

A European network to develop virtual twin technology for personalized stroke management in atrial fibrillation: the TARGET consortium

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Summary:

Atrial fibrillation (AF) is a prevalent heart arrhythmia that increases stroke risk, leading to severe complications, high costs, and poor recovery outcomes. To address this, the European Union's Horizon Europe research programme has funded the TARGET project to develop personalised stroke management strategies for AF-related stroke patients. To achieve this, TARGET will capitalise on the power of AI, virtual twin technologies and *in silico* trials, and will further advance the work in the direction of the personalisation of care.

What led to TARGET

Atrial fibrillation (AF) is the most common heart arrhythmia worldwide, leading to life-limiting complications, high financial burden and significant resource utilisation. Stroke is a debilitating complication of AF and is amongst the most common causes of death and the leading cause of disability and dementia. The pathophysiology of AF-related stroke (AFRS) is associated with severe neurological deficits due to larger clots, infarction of substantial cerebral areas and haemorrhagic transformation, a complication that significantly worsens prognosis¹. Functional recovery from AFRS is often unsatisfactory, leading to longer hospital stays, severe disability and high mortality.

In this context, the European Union, through the Horizon Europe research programme, has funded the "Health Virtual Twins for the Personalised Management of Stroke Related to Atrial Fibrillation" (TARGET) project (grant agreement no. 101136244). The consortium brings together the diverse expertise of nineteen leading institutions in ten countries (Figure 1A), representing eight academic partners, six hospitals, four companies and a charity. TARGET is led by Liverpool John Moores University (LJMU), the University of Liverpool (UoL) and Lund University (LU).

A



B

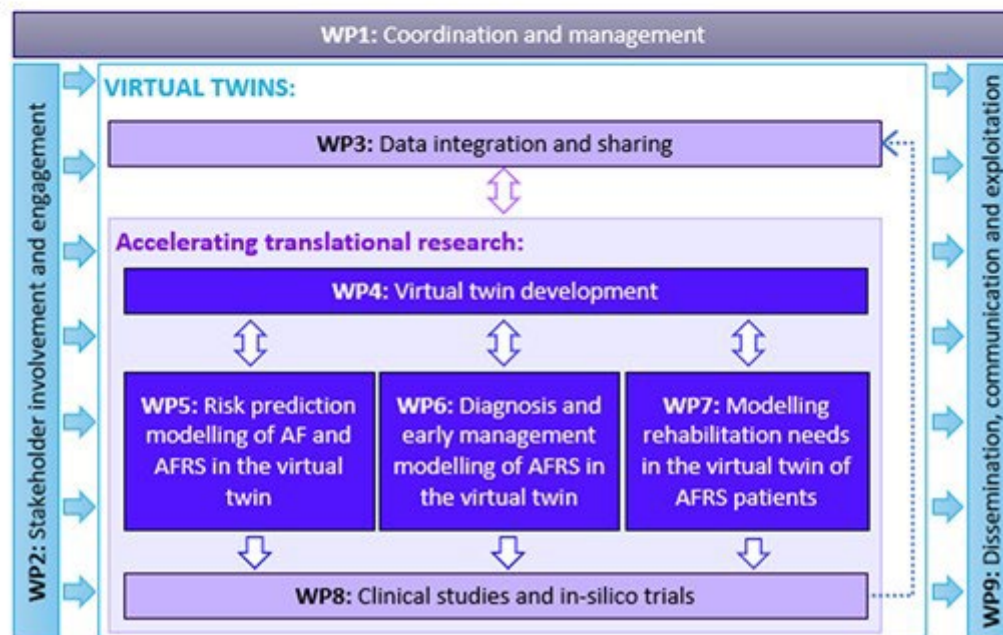


Figure 1. A) Consortium of the EU project TARGET. **B)** TARGET's programme of work is divided into nine work packages (WPs). AF: atrial fibrillation; AFRS: AF-relates stroke.

TARGET's ambition and timeliness

TARGET harnesses the power of Artificial Intelligence (AI) modelling, virtual twins and *in silico* trials to develop personalised computational models and decision-support tools with data from multiple countries,

covering the AFRS disease pathway, starting from the healthy state, pathophysiology and disease onset, progression, treatment and recovery. This is important given the dynamic nature of risk factors and comorbidities, the arrhythmia itself (including a spectrum of AF burden) and management strategies²⁻⁴. Hence, global guidelines have advocated a holistic or integrated care approach to AF management, and the need for regular re-assessment of risk and adherence to guideline-recommended care⁵⁻⁷.

AI solutions are being increasingly used in clinical practice. Coupled with AI, health virtual twins⁸ (which refer to digital representations of individuals based on their unique traits and medical history) aim to improve patient outcomes by enabling more accurate diagnoses, more personalised treatment plans, and more efficient resource allocation. TARGET's ambition is to develop novel virtual twin-based AI models involving hybrid modelling of mechanistic and data-driven virtual twins, together with causal AI, to facilitate the translation of basic research into clinical practice through an integrated multiscale approach.

The project is timely – virtual twins, AI, *in silico* trials and related technologies are increasingly prevalent in healthcare applications, taking advantage of a learning health system model approach. There has been an exponential growth of AI and machine learning publications aimed at advancing our understanding of AF, which has been mainly driven by the advances in deep neural networks and the availability of large, open-access databases⁹. TARGET will capitalise on this and the maturity of the technology, and will further advance the work in the direction of the personalisation of care. The project spans a timeline including i) development of personalised models and decision support tools, ii) validation (including *in silico* trials) of these models and tools and iii) testing on newly collected data (from observational clinical studies); all these with the participation (co-development and evaluation) of patients, healthcare professionals and relevant stakeholders.

TARGET's programme of work

The TARGET project started in January 2024 and its programme of work is based on nine work packages (WPs) to be delivered over a period of five years (Figure 1B). The project activities are coordinated and managed by WP1 under the scientific leadership of Prof Sandra Ortega-Martorell (Principal Investigator, LJMU), the methodological leadership in AI and virtual twins of Prof Ivan Olier (LJMU), the clinical leadership in AF and stroke of Prof Gregory Lip (UoL) and the coordination of Prof Mattias Ohlsson (LU).

A dedicated work package looking at the ethics and regulatory framework of developing virtual twins for health, and the engagement with healthcare professionals, societies and Patient and Public Involvement (PPI) groups (WP2), will help TARGET understand stakeholders' needs and level of acceptability/engagement with this technology. The close participation of Arrhythmia Alliance, a patient organisation, in the development of the research, will also ensure that patients remain at the heart of the project.

Powered by retrospective and prospective data

TARGET will capitalise on the existing retrospective data from the participating hospitals and from publicly available healthcare data repositories to develop a centralised data platform (WP3) to be used for modelling, employing state-of-the-art data integration and harmonisation techniques. We will combine established risk factors with comorbidities, imaging and biomarkers for all stages of the AFRS disease pathway. The resulting personalised models will advance clinical care and enable dynamic, longitudinal monitoring (WPs 4-7). This will help prevent AFRS, optimise acute stroke management, improve rehabilitation treatments, reduce long-term disability, enable a better quality of life for patients and caregivers, and lower healthcare costs (reducing challenges to healthcare systems). The integration of the developed models into monitoring devices and rehabilitation tools will accelerate clinical adoption.

New observational data will be collected during the span of the project via four carefully designed prospective clinical observational studies (WP8), which will be used to test and validate the personalised decision support tools and to evaluate the virtual twin models on specific scenarios using a clinical trial simulation (*in silico*), to demonstrate evidence of clinically meaningful results. TARGET will cover the different stages in the continuum of the innovation path, including clinical research and validation in real-world settings, ensuring appropriate pathways for dissemination and exploitation of its results (WP9).

Experienced industrial partners

TARGET's association with experienced industrial partners such as Siemens SRL, Siemens Healthineers, and Isansys, leaders in the healthcare sector, will warrant that novel technologies are swiftly adopted and implemented. Also, TARGET will contribute to the consolidation of existing mechanistic virtual twins of the heart, brain and neuromusculoskeletal system, enriching these twins to deliver more complex tasks, and supporting research to move towards a more integrated human virtual twin, enabling new studies, including other health conditions.

In conclusion, TARGET represents a milestone project to improve the care of patients in the AFRS pathway, introducing a paradigm shift in risk prediction, diagnosis and management of the disease, and accelerating translational research into practice. The project has an online presence (<https://target-horizon.eu/>) and on major social media platforms.

Supplementary material

TARGET leaders and Consortium members list.

TARGET leaders:

Prof Sandra Ortega-Martorell^{1,2}, Prof Ivan Olier^{1,2}, Prof Mattias Ohlsson³, Prof Gregory Y. H. Lip^{2,4}

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Consortium members list.

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