Title: "An Exploration of the Incorporation of Prediction Models in (inter) national clinical practice guidelines in cardiology"

Master of Science degree in Epidemiology (Medicine faculty-Utrecht University): Writing assignment

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Laymen's summary

A range of disorders associated with atherosclerosis affecting the heart and vascular system, collectively known as cardiovascular diseases, are the primary global cause of mortality. Each year, Cardiovascular Diseases (CVDs) claim the lives of millions due to heart attacks and strokes, underscoring the importance of prompt and preventive healthcare measures. The World Health Organization (WHO) has indicated that a significant proportion of global deaths are attributed to CVDs. The spectrum of these diseases is broad, extending beyond Coronary Heart Disease (CHD) to include heart failure, cerebrovascular disease, myocardial infarction, peripheral arterial disease, aortic disease, and arrhythmias. In the Netherlands, ischemic heart disease accounts for a substantial share of the mortality rate as well.

To address the issue of cardiovascular diseases (CVDs), associations and medical centres are crafting guidelines that enable swift and accurate medical decisions. These guidelines assist clinicians in forecasting the progression of CVDs, allowing for timely medication prescriptions or recommendations for a specific life style. Integral to these guidelines are risk estimates for patient outcomes. Clinicians have access to various tools within these guidelines, including prediction models. These models are mathematical constructs that factor in patient characteristics like blood pressure, cholesterol levels, physical activity, the disease's current state, etc. With these risk estimates, clinicians and healthcare professionals can determine the best medical management course. This research endeavour aimed to compile the prediction models, their outputs, and the patient groups they target, as outlined in the CVD guidelines.

In pursuit of this goal, an explorative review of cardiovascular disease (CVD) medical guidelines was conducted. The process involved identifying relevant guidelines and cataloguing the various models they contain, along with their intended outcomes and target patient groups. The sources providing explanations for these prediction models were also noted. Standardized instruments and checklists were employed to ensure methodological rigour. Data on the prediction models, including the publication year of the guidelines and any subsequent corrections, were compiled. The organization of these prediction models within the guidelines and details on their application for forecasting the progression of CVD is vitally important. It can significantly enhance the methodological approach to utilizing timely information for making specific decisions in CVD management.

The study uncovered 17 guidelines that describe 23 different models for forecasting the trajectory of cardiovascular diseases (CVDs). These models are mentioned in the guidelines as instruments for prediction. Yet, there's no guidance on the use or whether alternative models could be employed interchangeably for identical prognoses within the same guideline. Additionally, there's a lack of standardized definitions for risk estimations among similar patient groups, which may hinder accurate disease progression predictions. The focus of these models is mainly on assessing the risk of sudden cardiac death, overall long-term risk, mortality rates, or the probability of developing CVD. Although the guidelines cite external sources that elaborate and validate the creation methods of these models, the guidelines themselves fall short of explaining how the models were developed or their efficacy in predicting outcomes.

The project culminates with six principal insights. It points out that while the guidelines support healthcare professionals in the clinical application of these models, there is a pressing need for scientific advancements to thoroughly elucidate the application of these models, their benefits, drawbacks, and the processes for calculating outcomes related to CVD within the guidelines. The research community is called upon to enhance the detail and clarity of using these predictive models in the guidelines.

In conclusion, the guidelines should present multiple prediction models, providing medical professionals with diverse tools to forecast patient outcomes and determine suitable treatment plans.

Abstract

Cardiovascular diseases (CVDs) significantly impact survival and quality of life, highlighting the necessity for prompt and effective prevention and treatment strategies. Healthcare providers rely on guidelines from authoritative bodies like the ESC, AHA, and ACC to manage CVDs. These guidelines incorporate prediction models crucial for evaluating patient outcomes. This study assessed the integration of such models into international clinical practice guidelines. For example, a review of 146 guidelines part of ESC and AHA/ASCVD revealed 17 that described at least 23 distinct models predicting CVD progression, focusing on long-term risk, mortality, disease development likelihood, etc. While these models are referenced as predictive tools in the

guidelines, there is a lack of detailed explanation about their development and predictive accuracy within the guidelines. The study emphasizes the need for scientific progress in the guidelines to fully understand these models' applications, advantages, limitations, and outcome calculation methodologies. It recommends that guidelines offer various predictive models with comprehensive usage details, equipping healthcare professionals with a broad spectrum of tools for outcome evaluation and informed decision-making in patient care. The guidelines discussed did not endorse a particular prognostic model but referred to models from other guidelines or studies. Further research is required to provide clear recommendations on using various predictive models in a specific guideline, which will assist healthcare providers in making definitive choices for particular cardiovascular disease (CVD) cases.

Introduction

Cardiovascular diseases (CVDs) are a group of atherosclerosis-related disorders of the heart and blood vessels and are the leading cause of death globally. They severely impact the quality of life and mortality (McKearnan, Wolfson, Vock, Vazquez-Benitez & O'Connor, 2018). So, tackling these health problems on time is crucial for proper prevention and treatment.

Multiple guidelines have been formed to support healthcare professionals in managing cardiovascular conditions. The European Society of Cardiology (ESC) has created extensive guidelines covering various cardiovascular topics, continuously updating them based on the latest scientific findings and clinical practices (ESC Clinical Practice Guidelines, n.d.). In the United States, the American Heart Association (AHA) and the American College of Cardiology (ACC) offer comprehensive clinical guidelines to support healthcare professionals, which cover various aspects as well (American Heart Association, n.d.). Other guidelines are those from the World Health Organization (WHO), such as: "The Hearts technical package for cardiovascular disease management in primary health care" (World Health Organization, 2007). In the United Kingdom, the National Institute for Health and Care Excellence (NICE) has established a set of guidelines aimed at aiding health and social care professionals in preventing health issues, promoting overall well-being, and enhancing the standard of care across various topics, including cardiovascular conditions (National Institute for Health and Care Excellence, n.d.).

In the realm of healthcare, and especially in the clinical guidelines, prediction models play a crucial role in assessing outcomes. These multifactorial models aim to predict specific outcomes for individuals. There are two types of predicting models: a diagnostic and a prognostic model. Diagnostic models focus on an individual's current state and help determine whether a person has a particular condition or outcome. For example, a diagnostic model might predict a patient has diabetes based on various clinical features (e.g., blood glucose levels, family history, symptoms). On the other hand, prognostic models look into the future and estimate the likelihood of a specific outcome occurring over time. For instance, a predictive model could predict the risk of a heart attack (myocardial infarction) in the next five years based on risk factors such as age, cholesterol levels, and blood pressure (Wolff et al., 2019).

Integrating well-validated Clinical Prediction Models (CPMs) into guidelines can enhance patient care and resource allocation. Furthermore, integrating high-quality prediction models into clinical practice guidelines is crucial for evidence-based decision-making, enabling personalized medical decisions for individual patients. Additionally, it helps indirectly to shape policies promoting a healthy and high-quality lifestyle for the entire community. Evidence-based guidelines, coupled with specific prediction models, enhance health outcomes for individuals with illnesses by guiding effective practices for healthcare professionals and informing optimal program design for policymakers (Wang, Norris, & Bero, 2018). Using the prediction models within the clinical guidelines for early cardiovascular disease prediction can generate valuable health records. These records can inform policymakers, enabling targeted lifestyle interventions based on preemptive risk assessment (Deepa, Sadu, & Sivasamy, 2024).

Clinical Prediction modelling in cardiology utilizes multiple factors to estimate the risk of developing a CVD in individuals. Some of the models can estimate the 10-year risk of developing coronary heart disease (CHD), such as the Framingham Cardiovascular Risk Score, which is based on factors like age, sex, cholesterol levels, blood pressure, and smoking status and is among the first model developed in this regard. Another model the European Society of Cardiology (ESC) recommends to assess the 10-year risk of fatal cardiovascular events is the European Systematic Coronary Risk Evaluation (SCORE). The American Heart Association/Atherosclerotic Cardiovascular Disease (AHA/ASCVD) developed some algorithms which estimate the risk of atherosclerotic cardiovascular events (heart attack, stroke) over a specified time frame. Factors

considered include age, sex, cholesterol levels, blood pressure, and diabetes status (Arxiv, n.d.; American Heart Association, n.d.).

Additional models estimating cardiac risk include the PRIMaCY Childhood HCM Sudden Cardiac Death Risk Prediction Tool, preoperative mortality rate prediction for infective endocarditis surgery, the TIMI Risk Score for Unstable Angina/Non-ST-Elevation Myocardial Infarction (UA/NSTEMI), early and late risk stratification tools, the Revised Cardiac Risk Index (RCRI), and a random effects model for patient groups or studies. Additionally, the predictive approach for pulmonary hypertension linked to left heart disease (PH-LHD) involves assessing heart and blood vessel functions to categorize risk levels. Other models are as follows: Sudden Cardiac Death (SCD) risk prediction model; Logistic Models for Heart Failure (H.F) mortality that incorporate SDOH (social determinants of health); Stratification model; Feedforward Artificial Neural Network (ffANN); ankle-brachial index (ABI); Cardiac Disease in Pregnancy Risk Estimation (CARPREG II) Risk Prediction Mode; Logistic Regression; Multivariable models predicting risk of Atrial Fibrillation (Cohorts for Heart and Aging Research in Genomic Epidemiology - Atrial Fibrillation, (CHARGE-AF)) etc.

Clinical prediction models are closely related to individual patient models tailored to the individual patient. Their primary purpose is to guide treatment recommendations and provide personalized consultations. Individual patient models consider the patient's unique characteristics and preferences. So, they are essential in evidence-based medicine. These models guide critical decisions, including treatment options, risk assessment, and patient care. (Vogenberg, 2009).

Many prediction models addressing CVD and stroke have been analyzed in studies (Wessler et al., 2015). However, the extent to which they are incorporated in clinical practice guidelines is unknown. Therefore, this study aims to explore the incorporation of prediction models in (inter) national clinical practice guidelines in cardiology.

The objective of the research

To explore the incorporation of prediction models in (inter)national clinical practice guidelines in cardiology.

To achieve the main objective, an explorative review was conducted to identify clinical practice guidelines in cardiology, starting with the ESC and AHA/ASCVD guidelines and searching within these guidelines for clinical prediction models used for decision-making. This means we gather various predictive models instrumental in making decisions about cardiovascular disease outcomes. Occasionally, these models are cited in research to support the diagnostic process.

Methods

Data sources and searches

A comprehensive search was conducted on the 29th, 30th and 31st of May 2024 for guidelines that may originate from international or national heart associations related to cardiovascular disease (CVD). We aimed to recognize guidelines from reputable national or international health organizations, professional societies, or governmental bodies. We also aimed to identify guidelines recommending using different prediction models within clinical practice. Guidelines incorporating a prediction model on CVD were eligible for inclusion in this study.

We identified that two major associations in E.U. and USA settings are those from the ESC and AHA/ASCVD associations, respectively (American Heart Association (AHA), n.d.; ESC Clinical Practice Guidelines, n.d.). So, we started with the latest guidelines issued last year and a year before from ESC and AHA/ASCVD and wanted to search for additional guidelines if time allowed. For these purposes, and if time allows, we wanted to use guideline-specific databases. We tried to search for clinical practice guidelines in cardiology in databases such as Trip database, G-I-N library, U.S. Preventive Taskforce, NICE, and UpToDate.

We wanted to search for any prediction model taken into consideration within the selected guidelines connected with CVD as an output. In addition, and if time allows, we wanted to search for the latest developments in the science such as prediction Model for Assessment of Telemedicine in Chronic Heart Failure (MAGIC), Emergency Care Research Institute (ECRI), Dynamed, Biomarker-Integrated Approaches of Genomic and Genetic (AWMF), Grading of Recommendations Assessment, Development, and Evaluation (GRADEpro), and to use IEEE Xplore as a digital library for computational models for CVD prediction (Deepa, Sadu, & Sivasamy, 2024; Cai et al., 2024).

So, the process included a two-step procedure:

Step 1-Study selection- search for clinical practice guidelines in cardiology:

As an initial step, we followed the procedures outlined in Figure 1. We reported our study findings according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) guidelines. These guidelines include a 17-item checklist for systematic review protocols established by Moher and colleagues in 2015. Subsequently, we structured the presentation of our results based on this framework, as depicted in Figure 1.

We focused on relevant guidelines incorporating prediction models for cardiovascular disease (CVD) outcomes and recommended their use in clinical practice. These guidelines were developed in the European Union (E.U.) and the United States (USA). Initially, we included guidelines from the European Society of Cardiology (ESC) and the American Heart Association/American College of Cardiology (AHA/ASCVD) separately, considering their overall relevance to CVD management in both regions.

Inclusion criteria for a guideline:

- guideline originates from the well-recognized international health organizations, professional associations, or governmental bodies in two settings: the USA and the E.U.,
- had the outcome as CVD (including but not limited to coronary artery disease, heart failure, atrial fibrillation, hypertension, and other cardiovascular conditions),
- published in English,
- the guidelines should have been published within the last two years to be eligible for inclusion.

Step2: in the identified guidelines, search for prediction models:

As the next step, we reviewed all identified guidelines. When encountering a prediction model, we referred to the original article or guideline cited in the current guideline. Our goal was to extract details about the prediction model (at least one from each guideline identified and, if time allows to search for additional prediction models within the same guidelines), including its outputs, the DOI of the referenced article, and the specific patient population to which the model applies. We diligently documented the relevant information. So, we employed a self-reported tool customized for our screening process in relation to the prediction models outlined in the provided CVD

guideline or the so-called Customized Data Extraction Forms (CDEF) specific to clinical guidelines.

The interest was in all prediction models (regardless of the method) included in the identified guidelines or the source given. Due to time constraints, we initially identified at least one prediction model per guideline. Later, we revisited a subset of randomly chosen guidelines to explore additional models. We searched for a prediction model applicable to patients with cardiovascular diseases and patients with any other disease requiring cardio vascular (CV) treatment. We also searched for prediction models that report on the outcomes, such as improved risk stratification or treatment outcomes. Terms such as long risk of atherosclerotic cardiovascular events (including heart attacks and strokes) or coronary heart disease (CHD) events (such as heart attacks) were defined. CVD outcomes have been described as any of the following: Death due to myocardial infarction (heart attack) or other CHD-related causes, death resulting from a cerebrovascular event (e.g., ischemic stroke or hemorrhagic stroke), Preoperative mortality rate from CVD, Deaths related to heart failure, sudden cardiac arrest, or other cardiovascular causes, Surviving a cerebrovascular event a condition where the heart cannot pump blood effectively, Long term risk of all-cause mortality (GRACE risk), Peripheral artery disease (PAD): Reduced blood flow to the limbs due to narrowed arteries, Chest pain or discomfort due to reduced blood flow to the heart muscle etc.

No language or publication date restrictions are applied in this regard.

Inclusion criteria for a prediction model (based on Customized Data Extraction Forms (CDEF) specific to clinical guidelines)

- prediction model or risk calculator includes models for risk assessment, prognosis, treatment decision-making, and management strategies.
- Considered at least one risk factor in the prediction model simultaneously (such as age, blood pressure, cholesterol levels, etc.) when making predictions. In other words, it considers multiple risk factors together rather than focusing on just one. This approach helps improve the accuracy of the model's predictions.
- models are aimed at risk assessment, prognosis, treatment decision-making, and management strategies

- prediction model is given within the selected guideline and is fully explained in the given guideline or within the source identified (study/article, additional guideline)

Occasionally, we needed to consult additional referenced articles that originally defined the model and clearly outlined its usage steps.

Inclusion criteria for a study/article where the prediction model is defined and is given in the guideline selected:

- the study/article is given in full, not only the abstract
- the study/articles can be the original one with the model identified or a later one issued not only in the last two years

Articles published solely in abstracts or without available full-texts, letters or protocols, reviews, or case reports were not used for model confirmation or other justifications. We thoroughly reviewed complete articles concerning the particular prediction model cited in the guidelines, delving into its purpose, outcomes, and application methods, especially when time permitted and particularly for articles provided by ESC or AHA/ASCVD guidelines.

Data extraction:

We've identified at least one prediction model for every *guideline mentioned* in the provided Tables number one and two. We also studied whether the guideline gives suggestions on using different prediction models for the same output. We have extracted relevant data from the guidelines studied, as presented in Tables 1 and 2, for the model, outputs, and target group/ patients for whom the model was used. In cases where it's relevant, additional models have been identified, and we have gathered the subsequent information given herewith as a summary:

- guidelines in which it was incorporated

- data of guideline publication

-corrigendum publication date

- name of the model

- a reference to the original paper in which the development of the model was described

- if the guidelines presented different prediction models for the same output or not

- if different prediction models are suggested in the guideline to help clinicians arrive at a conclusive decision in a specific cardiovascular disease (CVD) scenario.

In addition, from the *original articles* we identified

- the Risk Score,
- the number of outcomes each prediction model addresses,
- confirmation on the outcome that is predicted by the model and patient population/indication (e.g., patients with atrial fibrillation)**,**
- we also searched if the models mentioned in different articles predict the same result/outcome or a unique one and where allowed the
- model relevance and
- its usage.

Data synthesis

As we explored prediction models incorporated in clinical practices connected with CVD, the analysis was purely descriptive, and no formal statistical analysis was performed. We have given an overview of the prediction models used in clinical practice and provided in the guidelines, together with other relevant data fully explained in the section Inclusion criteria for a study or a guideline.

Results

Step 1- Guideline search:

We found that the major associations in CVD that are issuing guidelines are those from ESC or AHA/ASCVD in E.U. and USA settings, respectively. So, we continue searching for the guidelines within these two associations as per the PRISMA tool. The data and findings are presented in Table

1 for the guidelines identified from ESC and Table 2 for the guidelines identified from AHA/ASCVD. The literature search yielded 146 Clinical Practice Guidelines in Cardiology (32 from ESC and 114 from AHA/ASCVD). After the title, a year of publishing and screening of the corrigendum of the existing guideline, 17 full-text guidelines (nine from ESC and eight from AHA/ASCVD) were gaged for inclusion that were issued in the last two years. All guidelines were initially extracted from the two leading CVD associations in the E.U. and USA, meaning that none of the included guidelines were mapped from the databases mentioned under the "Methods-Data sources" section because of the time constraint. The characteristics of the guidelines are elaborated upon in Tables 1 and 2. If multiple versions of a clinical practice guideline were identified, we considered the most recent version. We have also been focused only on the last two years of guideline publication. So, there were no guidelines unrelated to cardiology, which can be excluded, and guidelines lacking in any mention or incorporation of prediction models at ESC and AHA/ASCVD. Also, there were no outdated guidelines that more recent versions have superseded, which can be excluded.

Step 2- Prediction model search:

We yielded 15 unique results or prediction models defined in the ESC guidelines and eight different results or prediction models for CVD identified within AHA/ASCVD guidelines (Figures 1 and 2 show the results for E.U. and U.S. settings, respectively). The guidelines discussed did not endorse a particular prediction model but referred to models from other guidelines or studies/articles.

However, while the guidelines presented a specific type of model for use, they stopped short of offering explicit guidance on applying different prediction models to help clinicians arrive at a conclusive decision in a specific cardiovascular disease (CVD) scenario. These guidelines provide a structure for adopting established prognostic models into everyday clinical practice, enhancing decision-making. This method helps healthcare professionals comprehend the logic behind specific diagnostic or therapeutic choices.

Figures 2 and 3 provide an overview of the guidelines, tallying the number of prediction models each contains and categorizing them by the number of outcomes they address. Category 1 consists of models that predict the same result/outcome and are referenced in multiple guidelines/studies.

In contrast, category 2 comprises models that predict a unique outcome per model mentioned in each guideline.

Prediction models within the setting of Europe – defined by The European Society of Cardiology (ESC)

Models studied and included in the guidelines for the last two years at ESC are: model for the likelihood of hospitalization due to heart failure, termed the WATCH-DM Risk Score, models predicting the risk of sudden cardiac Death (SCD) across various age groups, the preoperative mortality rate for patients with infective endocarditis (I.E.) undergoing surgery, long-term all-cause mortality risk (GRACE risk), risk of immediate critical complications like ventricular fibrillation (V.F.) and risk associated with ECG findings indicating recurrent ischemic events as well as employing prediction tools without specifying the models, revised cardiac risk index (RCRI), a random effects model, and a stratification scheme.

The initial guideline in Table 1 encompassed individuals with a diabetes diagnosis. The researchers formulated a predictive model for the likelihood of hospitalization due to heart failure, termed the WATCH-DM Risk Score. This model, which is both innovative and based on machine learning techniques, estimates the risk of heart failure in patients with type 2 diabetes. Segar et al.'s 2019 publication details the model's development and validation. It is depicted as the first entry in Table 1 and classified as the second category in Figure 1, illustrating a single result/output from one prediction model.

Three sets of guidelines (given under entries 2, 4 and 14 in Table 1) detail five distinct models predicting the risk of sudden cardiac Death (SCD) across various age groups. The models in question are indexed as items 2, 3, 4, 5, and 14 in the first table, and the corresponding studies detailing them are cited in the fifth column of the same table, according to the guidelines reviewed. They are categorized as type one/first category in Figure 2 as they present a single output such as SCD. The primary patient groups include those with hypertrophic cardiomyopathy (HCM), both overall and specifically those diagnosed before the age of 16, as well as patients with different forms of heart failure, acute heart failure hospitalizations, type 2 diabetes with chronic kidney

disease, and ventricular arrhythmias (American College of Cardiology et al., 2020; Norrish et al., 2019a; Norrish et al., 2019b; O'Mahony et al., 2014; O'Mahony et al., 2019; Risgaard et al., 2014).

The fifth guideline in Table 1, given as entry number 6, predicts the preoperative mortality rate for patients with infective endocarditis (I.E.) undergoing surgery. It introduces 12 risk scores, including three traditional and nine IE-specific scores, focusing mainly on preoperative mortality (as a primary output) (Varela Barca et al., 2020). This is documented as type two/category two in Figure 2. The corresponding study detailing the model is cited in the fifth column of the same table.

The sixth guideline, given as entry numbers 7, 8 and 9 in Table 1, addresses the Management of acute coronary syndromes, crafted by the ESC's task force. It outlines three different models with three distinct outcomes: long-term all-cause mortality risk (GRACE risk), risk of immediate critical complications like ventricular fibrillation (V.F.), and risk associated with ECG findings indicating recurrent ischemic events. The models in question are indexed as items 7, 8 and 9 in Table 1 and are fully explained in articles (Morrow et al., 2000; Ambrosetti et al., 2021; Schwartz et al., 2001), respectively. They belong to category/type two in Figure 2, representing different outcomes from different models.

The seventh guideline, entry 10 in Table 1, pertains to cardio-oncology, employing prediction tools without specifying the models, focusing on cancer prognoses of less than six months, more than six months, or more than 12 months within a multidisciplinary team approach (O'Mahony et al., 2014). It highlights cardiovascular adverse events (CVAEs) as the primary outcome for patients with multiple myeloma (MM) receiving proteasome inhibitors (P.I.s). This information is found as entry number 10 in Table 1 and type two in Figure 2. The corresponding study detailing the model is cited in the fifth column of the same table.

The eighth guideline, given as entry numbers 11, 12 and 13 in Table 1, deals with cardiovascular assessment and Management for patients undergoing noncardiac surgery, including those with recent coronary stent implantation or peripheral artery disease (PAD). It utilizes models like the revised cardiac risk index (RCRI), a random effects model, and a stratification scheme (Smilowitz et al., 2018; Siller-Matula et al., 2017; Ashton et al., 1993). These are presented as entries 11, 12, and 13 in Table 1 and as type two in Figure 2, with outcomes including the prevalence of multiple cardiovascular risk factors and atherosclerotic cardiovascular disease (ASCVD), stent thrombosis,

and coronary artery disease as a significant perioperative infarction risk factor. The corresponding studies detailing the models are cited in the fifth column of the same table.

Lastly, the ninth guideline, given as entry number 15 in Table 1, focuses on diagnosing and treating pulmonary hypertension in patients with left heart disease (PH-LHD), right ventricular (R.V.) dysfunction, and various forms of heart failure, as well as valvular heart disease and conditions leading to postcapillary P.H. It employs a predictive approach based on cardiac and vascular function assessments to stratify risk levels (Hoeper et al., 2016). The primary concern is the causes of sudden cardiac death across different age groups. This is detailed as entry number 15 in Table 1 and as type two in Figure 2, showing different outcomes for different models. The corresponding study detailing this model is cited in the fifth column of the same table, according to the guidelines reviewed.

Prediction models within the setting of the USA- defined by the American Heart Association (AHA) and the American College of Cardiology (ACC)

Models studied and included in the guidelines for the last two years at AHA/ASCVD are the SCD risk prediction model, the Logistic model for H.F. mortality that incorporates SDOH (social determinants of health), ffANN, CARPREG II Risk Prediction Mode, ankle-brachial index (ABI), Stratification model, Logistic Regression and Multivariable model CHARGE-AF. The fifth column of Table 2 lists the citations for research papers referenced in the guidelines. These papers offer comprehensive descriptions of the models under review.

The model with SCD considered Sudden Cardiac Death Risk Prediction in Pediatric Hypertrophic Cardiomyopathy was recommended for use in the guideline referenced as item number 1 in Table 2. The model is designed to assess the risk of Sudden Cardiac Death (SCD) in young patients with Hypertrophic Cardiomyopathy. It calculates the risk by analyzing clinical and genetic variables through competing risk models and cause-specific hazard regression techniques. The model incorporates various predictors, including the patient's age when diagnosed, absence of prolonged ventricular tachycardia, unexplained fainting episodes, measurements of septal thickness, left ventricular posterior wall, and left atrial size, as well as the peak gradient in the left ventricular outflow tract and any pathogenic genetic mutations found. This model supports preventive

measures, particularly when implanting cardioverter-defibrillators (ICDs) for primary prevention (Miron et al., 2020). The guideline is categorized under Category 2 in Figure 3 because it presents a single outcome for each prediction model.

In the subsequent guideline, the model the researchers, created and confirmed is the logistic model to forecast mortality due to heart failure (H.F.), considering the social determinants of health (SDOH). The objective of using this specific model was to improve the precision of predictions regarding in-hospital death among heart failure patients by integrating SDOH, which is frequently neglected in conventional predictive models. The SDOH include elements such as an individual's socioeconomic status, level of education, community, and living conditions, all of which play a crucial role in determining health results. According to the referenced study in the guideline, the improved model can help healthcare providers identify high-risk patients better and tailor interventions accordingly. This can lead to more personalized and effective care, potentially reducing mortality rates (Segar et al., 2022). This prediction model in the guideline corresponds to a single outcome, placed in Category 2, as shown in Figure 3 and listed as entry number 2 in Table 2.

Utilizing logistic regression analysis and based on the study by de Oliveira Manoel and colleagues (2015), this prediction model was suggested for use in the guideline, listed as item 3 in Table 2. This model employs the VASOGRADE scale, which stratifies the risk of delayed cerebral ischemia (DCI) based on initial patient presentation after subarachnoid haemorrhage (SAH). The VASOGRADE, as a straightforward grading scale, integrates the World Federation of Neurosurgical Societies scale (WFNS) and the modified Fisher score. In Figure 3, this guideline falls under Category 2, indicating that it is associated with a distinct outcome for each predictive model.

A feedforward artificial neural network (ffANN) was utilized as a predictive model for forecasting three specific outcomes in patients who have experienced an aneurysmal subarachnoid haemorrhage (aSAH), as given in the following guideline. In this network, various inputs, such as the patient's age, the aneurysm's location, and the modified Fisher score, are fed into a series of processing units called nodes. These nodes analyze the inputs to discern patterns that follow the logic of "if this condition exists, then this outcome is likely," enabling the prediction of results.

The study involved enrolling patients who had aSAH to evaluate the ffANN's ability to predict in-hospital mortality, the likelihood of an unfavourable modified Rankin Scale (mRS) score six months post-event, and the incidence of delayed cerebral ischemia (DCI) (de Jong, G et al., 2021). The guideline, which presents three outcomes for each prediction model, is grouped into Category 2, as depicted in Figure 3 and is referenced as entry number 4 in Table 2.

Then, the ABI or ankle-brachial index (ABI) is used as a model for screening peripheral artery disease (PAD) among asymptomatic adults within the following guidelines. The study for this specific model given in the guideline highlights that a low ABI (<0.90) is linked to a higher risk of future cardiovascular events, such as myocardial infarction and stroke. Incorporating ABI into cardiovascular risk assessments can improve the identification of individuals at high risk for cardiovascular events, even if they are asymptomatic (Lin, J. S., Olson et al., 2013). The main output is peripheral artery disease (PAD) among asymptomatic adults. The guideline is allocated to Category 2 in Figure 3 due to its structure of assigning a single outcome to each prediction model, and it is recorded as entry number 5 in Table 2.

The CARPREG II (Cardiac Disease in Pregnancy II) risk prediction model is used to estimate the risk of cardiac complications as a principal output for mothers during pregnancy with pre-existing heart disease (recommended by the following guideline). With the model, pregnant women with heart disease are categorized according to a risk score into different risk groups. By identifying high-risk patients, the model aids in planning appropriate surveillance, interventions, and management strategies during pregnancy to mitigate risks. The individualized risk scores enable healthcare providers to offer personalized counselling and care plans for pregnant women with heart disease, aiming to improve maternal and fetal outcomes (Silversides et al., 2018). The guideline is designated to Category 2 in Figure 3, as it features a single result for each prediction model and is identified as item number 6 in Table 2.

The subsequent article, as per the recommendation given in the guideline, examines a logistic regression model referenced in the fifth column of Table 2 (Orkin et al., 2017). They calculated standardized case fatality rates and odds ratios for Survival to hospital discharge among cardiac arrest cases attributed to drug-related causes compared to those attributed to presumed cardiac causes after adjusting for potential confounding factors. The patients who had an out-of-hospital

cardiac arrest caused by drugs show comparable survival chances to cardiac arrest presumed to be of cardiac origin, however with adjustment of factors concerning demographic traits, circumstances surrounding the cardiac arrest, and the clinical course before hospitalization, drug-related cardiac arrest demonstrated higher odds of Survival compared to those with cardiac arrest by presumed cardiac cause. Yet, studying the epidemiology, care patterns, and prognosis of drug-related emergencies occurring before hospital admission could potentially better patient outcomes. As per Figure 3, this guideline is classified under Category 2, as it is associated with a singular outcome for its model and is noted as entry number 7 in Table 2.

The forthcoming guideline endorses the application of multivariate prediction models. According to the research by Himmelreich et al. (2020), these models can potentially improve primary atrial fibrillation (A.F.) screening by pinpointing those at elevated risk. A.F., a prevalent cardiac arrhythmia, is also associated with a heightened risk of stroke. The guideline's cited study evaluates which model could enhance the efficacy of future screenings. A systematic evaluation of multivariate prediction models could bolster A.F. prediction in community-dwelling populations. Of the 21 models reviewed for predicting A.F. risk in community-based cohorts, the CHARGE-AF model stood out for its exceptional performance and relevance. Notably, CHARGE-AF proved highly effective for initial screenings, especially among older individuals of European ancestry. This model is categorized under Category 2 in Figure 3 and is marked as number 8 in Table 2.

Figure 2 shows no recommendations for various models that address the same or a single outcome.

Discussion

This review investigates the integration of prediction models into cardiology clinical practice guidelines. These models are crucial for predicting patient outcomes and are sometimes referenced in guidelines to aid in diagnosing and forecasting fetal and neonatal outcomes in cardiovascular diseases. The findings lead to several conclusions:

First, an analysis of the last two years' guidelines from the ESC revealed nine guidelines and an additional eight guidelines from the AHA/ASCVD, which were thoroughly examined. This review

identified 15 distinct models from the ESC and eight from the AHA/ASCVD used in decision-making. Similar to other well-known models, in the guidelines a widely used model that estimates the 10-year risk of developing coronary heart disease (CHD), such as the Framingham Cardiovascular Risk Score was not identified. This might happen as the widely used Framingham Cardiovascular Risk Score lacks population diversification, potentially limiting its accuracy for broader populations (Lee, 2024). The ASCVD (Atherosclerotic Cardiovascular Disease) calculator, introduced by the ACC and AHA, considers multiple vascular endpoints beyond CHD (American College of Cardiology, n.d.). These contemporary models now guide clinical practice. They are innovative and based on machine learning techniques, which estimate patients' risk of heart failure in recent years (Gautam et al., 2023).

Secondly, lack of alternative predection models options in guidelines poses a risk. Models may become overly fitted to the original data, resulting in optimistic predictions. While they excel on known data, they might struggle to generalize to new data or miss underlying patterns. This discrepancy could mislead clinicians, potentially leading to inappropriate treatment decisions and harm to patients (Aliferis, C., & Simon, G., 2024). However, certain guidelines—such as the 2023 ESC Guidelines for Cardiomyopathies and the 2023 Focused Update on Heart Failure—deviate from this trend. They explore various prediction models for estimating sudden cardiac death risk, including HCM-SCD Risk calculators, HCM Risk-Kids, HCM Risk-SCD Calculator, PRIMaCY Childhood HCM Sudden Cardiac Death Risk Prediction Tool, and a stratification scheme.

The third finding highlights a lack of consistency across the guidelines. Specifically, guidelines 2, 3, and 8 each use distinct prediction models to achieve the same intended outcome. This discrepancy could be addressed by mentioning these models in a single section within each guideline rather than discussing them individually.

Moreover, the guidelines do not explain the prediction models used. Consequently, clinicians seeking to understand a particular model must consult the original articles. Since clinicians are not primarily researchers, this requirement could pose challenges or time constraints, potentially complicating the process of making informed therapeutic and timely decisions.

Regrettably, most models were constructed based on data collected at the time nearest to the diagnosis or consultation rather than from earlier periods, based on the data collected for the patients (population/indication- with atrial fibrillation). This approach could lead to an inflated

perception of the models' accuracy when applied to earlier patient care stages (Kim, 2022a; Kim, 2022b).

Finally, different outcome definitions were used, mainly for the combined outcome of sudden cardiac Death (SCD) (guidelines given under the following numbers in Table 1: 2, 3, 4, 5 and 14). In this regard, future research should increase generalizability and head-to-head comparisons (Adabag et al., 2010).

Given more time, we would have conducted additional searches in specialized cardiovascular disease (CVD) databases. Specifically, we would have explored guidelines within these databases that incorporate machine learning models such as random forests (R.F.), gradient-boosted machines (GBM), and extreme gradient-boosted models (XGBoost). These models showes practical effectiveness in predicting CVD risk in recent times (Ward et al., 2020).

Given time limitations, future research can expand the recommended list of guidelines and prediction models. Researchers should explore computational models for cardiovascular disease (CVD) prediction available in IEEE Xplore. By scrutinizing these models, we can create a comprehensive dataset of CVD guidelines, informing clinical decisions and potentially benefiting a broader community. Improving the predictive accuracy of the models highlighted in the guidelines should be a key focus for future analyses.

The main insights from this review align with findings from other research on predictive modelling across different medical disciplines. One such research is Cornell et al.'s 2019 study, which underscores the necessity for straightforward, universal guidelines. These guidelines would assist healthcare professionals in better understanding the implementation of prediction models in clinical settings. There's a call for the research community to better understand and provide more detailed reporting on the predictive models mentioned in these guidelines.

By conducting guideline searches and meticulously extracting data using Customized Data Extraction Forms (CDEF) specific to clinical guidelines, healthcare workers can make informed recommendations for specific prediction models. This approach enhances the accuracy of health course predictions and facilitates appropriate therapeutic decisions. Data extraction forms and the extraction process are pivotal in evidence-based medicine by improving research quality and informing clinical practice.

The study summarizes prediction models and their outcomes for cardiovascular disease (CVD) patients. Additionally, it addresses significant issues related to these models, suggesting using universal guidelines to enhance healthcare professionals' understanding of model implementation and reporting. However, the study was constrained by a five-week timeline, and the literature search was limited to prediction models for CVD patients from guidelines published only by the ESA and AHA within the last two years.

The clinical significance lies in utilizing precise predictive models to guide effective therapy and treatment decisions. On the other hand, from a scientific perspective, implementing robust data extraction processes can play a crucial role in evidence-based medicine by enhancing research quality.

In conclusion, this study has identified numerous prediction models for CVD outcomes in specific patient groups. It's possible that other valuable prediction models related to cardiovascular complications were not captured in our guideline search. Future investigations should expand to include data from cardiology guidelines of prior years, reaching back to 2017 through 2021 or even earlier. It's also crucial to examine guidelines from clinical areas that are not directly associated with cardiovascular association but are pertinent to cardiovascular diseases (CVD). Future research should aim to complete the compilation of all existing clinical guidelines and pursue the external validation of the prediction models mentioned in the guidelines using contemporary and recognized validation methods with standardized definitions for predictors and outcomes.

Figures:

Figure 1: PRISMA flow diagram.

Figure 2: Summary of different outputs derived from different prediction models within the setting of the E.U. guideline

Figure 3: Summary of different outputs derived from different prediction models within the setting of USA guideline

Tables

Table 1: Prediction models in the Europe setting for CVD guideline - ESC

Table 2: Prediction models within the setting of U.S. for CVD guideline- AHA/ASCVD

Figure 1: PRISMA flow diagram.

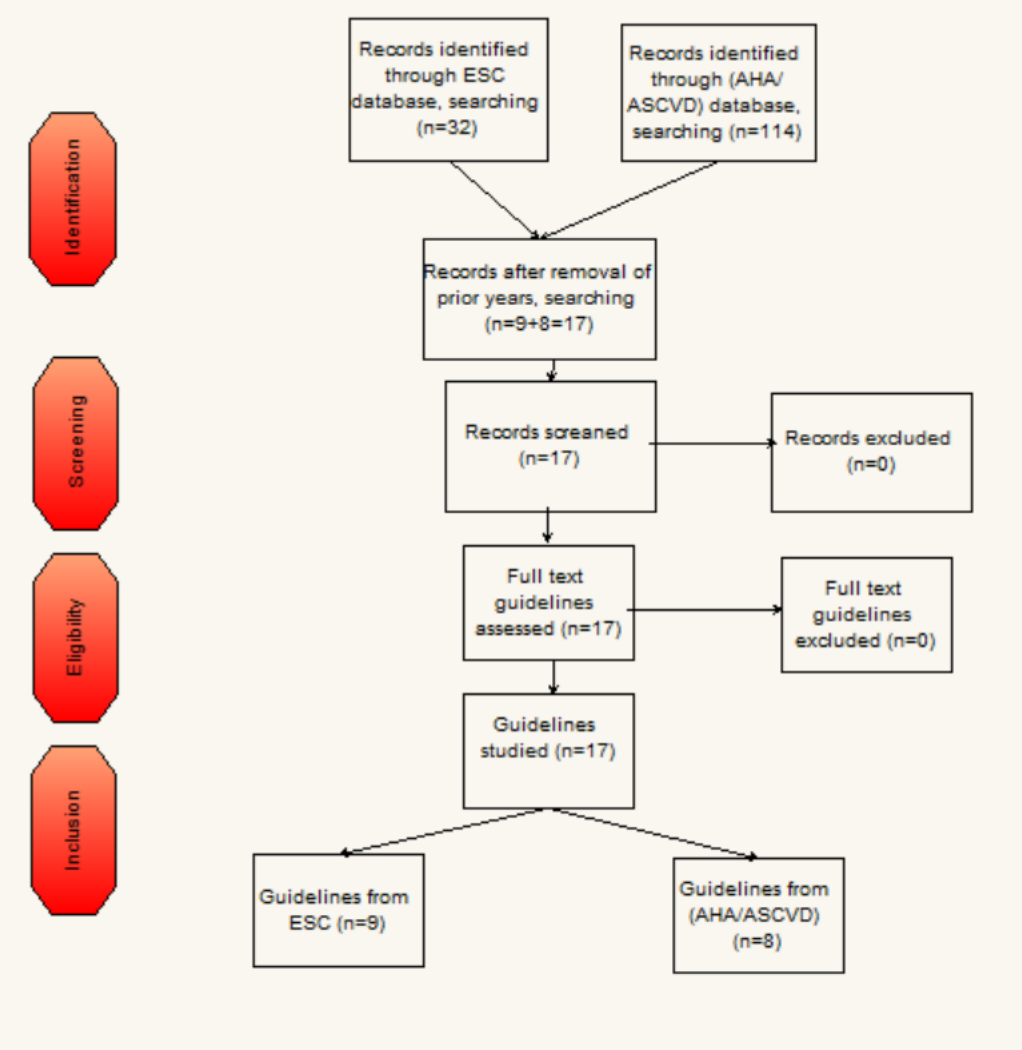

Figure legend: ESC = European Society of Cardiology, AHA/ASCVD = American Hearth Association/The American Heart Association/Atherosclerotic Cardiovascular Disease

Figure 2: Summary of different outputs derived from different prediction models within the setting of the E.U. guidelines:

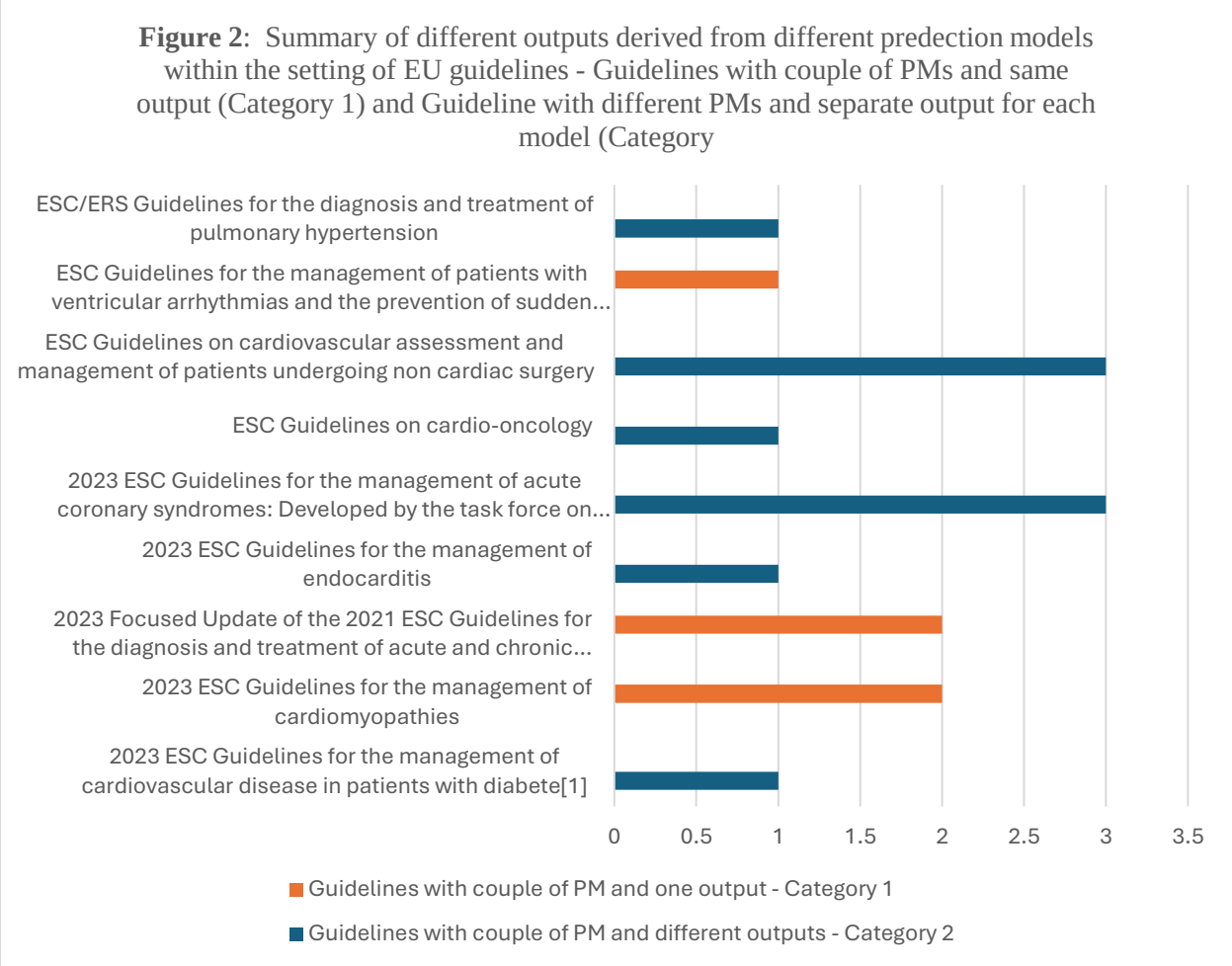

Figure 2: Summary of different outputs derived from different prediction models within the setting of the E.U. guidelines (Figure legend: ESC = European Society of Cardiology, ERS = European Respiratory Society, AHA/ASCVD = American Hearth Association/The American Heart Association/Atherosclerotic Cardiovascular Disease)

Figure 3: Summary of different outputs derived from different prediction models within the setting of USA guidelines:

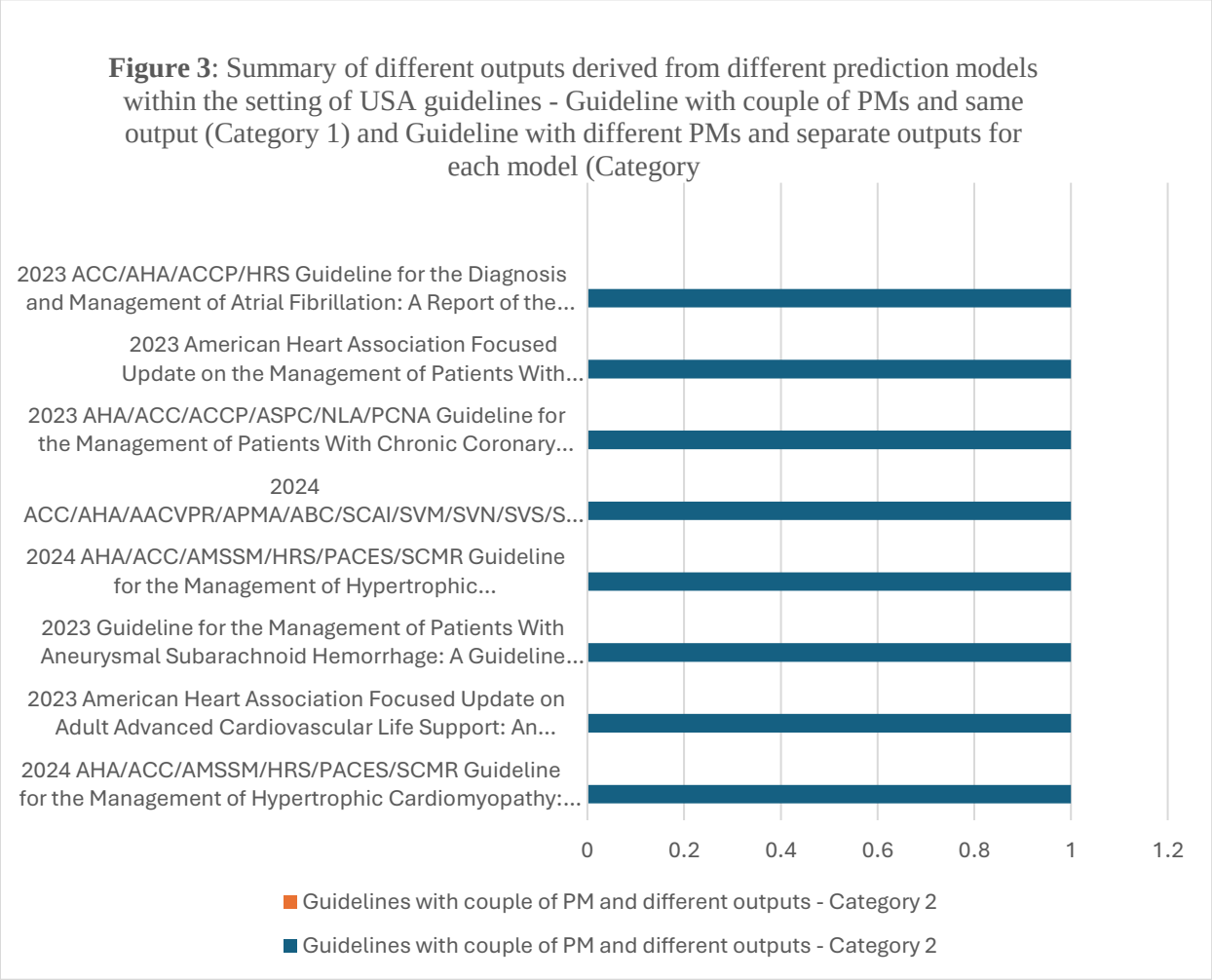

Figure 3: Summary of different outputs derived from different prediction models within the setting of USA guidelines (Figure legend: ESC = European Society of Cardiology, ERS= European Respiratory Society, AHA/ASCVD = American Hearth Association/The American Heart Association/Atherosclerotic Cardiovascular Disease)

Table 1*: Prediction models within the E.U. setting of CVD - ESC and guidelines*

	Prognostic model- name of the model	Guidelines in which it was incorporated	Date of guideline publication[1]	Reference to the paper in which the development of the model was described (given in the guideline)	The outcome that is predicted by the model	Patient population/indication- with atrial fibrillation)
1	The WATCH-DM Risk Score	2023 ESC Guidelines for the Management of cardiovascular disease in patients with diabetes[2]	November 15 2023 Corrigendum 22 January 2024	DOI: 10.2337/dc19-0587	Risk of Incident Heart Failure Hospitalization	Patients with T2DM
2	HCM-SCD Risk calculators	2023 ESC Guidelines for the Management of cardiomyopathies[3]	15 Nov 2023	DOI: 10.1161/CIR.0000000000000937	Risk of sudden cardiac Death (SCD)	Patients with hypertrophic cardiomyopathy (HCM)
3	HCM Risk-Kids			https://doi.org/10.1001/jamacardio.2019.2861 and https://doi.org/10.1093/europace/euz118	Risk of sudden cardiac Death (SCD)	HCM who are younger than 16 years old at diagnosis
4	HCM Risk-SCD	2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure[4]	August 25 2023 Corrigendum published : 23 November 2023	DOI: 10.1136/heartjnl-2018-313700 and DOI: 10.1093/eurheartj/eht439	The risk of sudden cardiac Death (SCD)	(1)Patients with symptomatic heart failure with mildly reduced ejection Fraction (2) patients with symptomatic heart failure with preserved ejection Fraction (3) patients hospitalized for acute heart failure

[1] retrived from: https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines

[2] Marx, N., Federici, M., Schütt, K., Müller-Wieland, D., Ajjan, R. A., Antunes, M. J., ... & Sattar, N. (2023). 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes: Developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC). European heart journal, 44(39), 4043-4140.

[3] Arbelo, E., Protonotarios, A., Gimeno, J. R., Arbustini, E., Barriales-Villa, R., Basso, C., ... & Kaski, J. P. (2023). 2023 ESC Guidelines for the management of cardiomyopathies: Developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC). European heart journal, 44(37), 3503-3626.

[4] Authors/Task Force Members:, McDonagh, T. A., Metra, M., Adamo, M., Gardner, R. S., Baumbach, A., ... & Zeppenfeld, K. (2024). 2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. European Journal of Heart Failure, 26(1), 5-17.

						(4)patients with type 2 diabetes mellitus and chronic kidney disease (5) patients with heart failure
5	PRIMaCY Childhood HCM Sudden Cardiac Death Risk Prediction Tool			DOI: 10.1136/heartjnl-2018-313700 And DOI: 10.1093/eurheartj/eht439	The risk of sudden cardiac Death (SCD)	(1)Patients (less than 16 years old)with symptomatic heart failure with mildly reduced ejection Fraction (2) patients (less than 16 years old)with symptomatic heart failure with preserved ejection Fraction (3) patients (less than 16 years old)hospitalized for acute heart failure
6	Preoperative mortality rate prediction in surgery for I.E.	2023 ESC Guidelines for the Management of Endocarditis[5]	November 15 2023 Corrigendum 13 December 2023	DOI: 10.1093/ejcts/ezz328	Preoperative mortality rate	Patients with, I.E. undergoing surgery
7	TIMI Risk Score for UA/NSTEMI	2023 ESC Guidelines for the Management of acute coronary syndromes: Developed by the task force on the Management of acute coronary syndromes of the European Society of Cardiology (ESC)[6]	August 25 2023 Corrigendum February 22 2024 (Previous guidelines on STEMI were published in 2017, and the previous	https://doi. org/10.1161/01.cir.102.17.2031	Longer-term risk of all-cause mortality (GRACE risk)	Patients presenting with acute coronary syndrome (ACS)
8	Early Risk Stratification of ACS			https://doi.org/10.1177/2047487320913379	A higher risk of immediate, life-threatening complications (e.g. ventricular fibrillation [V.F.]) ;	Patients with suspected ACS

[5] Delgado, V., Ajmone Marsan, N., de Waha, S., Bonaros, N., Brida, M., Burri, H., ... & Borger, M. A. (2023). 2023 ESC Guidelines for the management of endocarditis: Developed by the task force on the management of endocarditis of the European Society of Cardiology (ESC) Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Nuclear Medicine (EANM). *European heart journal*, *44*(39), 3948-4042.

[6] Byrne, R. A., Rossello, X., Coughlan, J. J., Barbato, E., Berry, C., Chieffo, A., ... & Ibanez, B. (2024). 2023 ESC guidelines for the management of acute coronary syndromes: developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). *European Heart Journal: Acute Cardiovascular Care*, *13*(1), 55-161.

9	Late risk stratification		guidelines on NSTE-ACS were published in 2020)	https:// doi.org/10.1001/jama.285.13.1711	Risk of ECG findings (recurrent ischemic events)	All ACS patients
10	Predictive tools	2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS): Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC)[7]	August 26 2022 Corrigendum published on May 7 2023	doi: 10.1200/JCO.19.00231	Cardiovascular adverse events (CVAEs)	Patients with multiple myeloma (MM) receiving P.I.s
11	Revised Cardiac Risk Index (RCRI)	2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing noncardiac surgery: Developed by the task force for the cardiovascular evaluation and management of patients undergoing noncardiac surgery of the European Society of Cardiology (ESC) Endorsed by the European Society of Anaesthesiology and Intensive Care (ESAIC)[8]	August 26 2022 Corrigendum 07 September 2023	DOI: 10.1136/heartjnl-2017-312391	Prevalence of multiple (≥2) cardiovascular risk factors and ASCVD And the Revised Cardiac Risk Index (RCRI)	Population undergoing noncardiac surgery
12	A random effects model patient groups or studies and aids in drawing broader inferences regarding the factors that predict cardiac			DOI: 10.1177/2048872615585516	Stent thrombosis	Patients with recent coronary stent implantation

[7] Lyon, A. R., López-Fernández, T., Couch, L. S., Asteggiano, R., Aznar, M. C., Bergler-Klein, J., ... & Van Der Pal, H. J. (2022). 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS) Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC). *European Heart Journal-Cardiovascular Imaging*, *23*(10), e333-e465.

[8] Halvorsen, S., Mehilli, J., Cassese, S., Hall, T. S., Abdelhamid, M., Barbato, E., ... & Zacharowski, K. (2022). 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery: Developed by the task force for cardiovascular assessment and management of patients undergoing non-cardiac surgery of the European Society of Cardiology (ESC) Endorsed by the European Society of Anaesthesiology and Intensive Care (ESAIC). *European heart journal*, *43*(39), 3826-3924.

	function around the time of surgery					
13	The stratification scheme			DOI: 10.7326/0003-4819-118-7-199304010-00004	Coronary artery disease is a major risk factor for perioperative infarction.	Patients with PAD
14	The stratification scheme	2022 ESC Guidelines for the Management of Patients with Ventricular Arrhythmias and the Prevention of sudden cardiac death: Developed by the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC) Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC)[9]	August 26 2022	DOI: 10.1161/CIRCEP.113.001421	Causes of sudden cardiac Death in different age groups	Patients with ventricular arrhythmias
15	The predictive approach discussed for pulmonary hypertension linked to left heart disease (PH-LHD) relies on measuring and evaluating heart and blood vessel functions to determine and	2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Endorsed by the International Society	August 26 2022	DOI: 10.1016/j.jchf.2015.12.016	a low DLCO level of risk.	Patients with LHD, P.H. and R.V. dysfunction. includes patients with H.F. with reduced, mildly reduced, or preserved ejection fraction (HFrEF, HFmrEF, or HFpEF), left-sided valvular heart disease, and

[9] Zeppenfeld, K., Tfelt-Hansen, J., De Riva, M., Winkel, B. G., Behr, E. R., Blom, N. A., ... & Volterrani, M. (2022). 2022 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Developed by the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC) Endorsed by the Association for European Paediatric and Congenital Cardiology (AEPC). European heart journal, 43(40), 3997-4126.

	categorize the level of risk.	for Heart and Lung Transplantation (ISHLT) and the European Reference Network on Rare Respiratory Diseases (ERN-LUNG). [10]				congenital/acquired cardiovascular conditions leading to postcapillary P.H.

Note: ESC: European Society of Cardiology; ERS: European Respiratory Society; AHA/ASCVD: American Hearth Association/The American Heart Association/Atherosclerotic Cardiovascular Disease; WATCH-DM: Weight, Age, Total cholesterol, HDL cholesterol, Diabetes duration, and Mean systolic blood pressure; HCM-SCD: Hypertrophic Cardiomyopathy-Sudden Cardiac Death; HCM Risk-Kids: Hypertrophic Cardiomyopathy Risk in Children; HCM Risk-SCD: Hypertrophic Cardiomyopathy Risk-Sudden Cardiac Death; PRIMaCY: Pediatric Risk of Mortality; I.E.: Infective Endocarditis; TIMI: Thrombolysis In Myocardial Infarction; UA/NSTEMI: Unstable Angina/Non-ST-Elevation Myocardial Infarction; ACS: Acute Coronary Syndrome; V.F.: Ventricular Fibrillation; CVAEs: Cardiovascular Adverse Events; P.I.s: Proteasome Inhibitors; RCRI: Revised Cardiac Risk Index; ASCVD: Atherosclerotic Cardiovascular Disease; PAD: Peripheral Artery Disease; PH-LHD: Pulmonary Hypertension linked to Left Heart Disease; DLCO: Diffusing Capacity of the Lungs for Carbon Monoxide; LHD: Left Heart Disease; R.V.: Right Ventricle; H.F.: Heart Failure; HFrEF: Heart Failure with reduced Ejection Fraction; HFmrEF: Heart Failure with mildly reduced Ejection Fraction; HFpEF: Heart Failure with preserved Ejection Fraction.

[10] Humbert, M., Kovacs, G., Hoeper, M. M., Badagliacca, R., Berger, R. M., Brida, M., ... & Rosenkranz, S. (2022). 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: Developed by the task force for the diagnosis and treatment of pulmonary hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Endorsed by the International Society for Heart and Lung Transplantation (ISHLT) and the European Reference Network on rare respiratory diseases (ERN-LUNG). *European heart journal*, *43*(38), 3618-3731.

Table 2*: Prediction models within the U.S. setting of CVD guideline – AHA/* ASCVD

	Prognostic model- name of the model	Guidelines in which it was incorporated[11]	Data of guideline publication	Reference to the paper in which the development of the model was described	An outcome that is predicted by the model	Patient population/indication- with atrial fibrillation)
1	SCD risk prediction model	2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines [12]	Published: May, 2024	https://doi.org/10.1161/CIRCULATIONAHA.120.047235	Sudden Cardiac Death Risk Prediction in Pediatric Hypertrophic Cardiomyopathy	In children with Hypertrophic Cardiomyopathy
2	Logistic Models for H.F. mortality that incorporate SDOH (social determinants of health)	2023 American Heart Association Focused Update on Adult Advanced Cardiovascular Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care[13]	18th December 2023 Updated	doi: 10.1001/jamacardio.2022.1900	in-hospital mortality	mortality for patients with heart failure (H.F.)
3	Stratification model	2023 Guideline for the Management of Patients With Aneurysmal	July 2023 Correction November 27, 2023	DOI: 10.1161/STROKEAHA.115.008728	Other DCI-specific prediction (predict DCI)	Patients With Aneurysmal

[11] Retrived from: (Guidelines & Statements Search - Professional Heart Daily | American Heart Association)

[12] Members, W. C., Ommen, S. R., Ho, C. Y., Asif, I. M., Balaji, S., Burke, M. A., ... & Waldman, C. B. (2024). 2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, *83*(23), 2324-2405.

[13] Perman, S. M., Elmer, J., Maciel, C. B., Uzendu, A., May, T., Mumma, B. E., ... & American Heart Association. (2024). 2023 American Heart Association Focused Update on Adult Advanced Cardiovascular Life Support: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*, *149*(5), e254-e273.

		Subarachnoid Hemorrhage: A Guideline From the American Heart Association/American Stroke Association[14]				(aneurysmal subarachnoid hemorrhage)
4	ffANN	2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines[15]	May 2024	DOI: 10.1093/neuros/nyaa581	Prediction capacity of a ffANN (predict (1) death during hospitalization (i.e., mortality) (n = 451), (2) unfavourable modified Rankin Scale (mRS) at six mo (n = 413), and (3) the occurrence of DCI (n = 362)	Patients suffering from SAH
5	ankle-brachial index (ABI)	2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines[16]	May 2024	DOI: 10.7326/0003-4819-159-5-201309030-00007	Predict cardiovascular disease (CVD) morbidity and mortality independent of Framingham Risk Score (FRS)	asymptomatic adults with PAD
6	CARPREG II Risk	2023 AHA/ACC/ACCP/ASPC/NLA/PCNA	July 2023	https://doi.org/10.1016/j.jacc.2018.02.076	Cardiac outcomes during	Pregnant women with heart disease

[14] Hoh, B. L., Ko, N. U., Amin-Hanjani, S., Chou, S. H. Y., Cruz-Flores, S., Dangayach, N. S., ... & Welch, B. G. (2023). 2023 guideline for the management of patients with aneurysmal subarachnoid hemorrhage: a guideline from the American Heart Association/American Stroke Association. *Stroke*, *54*(7), e314-e370.

[15] Members, W. C., Ommen, S. R., Ho, C. Y., Asif, I. M., Balaji, S., Burke, M. A., ... & Waldman, C. B. (2024). 2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, *83*(23), 2324-2405.

[16] Members, W. C., Gornik, H. L., Aronow, H. D., Goodney, P. P., Arya, S., Brewster, L. P., ... & Wilkins, L. R. (2024). 2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS guideline for the management of lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Journal of the American College of Cardiology*.

	Prediction Mode	Guideline for the Management of Patients With Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines[17]			pregnancy (Temporal trends in complications were examined)	
7	Logistic Regression	2023 American Heart Association Focused Update on the Management of Patients With Cardiac Arrest or Life-Threatening Toxicity Due to Poisoning: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care[18]	October 17, 2023	DOI:10.1371/journal.pone.0176441	Odds ratios of Survival to hospital discharge and fatality rates	Patients With Cardiac Arrest or Life-Threatening Toxicity Due to Poisoning
8	Multivariable models predicting risk of AF CHARGE-AF)	2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines[19]	January 2024	DOI: 10.1093/europace/euaa005	Incident A.F. in the community	At-risk individuals of A.F.

[17] Writing Committee Members, Virani, S. S., Newby, L. K., Arnold, S. V., Bittner, V., Brewer, L. C., ... & Williams, M. S. (2023). 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Journal of the American College of Cardiology*, *82*(9), 833-955.

[18] Lavonas, E. J., Akpunonu, P. D., Arens, A. M., Babu, K. M., Cao, D., Hoffman, R. S., ... & American Heart Association. (2023). 2023 American Heart Association Focused Update on the Management of Patients With Cardiac Arrest or Life-Threatening Toxicity Due to Poisoning: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*, *148*(16), e149-e184.

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Note: SCD: Sudden Cardiac Death; AHA: American Heart Association; ACC: American College of Cardiology; AMSSM: American Medical Society for Sports Medicine; HRS: Heart Rhythm Society; PACES: Pediatric and Congenital Electrophysiology Society; SCMR: Society for Cardiovascular Magnetic Resonance; H.F.: Heart Failure; SDOH: Social Determinants of Health; DCI: Delayed Cerebral Ischemia; ffANN: Feedforward Artificial Neural Network; SAH: Subarachnoid Hemorrhage; ABI: Ankle–Brachial Index; PAD: Peripheral Artery Disease; CVD: Cardiovascular Disease; FRS: Framingham Risk Score; CARPREG: Cardiac Disease in Pregnancy; A.F.: Atrial Fibrillation; CHARGE-AF: Cohorts for Heart and Aging Research in Genomic Epidemiology model for atrial fibrillation.

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