MI), CVA, TIA, PAD, HF	N.A	SCORE underestimated CV risk	moderate risk
Buchan et al. 2021 [94]	Coleman et al. 2007 [132]	UK	SCORE	3,898	0.77 (0.76; 0.78)	N.A	CV mortality	10.4	pooled effect: 0.77 (0.76; 0.78)	high risk
	Van der Heijen et al. 2009 [125]	NL	SCORE	125	0.74 (0.56; 0.92)	N.A	CV mortality	10		high risk
Zhang et al. 2024 [95]		UK	SCORE	20,527	0.63 (0.62; 0.65) f: 0.61 m: 0.60	slope: 0.331 (0.019)	CV mortality	10	low-modest discrimination and low calibration, with overprediction of observed risk. little numerical difference between sexes, slightly better performance in younger age group (40-59) and non-white ethnicities.	N.A

Abbreviations: ACS ... Acute Coronary Syndrome; CAD ... Coronary Artery Disease; CDN ... Canada; CV ... Cardiovascular; CVA ... Cerebrovascular Accident; E ... Spain; EULAR ... European League Against Rheumatism; GR ... Greece; HF ... Heart Failure; IT ... Italy; MEX ... Mexico; MI ... Myocardial Infarction; N ... Norway; N.A ... Not Available; NL ... Netherlands; NR. ... not reported; PAD ... Peripheral Arterial Disease; PVD ... Peripheral Vascular Disease; ROB ... Risk of Bias; SCORE ... Systematic Coronary Risk Evaluation; S ... Sweden; TIA ... Transient Ischemic Attack; UK ... United Kingdom; USA ... United States of America; ZA ... South Africa

Table A-4: QRISK characteristics and statistics

QRISK										
SR reference	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration: expected/observed	Outcomes	Mean FU(yrs.)	Major findings	PS RoB
Colaco et al. 2020 [89]	Alemao 2017 [115]	UK	QRISK 2	12,747	0.76	N.A	MI, CHD, stroke, TIA	6	QRISK 2 underestimates CV risk discrimination of QRISK2 was lower in the RA population compared to the general population. CRP addition was not associated with significant improvement in reclassification of CV risk	moderate risk
			QRISK 2+ CRP		0.77	NRI = –2.0% (95% CI: –5.8, 4.5)				
	Arts 2015 [119]	NL	QRISK2	1,157	0.79	N.A	ACS, angina, CVA, TIA, PVD, HF	N.A	QRISK2 overestimated the risk of future CV events	moderate risk
	Crowson 2017 [116]	UK, N, NL, USA, S; GR; ZA, E, CDN, MEX	QRISK 2	5,638	0.72	N.A	ACS, chronic ischemic heart disease, coronary revascularization, coronary death, other CV death, cerebrovascular events, peripheral vascular events	5.8	QRISK2 overestimated CV risk	high risk
	Crowson 2017 [120]	UK, N, NL, USA, ZA, CDN, MEX	QRISK2	1,796	0.72	QRISK2 vs PCE: NRI = –2.4% (95% CI: –10.9, 6.5) QRISK2 vs FRS: NRI = 25% (95% CI: –9.4, 34.7)	MI, ischemic stroke, CV death	6.9	QRISK2 Significantly overestimated CV risk RA specific risk calculators (like QRISK2) did not predict CV disease more accurately than traditional scores (like PCE, FRS)	high risk
	Navarini 2018 [118]	IT	QRISK2	155	0.87	N.A	CV death, CAD (stable and unstable angina, MI), CVA, TIA, PAD, HF	N.A	QRISK2 underestimated CV risk. EULAR multiplier did not increase discriminative ability or calibration	moderate risk
			QRISK2 + EULAR multiplier		0.87					
Erqou et al. 2025 [93]	McGurnaghan 2021 [124]	GB-SCT.	QRISK3	27,527	0.75 (0.74; 0.76)	E:O Ratio: 0.72	MI/stroke/UA/TIA/PVD or CAD/CVD/PAD/ACS	10	NA	6/7
		SE		33,183						

Abbreviations: ACS ... Acute Coronary Syndrome; CAD ... Coronary Artery Disease; CDN ... Canada; CHD ... Coronary Heart Disease; CI ... Confidence Interval; CRP ... C-Reactive Protein; CV ... Cardiovascular; CVA ... Cerebrovascular Accident; CVD ... Cardiovascular Disease; E ... Spain; E:O ... Expected to Observed; EULAR ... European League Against Rheumatism; FRS ... Framingham Risk Score; FU ... Follow-Up; GB-SCT ... Great Britain-Scotland; GR ... Greece; HF ... Heart Failure; IT ... Italy; MEX ... Mexico; MI ... Myocardial Infarction; N ... Norway; N.A ... Not Available; NL ... Netherlands; NRI ... Net Reclassification Improvement; PAD ... Peripheral Arterial Disease; PCE ... Pooled Cohort Equations; PS ... Primary Study; PVD ... Peripheral Vascular Disease; QRISK2 ... QRISK version 2; QRISK3 ... QRISK version 3; RA ... Rheumatoid Arthritis; RoB ... Risk of Bias; S ... Sweden; SR ... Systematic Review; TIA ... Transient Ischemic Attack; UA ... Unstable Angina; UK ... United Kingdom; USA ... United States of America; yrs ... Years; ZA ... South Africa

Table A-5: UKPDS characteristics and statistics

UKPDS										
SR ref- erence	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration expected/ observed	Outcomes	Mean FU (yrs.)	Major findings	PS RoB
Erquo et al. 2025 [93]	Zgibor 2006 [123]	US	UKPDS	537	0.76	H-L 324.1 (p < 0.0001)	fatal CHD, nonfatal MI	11.2	UKPDS Risk engine were poorly calibrated O/E >1 managing CVD risk in T1DM should not be based on scores developed for T2DM or general population	4/7
	Llaurado 2017 [121]	ES	UKPDS	84	0.56 (0.42; 0.69)	NR	SMI via perfusion stress	N.A		4/7
	Vistisen 2016 [122]	DK	UKPDS	4,306	0.77 (0.74; 0.79)	H-L 711.8 (p < 0.001)	CHD, CVA, PVD, HF	6.8		6/7
				2,118	0.74 (0.70; 0.78)	H-L 210.9 (p < 0.001)		6.6		6/7
Buchan et al. 2021 [94]	Van der Heijen 2009 [125]	NL	UKPDS Outcomes Model 1	125	0.72 (0.55; 0.89)	N.A	CV Mortality	10	UKPDS Model1 pooled C statistic: CV mortality: 0.7 (0.58;0.81) Stroke: 0.7 (0.66; 0.74) summary of calibration: overestimates risk for CV mortality may overestimate risk for stroke UKPDS Model 2 pooled C Statistic: CV Mortality: 0.68 (0.61;0.75) stroke: 0.60 (0.5;0.61) MI: 0.64 (0.58;0.70) summary of calibration: model has good calibration for CV Mortality for low risk patients and may overestimate risk for high-risk patients model may overestimate risk for MI inconsistent calibration for estimation of risk across studies	high risk
	Davis 2009 [129]	AU	UKPDS Outcomes Model 1	791	0.68 (0.53; 0.83)	N.A	CV Mortality	5		high risk
					0.86 (0.79; 0.93)		stroke			
	Yew 2019 [127]	MY	UKPDS Outcomes Model 2	660	0.71 (0.68; 0.74)	N.A	CV Mortality	10		high risk
					0.57 (0.19; 0.96)		stroke			
	Laxy 2019 [128]	DE	UKPDS Outcomes Model 2	456	0.64 (0.58; 0.70)	N.A	CV Mortality	N.A		high risk
					0.57 (0.48; 0.66)		stroke			
	Basu 2018 [131]	USA	UKPDS Outcomes Model 2	1,746	0.57 (0.55; 0.59)	N.A	MI	8		two low risk; two high risk (RoB by outcome)
					0.60 (0.5; 0.62)		stroke			
				1,555	0.60 (0.57; 0.63)		stroke	9.1		
	Tao 2013 [148]	DK, UK, NL	UKPDS Outcomes Model 2	2,899	0.72 (0.66; 0.78)	N.A	MI	5.3		low risk
			UKPDS Outcomes Model 1		0.70 (0.64; 0.76)		stroke			
	Basu 2017 [54]	USA	UKPDS Outcomes Model 2	9,635	0.62 (0.60; 0.64)	N.A	MI	10.6		four Low Risk RoB by outcome
					0.61 (0.56; 0.66)		stroke			
4,760				0.67 (0.65; 0.69)	MI		4.7			
				0.63 (0.58; 0.68)	stroke					
Tanaka 2013 [149]	J	UKPDS Outcomes Model 1	1,748	0.64 (0.57; 0.71)	N.A	stroke	7.2	high risk		

UKPDS										
SR ref- erence	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration expected/ observed	Outcomes	Mean FU (yrs.)	Major findings	PS RoB
Buchan et al. 2021 [94] (cont.)	Bannister 2014 [126]	UK	UKPDS Outcomes Model 1	36,746	f: 0.73 (0.72; 0.74)	N.A	stroke	4.2		high risk
				43,200	m: 0.71 (0.70; 0.72)					
	Yang, 2007 [109]	HK	UKPDS Outcomes Model 1	3,541	0.59 (0.55; 0.63)	N.A	stroke	5.4		low risk
Zhang et al. 2024 [95]		UK	UKPDS Outcomes Model 2	8,222	0.67 (0.66; 0.69) f: 0.67 m: 0.67	slope: 0.589 (0.026)	all-cause mortality	12	low-modest discrimination and low calibration, with overprediction of observed risk. little numerical difference between sexes, slightly better performance in younger age group (40-59) and non-white ethnicities.	N.A
					0.71 (0.70; 0.73) f: 0.74 m: 0.68	slope: 0.506 (0.013)	CV mortality			
					0.58 (0.56; 0.59) f: 0.55 m: 0.6	slope: 0.690 (0.085)	congestive HF			
					0.60 (0.58; 0.63) f: 0.59 m: 0.59	slope: 0.268 (0.034)	MI			
					0.60 (0.57; 0.62) f: 0.58 m: 0.6	slope: 0.489 (0.072)	stroke			
					0.50 (0.48; 0.51) f: 0.5 m: 0.52	slope: 0.391 (0.210)	ischaemic heart disease/coronary heart disease			

Abbreviations: AU ... Australia; CHD ... Coronary Heart Disease; CV ... Cardiovascular; CVA ... Cerebrovascular Accident; CVD ... Cardiovascular Disease; DE ... Germany; DK ... Denmark; ES ... Spain; F ... Female; FU ... Follow-Up; HF ... Heart Failure; HK ... Hong Kong; H-L ... Hosmer-Lemeshow; J ... Japan; M ... Male; MI ... Myocardial Infarction; MY ... Malaysia; N.A ... Not Available; NL ... Netherlands; NR. ... not reported; O/E ... Observed to Expected; PS ... Primary Study; PVD ... Peripheral Vascular Disease; RoB ... Risk of Bias; SMI ... Silent Myocardial Infarction; SR ... Systematic Review; T1DM ... Type 1 Diabetes Mellitus; T2DM ... Type 2 Diabetes Mellitus; UK ... United Kingdom; UKPDS ... United Kingdom Prospective Diabetes Study; US/USA ... United States of America; yrs ... Years

Table A-6: PCE characteristics and statistics

PCE										
SR reference	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration: expected/ observed	Outcomes	Mean FU (yrs.)	Major findings	PS RoB
Colaco et al. 2020 [89]	Crowson 2017 [116]	UK, N, NL, USA, S; GR; ZA, E, CDN, MEX	PCE	5,638	0.72	N.A	ACS, chronic ischemic heart disease, coronary revascularisation, coronary death, other CV death, cerebrovascular events, peripheral vascular events	5.8	PCE underestimated risk	high Risk
	Crowson 2017 [120]	UK, N, NL, USA, ZA, CDN, MEX	PCE	1,796	0.72	N.A	MI, ischemic stroke, CV death	6.9	PCE overestimated risk	high risk
			PCE+ EULAR		0.72					
Damen et al. 2019 [91]	Andersson 2015 [150]	N.A	PCE	m: 3,396	0.72 (0.69; 0.65)	0.84 (0.75; 0.94)	fatal or nonfatal CVD	10	pooled performance: male population: c-statistic: 0.7 (0.68; 0.72)	high risk
				f: 3,838	0.77 (0.72; 0.81)	0.67 (0.55; 0.83)				high risk
	Chia 2014 [105]	MAL	PCE	m: 307	0.55 (0.45; 0.64)	0.34 (0.23; 0.51)	fatal or nonfatal CVD	N.A	prediction interval: 0.7 (0.68; 0.79)	high risk
				f: 615	0.61 (0.49; 0.72)	0.55 (0.37; 0.83)				high risk
	De Filippis 2017 [112]	USA	PCE	m: 3,053	0.71 (0.67; 0.74)	0.52 (0.46; 0.59)	fatal or nonfatal CVD	N.A	O:E ratio: 0.66 (0.59; 0.73)	high risk
				f: 3,388	0.74 (0.70; 0.78)	0.50 (0.43; 0.83)				high risk
	De Las Heras Gala 2016 [108]	D	PCE (HNR study)	m: 2,584	0.67 (0.63; 0.71)	0.62 (0.54; 0.71)	fatal or nonfatal CVD	N.A	pooled performance +CI 0.66 (0.59; 0.73)	KORA: high risk, HNR: unclear risk
				f: 2,654	0.76 (0.70; 0.80)	0.59 (0.48; 0.73)				
			PCE (Kora study)	m: 2,584	0.74 (0.71; 0.76)	0.70 (0.62; 0.79)				
				f: 2,654	0.81 (0.77; 0.84)	0.80 (0.67; 0.95)				
	Emdin 2017 [151]	USA	PCE	m: 1,635	0.63 (0.54; 0.71)	0.41 (0.30; 0.55)	fatal or nonfatal CVD	N.A	female population: c-statistic: 0.74 (0.72; 0.76)	high risk
				f: 2,000	0.63 (0.57; 0.69)	0.33 (0.22; 0.49)				high risk
	Goff 2014 [50]	USA	PCE (white American)	m: 5,041	0.68 (0.66; 0.71)	0.73 (0.67; 0.78)	fatal or nonfatal CVD	N.A	predictive interval: 0.74 (0.63; 0.83)	high risk
				f: 6,509	0.74 (0.71; 0.76)	0.78 (0.71; 0.85)				
			PCE (African American)	m: 7,35	0.71 (0.66; 0.76)	0.944 (0.8; 1.12)				
				f: 1,367	0.71 (0.66; 0.75)	0.94 (0.8; 1.1)				
	Jung 2015 [106]	South Korea	PCE	m: 114,622	0.73 (0.72; 0.73)	0.63 (0.62; 0.65)	fatal or nonfatal CVD	N.A	O:E ratio: 0.76 (0.65; 0.88)	high risk
				f: 77,983	0.74 (0.73; 0.75)	0.57 (0.56; 0.59)				high risk
	Kavousi 2014 [107]	NL	PCE	m: 1,513	0.67 (0.63; 0.71)	0.59 (0.52; 0.68)	fatal or nonfatal CVD	N.A	prediction interval: 0.76 (0.38; 1.55)	unclear risk
				f: 1,920	0.68 (0.63; 0.72)	0.68 (0.58; 0.80)				

PCE										
SR ref- erence	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration: expected/ observed	Outcomes	Mean FU (yrs.)	Major findings	PS RoB
Damen et al 2019 [91] <i>(continuation)</i>	Khalili 2015 [110]	IR	PCE	m: 2,353	0.74 (0.70; 0.77)	0.76 (0.66; 0.87)	fatal or nonfatal CVD	N.A		high risk
				f: 2,749	0.82 (0.78; 0.86)	0.84 (0.69; 1.12)				
	Lee 2015 [152]	CHN	PCE	m: 679	0.71 (0.61; 0.80)	1.05 (0.87; 1.27)	fatal or nonfatal CVD	N.A		high risk
				f: 797	0.76 (0.68; 0.83)	1.44 (1.11; 1.87)				
	Mortensen 2017 [153]	DK	PCE	m: 19,383	0.71 (0.69; 0.72)	0.66 (0.01; 1)	fatal or nonfatal CVD	N.A		high risk
				f: 25,506	0.71 (0.69; 0.73)	1.28 (0.01; 1)				
	Muntner 2014 [154]	USA	PCE	m: N.A	0.65 (0.62 ;0.68)	0.72 (0.66; 0.79)	Fatal or nonfatal CVD	N.A		high risk
				f: N.A	0.74 (0.71; 0.76)	0.81 (0.73; 0.90)				
	Pike 2016 [155]	USA	PCE	m: 3,093	0.63 (0.59; 0.66)	0.61 (0.54; 0.69)	fatal or nonfatal CVD	N.A		high risk
				f: 5,690	0.69 (0.66; 0.72)	0.61 (0.54; 0.69)				
	Rana 2016 [156]	USA	PCE	m:118,080	0.68 (0.00;1.00)	N.A	fatal or nonfatal CVD	N.A		high risk
				f: 189,511	0.72 (0.00; 1.00)					
	Sussman 2017 [157]	USA	PCE	m: 143,593	0.66 (0.65; 0.66)	0.63 (0.62; 0.63)	fatal or nonfatal CVD	N.A		high risk
				f: 76,155	0.73 (0.70; 0.75)	0.91 (0.87; 0.96)				
	Yang 2016 [109]	CHN	PCE Cohort: InterASIA and China MUCA (1998) White men and women	m: 10,334	0.76 (0.74; 0.78)	0.66 (0.60; 0.72)	fatal or nonfatal CVD	N.A		high risk
				f: 10,986	0.78 (0.75; 0.82)	1.10 (0.98; 1.24)				
			PCE Cohort: China MUCA (1992) white men and women	m: 6,565	0.77 (0.73; 0.80)	0.645 (0.57; 0.74)				
				f: 7,558	0.77 (0.77; 0.80)	1.37 (1.18; 1.59)				
PCE CIMIC			m: 26,872	0.76 (0.74; 0.78)	0.64 (0.59; 0.68)					
			f: 43,966	0.79 (0.75; 0.82)	1.11 (1.03; 1.19)					

Abbreviations: ACS ... Acute Coronary Syndrome; CDN ... Canada; CHN ... China; CI ... Confidence Interval; CIMIC ... China Multi-Provincial Cohort Study; CV ... Cardiovascular; CVD ... Cardiovascular Disease; D ... Germany; DK ... Denmark; E ... Spain; EULAR ... European League Against Rheumatism; F ... Female; FU ... Follow-Up; GR ... Greece; HNR ... Heinz Nixdorf Recall; IR ... Iran; KORA ... Cooperative Health Research in the Region of Augsburg; M ... Male; MAL ... Malaysia; MEX ... Mexico; MI ... Myocardial Infarction; MUCA ... Multicenter Collaborative Study of Cardiovascular Epidemiology; N ... Norway; N.A ... Not Available; NL ... Netherlands; O:E ... Observed to Expected; PCE ... Pooled Cohort Equations; PS ... Primary Study; RoB ... Risk of Bias; S ... Sweden; SR ... Systematic Review; UK ... United Kingdom; USA ... United States of America; ZA ... South Africa

Table A-7: FRS-ATP characteristics and statistics

FRS- ATP										
SR ref- erence	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic	Calibration: expected/observed	Outcomes	Mean FU (yrs.)	Major findings	PS RoB
Colaco et al. 2020 [89]	Crowson 2017 [120]	UK, N, NL, USA, ZA, CDN, MEX	FRS-ATP	1,796	0.75	NR	MI, ischemic stroke, CV death	6.9	FRS underestimated risk in the highest risk groups	high risk
			FRS-ATP + EULAR multiplier		0.75					
Damen et al. 2019 [91]	Koller 2012 [111]	NL	ATP III (Rotterdam Study)	m: 1,454	0.60 (0.56; 0.63)	N.A	fatal or nonfatal CHD	N.A	pooled estimate: male population c-statistic: 0.64 (0.59;0.68) prediction interval: 0.64 (0.48,0.77) O:E ratio: 0.58 (0.37; 0.79)	unclear risk
				f: 2,849	0.65 (0.61; 0.68)					
			ATP III (Cardiovascular Health Study)	m: 1,917	0.60 (0.57; 0.63)					high risk
				f: 3,029	0.66 (0.63; 0.68)					
	Cooper 2005 [113]	UK	ATP III	m: 2,732	0.62 (0.58; 0.66)	0.47	fatal or nonfatal CHD	N.A	unclear risk	
	De Filippis 2015 [112]	USA	ATP III	m: 1,961	0.71 (0.65; 0.76)	0.39 (0.32; 0.47)	fatal or nonfatal CHD	N.A	prediction interval: 0.58(0.16;2.13) female population c-statistic: 0.66 (0.65;0.67) prediction interval: 0.66 (0.63;0.69) O:E ratio: 0.79 (0.6;0.97) prediction interval: 0.79 (0.27,2.23)	unclear risk
				f: 2,266	0.67 (0.59; 0.74)	0.69 (0.53; 0.90)				
	Kavousi 2014 [107]	NL	ATP III	m: 1,431	0.67 (0.62; 0.72)	0.42 (0.35; 0.52)	fatal or nonfatal CHD	N.A		
				f: 1,976	0.69 (0.63; 0.75)	0.57 (0.44; 0.74)				

Abbreviations: ATP III ... Adult Treatment Panel III; CDN ... Canada; CHD ... Coronary Heart Disease; CV ... Cardiovascular; EULAR ... European League Against Rheumatism; F ... Female; FRS-ATP ... Framingham Risk Score – Adult Treatment Panel; M ... Male; MEX ... Mexico; MI ... Myocardial Infarction; N ... Norway; N.A ... Not Available; NL ... Netherlands; NR ... not reported; O:E ... Observed to Expected; PS ... Primary Study; RoB ... Risk of Bias; SR ... Systematic Review; UK ... United Kingdom; USA ... United States of America; yrs ... Years; ZA ... South Africa

Table A-8: RECODE characteristics and statistics

RECODE											
SR ref- erence	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic [Cohort]		Calibration: expected/ observed	Outcomes	Mean follow- up (yrs.)	Major findings	PS RoB
Buchan et al. 2021 [94]	Basu 2018 [131]	USA	RECODE	[MESA] 1,555 [JHS] 1,746	[MESA] 0.81 (0.76; 0.86) [JHS] 0.78 (0.75; 0.81)		N.A	all-cause mortality	[MESA] 9.1	AC mortality: model has perfect calibration for low-risk patients. pooled C statistic: 0.75 (0.70; 0.80) high certainty evidence CV mortality: model has perfect calibration for low-risk patients pooled C statistic: 0.79 (0.75; 0.84) Low certainty evidence MI: MI model has perfect calibration for low-risk patients pooled C statistic: 0.72 (0.69 to 0.74) moderate certainty of evidence	four low risk four high risk (RoB by Outcome)
					[MESA] 0.81 (0.76; 0.86) [JHS] 0.87 (0.79; 0.95)			CV mortality			
					[MESA] 0.73 (0.69; 0.77) [JHS] 0.74 (0.72; 0.76)			MI	[JHS] 8		
					[MESA] 0.75 (0.71; 0.79) [JHS] 0.72 (0.70; 0.74)			stroke			
	Basu 2017 [54]	USA	RECODE	[Look AHEAD] 4,760 [ACCORD] 9,635	[Look AHEAD] 0.71(0.68; 0.74)		N.A	all-cause mortality	[Look AHEAD] 10.6		seven low risk (RoB by Outcome)
					[Look AHEAD] 0.79 (0.75; 0.83)	[ACCORD] 0.74 (0.71; 0.77)		CV mortality			
					Look [AHEAD] 0.71 (0.68; 0.74)	[ACCORD] 0.69 (0.68; 0.70)		MI	[ACCORD] 4.7		
					[Look AHEAD] 0.67 (0.63; 0.71)	[ACCORD] 0.70 (0.66; 0.74)		stroke			
	Copetti 2019 [130]	[GMS, FMS and PMS] IT	RECODE	1,082	0.74 (0.53; 0.95)		N.A	all-cause mortality	N.A	stroke: model may underestimate risk among low-risk patients. pooled C statistic: 0.71 (0.68 to 0.74) moderate certainty of evidence	low risk GMS FMS, PMS)
		[ACCORD] USA, CND		3,150	0.69 (0.65; 0.73)				5		high risk ACCORD)
Zhang et al. 2024 [95]		UK	RECODE	9,192	0.67 (0.65; 0.69) Female: 0.68 Male: 0.66		Slope: 1.765 (0.000)	All-cause mortality	10	RECODE had the best calibration performance for all comparable outcomes (CV mortality, congestive HF, MI, stroke) except all-cause mortality Low-modest discrimination and low calibration, with over- prediction of observed risk little numerical difference	N.A
					0.70 (0.67; 0.72) Female: 0.71 Male: 0.68		Slope: 1.420 (0.003)	CV mortality			
					0.71 (0.69; 0.72) Female: 0.69 Male: 0.71		Slope: 1.023 (0.016)	Congestive HF			

RECODE										
SR ref- erence	PS reference	Country of application of the model	Model version/ Model Comparison	Sample size	C – Statistic [Cohort]	Calibration: expected/ observed	Outcomes	Mean follow- up (yrs.)	Major findings	PS RoB
Zhang et al. 2024 [95] (cont.)					0.67 (0.65; 0.68) Female: 0.66 Male: 0.65	Slope: 1.541 (0.010)	MI		between sexes, slightly better performance in younger age group (40-59) and non-white ethnicities	
					0.65 (0.62; 0.68) Female: 0.67 Male: 0.64	Slope: 1.120 (0.021)	stroke			

Abbreviations: AC ... All-Cause; ACCORD ... Action to Control Cardiovascular Risk in Diabetes; CDN/CND ... Canada; CV ... Cardiovascular; FMS ... Foggia Monogenic Study; GMS ... Gargano Mortality Study; IT ... Italy; JHS ... Jackson Heart Study; HF ... heart failure; Look AHEAD ... Action for Health in Diabetes; MESA ... Multi-Ethnic Study of Atherosclerosis; MI ... Myocardial Infarction; N.A ... Not Available; PMS ... Padova Monogenic Study; PS ... Primary Study; RECODE/RECODE ... Risk Equations for Complications Of type 2 Diabetes; RoB ... Risk of Bias; SR ... Systematic Review; UK ... United Kingdom; USA ... United States of America; yrs ... Years

Search strategy

Search strategy for Cochrane

Search Name: Risk prediction models & scores for CVDs	
Last Saved: 28/05/2025 18:15:20	
Comment: JP/LG (Vorsorgeuntersuchungen)	
ID	Search
#1	MeSH descriptor: [Cardiovascular Diseases] explode all trees
#2	(cardio?vascular*) (Word variations have been searched)
#3	(cardio-vascular*) (Word variations have been searched)
#4	(CVD):ti,ab,kw (Word variations have been searched)
#5	#1 OR #2 OR #3 OR #4
#6	MeSH descriptor: [Predictive Value of Tests] explode all trees
#7	(predict* NEAR model*) (Word variations have been searched)
#8	#6 OR #7
#9	#5 AND #8
#10	MeSH descriptor: [Risk Assessment] explode all trees
#11	MeSH descriptor: [Risk Factors] explode all trees
#12	(risk* NEAR (predict* OR model* OR score*)) (Word variations have been searched)
#13	#10 OR #11 OR #12
#14	#9 AND #13
#15	#9 AND #13 in Cochrane Reviews, Cochrane Protocols
#16	#9 AND #13 with Cochrane Library publication date Between Jan 2015 and May 2025, in Cochrane Reviews, Cochrane Protocols
Total hits: 46	

Search strategy for Embase

Search Name:		
Search date: 28 May 2025		
No.	Query Results	Results
#27.	#23 NOT #2	617
#26.	#24 OR #25	339,462
#25.	'clinical trial':dtype	339,305
#24.	#23 AND 'conference abstract'/it	157
#23.	#22 AND [2015-2025]/py	782
#22.	#19 OR #21	937
#21.	#18 AND #20	927
#20.	('meta analysis'/exp OR 'systematic review'/exp OR ((meta NEAR/3 analy*):ab,ti) OR metaanaly*:ab,ti OR review*:ti OR overview*:ti OR ((synthes* NEAR/3 (literature* OR research* OR studies OR data)):ab,ti) OR (pooled AND analy*:ab,ti) OR (((data NEAR/2 pool*):ab,ti) AND studies:ab,ti) OR medline:ab,ti OR medlars:ab,ti OR embase:ab,ti OR cinahl:ab,ti OR scisearch:ab,ti OR psychinfo:ab,ti OR psycinfo:ab,ti OR psychlit:ab,ti OR psyclit:ab,ti OR cinhal:ab,ti OR cancerlit:ab,ti OR cochrane:ab,ti OR bids:ab,ti OR pubmed:ab,ti OR ovid:ab,ti OR (((hand OR manual OR database* OR computer*) NEAR/2 search*):ab,ti) OR ((electronic NEAR/2 (database* OR 'data base' OR 'data bases')):ab,ti) OR bibliograph*:ab OR 'relevant journals':ab OR (((review* OR overview*) NEAR/10 (systematic* OR methodologic* OR quantitativ* OR research* OR literature* OR studies OR trial* OR effective*)):ab)) NOT (((retrospective* OR record* OR case* OR patient*) NEAR/2 review*):ab,ti) OR (((patient* OR review*) NEAR/2 chart*):ab,ti) OR rat:ab,ti OR rats:ab,ti OR mouse:ab,ti OR mice:ab,ti OR hamster:ab,ti OR amsters:ab,ti OR animal:ab,ti OR animals:ab,ti OR dog:ab,ti OR dogs:ab,ti OR cat:ab,ti OR cats:ab,ti OR bovine:ab,ti OR sheep:ab,ti) NOT ('editorial'/exp OR 'erratum'/de OR 'letter'/exp) NOT (('animal'/exp OR 'nonhuman'/exp) NOT (('animal'/exp OR 'nonhuman'/exp) AND 'human'/exp))	1,905,525
#19.	#18 AND [systematic review]/lim	409
#18.	#10 AND #17	11,912

#17.	#11 OR #12 OR #13 OR #14 OR #15 OR #16	292,436
#16.	risk* NEAR/3 (predict* OR model* OR score*)	292,426
#15.	'risk prediction tool'/exp	11
#14.	'score'/exp	22
#13.	'risk prediction score'/exp	16
#12.	'risk prediction model'/exp	107
#11.	'risk prediction'/exp	113
#10.	#5 AND #9	48,747
#9.	#6 OR #7 OR #8	531,013
#8.	predict* NEAR/2 model*	255,178
#7.	'predictive model'/exp	30,214
#6.	'predictive value'/exp	295,672
#5.	#1 OR #2 OR #3 OR #4	2,210,676
#4.	cvd:ti,ab	92,950
#3.	'cardio vascular*'	8,528
#2.	cardio*vascular*	2,198,822
#1.	'cardiovascular disease'/de	423,462
Total hits: 617		

Search strategy for Medline via Ovid

Database: Ovid MEDLINE(R) ALL <1946 to May 27, 2025>	
Search date: 28.05.2025	
ID	Search
1	*Cardiovascular Diseases/ (144145)
2	cardio?vascular*.mp. (768135)
3	cardio-vascular*.mp. (2890)
4	CVD.ti,ab. (59158)
5	1 or 2 or 3 or 4 (778674)
6	exp "Predictive Value of Tests"/ (234152)
7	(predict* adj3 model*).mp. (233158)
8	6 or 7 (456264)
9	5 and 8 (25313)
10	exp Risk Assessment/ (332956)
11	exp Risk Factors/ (1039703)
12	(risk* adj5 (predict* or model* or score*)).mp. (260324)
13	10 or 11 or 12 (1413899)
14	9 and 13 (13728)
15	limit 14 to "systematic review" (266)
16	((comprehensive* or integrative or systematic*) adj3 (bibliographic* or review* or literature)) or (meta-analy* or metaanaly* or "research synthesis" or ((information or data) adj3 synthesis) or (data adj2 extract*)).ti,ab. or (cinahl or (cochrane adj3 trial*) or embase or medline or psycit or (psycinfo not "psycinfo database") or pubmed or scopus or "sociological abstracts" or "web of science").ab. or ("cochrane database of systematic reviews" or evidence report technology assessment or evidence report technology assessment summary).jn. or Evidence Report: Technology Assessment*.jn. or ((review adj5 (rationale or evidence or safety or effectiveness)).mp. and review.pt.) or meta-analysis as topic/ or Meta-Analysis.pt. (884290)
17	14 and 16 (655)
18	15 or 17 (658)
19	limit 18 to yr="2015 - 2025" (477)
20	remove duplicates from 19 (474)
Total hits: 474	



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