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Global Spotlights

iCARE4CVD: an innovative European consortium aiming to improve personalized cardiovascular care

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Introduction

Cardiovascular disease (CVD) remains a major cause of morbidity and mortality, demanding innovative and more effective strategies to decrease their impact. In 2019, a staggering 113 million people living in the 57 European Society of Cardiology member countries were reported to suffer from CVD,[1] and at a global scale, almost 18 million deaths are yearly caused by atherosclerotic CVD.[2] Its prevalence is further increasing due to the aging population, changes in lifestyle, and environmental factors. Despite decades of research and advances in treatment, CVD remains a leading health challenge. Traditional models of care often follow a 'one-size-fits-all' approach, which does not account for the individual variability in disease progression, treatment responses, and clinical outcomes. Furthermore, the exact role of most causal and disease modifying factors in CVD, like diabetes, chronic kidney disease, and obesity, is not fully understood.

Current state of cardiovascular disease management

The contemporary management of CVD typically involves evidence-based therapy, based on large randomized controlled trials. Good examples are the administration of lipid-lowering drugs, antihypertensive medication, heart failure (HF) treatment, and glucose-lowering medication with cardio- and reno-protective effects.[3,4] Target populations for guideline-based treatment are mostly defined by the inclusion criteria for participation in these trials but may not necessarily reflect the profile of the broader population. While effective for some, this approach does not account for the complex interplay of biological, environmental, and lifestyle factors unique to each patient. For example, the indiscriminate use of beta-blockers in HF with reduced ejection fraction negates the variability in response rates, potentially leading to suboptimal outcomes for some patients, particularly in those with atrial fibrillation.[5] Risk prediction models have claimed to enable a more personalized approach. However, risk prediction does not necessarily point towards the best treatment strategy in an individual patient.[6] Therefore, there are gaps of data and evidence for improving outcome in different settings and patient populations. In addition, although recommendations, e.g. for the use of glucose and/or lipid-lowering medications, are provided on assessed risk,[4] these recommendations using risk scores mostly rely on the estimated number needed to treat but have not been evaluated prospectively. Therefore, there are medical needs to better delineate clinical courses and trajectories including treatment responses and finally to evaluate these learnings in prospective clinical trials.

Innovative strategy and objectives

Against this background, the European Union through the Innovative Health Initiative has funded the 'Individualized care from early risk of CVD to established HF' (iCARE4CVD, https://icare4cvd.eu) project, which started in October 2023. It represents a significant leap forward in personalized cardiovascular (CV) care, by integrating cutting-edge technologies with patient-centred approaches to fundamentally

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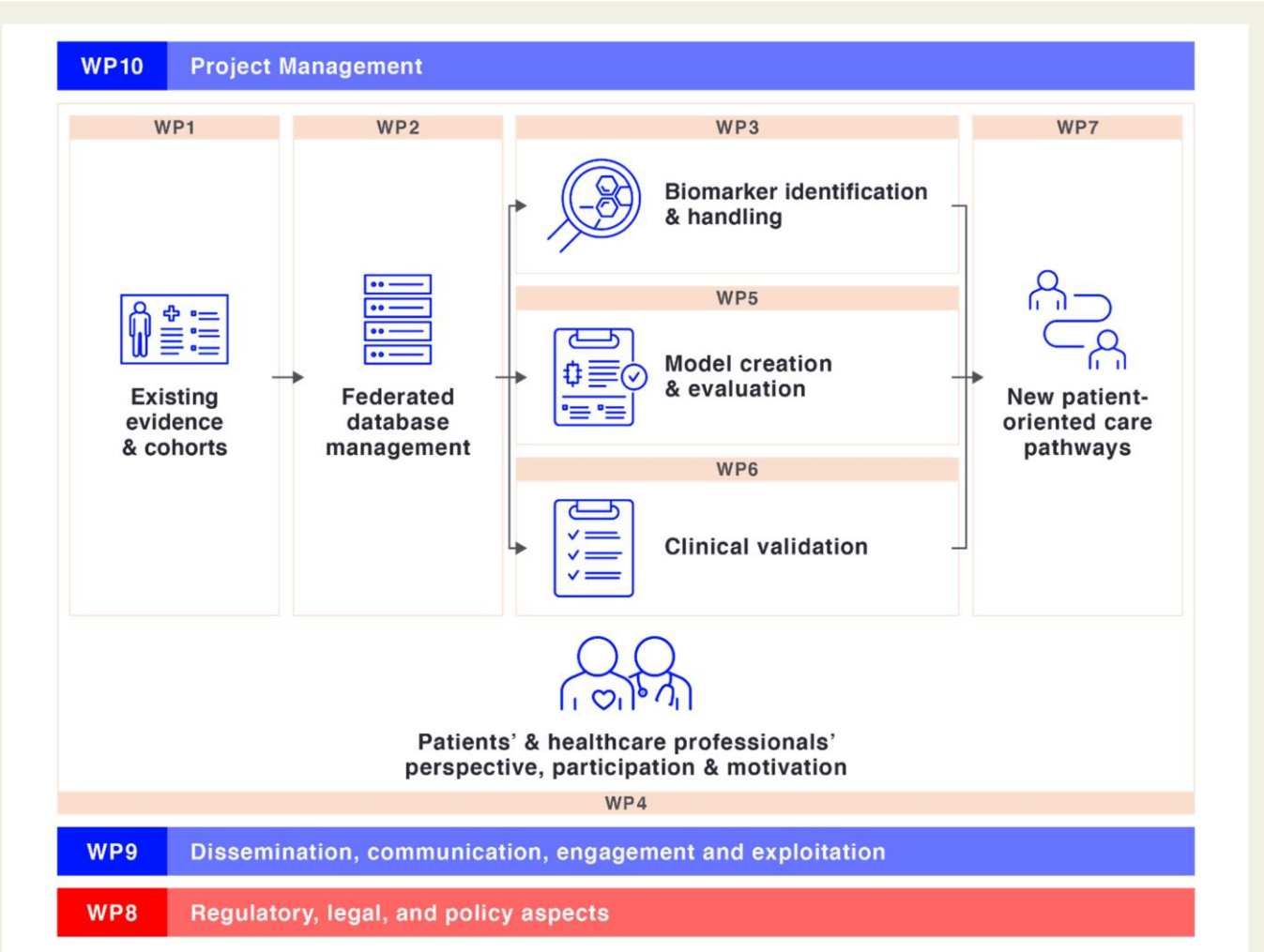

Figure 1 The iCARE4CVD programme structure. WP, work package

transform the management of CV health. Jointly led by Maastricht University and Novo Nordisk, iCARE4CVD addresses the challenges by leveraging a consortium of 36 leading academic institutions, healthcare providers, and pharmaceutical and technology companies across Europe and beyond (see https://icare4cvd.eu). This collaborative approach aims to harmonize diverse data sets of different cohorts with broad phenotyping including biomarkers, genetics, treatment, and patient-reported outcomes from more than a million individuals, to develop a nuanced understanding of CVD.

To enhance patient outcomes across the full spectrum of CVD—from early risk stages to advanced HF—the iCARE4CVD project focuses on four critical areas: (i) early diagnosis and classification into clinically meaningful subgroups; (ii) risk stratification to determine the urgency of interventions; (iii) prediction of individual treatment response; and (iv) incorporation of patient-centred outcomes. Over a period of 4½ years, 10 work packages (WPs) will systematically address these components (*Figure 1*). The initial phase of the project involves developing precise predictive models that incorporates patient profiles including biomarkers and advanced artificial intelligence (AI) techniques. The subsequent phase will focus on validating these models. Concurrently, iCARE4CVD will develop innovative care pathways derived from these results. Throughout the project, patient perspectives are integral to the development process (WP4), alongside the interpretation and management of biomarkers (WP3) and addressing legal and ethical considerations (WP8). The following elements are pivotal in achieving the goals of iCARE4CVD:

(1) *Development of a federated data ecosystem*: iCARE4CVD is creating a federated data platform (WP2) that integrates data from numerous sources (WP1) while ensuring privacy and adherence to General Data Protection Regulation. This platform uses blockchain technology for secure data sharing and advanced analytics on individual patient levels.
(2) *Advanced predictive models using AI*: iCARE4CVD is applying AI to develop predictive models that allow early disease modelling and assess risk and treatment efficacy more accurately than currently possible (WP5). These models are designed to facilitate early intervention and customize treatment plans based on individual patient profiles, significantly improving outcomes.
(3) *Prospective validation of AI-based models*: A cornerstone of iCARE4CVD is the comprehensive prospective validation of the models (WP6) to ensure the added clinical value and the reliability for broader adoption.[7] To validate these models, additional cohorts will be sought and added to the federated database. However, the central point will be the deployment

of the most promising model in a randomized, controlled intervention trial. This approach positions iCARE4CVD at the forefront of implementing precision medicine in clinical studies, establishing a methodological framework as standard for future research in the field.

(4) *Patient-centric care pathways*: Central to the initiative is the development of innovative care pathways (WP7) that are not only informed by clinical data but also by patient preferences (WP4). This approach ensures that care delivery is both scientifically sound and aligned with patient needs, enhancing adherence and satisfaction.

(5) *Stakeholder engagement and policy development*: Recognizing the importance of multi-stakeholder involvement, iCARE4CVD is establishing frameworks for engaging with patients, healthcare providers, policymakers, and payers (WP4, WP7, WP8) as well as for disseminating and exploiting results (WP9). This inclusive strategy ensures that the solutions developed are practical, scalable, and aligned with the existing healthcare policies and economic models.

Expected impact and future directions

iCARE4CVD is set to redefine the landscape of CVD management through its holistic approaches. By the end of the project, we anticipate a suite of validated tools and protocols to improve CVD care and outcomes and cut healthcare costs. Furthermore, the project's emphasis on secure and ethical data use paves the way for future research initiatives, providing a blueprint for integrating large-scale data analytics and validation in healthcare. iCARE4CVD will foster CVD management moving towards more personalized and preventative models.

In conclusion, the iCARE4CVD project not only promises to improve outcomes for patients with CVD but also aims to set new standards for integrating patient data and technology, making a significant impact on public health in Europe and globally.

Declarations

Disclosure of Interest

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References

1. Timmis A, Vardas P, Townsend N, Torbica A, Katus H, De Smedt D, *et al.* European Society of Cardiology: cardiovascular disease statistics 2021. *Eur Heart J* 2022;**43**:716–99. https://doi.org/10.1093/eurheartj/ehab892
2. WHO. Cardiovascular diseases (CVDs). https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).
3. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, *et al.* 2023 focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2023;**44**:3627–39. https://doi.org/10.1093/eurheartj/ehad195
4. Marx N, Federici M, Schütt K, Müller-Wieland D, Ajjan RA, Antunes MJ, *et al.* 2023 ESC guidelines for the management of cardiovascular disease in patients with diabetes. *Eur Heart J* 2023;**44**:4043–140. https://doi.org/10.1093/eurheartj/ehad192
5. Kotecha D, Holmes J, Krum H, Altman DG, Manzano L, Cleland JG, *et al.* Efficacy of beta blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis. *Lancet* 2014;**384**:2235–43. https://doi.org/10.1016/S0140-6736(14)61373-8
6. Brunner-La Rocca H-P, Sanders-van Wijk S, Knackstedt C. Biomarkers in patients with acute dyspnoea: what for? *Eur Heart J* 2012;**33**:2124–6. https://doi.org/10.1093/eurheartj/ehs212
7. Hawkins JR, Olson MP, Harouni A, Qin MM, Hess CP, Majumdar S, *et al.* Implementation and prospective real-time evaluation of a generalized system for in-clinic deployment and validation of machine learning models in radiology. *PLOS Digit Health* 2023;**2**:e0000227. https://doi.org/10.1371/journal.pdig.0000227