HOW DATA SCIENCES TRANSFORM PATIENT MANAGEMENT: BEST PRACTICE SHARING

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The healthcare system as it stands misses the potential of technological breakthroughs

6.1 million new cases of CVD in the EU in 2015. Half of new CVD cases due to CHD, while around 10% of new CVD cases were due to stroke

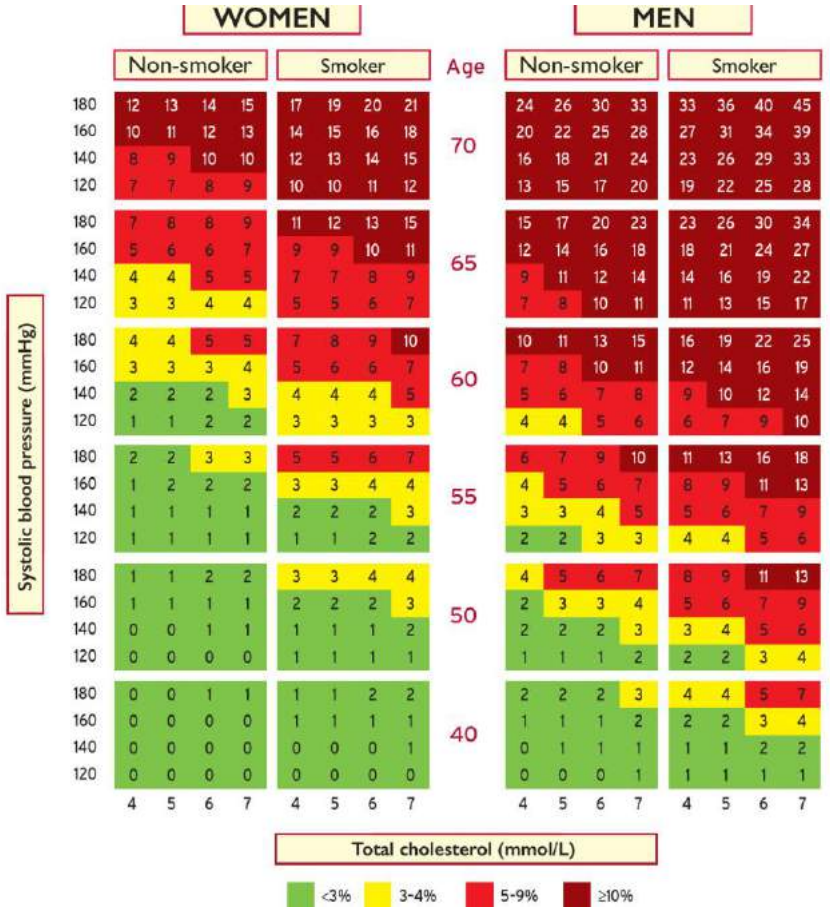
Structures and Incentives focused on unspecific reactive “Break & Fix”

Note: Europe refers to the 28 European Union (EU) member states. Data are based on latest available year for each European country. CV, cardiovascular.

Wilkins E, et al. European Cardiovascular Disease Statistics 2017. Accessed at: http://www.ehnheart.org/cvd-statistics.html. November 2018.

Current CV Risk estimation: one size fits all?

- **Individual 10-year risk**
  - **Always a high 10-year risk ≠ always a high benefit of medication**
  - **Always a low 10-year risk ≠ a low lifetime risk**
- **CV-risk categories**
- **SCORE not designed to be used in secondary prevention**
- **Other tools :ASCVD, SMART, ADVANCE, SMART-Reach, Life CVD Model, Elderly**



Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. DM with target organ damage,[a] or at least three major risk factors, or early onset of T1DM of long duration (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.
High-risk	People with: Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage,[a] with DM duration ≥10 years or another additional risk factor. Moderate CKD (eGFR 30–59 mL/min/1.73 m^2). A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.

ESC guidelines, 2019

The present and future steps

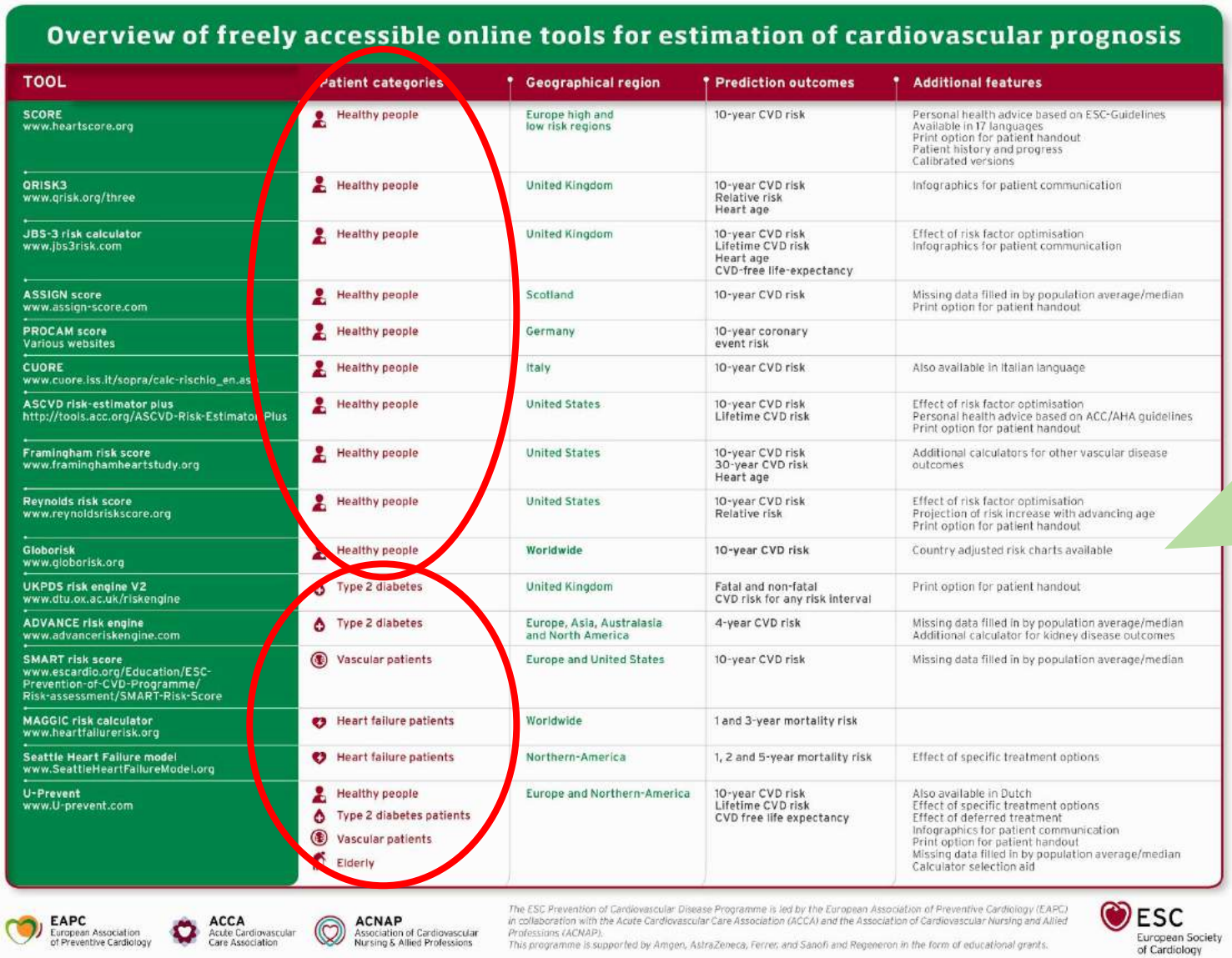
Medical challenges:

- Patients with acute coronary syndromes (ACS) are at increased risk of experiencing recurrent ACS.
- The predictive power of traditional risk scores remains relatively low, thus limiting the prediction of future events.
- Physicians adherence to guidelines remains suboptimal
- On the other hand, patient adherence and persistence on drugs and lifestyle changes remains a challenge
- Value of parameter analysis using machine learning algorithms in this field remains largely unexplored.

Unmet medical needs:

- Can you accurately predict the risk of your post-ACS patients?
- Can you define the best therapeutic approach in order to get the best outcome?
- Does each post-ACS patient achieve optimal risk reduction?
- Should every post-ACS patient receive the same therapy?

ESC recognizes the importance of risk prediction solutions for CV; report revealing the gap in secondary CV risk prediction



Overview of freely accessible online tools for estimation of cardiovascular prognosis

TOOL	Patient categories	Geographical region	Prediction outcomes	Additional features
SCORE www.heartscore.org	Healthy people	Europe high and low risk regions	10-year CVD risk	Personal health advice based on ESC-Guidelines Available in 17 languages Print option for patient handout Patient history and progress Calibrated versions
QRISK3 www.qrisk.org/three	Healthy people	United Kingdom	10-year CVD risk Relative risk Heart age	Infographics for patient communication
JBS-3 risk calculator www.jbs3risk.com	Healthy people	United Kingdom	10-year CVD risk Lifetime CVD risk Heart age CVD-free life-expectancy	Effect of risk factor optimisation Infographics for patient communication
ASSIGN score www.assign-score.com	Healthy people	Scotland	10-year CVD risk	Missing data filled in by population average/median Print option for patient handout
PROCAM score Various websites	Healthy people	Germany	10-year coronary event risk	
CUORE www.cuore.iss.it/sopra/calc-rischio_en.as	Healthy people	Italy	10-year CVD risk	Also available in Italian language
ASCVD risk-estimator plus http://tools.acc.org/ASCVD-Risk-Estimator-Plus	Healthy people	United States	10-year CVD risk Lifetime CVD risk	Effect of risk factor optimisation Personal health advice based on ACC/AHA guidelines Print option for patient handout
Framingham risk score www.framinghamheartstudy.org	Healthy people	United States	10-year CVD risk 30-year CVD risk Heart age	Additional calculators for other vascular disease outcomes
Reynolds risk score www.reynoldsriskscore.org	Healthy people	United States	10-year CVD risk Relative risk	Effect of risk factor optimisation Projection of risk increase with advancing age Print option for patient handout
Globorisk www.globorisk.org	Healthy people	Worldwide	10-year CVD risk	Country adjusted risk charts available
UKPDS risk engine V2 www.dtu.ox.ac.uk/riskengine	Type 2 diabetes	United Kingdom	Fatal and non-fatal CVD risk for any risk interval	Print option for patient handout
ADVANCE risk engine www.advanceriskengine.com	Type 2 diabetes	Europe, Asia, Australasia and North America	4-year CVD risk	Missing data filled in by population average/median Additional calculator for kidney disease outcomes
SMART risk score www.escardio.org/Education/ESC-Prevention-of-CVD-Programme/Risk-assessment/SMART-Risk-Score	Vascular patients	Europe and United States	10-year CVD risk	Missing data filled in by population average/median
MAGGIC risk calculator www.heartfailurerisk.org	Heart failure patients	Worldwide	1 and 3-year mortality risk	
Seattle Heart Failure model www.SeattleHeartFailureModel.org	Heart failure patients	Northern-America	1, 2 and 5-year mortality risk	Effect of specific treatment options
U-Prevent www.U-prevent.com	Healthy people Type 2 diabetes patients Vascular patients Elderly	Europe and Northern-America	10-year CVD risk Lifetime CVD risk CVD free life expectancy	Also available in Dutch Effect of specific treatment options Effect of deferred treatment Infographics for patient communication Print option for patient handout Missing data filled in by population average/median Calculator selection aid

EAPC European Association of Preventive Cardiology · ACCA Acute Cardiovascular Care Association · ACNAP Association of Cardiovascular Nursing & Allied Professions

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

ESC European Society of Cardiology

Most existing CV risk scores are developed for primary prevention; the few secondary prevention solutions focus on specific subgroups of CV patients.

Source:
Risk prediction tools in cardiovascular disease prevention: A report from the ESC Prevention of CVD Programme led by the European Association of Preventive Cardiology (EAPC) in collaboration with the Acute Cardiovascular Care Association (ACCA) and the Association of Cardiovascular Nursing and Allied Professions (ACNAP); published Jun 24, 2019,
European Journal of Preventive Cardiology.

https://journals.sagepub.com/doi/10.1177/2047487319846715

Rev Port Cardiol. 2017;36(2):77–83

Revista Portuguesa de
Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

ORIGINAL ARTICLE

ProACS risk score: An early and simple score for risk stratification of patients with acute coronary syndromes

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Received 29 March 2016; accepted 18 May 2016
Available online 31 January 2017

KEYWORDS
Risk stratification score;
Acute coronary syndromes;
Prognosis

Abstract
Introduction: There are barriers to proper implementation of risk stratification scores in patients with acute coronary syndromes (ACS), including their complexity. Our objective was to develop a simple score for risk stratification of all-cause in-hospital mortality in a population of patients with ACS.
Methods: The score was developed from a nationwide ACS registry. The development and internal validation cohorts were obtained from the first 31 829 patients, randomly separated (60% and 40%, respectively). The external validation cohort consisted of the last 8586 patients included in the registry. This cohort is significantly different from the other cohorts in terms of baseline characteristics, treatment and mortality. Multivariate logistic regression analysis was used to select four variables with the highest predictive potential. A score was allocated to each parameter based on the regression coefficient of each variable in the logistic regression model: 1 point for systolic blood pressure ≤116 mmHg, Killip class 2 or 3, and ST-segment elevation; 2 points for age ≥72 years; and 3 points for Killip class 4.
Results: The new score had good discriminative ability in the development cohort (area under the curve [AUC] 0.796), and it was similar in the internal validation cohort (AUC 0.785, p=0.333). In the external validation cohort, there was also excellent discriminative ability (AUC 0.815), with an adequate fit.

Amgen led initiative investigating the role of machine learning presents a potential solution

- **Detect**
- **Evaluate**
- **Engage**
- **Protect**

What?

- **DEEP™ is a platform** that harnesses the power of advanced data science to create solutions for predicting and preventing serious health conditions, helping patients live healthier lives, and unlocking value and efficiency for the healthcare system.

How?

- An AI-based clinical risk prediction model that uses routine EHR data to identify individual patient's risk and break down the risk drivers.
- Trained and cross validated on multiple real-world datasets.
- Jointly developed with the healthcare community in a value-based partnership model.

System uses AI and real world data to support a paradigm shift towards personalised and preventative healthcare

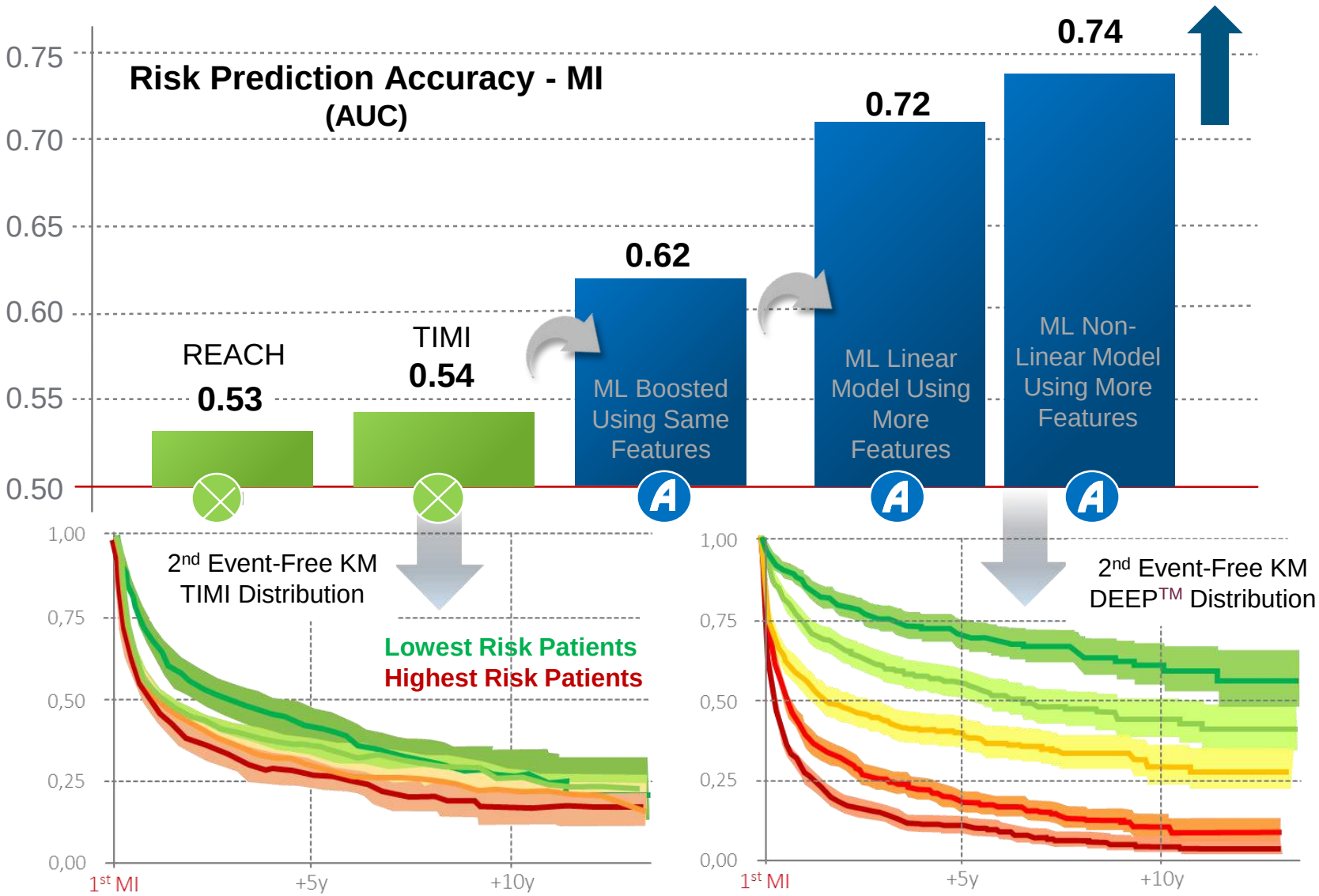
Predict at the individual patient level

- Risk of a subsequent event
- Drivers of event risks

Provide insights to

- Personalize treatment plans
- Optimize patient care management and improve health outcomes
- Allocate resources more efficiently to patients most at risk and in need

The DEEP™ algorithm today has already demonstrated superior risk prediction accuracy in primary care setting

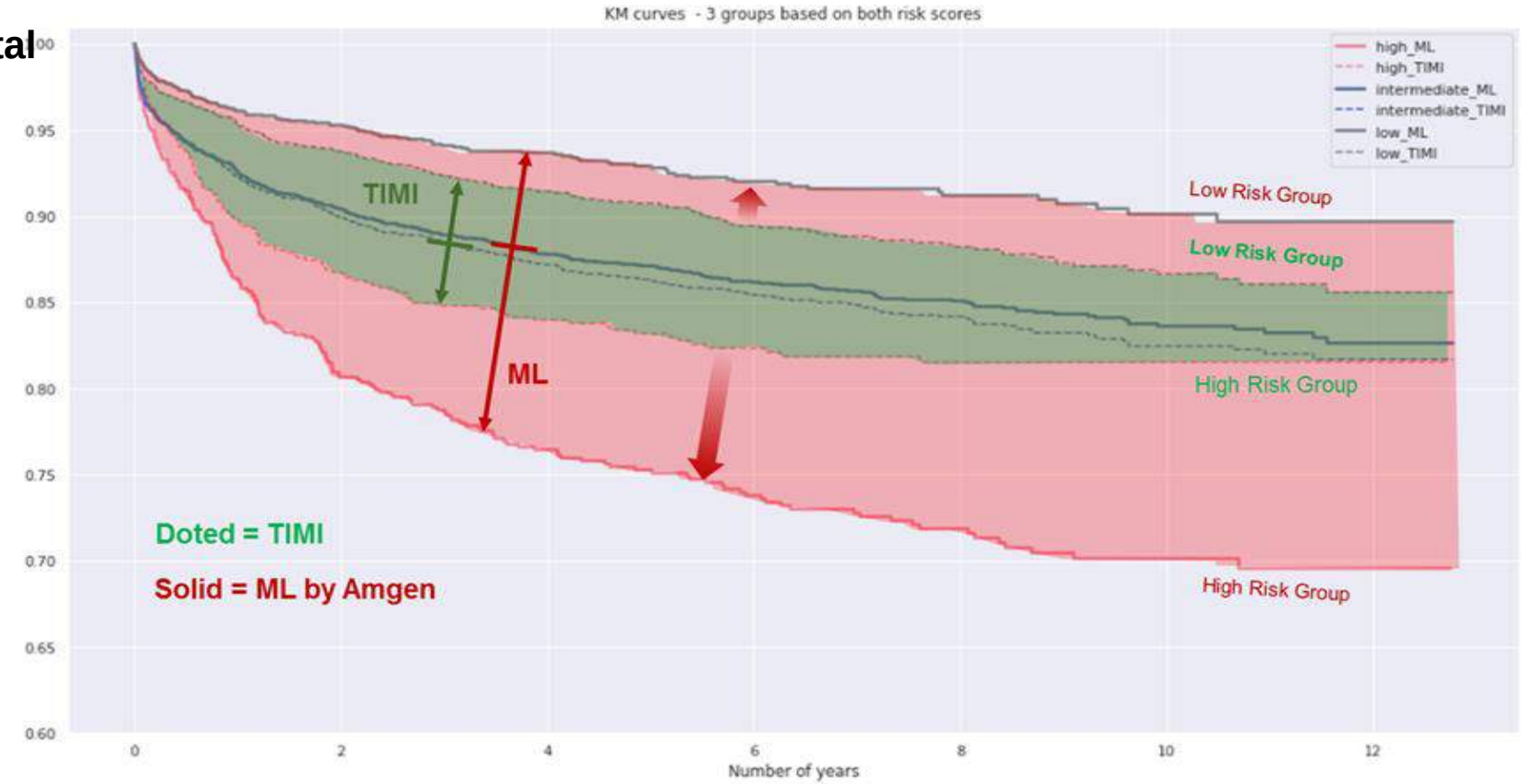


- Existing CV risk scores have been developed in clinical trial settings with almost perfect data. When applied to **real-world primary care data**, their prediction isn't accurate enough to meaningfully differentiate patients.
- With the level of **precise patient stratification** possible with DEEP, physicians can create **personalized treatment plans** based on each patient's risk profile.

Similar results were achieved on data from hospital setting

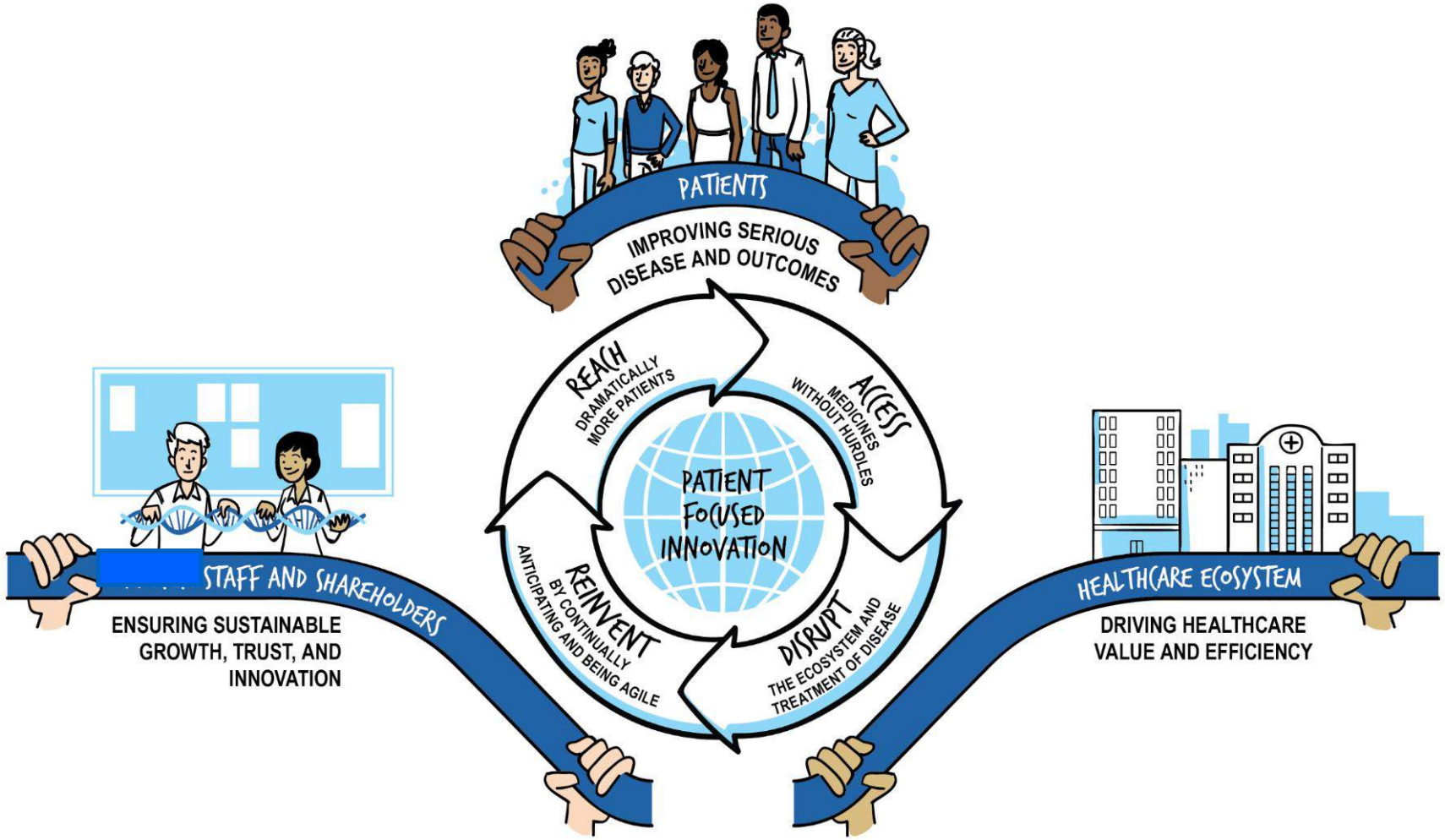
- As DEEP™ Cardiology focuses on **secondary prevention of CV events**, our target clinical setting is hospitals, where real-world post-MI/stroke patients' data sit.
- In this setting, DEEP™ Machine Learning algorithm has similarly proven to be **powerful in differentiating high vs. low risk patients** compared to TIMI.

Coimbra University Hospital
7.000 ACS Patients from UCU
Special interest on CV risk



DEEP™ is a concrete step towards changing the healthcare landscape

AI and machine learning have the power to change the healthcare landscape



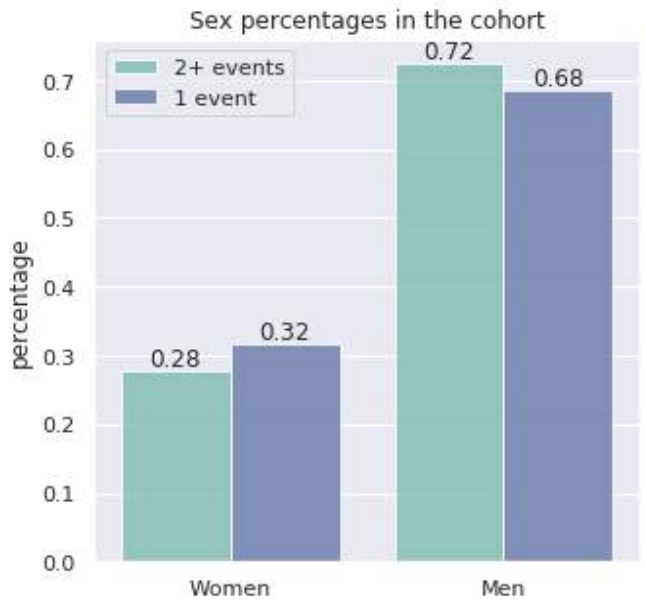
DEEP™ STUDY AT THE UNIVERSITY OF COIMBRA

- Our study is a long term, longitudinal, single center cohort study, where we collected data prospectively on 5977 ACS patients admitted for ACS and discharged alive.
- Using machine learning algorithms involving data collected on 119 variables
- Kaplan Meier event free survival curves were compared for parameters with highest ranked interaction with diabetes mellitus to predict readmission.

COIMBRA PATIENT POPULATION (N=5977)

Sex

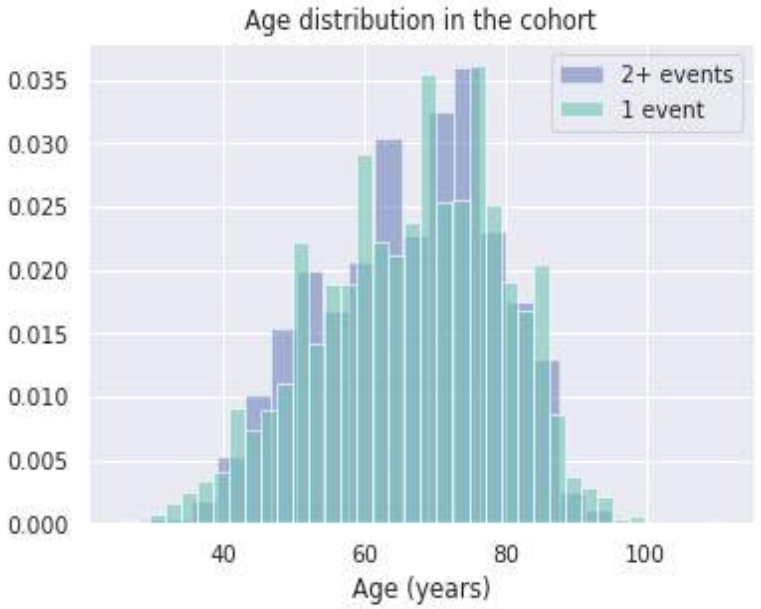
Women	Men
31%	69%



Age

Mean 66 years old

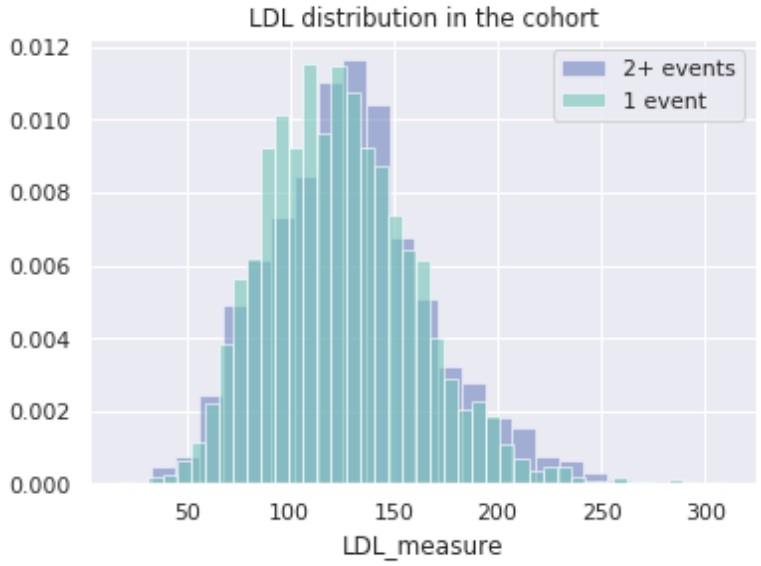
Median 68 years old



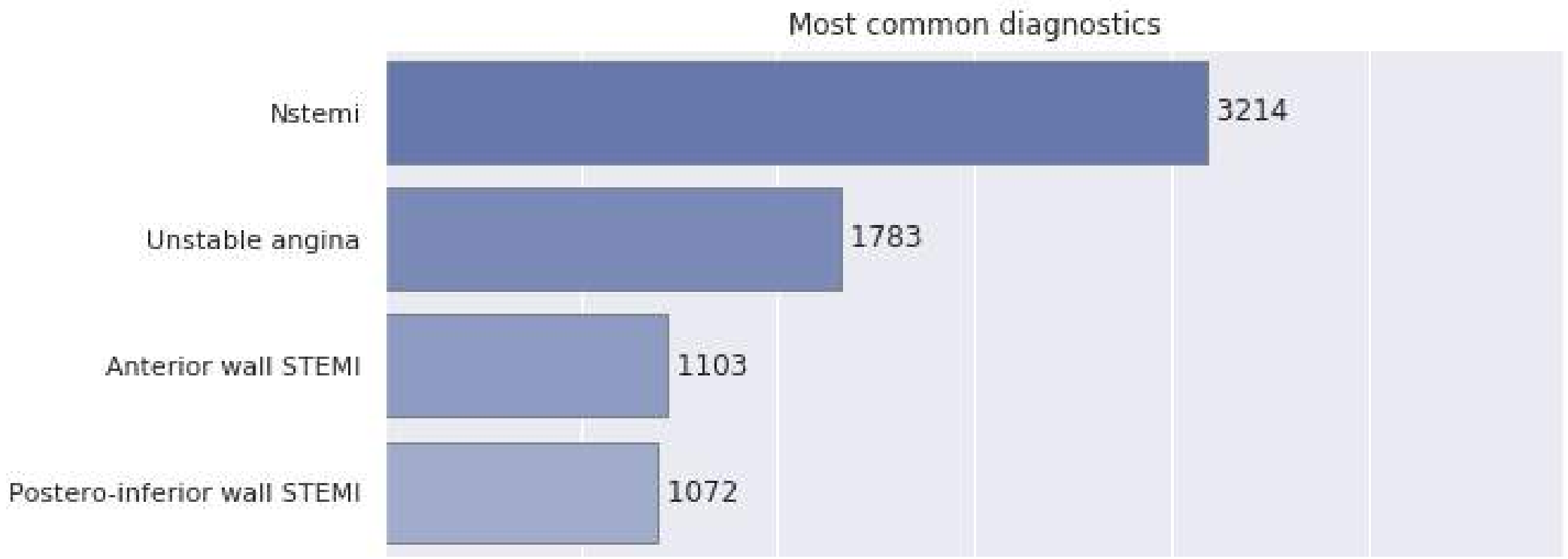
LDL

Mean 125 mg/dL

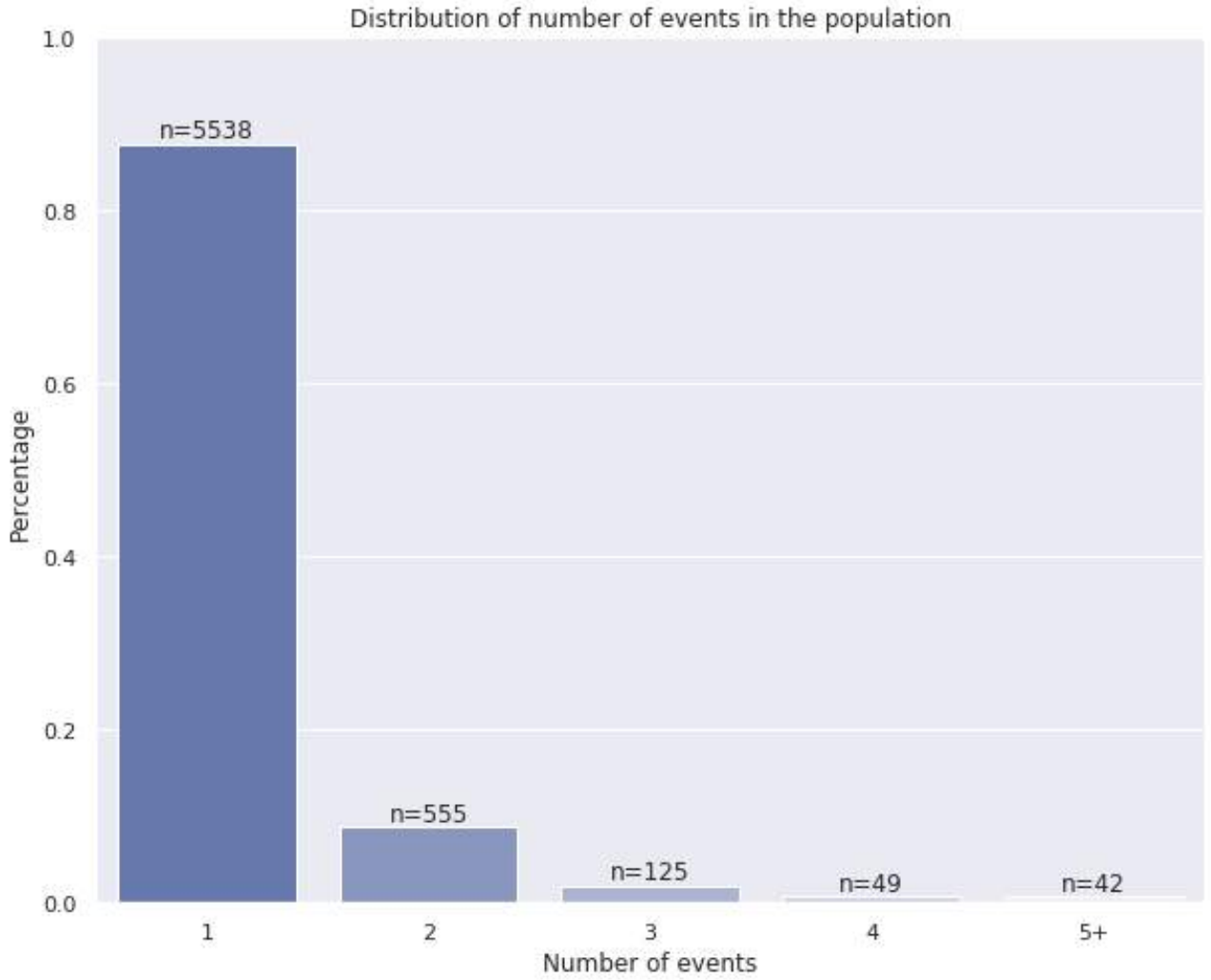
Median 123 mg/dL



ADMISSION DIAGNOSIS



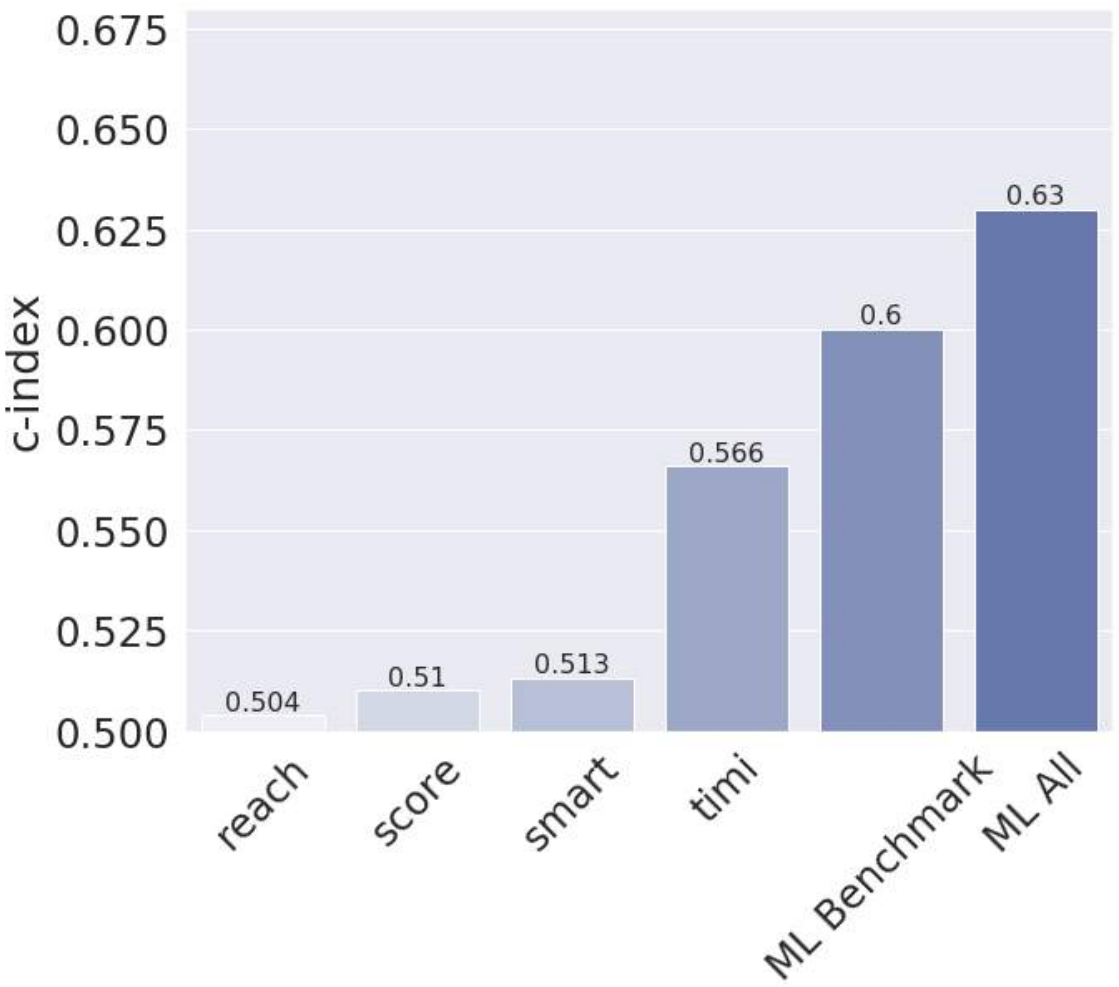
EVENT DISTRIBUTION



RESULTS

- 770 patients (13%) have at least a second cardiovascular event
- For the 5977 overall patients, re-event rates were 13% (771)
- Half of all recurrent events occur within (338 days) and the majority (90%) of recurrent events occur within 2000 days
- 42% of patients without readmission are observed under 2000 days (n=2186)

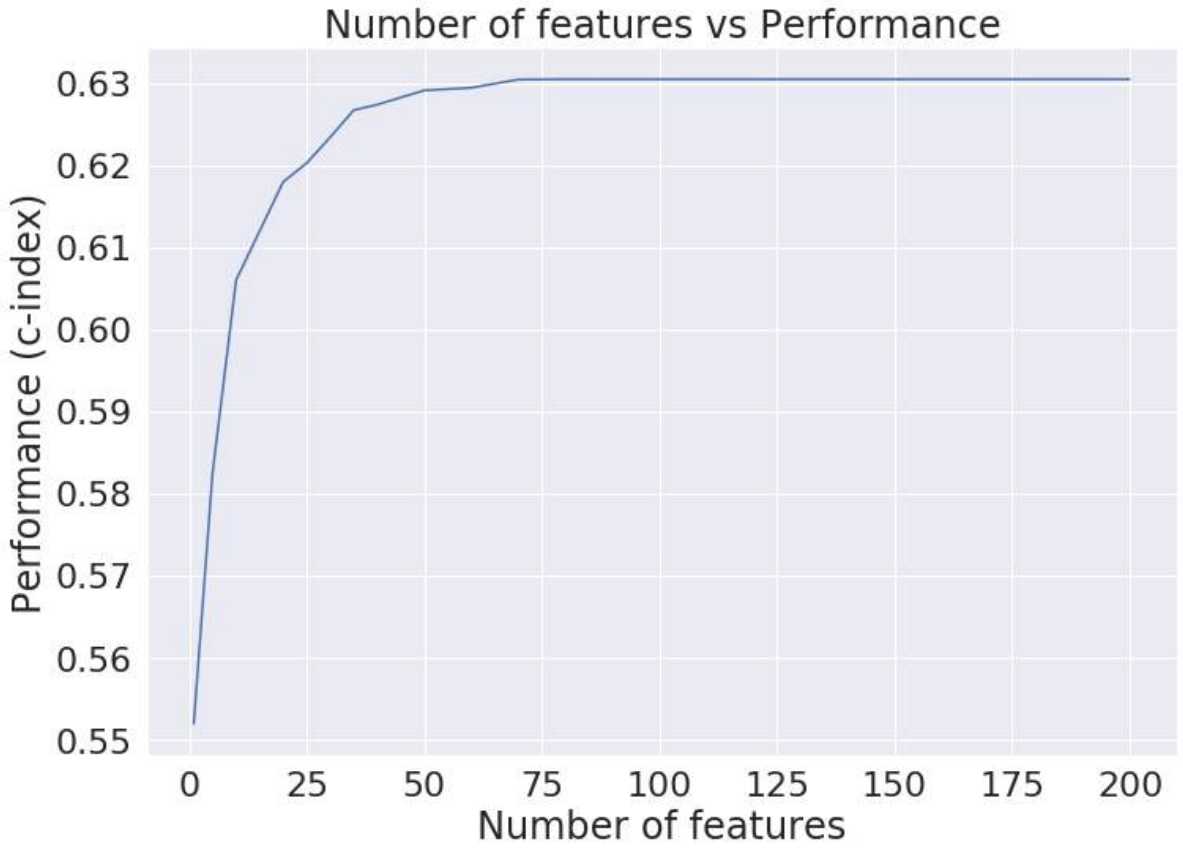
DEEP™ PREDICTION ACCURACY: SUBSEQUENT EVENTS



RESULTS

- The prediction accuracy for secondary CV events of existing scores is very limited with TIMI being the best among them (0.56)
- Combing the 17 features from all existing scores improves the accuracy to 0.6
- The DEEP algorithm using 273 features achieves delivers the highest prediction power with a C-index of 0.63

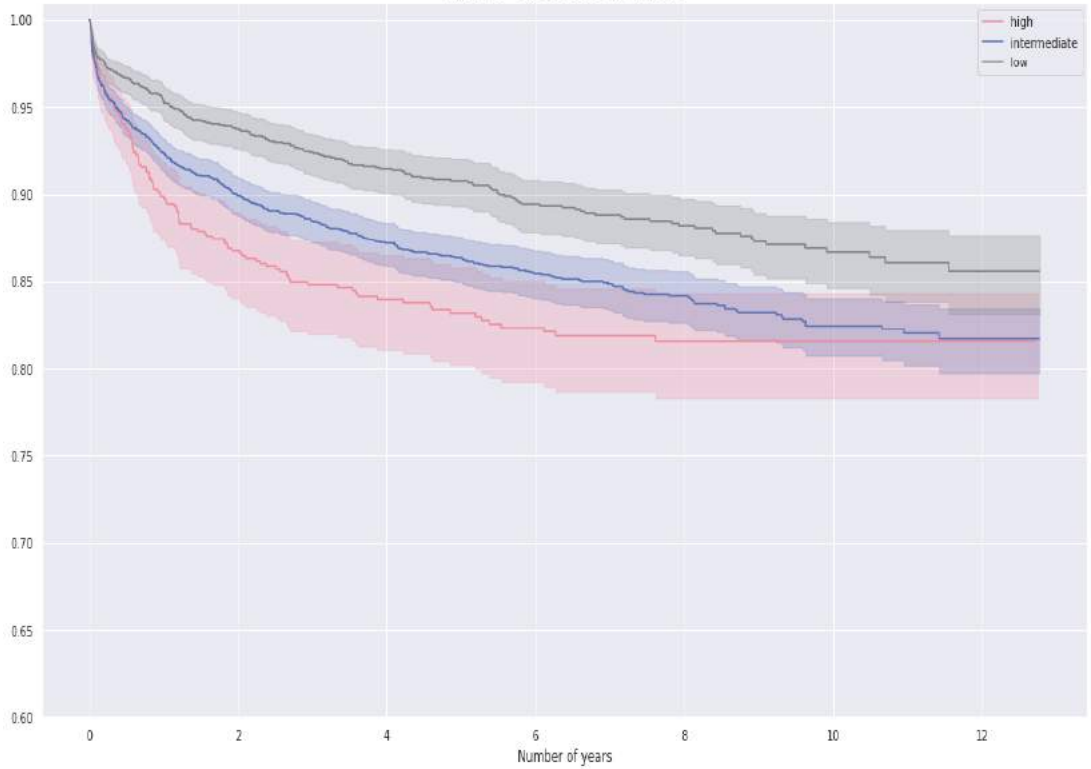
DEEP™ PERFORMANCE VS. NUMBER OF FEATURES



- With 50 features we achieve almost the highest performance
- The marginal gain in prediction accuracy of more attributes is low
- For future use in clinical practice a “mini-max” approach should be applied

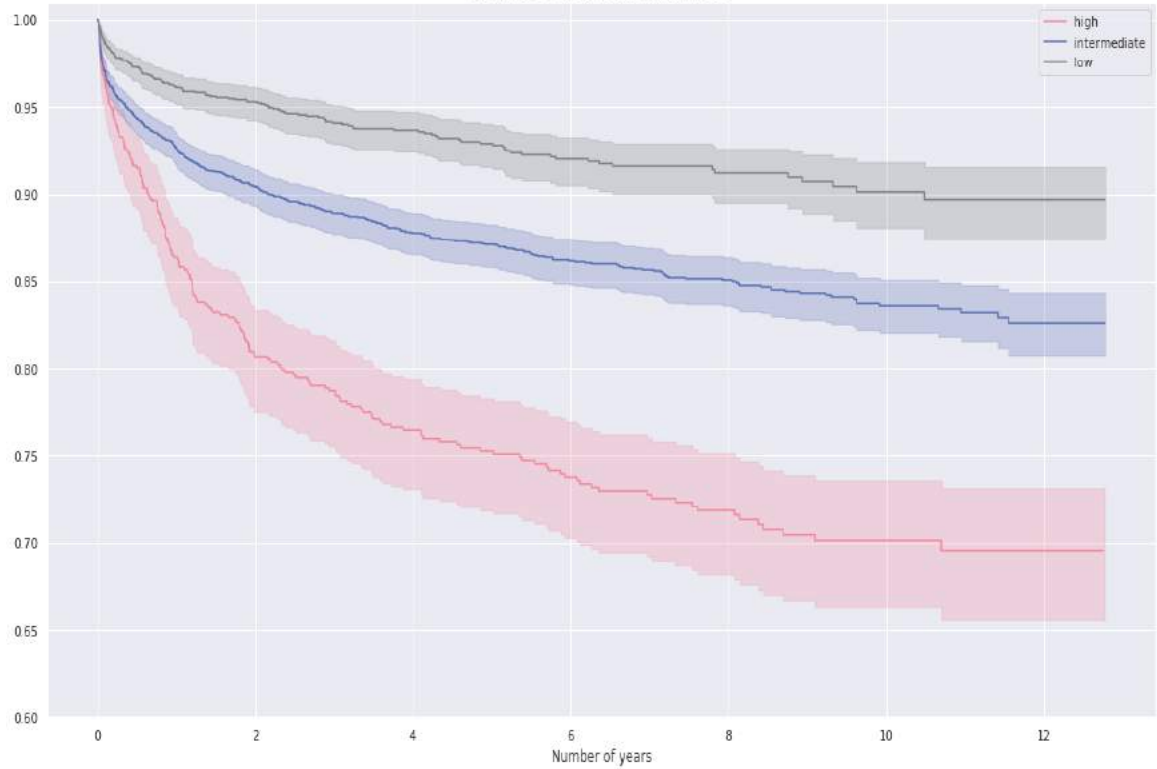
PATIENT RISK SEGMENTATION – TIMI VS. DEEP™ SCORE

BASED ON TIMI SCORE



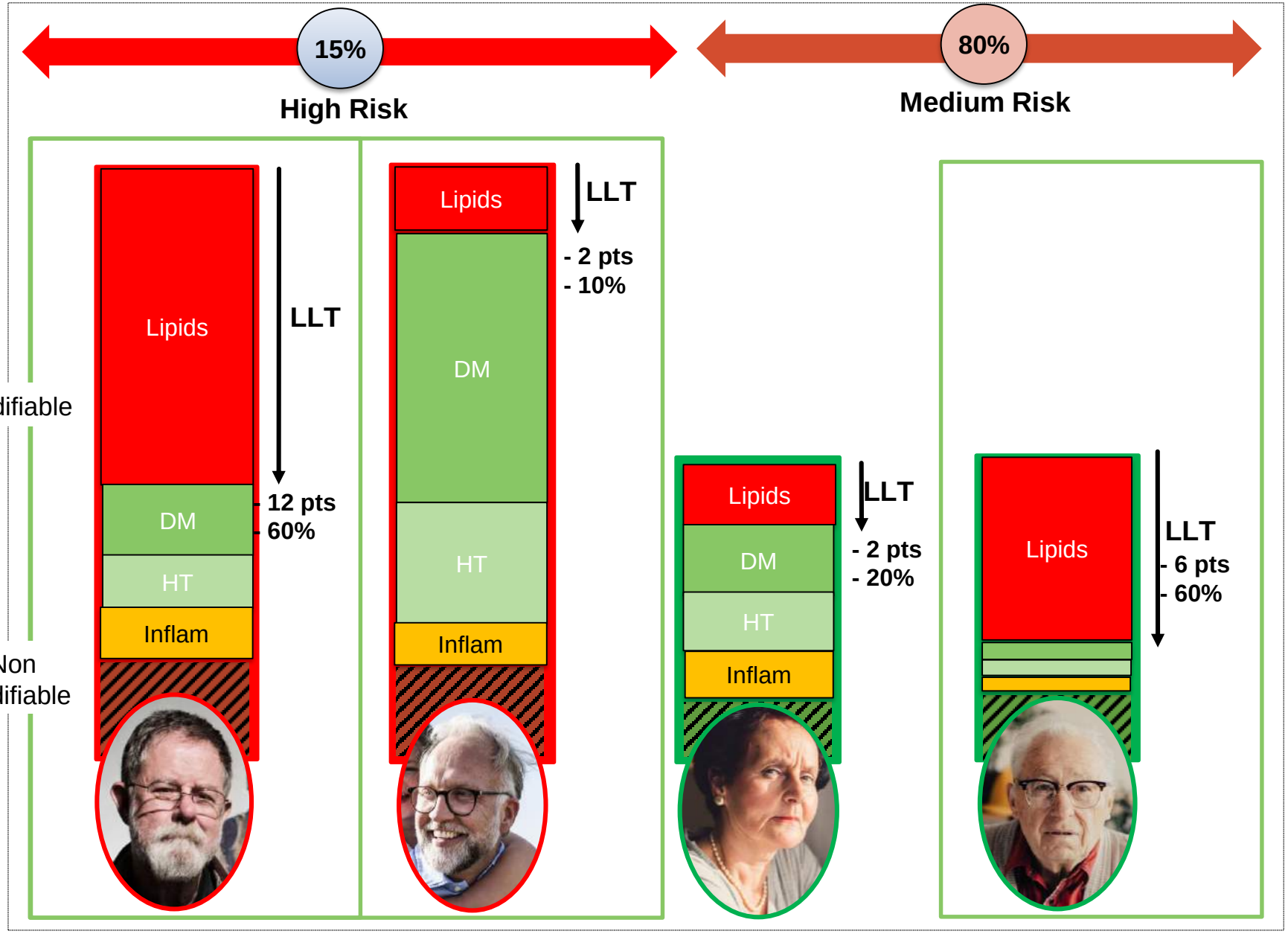
low: 0-1 (36%) -- medium: 2-3 (52%) -- high: 4+ (12%)

BASED ON DEEP SCORE



low: 36% -- medium: 52% -- high: 12%

PERSONALISED MANAGEMENT OF INDIVIDUAL CV RISKS - EXAMPLES



The present and future steps

- This algorithm is being trained and validated in different European databases
- And also applied in present and future clinical trial databases
- In Coimbra, the current algorithm is already used to predict outcomes and define the best secondary prevention strategy for each post-ACS patient
- For 2020 we envision:

1. A further refinement of the algorithm (making it mo accurate and more individualized)
2. The publication of the first results of our combined databases
3. Working on the setup of an user-friendly app for rapid assessment of risk and optimized risk management strategies

CONCLUSIONS

- Big data, Machine learning and Artificial intelligence are here to stay
- They are already everywhere and this trend will only become stronger
- There are lots of areas in Medicine that can benefit from these innovations
- As in other fields, this can lead to miracles or profound disasters
- If we own this process, we can influence its outcomes; if not...
- Clinicians and the Healthcare industry must thus cooperate on this issue to deliver better solutions for the patients and the society as a whole

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