

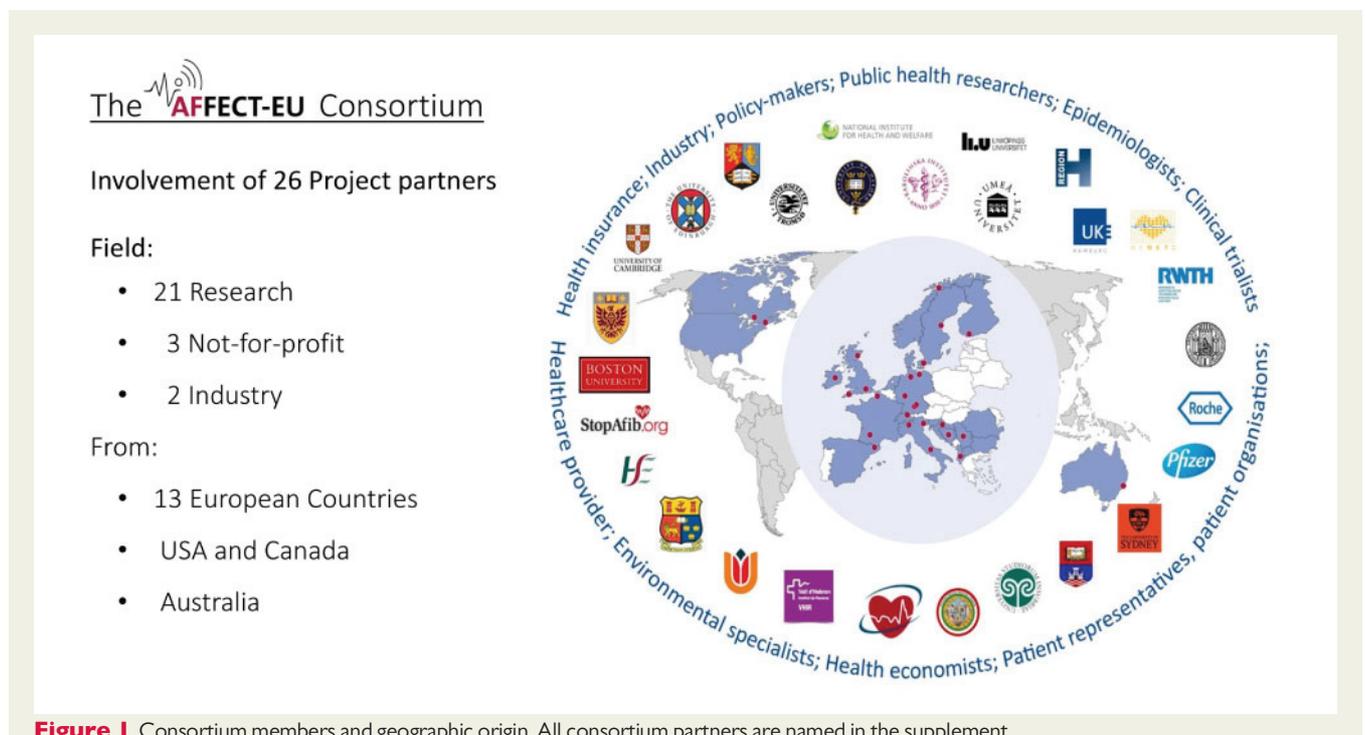
# Digital, risk-based screening for atrial fibrillation in the European community—the AFFECT-EU project funded by the European Union

Daniel Engler <sup>1,2</sup>, Hein Heidbuchel<sup>3</sup>, and Renate B. Schnabel <sup>1,2\*</sup>; for the AFFECT-EU Investigators

<sup>1</sup>Department of Cardiology, University Heart and Vascular Center Hamburg Eppendorf, Hamburg, Germany <sup>2</sup>German Center for Cardiovascular Research (DZHK) Partner Site Hamburg/Kiel/Lübeck; and <sup>3</sup>Department of Cardiology, Antwerp University and Antwerp University Hospital, Antwerp, Belgium

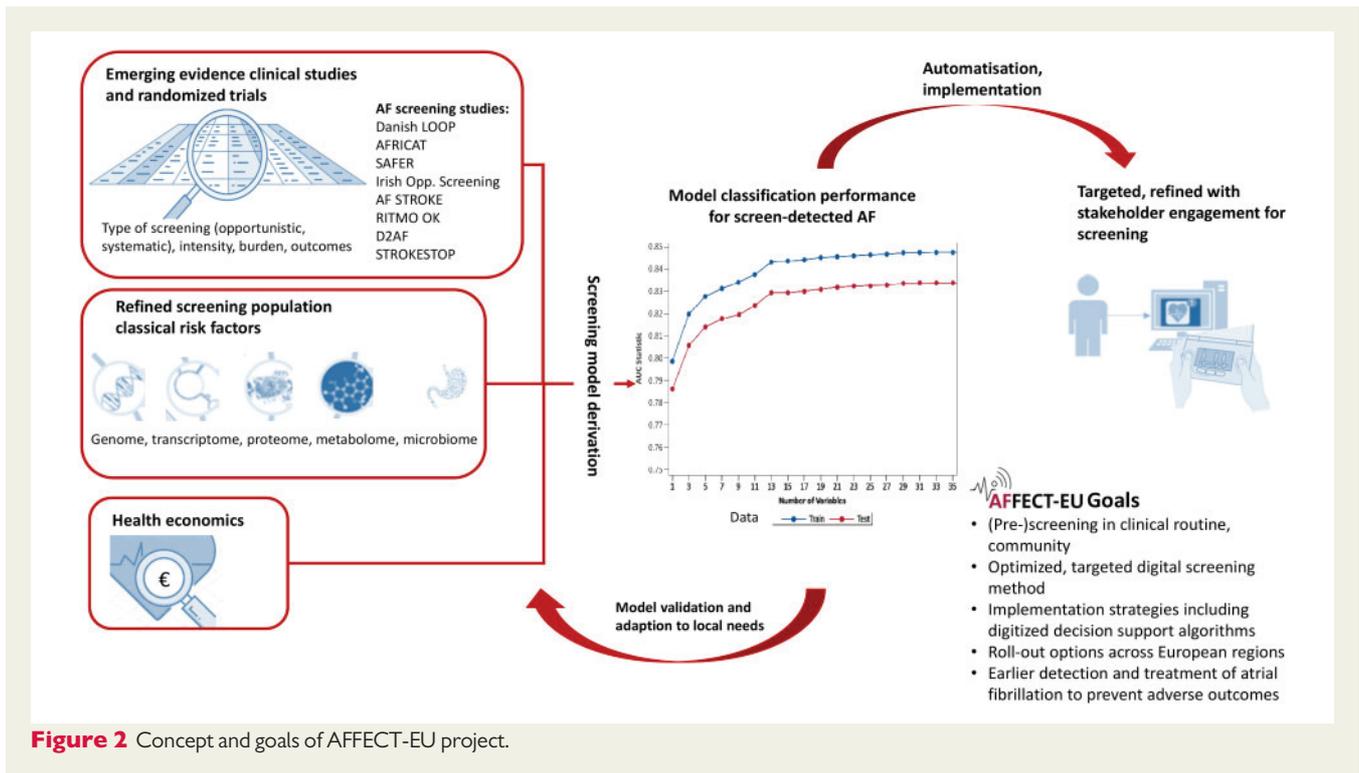
Owing to the demographic changes, we are facing an epidemic of atrial fibrillation (AF) in the aging population with a prevalence of approximately 2.5–3%<sup>1</sup> (twice as high in men and 5% prevalence in individuals  $\geq 65$  years) and a projected doubling of this number by 2050.<sup>2</sup> Atrial fibrillation is often asymptomatic with its first manifestation being debilitating stroke in more than 10 of patients.<sup>3</sup> Atrial fibrillation produces significant healthcare costs for the European society and

precludes healthy aging. The European Society of Cardiology (ESC) guidelines recommend screening for AF to prevent complications and optimize treatment, including the use of highly effective oral anti-coagulation (OAC) in patients at risk of stroke.<sup>4</sup> However, questions on whom to screen, how to screen, and the optimal setting for screening with highest efficiency remain unanswered. In this context, the EU-funded AFFECT-EU project ([www.affect-eu.eu](http://www.affect-eu.eu), *Figure 1*) aims



**Figure 1** Consortium members and geographic origin. All consortium partners are named in the supplement.

\* Corresponding author. Email: [r.schnabel@uke.de](mailto:r.schnabel@uke.de)



**Figure 2** Concept and goals of AFFECT-EU project.

at developing a risk-based AF screening strategy using digital applications for rhythm monitoring to reduce the burden of stroke and other AF-related comorbidities.

Over the last decade, an increasing number of studies have addressed diverse AF screening strategies in heterogeneous settings using different digital devices from traditional ECG recordings to intermittent or semi-continuous pulse-based or electrocardiographic monitoring to continuous monitoring by external or implantable loop recorders.

It is common sense that prolonged monitoring for AF will increase the yield of screen-detected AF. However, little is known on the screening yield by different screening strategies in primary care and in the community. Currently, an arrhythmia must have a duration of at least 30 s to be defined as AF. Shorter episodes of irregular atrial rhythms are summarized under the general term atrial tachycardia or micro AF. Longer-lasting (minutes to hours) episodes of asymptomatic atrial arrhythmias are increasingly detected with the use of long-term, continuous monitoring such as implanted devices. Although micro AF and other episodes may be precursors of clinical AF, screening detection of such arrhythmias may be associated with a lower risk of stroke than clinical AF and the use of OAC to treat individuals with such episodes is still a matter of controversy.<sup>5</sup>

In AFFECT-EU, study information from eight European screening studies (Figure 2) will permit to estimate the efficiency of different screening methods. Based on data from continuous monitoring studies (e.g. Danish Loop<sup>6</sup>), the total AF burden from AF detected by different types of screening, screening intensity, and screening intervals will be simulated.

The number needed to provide robust outcome data in a screening study is larger than could be enrolled in a single RCT.<sup>7</sup> Therefore, a systematic review and participant-level meta-analysis of outcome trials including worldwide data from the AF Screen International Collaboration<sup>8</sup> consortium will summarize all available evidence and assess the risks and benefits of AF screening. Simulations will be performed to derive risk estimates for adverse outcomes across the spectrum of screening types and intensity of AF screening.

Established, contemporary European [MORGAM, MOnica Risk, Genetics, Archiving, and Monograph The MORGAM Project (thl.fi)] population cohorts<sup>9,10</sup> permit refinement of AF screening to increase accuracy and reduce the number needed to screen through optimized clinical prediction models. They will integrate health modifiers from epidemiological and biomarker data sources to identify high-risk populations to tailor early AF detection.

Health economics flank the project. Decision analytic models including an updated stroke risk equation as well as updated parameters on the prognosis of screen-detected AF, effectiveness, and adherence of OAC treatment and long-term cost and effects of AF-related complications will be developed. The budget impact on the health care system of implementing different AF screening programs in a variety of European countries will be assessed. Economic evaluations of different screening strategies including a variety of devices in combination with other diagnostic methods evaluating the marginal long-term cost-effectiveness from both health care providers and societal perspectives will be performed.

The European Society of Cardiology represented by the European Heart Rhythm Association (EHRA) leads the implementation. First,

the obstacles of AF screening uptake in Europe will be assessed in structured interviews and a survey addressed at healthcare professionals and regulators. The project will review healthcare systems and infrastructure, national non-communicable disease plans, and measures and policies addressing AF burden across European countries.

Following the Medical Research Council framework for evaluating complex interventions the implementation of AF screening across participating European countries will be examined to determine how AF screening is delivered in practice. The project will develop an understanding of how the mechanisms of impact of AF screening relate to the mechanisms through which the intervention works and produces changes in the intervention recipients. The country-specific context on how factors external to the intervention that might influence how the intervention operates will be examined. Implementation will be assessed in a pilot study for opportunistic AF screening with a potential roll-out across Europe.

Major considerations that AFFECT-EU will focus on

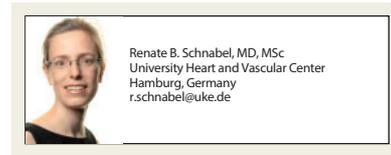
- Dimension of the healthcare problem, relevance of screen-detected atrial fibrillation
- Accuracy of digital screening methods
- Comparison of different screening methods (opportunistic, systematic, single-timepoint, prolonged)
- Cost–benefit ratio, effectiveness, and efficiency
- Feasibility, screenee, and healthcare professional acceptance
- Adaption to the regional, local environment also overcoming inequities
- Health economics of digitized screening
- Outline of structured post-screening work-up processes
- Raising the awareness of the detrimental effects of undetected AF will be raised in healthcare professionals, regulators, and the target population.

Overall, the project is intended to reduce the burden of AF-related diseases and improve AF-associated health equity across Europe.

## Funding

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme under the grant agreement No 847770 (AFFECT-EU).

**Conflict of interest:** none declared.



## References

1. Magnussen C, Ojeda FM, Wild PS, Sørensen N, Rostock T, Hoffmann BA, Prochaska J, Lackner KJ, Beutel ME, Blettner M, Pfeiffer N, Rzyayeva N, Sinning CR, Blankenberg S, Münzel T, Zeller T, Schnabel RB. Atrial fibrillation manifestations risk factors and sex differences in a population-based cohort (From the Gutenberg Health Study). *Am J Cardiol* 2018;**122**:76–82.
2. Di Carlo A, Bellino L, Consoli D, Mori F, Zaninelli A, Baldereschi M, Cattarinussi A, D'Alfonso MG, Gradia C, Sgherzi B, Pracucci G, Piccardi B, Polizzi B, Inzitari D, Aliprandi ML, Bonsangue E, Locatelli P, Saurgnani P, Senziani LG, Tarantini D, Rota RP, Boninsegni R, Feltrin T, Lancia E, Latella F, Monici G, Portera F, Ceccherini S, Borello G, Contartese A, D'Amico A, D'Urzo G, Grillo GC, Mellea F, Ramondino C, National Research Program: Progetto FAI. La Fibrillazione Atriale in Italia. Prevalence of atrial fibrillation in the Italian elderly population and projections from 2020 to 2060 for Italy and the European Union: the FAI Project. *Eurpace* 2019;**21**:1468–1475.
3. Kishore A, Vail A, Majid A, Dawson J, Lees KR, Tyrrell PJ, Smith CJ. Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis. *Stroke* 2014;**45**:520–526.
4. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). 2020.
5. Van Gelder IC, Healey JS, Crijns HJGM, Wang J, Hohnloser SH, Gold MR, Capucci A, Lau C-P, Morillo CA, Hobbelt AH, Rienstra M, Connolly SJ. Duration of device-detected subclinical atrial fibrillation and occurrence of stroke in ASSERT. *Eur Heart J* 2017;**38**:1339–1344.
6. Diederichsen SZ, Haugan KJ, Kronborg C, Graff C, Højberg S, Køber L, Krieger D, Holst AG, Nielsen JB, Brandes A, Svendsen JH. Comprehensive evaluation of rhythm monitoring strategies in screening for atrial fibrillation. *Circulation* 2020;**141**:1510–1522.
7. Mandrola J, Foy A, Naccarelli G. Screening for atrial fibrillation comes with many snags. *JAMA Internal Med* 2018;**178**:1296–1298.
8. Freedman B. AF-SCREEN international collaboration. *Eur Heart J* 2016;**37**:3490–3491.
9. Schnabel RB, Sullivan LM, Levy D, Pencina MJ, Massaro JM, D'Agostino RB, Newton-Cheh C, Yamamoto JF, Magnani JW, Tadros TM, Kannel WB, Wang TJ, Ellinor PT, Wolf PA, Vasan RS, Benjamin EJ. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. *Lancet* 2009;**373**:739–745.
10. Schnabel RB, Aspelund T, Li G, Sullivan LM, Suchy-Dicey A, Harris TB, Pencina MJ, D'Agostino RB, Levy D, Kannel WB, Wang TJ, Kronmal RA, Wolf PA, Burke GL, Launer LJ, Vasan RS, Psaty BM, Benjamin EJ, Gudnason V, Heckbert SR. Validation of an atrial fibrillation risk algorithm in whites and African Americans. *Arch Intern Med* 2010;**170**:1909–1917.