**Quality indicators for the care and outcomes of adults with atrial fibrillation.**

**Task Force for the development of quality indicators in Atrial Fibrillation of the European Heart Rhythm Association (EHRA) of the European Society of Cardiology (ESC): Developed in collaboration with the Heart Rhythm Society (HRS), the Asia Pacific Heart Rhythm Society (APHRS) and the Latin-American Heart Rhythm Society (LAHRS)**

Elena Arbelo (Chair)1, Suleman Aktaa2, Andreas Bollmann3, André D’Avila4, Inga Drossart5, Jeremy Dwight6, Mellanie True Hills7, Gerhard Hindricks3, Fred M. Kusumoto8, Deirdre A Lane9, Dennis H. Lau10, Maddalena Lettino11, Gregory Y. H. Lip9, Trudie Lobban12, Hui-Nam Pak13, Tatjana Potpara14, Luis C. Saenz15, Isabelle C. Van Gelder16, Paul Varosy17, Chris P Gale2, Nikolaos Dagres (Co-chair)3.

1Arrhythmia Section, Cardiology Department, Hospital Clínic, Universitat de Barcelona. Barcelona (Spain). IDIBAPS, Institut d’Investigació August Pi i Sunyer (IDIBAPS). Barcelona (Spain). Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Madrid (Spain)

2Leeds Institute for Data Analytics, University of Leeds, UK; Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, UK; Department of Cardiology, Leeds Teaching Hospitals NHS Trust, UK

3Department of Electrophysiology, Heart Center Leipzig at University of Leipzig, Leipzig, Germany

4Cardiac Arrhythmia Service, Hospital SOS Cardio, Florianopolis, SC, Brazil; Harvard-Thorndike Electrophysiology Institute, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA.

5European Society of Cardiology, Sophia Antipolis, France. ESC Patient Forum, Sophia Antipolis, France.

6ESC Patient Forum, Sophia Antipolis, France.

7StopAfib.org, American Foundation for Women’s Health, Decatur, Texas 76234, United States of America

8Mayo Clinic Hospital, Cardiology Department, Jacksonville, United States of America

9Liverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool Heart & Chest Hospital, Liverpool, United Kingdom; Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark

10Centre for Heart Rhythm Disorders, The University of Adelaide and Department of Cardiology, Royal Adelaide Hospital, Adelaide, South Australia, Australia.

11San Gerardo Hospital, Cardiovascular Dept, ASST-Monza, Monza - Italy

12Arrhythmia Alliance/AF Assoc/STARS; Essex House, Cromwell Business Park, OX7 5SR Chipping Norton, UK

13Yonsei University Health System, Seoul, Republic of Korea

14School of Medicine, University of Belgrade, Serbia; Cardiology Clinic, Clinical Center of Serbia, Visegradska 26, 11000 Belgrade, Serbia

15Fundación Cardio Infantil-Instituto de Cardiología, Bogotá, Colombia

16University of Groningen, University Medical Center Groningen, Department Of Cardiology, Groningen, The Netherlands

17Rocky Mountain Regional Veterans Affairs Medical Center and the University of Colorado Anschutz Medical Campus, Aurora, Colorado, United States of America.

Corresponding author:

Elena Arbelo, MD, PhD, MSc

Institut Clínic Cardiovascular

Hospital Clínic de Barcelona

C. Villarroel 170, Esc 3, Planta 6

08036 Barcelona. SPAIN

Ph: (+34) 93 227 5551

Fax: (+34) 93

Email: elenaarbelo@secardiologia.es

REVIEWERS

Serge Boveda (review coordinator): Clinique Pasteur, Heart Rhythm Department, 31076 Toulouse, France.

Thomas Deneke: Clinic for Interventional Electrophysiology, Heart Center RHÖN-KLINIKUM Campus Bad Neustadt, Germany

Pascal Defaye : CHU Grenoble Alpes, Unite de Rythmologie Service De Cardiologie, CS10135, 38043 Grenoble Cedex 09, France

Giulio Conte : Cardiology Department, Cardiocentro Ticino, Lugano, Switzerland

Radoslaw Lenarczyk : First Department of Cardiology and Angiology, Silesian Centre for Heart Disease, Curie-Sklodowskiej Str 9, 41-800 Zabrze, Poland

Rui Providencia: - St Bartholomew’s Hospital, Barts Heart Centre, Barts Health NHS Trust, London, UK and Institute of Health Informatics, University College of London, London, UK

Jose M Guerra: Department of Cardiology, Hospital de la Santa Creu i Sant Pau, Universidad Autonoma de Barcelona, CIBERCV, Barcelona, Spain

Yoshihide Takahashi : Deparment of Advanced Arrhythmia Research, Tokyo Medical and Dental University

Cristiano Pisani: Heart Institute, Arrhytmia Unit, Sao Paulo, Brazil

Santiago Nava: Head of Electrocardiology department, Instituto Nacional de Cardiologia “Ignacio Chavez”, Mexico

Andrea Sarkozy, MD, pHd: University Hospital of Antwerp, University of Antwerp, Antwerp, Belgium

Taya V. Glotzer: Hackensack Meridian-Seton Hall School of Medicine, Rutgers New Jersey Medical School

Director of Cardiac Research, Hackensack University Medical Center, Hackensack, USA

Mario Martins Oliveira : Hospital Santa Marta, Department of Cardiology, Rua Santa Marta, 1167-024 Lisbon, Portugal

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**STRUCTURED ABSTRACT**

**Aims**

To develop quality indicators (QIs) that may be used to evaluate the quality of care and outcomes for adults with atrial fibrillation (AF).

**Methods**

We followed the ESC methodology for QI development. This methodology involved 1) the identification of the domains of AF care for the diagnosis and management of AF (by a group of experts including members of the ESC Clinical Practice Guidelines for AF); 2) the construction of candidate QIs (including a systematic review of the literature); and 3) the selection of the final set of QIs (using a modified-Delphi method).

**Results**

Six domains of care for the diagnosis and management of AF were identified: 1) Patient assessment (baseline and follow-up), 2) Anticoagulation therapy, 3) Rate control strategy, 4) Rhythm control strategy, 5) Risk factor management, and 6) Outcomes measures, including patient-reported outcome measures (PROMs). In total, 17 main and 17 secondary QIs, which covered all six domains of care for the diagnosis and management of AF were selected. The outcome domain included measures on the consequences and treatment of AF, as well as PROMs.

**Conclusion**

This document defines 6 domains of AF care (patient assessment, anticoagulation, rate control, rhythm control, risk factor management and outcomes), and provides 17 main and 17 secondary QIs for the diagnosis and management of AF. It is anticipated that implementation of these QIs will improve the quality of AF care.

**KEYWORDS:** Atrial Fibrillation. Quality Indicators. Outcome measures.

**ABBREVIATIONS**

AF: atrial fibrillation

EORP: EURObservational Research Programme

ESC: European Society of Cardiology

QI: quality indicator

QoL: quality of life

RCT: randomised controlled trial

PROMs: patient-reported outcome measures

**INTRODUCTION**

Atrial fibrillation (AF) is a key public health challenge and major source of morbidity, mortality and economic burden for governments worldwide1. Despite progress in the management of patients with AF, this arrhythmia is still a major cause of stroke, heart failure, and cardiovascular morbidity and mortality globally2. Additionally, AF is associated with cognitive impairment3-5, reduced quality of life (QoL)6, 7, depression8, and frequent hospital admissions9-11. The magnitude of the economic burden of AF is increasing, mainly driven by AF-related complications and management costs, particularly those associated with hospitalizations2, 12, 13.

Data from the EURObservational Research Programme in AF (EORP-AF) found that adherence to guideline recommended therapies in the treatment of AF is associated with lower mortality14, yet large variability persists in the delivery of such therapies across Europe15, 16. To improve the implementation of evidence-based medicine17, some professional organisations have developed quality standards, clinical indicators and quality measures to evaluate and improve the quality of AF care18-20,21, 22. However, no AF quality indicators (QIs) have been specifically designed for the wider international community.

Hence, the European Heart Rhythm Association (EHRA), in collaboration with the Asian Pacific Heart Rhythm Society (APHRS), the Heart Rhythm Society (HRS) and the Latin-American Heart Rhythm Society (LAHRS), established the AF QI Working Group, which was tasked with the development of QIs for the diagnosis and management of adults with AF. It is hoped that these QIs can serve as a mechanism to improve the quality of AF care, and be used by healthcare providers to evaluate care delivery at the patient, centre, and national levels.

To enhance the translation of guideline recommendations into clinical practice and provide healthcare providers with tools to identify opportunities for improvement, a summary of the AF QIs has been embedded in the 2020 ESC Clinical Practice Guidelines for AF23. Efforts were made to ensure alignment between the developed QIs and the ESC Guidelines for AF, which may differ from recommendations developed by other professional organisations.

**METHODS**

The detailed methodology for the development of QIs for the quantification of cardiovascular care and outcomes for the ESC Clinical Practice Guidelines is published separately24. This methodology consists of a four-step process: identification of the key domains of care; construction of candidate indicators; selection of a final QI set; and undertaking of a feasibility assessment. In this document, we have identified important domains of AF care, and developed QIs for each domain. The development process involved conducting a systematic review of the literature, and using a modified Delphi method25 to derive the final set of QIs and divide them into main and secondary QIs. The next step would be to conduct a feasibility assessment of the developed QIs using existing AF registries24.

Quality indicators may be divided into structural, process, and outcome indicators26. For each proposed QI, we provided relevant specifications, including numerator, denominator, measurement period, and measurement duration. However, no care settings were suggested, because the proposed QIs are applicable in both the inpatient and outpatient care. It is, thus, important to determine locally the clinical setting during which QIs are applied in order to ensure the same processes of care are evaluated between healthcare providers.

**2.1 Members of the Working Group**

The Working Group comprised of members of the ECG Clinical Practice Guidelines Task Force, as well as international experts in AF management, patients with AF, and representatives from patient organisations. Six domains of AF care were defined: 1) Patient assessment (baseline and follow-up), 2) Anticoagulation therapy, 3) Rate control strategy, 4) Rhythm control strategy, 5) Risk factor management, and 6) Outcomes measures, including patient-reported outcome measures (PROMs). The names, affiliations, and conflicts of interest of the AF QIs Working Group is provided in APPENDIX 1.

**2.2 Systematic review**

*Search strategy*

We conducted a systematic review of the published literature in accordance with the Preferred Reporting Items for Systematic Review and Meta-analyses statement27, 28 (APPENDIX 2). We searched two online bibliographic databases; MEDLINE and Embase via OVID®. The initial search strategy was developed in MEDLINE using keywords and, when available, medical subject headings (MesH) terms based on three main terms: “atrial fibrillation”, “quality indicators”, and “outcome measures”, (APPENDIX 3). The final search strategies were, then, developed using an iterative process, which also included citations search, grey literature, and hand search of the reference lists of the selected studies.

We included randomised controlled trials (RCTs) and observational studies, including local, national, and international registries. We excluded systematic reviews, meta-analyses, editorial letters and conference proceedings. We only included the main publications of major trials and registries from which our search obtained only their sub-studies. The search was restricted to those full-text articles published in English language and publication date between 01 January 2014 and 05 October 2019, to capture QIs and outcome measures for AF from contemporary practice.

*Eligibility criteria*

We included articles which fulfilled the following criteria: 1) the study population was adult patients (≥18 years old) with AF, 2) the study explicitly stated at least one QI or outcome measure to define best practice for AF diagnosis and/or management, 3) the study provided specifications for the QI or outcome measure (e.g., definition, data collection source, method of reporting), 4) RCT or registry, and 5) full-text publication. No restrictions were applied to the presence of, or the type of, intervention or comparison in the study.

*Study selection*

A reference manager software (Zotero) was used for duplicates removal and data management. Two authors (Suleman Aktaa and Elena Arbelo) independently examined the abstracts of the studies retrieved from the search against the inclusion criteria. Disagreements were resolved through discussion and review of the full text of the article when required.

*Data extraction*

The full texts of the included studies were independently reviewed by two authors (Suleman Aktaa and Elena Arbelo). All QIs relevant to the agreed 6 domains of AF care, namely: 1) Patient assessment (baseline and follow-up), 2) Anticoagulation therapy, 3) Rate control strategy, 4) Rhythm control strategy, 5) Risk factor management, and 6) Outcomes measures (including PROMs) were extracted and listed on an Excel spreadsheet. When available, the following information was obtained for the extracted QIs: definition (including numerator, denominator, and exclusions), objective, type of QI (structural, process, outcome, or PROM), domain of application, and potential data collection source.

**2.3 Clinical Practice Guidelines and Existing QIs**

In addition to the systematic review outlined above, we reviewed relevant Clinical Practice Guidelines and existing QIs from different professional organizations (Table 1). The goal of the Clinical Practice Guidelines review was to identify the recommendations with the strongest association with benefit or harm and to assess these recommendations against the ESC criteria for QIs (Table 2)24. Additionally, existing publications on QIs for patients with AF were also reviewed and, when applicable, information about the feasibility and/or validity of these measures was obtained.

**Table 1. Existing Clinical Practice Guidelines and QIs used during the development process**

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| **Organisation** | **Type**  | **Year** | **Country/Region** |
| ESC Guideline for the Management of Patients with Atrial Fibrillation23  | Clinical Practice Guidelines | 2020 | Europe |
| ICHOM International Standard Set of Outcome Measures for patients with Atrial Fibrillation29 | QIs | 2020 | Worldwide |
| AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation30 | Clinical Practice Guidelines | 2019 | United States |
| Canadian Quality Indicators for Atrial Fibrillation and Atrial Flutter20 | QIs | 2019 | Canada  |
| Harmonized outcome measures for use in atrial fibrillation patient registries and clinical practice31 | QIs | 2019 | United States |
| ACC/AHA Clinical Performance and Quality Measures for Adults with Atrial Fibrillation or Atrial Flutter32 | QIs  | 2016 | United States |
| ESC Guidelines for the management of atrial fibrillation developed33 | Clinical Practice Guidelines  | 2016 | Europe  |
| NICE Atrial Fibrillation Quality standard [QS93]34 | QIs | 2015 | United Kingdom |
| AHA/ACC/HRS Guidelines for the Management of Patients with Atrial Fibrillation35 | Clinical Practice Guidelines | 2014 | United States |

QI=quality indicators; AHA=American Heart Association; ACC=American College of Cardiology; ESC=European Society of Cardiology; ICHOM=International Consortium for Health Outcomes Measurement; NICE=National Institute of Clinical Excellence;

**2.4 Data synthesis**

*Candidate QIs*

A list of candidate QIs was derived from the aforementioned systematic review and classified into structural, process, or outcome measures depending on the aspect of care being measured26. For each QI, a detailed definition was provided in order to facilitate the evaluation process.

*Modified Delphi process*

We used the modified Delphi process25, 36 to evaluate the candidate QIs and arrive at the final set of QIs. Instructions on the voting process, including QIs criteria (Table 2) were sent to the Working Group before the vote. All measures were independently graded by each member of the Group using the SurveyMonkey platform. Three rounds of voting were conducted, with a teleconference after each round to discuss the results of the vote. In the first voting round, we used a 9-point ordinal scale, where ratings of 1 to 3 signified that the QI was not valid; ratings of 4 to 6 meant that the QI was of uncertain validity; and ratings of 7 to 9 indicated that the QI was valid. Candidate QIs were included if ≥75% of the Working Group members ranked them between 7 and 9, and were excluded if ≥75% of the Working Group members ranked them between 1 and 3. Indicators that did not fall in the two categories above where carried forward to the second voting round, where a 3-point scale (should not be included, maybe, and should be included) was implemented, but same percentage agreement (≥75% of the Working Group members) cut-off was used. The final round comprised a binary, ‘yes’ or ‘no’ questionnaire to obtain the Working Group members’ agreement on the proposed final set of QIs.

**Table 2.** Criteria for the development and evaluation of the ESC quality indicators for cardiovascular disease24.

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| **Domain** | **Criteria** |
| **Importance**  | QI reflects a clinical area that is of high importance (e.g., common, major cause for morbidity, mortality, and/or health-related quality of life impairment). |
| QI relates to an area where there are disparities or suboptimal care.  |
| QI implementation will result in an improvement in patient outcomes. |
| QI may address appropriateness of medical interventions. |
| **page26image211549376Evidence base**  | QI is derived from an acceptable evidence consistent with contemporary knowledge.  |
| QI aligns with the respective ESC Clinical Practice Guideline recommendations. |
| **Specification** **page26image211536512** | QI has a clearly defined patient group to whom the measurement applies (denominator), including explicit exclusions.  |
| QI has clearly accomplishment criteria (numerator).  |
| **Validity**  | QI is able to correctly assess what it is intended to, adequately distinguishes between good and poor quality of care, and compliance with the indicator would confer health benefits. |
| **Reliability**  | QI is reproducible even when data is extracted by different people and estimates of performance on the basis of available data are likely to be reliable and unbiased.  |
| **Feasibility**  | QI may be identified and implemented with reasonable cost and effort.  |
| Data needed for the assessment is (or should be) readily available and easily extracted within an acceptable time frame. |
| **Interpretability** | QI is interpretable by healthcare providers, so that practitioners can understand the results of the assessment and take actions accordingly.  |
| **Actionability** | QI is influential to the current practice, where a large proportion of the determinants of adherence to the QI are under the control of healthcare providers.  |
| This influence of QI on behaviour will likely improve care delivery.  |
| QI is unlikely to cause negative unintended consequences. |

QI=quality indicator

**RESULTS**

**Search results**

The literature search retrieved 2954 articles, of which 441 met the inclusion criteria (Figure 1). These articles were used to extract a total of 352 candidate QIs (17 related to structure, 162 to process and 173 related to outcomes) before the first voting round. Of these 34 QIs (19 related to process and 15 related to outcomes) were selected by the end of the second round (Table 3). Over 93% of the Working Group members agreed on this final set of QIs in the third voting round.

Figure 1. PRISMA flow diagram for selection of included studies



**Table 3.** Primary (green) and secondary (yellow) quality indicators for the diagnosis and management of AF.

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| **Code** | **Quality Indicators** |
|  | **Domain 01: Patient assessment (at baseline and follow-up)** |
| **01MQI1** | Proportion of patients with cardioembolic risk assessment using CHA2DS2-VASc score |
| **01MQI2** | Proportion of patients with bleeding risk assessment using a validated method, such as the HAS-BLED score |
| **01MQI3** | Proportion of patients with a measurement of their serum creatinine (or creatinine clearance) |
| **01SQI1** | Proportion of people ≥65 years of age with risk factors for AF who have pulse check |
| **01SQI2** | Proportion of patients with atrial high-rate episodes (AHREs) detected on implantable cardiac devices who undergo further cardiovascular evaluation |
| **01SQI3** | Proportion of cryptogenic stroke patients who have been screened for AF |
| **01SQI4** | Proportion of patients with an ECG documentation of AF  |
| **01SQI5** | Proportion of patients who have been engaged in shared decision-making when deciding treatment strategy |
|  | **Domain 02: Anticoagulation** |
| **02MQI1** | Proportion of patients who are appropriately prescribed anticoagulation according to CHA2DS2-VASc score\* |
| **02MQI2** | Proportion of patients with a CHA2DS2-VASc score of 0 for men and 1 for women who are inappropriately prescribed long-term anticoagulation |
| **02MQI3** | Proportion of patients with ‘appropriate anticoagulation’ at every follow-up visit, defined as:1. Time in therapeutic range TTR\*\* ≥70% for vitamin-K antagonist.
2. Appropriate dose for NOAC according to manufacturer recommendations.
 |
|  | **Domain 03: Rate control** |
| **03MQI1** | Proportion of patients with permanent AF (i.e. where no attempt to restore sinus rhythm is planned), who are inappropriately prescribed antiarrhythmic drugs |
| **03SQI1** | Proportion of patients with LVEF <40% who are inappropriately prescribed non-dihydropyridine calcium channel blockers  |
|  | **Domain 04: Rhythm control** |
| **04MQI1** | Proportion of patients with structural heart disease who are inappropriately prescribed class IC antiarrhythmic drugs  |
| **04MQI2** | Proportion of patients with end-stage kidney disease who are inappropriately prescribed dofetilide or sotalol  |
| **04MQI3** | Proportion of patients with symptomatic paroxysmal or persistent AF who are offered AF catheter ablation after failure of, or intolerance to, one class I or class III antiarrhythmic drug |
| **04SQI1** | Proportion of patients with complete electrical isolation of the PVs during AF catheter ablation procedures |
| **04SQI2** | Proportion of patients with new onset persistent AF who are offered cardioversion |
|  | **Domain 05: Risk factor management** |
| **05MQI1** | Proportion of patients who have their modifiable risk factors identified |
|  | **Domain 06: Outcomes** |
|  | **Sub-domain 06.1: Consequences of the disease** |
| **06.1MQI1** | Annual rate of all-cause mortality\*\*\*  |
| **06.1MQI2** | Annual rate of ischaemic stroke or transient ischaemic attack\*\*\* |
| **06.1SQI1** | Annual rate of cardiovascular mortality\*\*\* |
| **06.1SQI2** | Annual rate of cardiovascular hospitalization \*\*\* |
| **06.1SQI3** | Annual rate of overall thromboembolic event \*\*\* |
| **06.1SQI4** | Annual rate of clinician-reported symptom status assessment |
|  | **Sub-domain 06.2: Consequences of treatment** |
| **06.2MQI1** | Annual rate of life-threatening or major bleeding events |
| **06.2MQI2** | Annual rate of procedure-related 30-day mortality  |
| **06.2MQI3** | Annual rate of procedure-related major complications or drug-related serious adverse events |
| **06.2SQI1** | Annual rate of haemorrhagic stroke |
|  | **Sub-domain 06.3: Patient-reported outcomes** |
| **06.3MQI1** | Proportion of patients with health-related quality of life assessment  |
| **06.3SQI1** | Proportion of patients with patient-reported symptom status assessment  |
| **06.3SQI2** | Proportion of patients with physical function assessment  |
| **06.3SQI3** | Proportion of patients with emotional wellbeing (including anxiety and depression) assessment  |
| **06.3SQI4** | Proportion of patients with cognitive function assessment  |
| \*Appropriateness of anticoagulation prescription is defined as CHA2DS2-VASc score of ≥1 for men and ≥2 for women in the 2020 ESC Guidelines (REF). The 2014 ACC/AHA Guidelines (and 2019 focused update) define anticoagulation prescription appropriateness and CHA2DS2-VASc score of ≥2 for men and ≥3 for women30, 35. \*\*TTR calculated using Rosendaal method.\*\*\*Crude and risk-adjusted rates (risk-adjustment should, as a minimum, consider age, sex, and comorbidities. |

The domains for AF care identified by the Working Group were: 1) Patient assessment (baseline and follow-up), 2) Anticoagulation therapy, 3) Rate control strategy, 4) Rhythm control strategy, 5) Risk factor management, and 6) Outcome measures (including PROMs). For each domain main, and for some secondary, QIs have been developed. Figure 2 shows the main QIs according to their respective domain of care. The full set of main and secondary QIs, alongside their definitions, proposed measurement period (the timepoint at which the assessment is performed), proposed measurement duration (the time frame needed for enough cases to be collected), and when applicable, the corresponding ESC Clinical Practice Guidelines recommendations are illustrated in APPENDIX 4. For each QI, a unique code was developed using the domain number and indicating whether the QI is main or secondary.

Figure 2. Domains of AF care with their respective main quality indicators



AAD, antiarrhythmic drug; AF, atrial fibrillation; CA, catheter ablation; ESRD, end-stage renal disease; HRQoL, health-related quality of life; NOAC, non-vitamin K antagonist oral anticoagulant; OAC, oral anticoagulants; TTR, time in therapeutic range; TIA, transient ischaemic attack

***Quality Indicators***

***Domain 1: Patient assessment (baseline and follow-up)***

Stroke prevention is the cornerstone of the AF patient management pathway, and ‘Avoid Stroke/Anticoagulation’ is the ‘A’ of the ABC pathway37, within the 2020 ESC guidelines23.

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| **01MQI1: Proportion of patients with cardioembolic risk assessment using CHA2DS2-VASc score**  |
| ***Numerator*:** Number of patients with AF who have their CHA2DS2-VASc score documented at the time of diagnosis and at every follow up appointment. ***Denominator*:** Number of patients with AF.  |
| **01MQI2: Proportion of patients with bleeding risk assessment using a validated method, such as the HAS-BLED score** |
| ***Numerator*:** Number of patients with AF who have their bleeding risk assessment documented at the time of diagnosis and at every follow up appointment using a validated bleeding risk score. ***Denominator*:** Number of patients with AF.  |
| **01MQI3: Proportion of patients with a measurement of their serum creatinine (or creatinine clearance)** |
| ***Numerator*:** Number of patients with AF who have their serum creatinine checked at the time of diagnosis and at every follow up appointment.***Denominator*:** Number of patients with AF.  |

Stroke risk in AF is not homogeneous and depends on the presence of various stroke risk factors38. The CHA2DS2-VASc score is recommended to assess stroke risk where the default should be to offer stroke prevention, unless the patient is low risk; hence use the CHA2DS2-VASc score to initially define low risk patients (CHA2DS2-VASc score 0 in males, 1 in females) who do not need antithrombotic therapy (indicator 01MQI1). The subsequent step is to offer stroke prevention in those with 1 or more risk factors (CHA2DS2-VASc score ≥1 in males, ≥2 in females). Since stroke risk is dynamic, and influenced by ageing and incident risk factors, risk reassessment should occur at every follow-up visit39.

Bleeding risk also changes over time and should also be assessed at every patient contact, initially to identify modifiable bleeding risks that should be mitigated, and to identify the ‘high bleeding risk’ patient who should be scheduled for early follow-up40 (indicator 01MQI2). Based on a Patient-Centered Outcomes Research Institute (PCORI) systematic review and evidence appraisal, the best validated bleeding risk score is the HAS-BLED score41. While stroke and bleeding risks track each other, the evidence shows that a formal bleeding risk score (HAS-BLED) is superior to stroke risk scores (e.g. CHADS2, CHA2DS2-VASc) for assessing bleeding risk42, 43. A strategy for dynamic bleeding risk assessment using the HAS-BLED score has been shown to reduce bleeding risk and to increase oral anticoagulation (OAC) use44.

Given that renal function has implications for both stroke and bleeding risk45, as well as prescriptions of OAC (choice of agent and dose), regular measurements of serum creatinine or creatinine clearance (based on the Cockroft-Gault formula) are needed, the frequency of which is determined by the renal function at baseline46 (indicator 01MQI3).

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| **01SQI1: Proportion of people ≥65 years of age with risk factors for AF who have pulse check** |
| ***Numerator*:** Number of people ≥65 years of age with risk factors for AF who have a documentation of pulse check (or ECG) to identify rhythm.***Denominator*:** Number of people ≥65 years of age with risk factors for AF. |
| **01SQI2: Proportion of patients with atrial high-rate episodes (AHREs) detected on implantable cardiac devices who undergo further cardiovascular evaluation** |
| ***Numerator*:** Number of patients with AHREs detected on implantable cardiac devices who have documentation of complete cardiovascular evaluation.***Denominator*:** Number of patients with atrial high-rate episodes detected on implantable cardiac devices. |
| **01SQI3: Proportion of cryptogenic stroke patients who have been screened for AF** |
| ***Numerator*:** Number of patients with cryptogenic stroke\* who have documentation of AF screening using continuous ECG recording. ***Denominator*:** Number of patients with cryptogenic stroke with no previous history of AF |
| **01SQI4: Proportion of patients with an ECG documentation of AF**  |
| ***Numerator*:** Number of patients with AF who have a documentation of an ECG confirming AF diagnosis.***Denominator*:** Number of patients with AF.  |
| **01SQI5: Proportion of patients who have been engaged in shared decision-making when deciding treatment strategy** |
| ***Numerator*:** Number of patients with AF who have a documentation of patient engagement when deciding treatment strategy.***Denominator*:** Number of patients with AF.  |

Asymptomatic AF is associated with a higher risk of stroke and mortality compared to symptomatic AF47-50. An observational study indicated that the application of standard care treatments for subclinical AF detected on screening improves outcomes50 and a systematic review and economic analysis suggested that screening programmes for AF are likely to represent a cost-effective use of resources51. Thus, screening for AF amongst people ≥65 years of age by checking their pulse may have therapeutic implications as these individuals need to be considered for thromboprophylaxis (indicator 01SQI1).

To that end, atrial high rate episodes (AHRE) detected by implanted cardiac devices, which may represent asymptomatic AF, should be investigated52, 53. Ideally, AHRE detection should be performed at every device interrogation, including home monitoring transmission as it determines whether or not subclinical AF is confirmed and whether anticoagulation and/or regular follow-up is warranted23, indicator 01SQI2. Furthermore, the detection of previously unknown AF following a stroke has relevant implications for secondary prevention54, 55. Thus, it is recommended to screen for AF following a cryptogenic stroke23, 56-58 (indicator 01SQI3).

However, screening for AF should be accompanied by confirming the diagnosis by traditional means, such as by 12-lead ECG or >30 seconds recording of a single-lead ECG, Holter monitor, or event recorder (indicator 01SQI4). Following the diagnosis, a dialogue between treating physician and patient to ensure patient involvement in decision-making is recommended23, 59. Thus, the indicator 01SQI5 captures shared decision-making when deciding on the treatment strategy.

***Domain 2: Anticoagulation***

Oral anticoagulation is an essential part of AF management and the ESC 2020 guidelines recommend oral anticoagulation for stroke prevention in males with CHA2DS2-VASc scores of ≥1, and females with scores ≥223. Accordingly, it is important that a set of QIs to regularly assesses the proportion of patients with CHA2DS2-VASc score ≥1 in males, ≥2 in females who are offered stroke prevention (indicator 02MQI1), as well as the inappropriate use of long-term antithrombotic therapy in low risk patients (CHA2DS2-VASc score 0 in males, and 1 in females) (indicator 02MQI2).

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| **02MQI1: Proportion of patients who are appropriately prescribed anticoagulation according to CHA2DS2-VASc score\*\*** |
| ***Numerator*:** Number of patients with AF who have CHA2DS2-VASc score of ≥1 for men or ≥2 for women and are prescribed anticoagulation for AF\*\*.***Denominator*:** Number of patients with AF who have CHA2DS2-VASc score of ≥1 for men or ≥2 for women and are eligible for anticoagulation with no contraindication or refusal\*\*. |
| **02MQI2: Proportion of patients with a CHA2DS2-VASc score of 0 for men and 1 for women who are inappropriately prescribed long-term anticoagulation** |
| ***Numerator*:** Number of patients with AF who have CHA2DS2-VASc score of 0 for men or 1 for women and are inappropriately prescribed long-term anticoagulation for AF. ***Denominator*:** Number of patients with AF who have CHA2DS2-VASc score of 0 for men and 1 for women and do not have other indication for anticoagulation. |
| **02MQI3: Proportion of patients with ‘appropriate anticoagulation’ at every follow-up visit, defined as:**1. **Time in therapeutic range TTR ≥70% for vitamin-K antagonist.**
2. **Appropriate dose for NOAC according to manufacturer recommendations\*\*\*.**
 |
| ***Numerator*:** Number of patients with AF who are appropriate anticoagulation defined as TTR ≥70% for vitamin-K antagonist, or appropriate dose for NOAC according to manufacturer recommendations\*\*\*.***Denominator*:** Number of patients with AF on anticoagulation.  |
| *\*\*Appropriateness of anticoagulation prescription is defined as CHA2DS2-VASc score of ≥1 for men and ≥2 for women in the 2020 ESC Guidelines23. The 2014 ACC/AHA Guidelines (and 2019 focused update) define anticoagulation prescription appropriateness and CHA2DS2-VASc score of ≥2 for men and ≥3 for women30, 35.* *\*\*\*Manufacturer recommendations are defined in APPENDIX 5.* |

Assessment of the quality of anticoagulation is also important. If patients are taking a non-vitamin K antagonist oral anticoagulant (NOAC), the label-adherent dose of the respective NOAC should be prescribed and the proportion appropriately dosed is indicative of quality of care. Regular audits should be performed to ensure that under- or over-dosing of the respective NOAC does not occur, given the association with worse outcomes60-62 (indicator 02MQI3). Oral anticoagulation can also be offered as well-managed vitamin K antagonist (VKA) (e.g., warfarin, acenocoumarol, phenprocoumon etc.), with a high (≥70%) time in therapeutic range (TTR) calculated using Rosendaal method, with INR 2.0-3.0. High TTR has been associated with low rates of stroke and bleeding, as well as reduced mortality63-65. Thus, the proportion of patients with TTR ≥70% is a good QI of anticoagulation control for patients on VKA.

***Domain 3: Rate control***

Rate control is an integral part of AF management, and may be sufficient to improve AF-related symptoms66. In patients for whom a decision has been made not to restore or maintain sinus rhythm (permanent AF), rate control can be achieved by rate-limiting medications (e.g., beta-blockers, digoxin, diltiazem, or verapamil). The use of antiarrhythmic drugs, such as amiodarone, dronedarone, or sotalol for rate-control is not recommended when no attempts to restore sinus rhythm is planned67-70 (indicator 03MQI1).

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| **03MQI1: Proportion of patients with permanent AF (i.e. where no attempt to restore sinus rhythm is planned), who are inappropriately prescribed antiarrhythmic drugs$**  |
| ***Numerator*:** Number of patients with permanent AF who are prescribed one or more antiarrhythmic drugs$ for rhythm control. ***Denominator*:** Number of patients with permanent AF. |
| **03SQI1: Proportion of patients with LVEF <40% who are inappropriately prescribed non-dihydropyridine calcium channel blockers** |
| ***Numerator*:** Number of patients with AF who have LVEF <40% and/or decompensated heart failure, and are inappropriate prescription of non-dihydropyridine calcium channel blockers.***Denominator*:** Number of patients with AF who have LVEF <40% and/or decompensated heart failure. |

The use of certain types of rate control drugs, such as non-dihydropyridine calcium channel blockers can influence outcomes in patients with heart failure and/or left ventricular ejection fraction (LVEF) of ≤40%9, 71. Thus the indicator 03SQI1, evaluates the inappropriate use of non-dihydropyridine calcium channel blockers in AF patients with concomitant reduced LVEF72.

***Domain 4: Rhythm control***

Rhythm control therapy is central for the reduction and/or relief of AF symptoms and improvement of patients’ quality of life (QoL)73-75. Given that the safety profile of an antiarrhythmic agent is a major determinant of treatment choice, the Working Group selected QIs based on this notion. Certain antiarrhythmic drugs have major contraindications that increase the likelihood of adverse events, such as the presence of structural heart disease (for instance ischemic heart disease, LV dysfunction and/or significant cardiomyopathy) for class IC antiarrhythmic drugs (indicator 04MQI1), and advanced chronic kidney disease for dofetilide and sotalol (indicator 04MQI2)23.

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| **04MQI1: Proportion of patients with structural heart disease who are inappropriately prescribed class IC antiarrhythmic drugs** |
| ***Numerator:*** Number of patients with AF who have structural heart disease and are inappropriately prescribed class IC antiarrhythmic drugs.***Denominator:*** Number of patients with AF who have structural heart disease |
| **04MQI2: Proportion of patients with end-stage kidney disease who are inappropriately prescribed dofetilide or sotalol** |
| ***Numerator:*** Number of patients with AF who have end-stage kidney disease and/or on dialysis$$ and are inappropriately prescribed dofetilide or sotalol.***Denominator:*** Number of patients with AF who have end-stage kidney disease, including patients on dialysis. |
| **04MQI3: Proportion of patients with symptomatic paroxysmal or persistent AF who are offered AF catheter ablation after failure of, or intolerance to, one class I or class III antiarrhythmic drug** |
| ***Numerator:*** Number of patients with paroxysmal or persistent AF who are offered catheter ablation after the failure of, or intolerance to, one class I or class III antiarrhythmic drug.***Denominator:*** Number of patients with paroxysmal or persistent AF with no contraindications (or refusal) to catheter ablation who remain symptomatic on, or intolerant to, one class I or class III antiarrhythmic drug. |

Catheter ablation is effective in maintaining sinus rhythm and improving symptoms in patients with AF76-87. Ablation is generally recommended in symptomatic patients after failure or intolerance to one class I or class III antiarrhythmic drugs (indicator 04MQI3). Several factors may influence the decision between conservative and invasive treatment for AF, including age, AF duration, left atrial size, co-morbidities, and substrate visualization by cardiac magnetic resonance88-94. Ultimately, patient preference supported by treating physician recommendation are the main determinants of the type of rhythm control strategy employed23, 59.

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| **04SQI1: Proportion of patients with complete electrical isolation of the PVs during AF catheter ablation procedures** |
| ***Numerator:*** Number of patients with AF who have complete electrical isolation (entrance and exit block) of the PVs during AF catheter ablation procedures.***Denominator:*** Number of patients with AF treated with catheter ablation procedures. |
| **04SQI2: Proportion of patients with new onset persistent AF who are offered cardioversion** |
| ***Numerator:*** Number of patients with new onset persistent AF who are haemodynamically stable and are offered cardioversion.***Denominator:*** Number of patients with new onset persistent AF who are haemodynamically stable and in whom attempts to restore sinus rhythm were deemed appropriate.  |

A QI to assess the complete electrical isolation (entrance and exit block) of the pulmonary veins during AF catheter ablation procedures (indicator 04SQI1) was developed given that this is the desired outcome of AF ablation76, 80, 81, 95-106. In addition, the indicator 04SQI2 assesses the consideration of cardioversion for patients with new onset persistent AF.

***Domain 5: Risk factor management***

The Working Group considered the role of risk factors in AF and developed a QI accordingly (indicator 05MQI1). Recent research has highlighted the potential benefits of risk factor management as upstream non-invasive therapy to lower the risk of AF progression and recurrence107-113. A large proportion of these risk factors are lifestyle related and, therefore, are amenable to be targeted and modified114. It is recommended that in the assessment of AF patients, practitioners actively evaluate and document these modifiable risk factors, such as smoking, obesity107, 109, 115, physical inactivity116-118, alcohol intake112, 119-121, sleep122 apnea123, 124, hypertension122, 125, 126 and poor glycaemic control127. Where necessary, appropriate education, support, and intervention (e.g., smoking cessation options, continuous positive airway pressure (CPAP), exercise prescription, etc.) can be provided to the patient to address the risk factors that may improve health outcomes.

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| **05MQI1: Proportion of patients who have their modifiable risk factors identified** |
| ***Numerator***: Number of patients with AF who have their modifiable risk factors (e.g., blood pressure, obesity, obstructive sleep apnoea, alcohol excess, lack of exercise, poor glycaemic control and smoking) identified. ***Denominator***: Number of patients with AF. |

***Domain 6: Outcome measures***

*Consequences of the disease*

Reducing the risk of death is one of the primary aims of AF management, and healthcare in general23. As such, annual assessment of crude and risk-adjusted rates of all-cause mortality is recommended (indicator 06.1MQI1). Risk-adjustment should, as a minimum, consider age, sex, and comorbidities. In addition, the inclusion of lifestyle factors (e.g., smoking status, body mass index, physical activity, and alcohol intake) provides a better insight to the adjustment process. Given that ischaemic stroke is a major complication of AF and, that most AF patients (CHA2DS2-VASc score of ≥1 in men and ≥2 in women) will be eligible for stroke prevention, the overall and risk-adjusted annual incidence of stroke and, separately, transient ischaemic attack should be recorded as QI (indicator 06.1MQI2). Other outcomes measures, which may provide an illustration of the quality of AF care include, the rate of cardiovascular mortality (indicator 06.1SQI1), cardiovascular hospitalization (indicator 06.1SQI2), overall thromboembolic events (indicator 06.1SQI3), and clinician-reported AF symptom status (indicator 06.1SQI4).

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| **06.1MQI1: Annual rate of all-cause mortality\***  |
| ***Numerator*:** Number of patients with AF who died during the measurement duration. ***Denominator*:** Number of patients with AF.  |
| **06.1MQI2: Annual rate of ischaemic stroke or transient ischaemic attack\*** |
| **Numerator**: Number of patients with AF who had documented ischaemic stroke or transient ischaemic attack during the measurement duration. ***Denominator***: Number of patients with AF.  |
| \*Crude and risk-adjusted rates (risk-adjustment should, as a minimum, consider age, sex, and comorbidities. |

In the ABC pathway of AF management mentioned above, the ‘B’ component pertains to ‘better’ symptom management37. Many AF patients may not be overtly symptomatic. However, assessment of AF-related symptoms can be a useful subjective measure of both the clinical consequences of AF and the success of rate- and rhythm-control treatment from the patients’ perspective. Using a validated method, such as the modified European Heart Rhythm Association (EHRA) score128 is recommended to assess symptom status (indicator 06.1SQI4).

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| **06.1SQI1: Annual rate of cardiovascular mortality\*** |
| ***Numerator***: Number of patients with AF who died from cardiovascular cause during the measurement duration.***Denominator***: Number of patients with AF.  |
| **06.1SQI2: Annual rate of cardiovascular hospitalization\*** |
| ***Numerator***: Number of patients with AF who had unplanned hospitalization for a cardiovascular cause during the measurement duration.***Denominator*:** Number of patients with AF.  |
| **06.1SQI3: Annual rate of overall thromboembolic events\*** |
| ***Numerator***: Number of documented AF-related thromboembolic events during the measurement duration.***Denominator*:** Number of AF patients. |
| **06.1SQI4: Annual rate of clinician-reported symptom status assessment**  |
| ***Numerator***: Number of patients with AF who had their clinician-reported symptom status assessed using a validated tool (e.g., EHRA symptom score) during the measurement duration.***Denominator*:** Number of patients with AF. |
| \*Crude and risk-adjusted rates (risk-adjustment should, as a minimum, consider age, sex, and comorbidities. |

*Complications of treatment*

OAC treatment conveys an increased risk of major bleeding. However, bleeding complications can also occur in the absence of OAC treatment129. The incidence of life-threatening or major bleeding events, defined by the International Society of Thrombosis and Haemostasis criteria,130, 131 should be reported annually as a QI (indicator 06.2MQI1). The annual rate of haemorrhagic stroke is of particular importance (indicator 06.2SQI1) and should be documented as a QI.

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| **06.2MQI1: Annual rate of life-threatening or major bleeding events&** |
| ***Numerator*:** Number of patients with AF who are on anticoagulation and had documented life-threatening or major bleeding events during the measurement duration.***Denominator*:** Number of patients with AF on anticoagulation.  |
| **06.2MQI2: Annual rate of procedure-related&& 30-day mortality**  |
| ***Numerator*:** Number of patients with AF who died due to an invasive procedure for AF management during the measurement duration. ***Denominator*:** Number of patients with AF treated with invasive procedures.  |
| **06.2MQI3: Annual rate of procedure-related&& major complications or drug-related serious adverse events$** |
| ***Numerator*:** Number of patients with AF who had documented major procedural complications and/or drug-related serious adverse events during the measurement duration. ***Denominator*:** Number of patients with AF. |
| **06.2SQI1: Annual rate of haemorrhagic stroke**  |
| ***Numerator:*** Number of patients with AF who had documented haemorrhagic stroke during the measurement duration. ***Denominator:*** Number of patients with AF on anticoagulation. |

AF procedure-related deaths occurring within the first 30 days following catheter-based ablation, surgical ablation procedure, hybrid catheter and surgical ablation, left atrial appendage closure/occlusion (device), left atrial appendage ligation/excision (surgical), electrical cardioversion, or pacemaker implantation, should be reported annually as a QI (indicator 06.2MQI2). Furthermore, any procedure-related major complication or drug-related serious adverse event, defined as any untoward medical occurrence that results in death, life-threatening outcomes, hospitalization (initial inpatient hospitalization or prolongation of existing hospitalization for ≥24h), or permanent injury, should be reported in real-time according to local or national policy, and annually as a marker of quality (indicator 06.2MQI3). Although a single QI is suggested for procedural complications (e.g., atrio-oesophageal fistula, cardiac tamponade, PV stenosis, phrenic nerve palsy, etc.), and drug-related adverse events (e.g., arrhythmias, sudden cardiac death, etc.), individual events may be collected in each centre for local monitoring and between centre comparisons.

*Patient-reported outcomes*

PROMs are important determinants of the patients’ perceived quality and success of treatment132-134. The 2020 ESC guidelines recommend that patient-reported outcomes should be routinely collected to measure treatment success and improve patient care23. Health-related quality of life (HRQoL) is considered the main QI and should be assessed at baseline and at follow-up visits (indicator 06.3MQI1).

Several validated tools are available to measure general HRQoL135 (e.g., the Short-Form 12 [SF-12])136, while others specifically measure AF-specific HRQoL137 (e.g., the Atrial Fibrillation Effect on QualiTy of life [AFEQT] or the Atrial Fibrillation Severity Scale [AFSS])138-141. Both the SF-12 and the AFEQT are validated, psychometrically robust assessments of HRQoL, and are recommended by the International Consortium of Healthcare Outcome Measures (ICHOM) for AF 142. Regardless of which validated tool is employed, it is important that the same PROM is used consecutively to assess HRQoL to permit temporal comparison of scores and allow the determination of response to treatment.

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| **06.3MQI1: Proportion of patients with health-related quality of life assessment** |
| ***Numerator*:** Number of patients with AF who have their health-related quality of life assessed at the time of diagnosis and least annually afterwards using a validated instrument. ***Denominator*:** Number of patients with AF. |
| **06.3SQI1: Proportion of patients with patient-reported symptom status assessment** |
| ***Numerator*:** Number of patients with AF who have their patient-reported symptom status assessed at the time of diagnosis and least annually afterwards using a validated instrument. ***Denominator*:** Number of patients with AF.  |
| **06.3SQI2: Proportion of patients with physical function assessment** |
| ***Numerator*:** Number of AF patients who have their physical function assessed at the time of diagnosis and at every follow up appointment using a validated instrument. ***Denominator*:** Number of AF patients. |
| **06.3SQI3: Proportion of patients with emotional wellbeing (including anxiety and depression) assessment**  |
| ***Numerator*:** Number of patients with AF who have their emotional wellbeing (including anxiety and depression) assessed at the time of diagnosis and at every follow up appointment using a validated instrument. ***Denominator*:** Number of patients with AF. |
| **06.3SQI4: Proportion of patients with cognitive function assessment**  |
| ***Numerator*:** Number of patients with AF who have their cognitive function assessed at the time of diagnosis and at least annually afterwards using a validated instrument. ***Denominator*:** Number of patients with AF. |

Determining the impact of AF and its treatment on the patient are important considerations in the management of AF and may contribute to patient and healthcare provider decisions regarding continuation/cessation of certain treatments and/or initiating alternatives. In addition to HRQoL, the assessment of other PROMs, such patient reported symptom status (indicator 06.3SQI1), physical functioning (indicator 06.3SQI2), emotional wellbeing (indicator 06.3SQI3), and cognitive function (indicator 06.3SQI4), could also be considered. The assessment of HRQoL, patient-reported symptom status, physical functioning and emotional wellbeing is recommended at baseline and once to twice annually, while the assessment of cognitive function is recommended at baseline and annually thereafter, given that it may show little variation over a shorter period of time. Validated tools, such as the ones recommended by the ICHOM for AF142 (PROMIS Global Health for physical and emotional wellbeing, and PROMIS for cognitive function) can be used.

**Comparison with other quality metrics**

Table 4 shows a comparison between the 2020 ESC QIs for AF and quality metrics from other professional organisations, such as the American College of Cardiology and the American Heart Association (ACC/AHA), the National Institute for Clinical Excellence (NICE), the Canadian Cardiovascular Society (CCS), and ICHOM. There are major differences between the process QIs proposed here, and those developed by ACC/AHA, NICE and CCS. These differences may be explained by the variation in Clinical Practice Guidelines endorsed by different societies and/or local needs to address certain gaps in AF care. Outcome QIs were relatively similar compared to those proposed by ICHOM.

**Table 4.** Comparison between the 2020 ESC AF QIs, and the ACC/AHA, NICE, CCS, and ICHOM indicators for AF. Green colour represent measures with similar definition; orange represent measures with different definitions, and white represent no corresponding measure.

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| **Domain**  | **2020 ESC QIs** | **2016 ACC/AHA** | **2017 NICE**  | **2019 CCS** | **2020 ICHOM** |
| **Patient assessment (at baseline and follow-up)** | CHA2DS2-VASc score risk assessment  |  |  |  |  |
| Bleeding risk assessment  |  |  |  |  |
| Serum creatinine  |  |  |  |  |
| Screening people ≥65 years of age with risk factors for AF  |  |  |  |  |
| Evaluating AHREs detected on implantable cardiac devices  |  |  |  |  |
| Screening for AF after cryptogenic stroke  |  |  |  |  |
| ECG documentation of AF diagnosis |  |  |  |  |
| Shared decision-making when deciding treatment strategy |  |  |  |  |
| **Anticoagulation** | Anticoagulation with CHA2DS2-VASc score ***≥*** 1 for men and ***≥*** 2 for women  |  |  |  |  |
| Inappropriate anticoagulation with CHA2DS2-VASc score 0 for men and 1 for women |  |  |  |  |
| Appropriate anticoagulation (TTR ≥70% or appropriate NOAC dose) |  |  |  |  |
| **Rate control** | Inappropriate AAD use for patients with permanent AF  |  |  |  |  |
| Inappropriate non-dihydropyridine CCBs use for patients with LVEF <40%  |  |  |  |  |
| **Rhythm control** | Inappropriate class IC AAD use for patients with structural heart disease |  |  |  |  |
| Inappropriate dofetilide or sotalol use for patients with end-stage kidney disease  |  |  |  |  |
| Offering CA for symptomatic paroxysmal or persistent AF after single AAD failure  |  |  |  |  |
| Complete PVs electrical isolation during all AF CA procedures |  |  |  |  |
| Cardioversion for patients with new onset AF  |  |  |  |  |
| **Risk factor management** | Identifying modifiable risk factors for AF patients  |  |  |  |  |
| **Outcomes: Consequences of the disease** | Rate of all-cause mortality  |  |  |  |  |
| Rate of ischaemic stroke or TIA  |  |  |  |  |
| Rate of CV mortality |  |  |  |  |
| Rate of CV hospitalization  |  |  |  |  |
| Rate of overall thromboembolic event  |  |  |  |  |
| Rate of clinician-reported symptom status assessment |  |  |  |  |
| **Outcome: Consequences of treatment** | Rate of life-threatening or major bleeding events |  |  |  |  |
| Rate of procedure-related 30-day mortality  |  |  |  |  |
| Rate of procedure-related major complications or drug-related serious adverse events |  |  |  |  |
| Rate of haemorrhagic stroke |  |  |  |  |
| **Outcome: Patient-reported outcomes** | Assessment of health-related quality of life assessed |  |  |  |  |
| Assessment of patient-reported symptom status  |  |  |  |  |
| Assessment of physical function  |  |  |  |  |
| Assessment of emotional wellbeing (including anxiety and depression)  |  |  |  |  |
| Assessment of cognitive function  |  |  |  |  |

AAD=anti-arrhythmic drug; ACC=American College of Cardiology; AF=atrial fibrillation; AHA=American Heart Association; AHRE=atrial high-rate episodes; CA=catheter ablaton; CCB=calcium-channel blockers; CCS=Canadian Cardiovascular Society; CV=cardiovascular; ECG=electrocardiogram; ESC=European Society of Cardiology; ICHOM= International Consortium of Healthcare Outcome Measures, LVEF=left ventricular ejection fraction; NICE=National Institute for National Excellence, NOAC=Non-vitamin k oral anti-coagulant; PVs=pulmonary veins; QI=quality indicator; TIA=transient ischaemic attack; TTR-time in therapeutic range;

**DISCUSSION**

Evaluating the quality of care delivered and measuring meaningful outcomes of both the condition and its treatment have become an essential element of modern health care143. AF is the most common cardiac arrhythmia, affecting 2-4% of the population, and is a major cause of significant morbidity144. Although evidence suggests that adherence to guideline recommended therapies for AF is associated with improved outcomes145, 146, data from AF registries continue to show room for improvement and significant geographical variation in AF quality of care and outcomes61, 62, 147-160. QIs have been developed to evaluate the quality of AF care18, 20, 22, 31, 161. Furthermore, QIs provide the mechanism to assess the effectiveness of quality improvement initiatives162. However, standardized measures to facilitate ongoing efforts to quantify the adherence to guidelines are needed.

The present document is the first effort undertaken by the ESC to develop a set of QIs to assess the quality of care for patients with AF. Using the ESC methodology for QIs development24, we have established a comprehensive set of QIs for AF care, which are supported by evidence and underpinned by expert consensus. Thus, they provide tools to quantify the quality of AF care and can be used as a basis for quality improvement. The simultaneous development of the ESC AF QIs and the ESC Clinical Practice Guidelines for AF facilitated seamless incorporation of QIs within the guidelines document. As such, a summary form of the developed QIs is embedded within the ESC Clinical Practice Guidelines for AF, with the hope to enhance their dissemination and, therefore, uptake into clinical practice23.

This document is the result of an international collaboration (12 countries) from seven professional societies/associations with a Working Group consisting of a wide range of stakeholders, including patients. In addition, the application of ESC criteria ensured that developed QIs are not only based on evidence, but also cover broad aspects of AF care where there is gap in care delivery, potential for quality improvement, and the availability of reliable data collection sources. To that end, different types of QIs including structural, process and outcome indicators26 were included in the initial set of candidate QIs.

The Working Group, however, considered structural QIs, such as the volume of catheter ablation cases for centres and individual operators not to be directly under the control of healthcare providers. Thus, structural QIs, although important, were given less priority compared to other process ones which may influence providers’ behaviour and practice and were not included in the final set of indicators. Other QIs, such as the reintroduction of OAC after a severe bleeding event, once the condition leading to the bleeding event has been appropriately addressed63, 163, and the use of strict versus lenient rate-control treatment164 were proposed in the initial set of candidate QIs, but were deemed difficult to operationalise, and, thus, were not included.

On the other hand, and to emphasise that improving outcomes is the ultimate aim of quality of care assessment (Figure 1), particular attention was given to outcome QIs. The term ‘outcome measures’ was used separately and in different variations in the systematic review search strategy (APPENDIX 3). The outcome QIs selected are applicable to all domains of AF care, and are in line with the recent ICHOM recommendations165.

One important type of outcome QIs are PROMs, which are increasingly used in everyday practice. Although a structured methodology for developing and reporting PROMs exist166, there is uncertainty around the best instruments to collect such measures. By defining specific PROMs and recommending tools for their measurement, the Working Group hopes to promote PROMs use in a systematic manner. However, developing outcome QIs to measure the results of PROMs assessment, as well as its temporal trends may not be feasible in contemporary practice. Thus, process QIs to measure and encourage PROMs assessment were developed instead.

The Working Group acknowledges that high-quality evidence supporting PROMs use is limited, widely accepted tools to collect them are lacking, and little experience exist on how PROMs can guide AF treatment decisions. The same argument can be levelled at shared-decision making in AF management. However, these aspects of AF care were deemed essential by the Working Group, thus QIs for PROMs and shared-decision making were developed.

The patient’s perspective is a fundamental element of optimal AF care given that most therapies are aimed at improving patients’ symptoms, wellbeing, and overall quality of life. Measuring patient-centred outcomes in a standardized way may allow comparison of performance, allow clinicians to learn from each other, and improve the care we provide to our patients. However, further validation of the tools and methods used to collect patient’s perspective in routine clinical practice is needed. As such, these tools may be used to guide the development of, and the effect of, treatment strategies for AF patients.

The methodology used for the selection of QIs has limitations. We relied on expert opinion to arrive at the final set of QIs following the comprehensive systematic review of the literature. A different panel of experts may have selected different QIs. We addressed this challenge by using the modified Delphi method, and involving AF specialists with different areas of expertise, as well as patients and representatives from AF patient associations.

Another challenge is that, if considered in isolation, QIs may cause some unintended consequences, such as anticoagulation prescription for patients with very high bleeding risk or recommending catheter ablation for frail patients with major risk factors for AF recurrence. We have sought to circumvent this issue by clearly defining eligible patients for each QI and specifying relevant exclusions. The suggested QIs are intended to drive a holistic patient assessments and tailor treatments to individual patient to improve patient care. More refinement of these QIs and/or their definitions may be needed in the future when more ‘real-world’ and feasibility data become available.

It is hoped that the developed set of QIs can be used in a wider quality assessment and improvement initiatives. As such, integration between different efforts (e.g., the ESC Clinical Practice Guidelines and registries), can be achieved and performance gaps addressed. Ongoing projects, such as the European Unified Registries on Heart care Evaluation and Randomized Trials (EuroHeart) of the ESC167 or the Stroke prevention and rhythm control Therapy: Evaluation of an Educational Programme of the European society of cardiology in a cluster-Randomised trial in patients with Atrial Fibrillation (STEEER-AF) Study168 may favour the use of systematically developed QIs for future AF registries in Europe, which this statement uniquely provides.

***Conclusion***

This document defines 6 domains of AF care (patient assessment, anticoagulation, rate control, rhythm control, risk factor management and outcomes), and provides 17 main and 17 secondary QIs for AF diagnosis and management. For each QI, relevant specifications were described to enhance their use in practice. The recommended set of QIs may facilitate the implementation of, and assess the adherence to, Clinical Practice Guidelines and enable institutions to monitor, compare and improve quality of care in patients with AF.

**REFERENCES**

1. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide Epidemiology of Atrial Fibrillation. A Global Burden of Disease 2010 Study. *Circulation*. 2014;129(8):837-847. doi:10.1161/circulationaha.113.005119

2. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *European Heart Journal*. 2016;37(38):2893-2962. doi:10.1093/eurheartj/ehw210

3. Ott A, Breteler MMB, de Bruyne MC, van Harskamp F, Grobbee DE, Hofman A. Atrial Fibrillation and Dementia in a Population-Based Study. The Rotterdam Study. *Stroke*. 1997;28(2):316-321. doi:10.1161/01.str.28.2.316

4. Knecht S, OelschlÃ¤ger C, Duning T, et al. Atrial fibrillation in stroke-free patients is associated with memory impairment and hippocampal atrophy. *European Heart Journal*. September 1, 2008 2008;29(17):2125-2132. doi:10.1093/eurheartj/ehn341

5. Ball J, Carrington MJ, Stewart S, investigators obotS. Mild cognitive impairment in high-risk patients with chronic atrial fibrillation: a forgotten component of clinical management? *Heart*. April 15, 2013 2013;99(8):542-547. doi:10.1136/heartjnl-2012-303182

6. Marzona I, O’Donnell M, Teo K, et al. Increased risk of cognitive and functional decline in patients with atrial fibrillation: results of the ONTARGET and TRANSCEND studies. *Canadian Medical Association Journal*. April 3, 2012 2012;184(6):E329-E336. doi:10.1503/cmaj.111173

7. Thrall G, Lane D, Carroll D, Lip GYH. Quality of Life in Patients with Atrial Fibrillation: A Systematic Review. *American Journal of Medicine*. 2006;119(5):448.e1-448.e19.

8. von Eisenhart Rothe A, Hutt F, Baumert J, et al. Depressed mood amplifies heart-related symptoms in persistent and paroxysmal atrial fibrillation patients: a longitudinal analysis—data from the German Competence Network on Atrial Fibrillation. *EP Europace*. 2015;17(9):1354-1362. doi:10.1093/europace/euv018

9. Kotecha D, Holmes J, Krum H, et al. Efficacy of β blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis. *Lancet*. 2014;384(9961):2235-2243. doi:[http://dx.doi.org/10.1016/S0140-6736(14)61373-8](http://dx.doi.org/10.1016/S0140-6736%2814%2961373-8)

10. Steinberg BA, Kim S, Fonarow GC, et al. Drivers of hospitalization for patients with atrial fibrillation: Results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *American Heart Journal*. 5// 2014;167(5):735-742.e2. doi:<http://dx.doi.org/10.1016/j.ahj.2014.02.003>

11. Kirchhof P, Schmalowsky J, Pittrow D, et al. Management of Patients With Atrial Fibrillation by Primary-Care Physicians in Germany: 1-Year Results of the ATRIUM Registry. *Clinical Cardiology*. 2014;37(5):277-284. doi:10.1002/clc.22272

12. Wattigney WA, Mensah GA, Croft JB. Increased atrial fibrillation mortality: United States, 1980-1998. *Am J Epidemiol*. May 1 2002;155(9):819-26.

13. Wattigney WA, Mensah GA, Croft JB. Increasing Trends in Hospitalization for Atrial Fibrillation in the United States, 1985 Through 1999: Implications for Primary Prevention. *Circulation*. August 12, 2003 2003;108(6):711-716. doi:10.1161/01.cir.0000083722.42033.0a

14. Boriani G, Proietti M, Laroche C, et al. Association between antithrombotic treatment and outcomes at 1-year follow-up in patients with atrial fibrillation: the EORP-AF General Long-Term Registry. *EP Europace*. 2019;doi:10.1093/europace/euz032

15. Boriani G, Proietti M, Laroche C, et al. Contemporary stroke prevention strategies in 11 096 European patients with atrial fibrillation: a report from the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Long-Term General Registry. *Europace*. 2018 2018;20(5):747-757. doi:10.1093/europace/eux301

16. Wu J, Alsaeed ES, Barrett J, Hall M, Cowan C, Gale CP. Prescription of oral anticoagulants and antiplatelets for stroke prophylaxis in atrial fibrillation: nationwide time series ecological analysis. *EP Europace*. 2020;doi:10.1093/europace/euaa126

17. Trivedi AN, Nsa W, Hausmann LRM, et al. Quality and Equity of Care in U.S. Hospitals. *New England Journal of Medicine*. 2014;371(24):2298-2308. doi:10.1056/NEJMsa1405003

18. Heidenreich PA, Solis P, Estes NAM, et al. 2016 ACC/AHA Clinical Performance and Quality Measures for Adults With Atrial Fibrillation or Atrial Flutter. 10.1016/j.jacc.2016.03.521. *Journal of the American College of Cardiology*. 2016;68(5):525.

19. Cox JL, Dai S, Gong Y, et al. The Development and Feasibility Assessment of Canadian Quality Indicators for Atrial Fibrillation. *Canadian Journal of Cardiology*. 2016;32(12):1566-1569. doi:10.1016/j.cjca.2016.02.059

20. Sandhu RK, Wilton SB, Cruz J, et al. An Update on the Development and Feasibility Assessment of Canadian Quality Indicators for Atrial Fibrillation and Atrial Flutter. *CJC Open*. 2019/07/01/ 2019;1(4):198-205. doi:<https://doi.org/10.1016/j.cjco.2019.05.007>

21. Inohara T, Kimura T, Ueda I, et al. Effect of Compliance to Updated AHA/ACC Performance and Quality Measures Among Patients With Atrial Fibrillation on Outcome (from Japanese Multicenter Registry). *The American Journal of Cardiology*. 2017/08/15/ 2017;120(4):595-600. doi:<https://doi.org/10.1016/j.amjcard.2017.05.029>

22. The National Institute for Health and Care Excellence (NICE). NICE Atrial fibrillation Quality standard [QS93]. <https://www.nice.org.uk/guidance/qs93>. Updated July 2015. <https://www.nice.org.uk/guidance/qs93>

23. Hindricks G 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). European Heart Journal (2020) doi:10.1093/eurheartj/ehaa612.

24. Aktaa S, Batra G, Wallentin L, et al. European Society of Cardiology methodology for the development of quality indicators for the quantification of cardiovascular care and outcomes. *Eur Heart J Qual Care Clin Outcomes*. 2020;doi:10.1093/ehjqcco/qcaa069

25. Hsu C, Sandford B. The Delphi Technique: Making Sense Of Consensus. . *Practical Assessment, Research & Evaluation*. 2007;Vol 12, No 10:1-8

26. Donabedian A. Evaluating the Quality of Medical Care. *The Milbank Memorial Fund Quarterly*. 1966;44(3):166-206. doi:10.2307/3348969

27. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. journal article. *Systematic Reviews*. 2015;4(1):1-9. doi:10.1186/2046-4053-4-1

28. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ : British Medical Journal*. 2015;349:g7647. doi:10.1136/bmj.g7647

29. Seligman WH, Das-Gupta Z, Jobi-Odeneye AO, et al. Development of an international standard set of outcome measures for patients with atrial fibrillation: a report of the International Consortium for Health Outcomes Measurement (ICHOM) atrial fibrillation working group. *European Heart Journal*. 2020;41(10):1132-1140. doi:10.1093/eurheartj/ehz871

30. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society in Collaboration With the Society of Thoracic Surgeons. *Circulation*. 2019;140(2):e125-e151. doi:doi:10.1161/CIR.0000000000000665

31. Calkins H, Gliklich RE, Leavy MB, et al. Harmonized outcome measures for use in atrial fibrillation patient registries and clinical practice: Endorsed by the Heart Rhythm Society Board of Trustees. *Heart Rhythm*. 2019/01/01/ 2019;16(1):e3-e16. doi:<https://doi.org/10.1016/j.hrthm.2018.09.021>

32. Heidenreich PA, Solis P, Estes NAM, et al. 2016 ACC/AHA Clinical Performance and Quality Measures for Adults With Atrial Fibrillation or Atrial Flutter: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *Journal of the American College of Cardiology*. 2016/08/02/ 2016;68(5):525-568. doi:<https://doi.org/10.1016/j.jacc.2016.03.521>

33. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *European Heart Journal*. 2016;37(38):2893-2962. doi:10.1093/eurheartj/ehw210

34. The National Institute for H, Care E. NICE Atrial fibrillation Quality standard [QS93]. [*https://wwwniceorguk/guidance/qs93*](https://wwwniceorguk/guidance/qs93). 2015/07//Published date: Last updated: February 2018 2015;

35. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation. *Circulation*. 2014;130(23):e199-e267. doi:doi:10.1161/CIR.0000000000000041

36. Brook RH, McGlynn EA, Cleary PD. Measuring Quality of Care. *New England Journal of Medicine*. 1996;335(13):966-970. doi:doi:10.1056/NEJM199609263351311

37. Lip GYH. The ABC pathway: an integrated approach to improve AF management. *Nat Rev Cardiol*. 2017/11/01 2017;14(11):627-628. doi:10.1038/nrcardio.2017.153

38. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. *Chest*. Nov 2018;154(5):1121-1201. doi:10.1016/j.chest.2018.07.040

39. Chao TF, Lip GYH, Liu CJ, et al. Relationship of Aging and Incident Comorbidities to Stroke Risk in Patients With Atrial Fibrillation. *Journal of the American College of Cardiology*. Jan 16 2018;71(2):122-132. doi:10.1016/j.jacc.2017.10.085

40. Chao TF, Lip GYH, Lin YJ, et al. Incident Risk Factors and Major Bleeding in Patients with Atrial Fibrillation Treated with Oral Anticoagulants: A Comparison of Baseline, Follow-up and Delta HAS-BLED Scores with an Approach Focused on Modifiable Bleeding Risk Factors. *Thrombosis and haemostasis*. Apr 2018;118(4):768-777. doi:10.1055/s-0038-1636534

41. Borre ED, Goode A, Raitz G, et al. Predicting Thromboembolic and Bleeding Event Risk in Patients with Non-Valvular Atrial Fibrillation: A Systematic Review. *Thrombosis and haemostasis*. Dec 2018;118(12):2171-2187. doi:10.1055/s-0038-1675400

42. Roldan V, Marin F, Manzano-Fernandez S, et al. The HAS-BLED score has better prediction accuracy for major bleeding than CHADS2 or CHA2DS2-VASc scores in anticoagulated patients with atrial fibrillation. *Journal of the American College of Cardiology*. Dec 10 2013;62(23):2199-204. doi:10.1016/j.jacc.2013.08.1623

43. Apostolakis S, Lane DA, Buller H, Lip GY. Comparison of the CHADS2, CHA2DS2-VASc and HAS-BLED scores for the prediction of clinically relevant bleeding in anticoagulated patients with atrial fibrillation: the AMADEUS trial. *Thrombosis and haemostasis*. Nov 2013;110(5):1074-9. doi:10.1160/TH13-07-0552

44. Guo Y, Lane DA, Chen Y, Lip GYH, m AFAIITi. Regular bleeding risk assessment associated with reduction in bleeding outcomes: The mAFA II randomised trial. *The American journal of medicine*. Apr 11 2020;doi:10.1016/j.amjmed.2020.03.019

45. Kumar S, Lim E, Covic A, et al. Anticoagulation in Concomitant Chronic Kidney Disease and Atrial Fibrillation: JACC Review Topic of the Week. *Journal of the American College of Cardiology*. 2019/10/29/ 2019;74(17):2204-2215. doi:<https://doi.org/10.1016/j.jacc.2019.08.1031>

46. Steffel J, Verhamme P, Potpara TS, et al. The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation: executive summary. *EP Europace*. 2018;20(8):1231-1242. doi:10.1093/europace/euy054

47. Potpara TS, Polovina MM, Marinkovic JM, Lip GY. A comparison of clinical characteristics and long-term prognosis in asymptomatic and symptomatic patients with first-diagnosed atrial fibrillation: the Belgrade Atrial Fibrillation Study. *Int J Cardiol*. Oct 12 2013;168(5):4744-9. doi:10.1016/j.ijcard.2013.07.234

48. Boriani G, Laroche C, Diemberger I, et al. Asymptomatic atrial fibrillation: clinical correlates, management, and outcomes in the EORP-AF Pilot General Registry. *Am J Med*. May 2015;128(5):509-18 e2. doi:10.1016/j.amjmed.2014.11.026

49. Siontis KC, Gersh BJ, Killian JM, et al. Typical, atypical, and asymptomatic presentations of new-onset atrial fibrillation in the community: Characteristics and prognostic implications. *Heart Rhythm*. Jul 2016;13(7):1418-24. doi:10.1016/j.hrthm.2016.03.003

50. Martinez C, Katholing A, Freedman SB. Adverse prognosis of incidentally detected ambulatory atrial fibrillation. A cohort study. *Thrombosis and haemostasis*. Aug 2014;112(2):276-86. doi:10.1160/TH4-04-0383

51. Welton NJ, McAleenan A, Thom HH, et al. Screening strategies for atrial fibrillation: a systematic review and cost-effectiveness analysis. *Health Technol Assess*. May 2017;21(29):1-236. doi:10.3310/hta21290

52. Pollak WM, Simmons JD, Interian Jr. A, et al. Clinical Utility of Intraatrial Pacemaker Stored Electrograms to Diagnose Atrial Fibrillation and Flutter. *Pacing and Clinical Electrophysiology*. 2001;24(4):424-429. doi:10.1046/j.1460-9592.2001.00424.x

53. Kaufman ES, Israel CW, Nair GM, et al. Positive predictive value of device-detected atrial high-rate episodes at different rates and durations: An analysis from ASSERT. *Heart Rhythm*. 2012/08/01/ 2012;9(8):1241-1246. doi:<https://doi.org/10.1016/j.hrthm.2012.03.017>

54. Kishore A, Vail A, Majid A, et al. Detection of atrial fibrillation after ischemic stroke or transient ischemic attack: a systematic review and meta-analysis. *Stroke*. Feb 2014;45(2):520-6. doi:10.1161/STROKEAHA.113.003433

55. Sposato LA, Cipriano LE, Saposnik G, Ruiz Vargas E, Riccio PM, Hachinski V. Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol*. Apr 2015;14(4):377-87. doi:10.1016/S1474-4422(15)70027-X

56. Gladstone DJ, Spring M, Dorian P, et al. Atrial Fibrillation in Patients with Cryptogenic Stroke. *New England Journal of Medicine*. 2014;370(26):2467-2477. doi:10.1056/NEJMoa1311376

57. Sanna T, Diener H-C, Passman RS, et al. Cryptogenic Stroke and Underlying Atrial Fibrillation. *New England Journal of Medicine*. 2014;370(26):2478-2486. doi:doi:10.1056/NEJMoa1313600

58. Thijs VN, Brachmann J, Morillo CA, et al. Predictors for atrial fibrillation detection after cryptogenic stroke. *Results from CRYSTAL AF*. 2016;86(3):261-269. doi:10.1212/wnl.0000000000002282

59. Piccini JP, Sr., Allred J, Bunch TJ, et al. HRS white paper on atrial fibrillation centers of excellence: Rationale, considerations, and goals. *Heart Rhythm*. May 5 2020;doi:10.1016/j.hrthm.2020.04.033

60. Steinberg BA, Kim S, Fonarow GC, et al. Drivers of hospitalization for patients with atrial fibrillation: Results from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF). *Am Heart J*. May 2014;167(5):735-42.e2. doi:10.1016/j.ahj.2014.02.003

61. Steinberg BA, Gao H, Shrader P, et al. International trends in clinical characteristics and oral anticoagulation treatment for patients with atrial fibrillation: Results from the GARFIELD-AF, ORBIT-AF I, and ORBIT-AF II registries. *American Heart Journal*. 2017/12/01/ 2017;194:132-140. doi:<https://doi.org/10.1016/j.ahj.2017.08.011>

62. Steinberg BA, Shrader P, Pieper K, et al. Frequency and Outcomes of Reduced Dose Non-Vitamin K Antagonist Anticoagulants: Results From ORBIT-AF II (The Outcomes Registry for Better Informed Treatment of Atrial Fibrillation II). *Journal of the American Heart Association*. 2018;7(4):e007633. doi:doi:10.1161/JAHA.117.007633

63. Wan Y, Heneghan C, Perera R, et al. Anticoagulation control and prediction of adverse events in patients with atrial fibrillation: a systematic review. *Circulation Cardiovascular quality and outcomes*. Nov 2008;1(2):84-91. doi:10.1161/CIRCOUTCOMES.108.796185

64. Sjalander S, Sjogren V, Renlund H, Norrving B, Sjalander A. Dabigatran, rivaroxaban and apixaban vs. high TTR warfarin in atrial fibrillation. *Thrombosis research*. Jul 2018;167:113-118. doi:10.1016/j.thromres.2018.05.022

65. Amin A, Deitelzweig S, Jing Y, et al. Estimation of the impact of warfarin's time-in-therapeutic range on stroke and major bleeding rates and its influence on the medical cost avoidance associated with novel oral anticoagulant use-learnings from ARISTOTLE, ROCKET-AF, and RE-LY trials. *J Thromb Thrombolysis*. 2014;38(2):150-9. doi:10.1007/s11239-013-1048-z

66. Al-Khatib SM, Allen LaPointe NM, Chatterjee R, et al. Rate- and rhythm-control therapies in patients with atrial fibrillation: a systematic review. *Ann Intern Med*. Jun 3 2014;160(11):760-73. doi:10.7326/M13-1467

67. Camm AJ. Hopes and disappointments with antiarrhythmic drugs. *Int J Cardiol*. Jun 15 2017;237:71-74. doi:10.1016/j.ijcard.2017.03.056

68. De Vecchis R. Long-term antiarrhythmic drug treatment after atrial fibrillation ablation: does a too obstinate rhythm control strategy bring serious risk of proarrhythmia to ablated patients? *Eur Heart J Cardiovasc Pharmacother*. Apr 1 2019;5(2):117-118. doi:10.1093/ehjcvp/pvy043

69. Fabritz L, Kirchhof P. Predictable and less predictable unwanted cardiac drugs effects: individual pre-disposition and transient precipitating factors. *Basic Clin Pharmacol Toxicol*. Mar 2010;106(3):263-8. doi:10.1111/j.1742-7843.2010.00547.x

70. Reimold FR, Reynolds MR. Proarrhythmia and death with antiarrhythmic drugs for atrial fibrillation, and the unfulfilled promise of comparative effectiveness research. *American heart journal*. Nov 2018;205:128-130. doi:10.1016/j.ahj.2018.08.011

71. Darby AE, DiMarco JP. Management of Atrial Fibrillation in Patients With Structural Heart Disease. *Circulation*. 2012;125(7):945-957. doi:doi:10.1161/CIRCULATIONAHA.111.019935

72. Goldstein RE, Boccuzzi SJ, Cruess D, Nattel S. Diltiazem increases late-onset congestive heart failure in postinfarction patients with early reduction in ejection fraction. The Adverse Experience Committee; and the Multicenter Diltiazem Postinfarction Research Group. *Circulation*. 1991;83(1):52-60. doi:10.1161/01.cir.83.1.52

73. Singh BN, Singh SN, Reda DJ, et al. Amiodarone versus sotalol for atrial fibrillation. *The New England journal of medicine*. May 5 2005;352(18):1861-72. doi:10.1056/NEJMoa041705

74. Capucci A, Piangerelli L, Ricciotti J, Gabrielli D, Guerra F. Flecainide-metoprolol combination reduces atrial fibrillation clinical recurrences and improves tolerability at 1-year follow-up in persistent symptomatic atrial fibrillation. *Europace*. Nov 2016;18(11):1698-1704. doi:10.1093/europace/euv462

75. Shiga T, Yoshioka K, Watanabe E, et al. Paroxysmal atrial fibrillation recurrences and quality of life in symptomatic patients: A crossover study of flecainide and pilsicainide. *J Arrhythm*. Aug 2017;33(4):310-317. doi:10.1016/j.joa.2017.03.005

76. Mont L, Bisbal F, Hernandez-Madrid A, et al. Catheter ablation vs. antiarrhythmic drug treatment of persistent atrial fibrillation: a multicentre, randomized, controlled trial (SARA study). *Eur Heart J*. Feb 2014;35(8):501-7. doi:10.1093/eurheartj/eht457

77. Morillo CA, Verma A, Connolly SJ, et al. Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation (RAAFT-2): a randomized trial. *JAMA*. Feb 19 2014;311(7):692-700. doi:10.1001/jama.2014.467

78. Hakalahti A, Biancari F, Nielsen JC, Raatikainen MJ. Radiofrequency ablation vs. antiarrhythmic drug therapy as first line treatment of symptomatic atrial fibrillation: systematic review and meta-analysis. Journal Article. *Europace*. Mar 2015;17(3):370-8. doi:10.1093/europace/euu376

79. Di Biase L, Mohanty P, Mohanty S, et al. Ablation Versus Amiodarone for Treatment of Persistent Atrial Fibrillation in Patients With Congestive Heart Failure and an Implanted Device: Results From the AATAC Multicenter Randomized Trial. *Circulation*. Apr 26 2016;133(17):1637-44. doi:10.1161/CIRCULATIONAHA.115.019406

80. Kuck KH, Brugada J, Furnkranz A, et al. Cryoballoon or Radiofrequency Ablation for Paroxysmal Atrial Fibrillation. *The New England journal of medicine*. Jun 9 2016;374(23):2235-45. doi:10.1056/NEJMoa1602014

81. Sohara H, Ohe T, Okumura K, et al. HotBalloon Ablation of the Pulmonary Veins for Paroxysmal AF: A Multicenter Randomized Trial in Japan. *J Am Coll Cardiol*. Dec 27 2016;68(25):2747-2757. doi:10.1016/j.jacc.2016.10.037

82. Nyong J, Amit G, Adler AJ, et al. Efficacy and safety of ablation for people with non-paroxysmal atrial fibrillation. *Cochrane Database Syst Rev*. Nov 22 2016;11(11):CD012088. doi:10.1002/14651858.CD012088.pub2

83. Nielsen JC, Johannessen A, Raatikainen P, et al. Long-term efficacy of catheter ablation as first-line therapy for paroxysmal atrial fibrillation: 5-year outcome in a randomised clinical trial. *Heart*. Mar 2017;103(5):368-376. doi:10.1136/heartjnl-2016-309781

84. Chen C, Zhou X, Zhu M, et al. Catheter ablation versus medical therapy for patients with persistent atrial fibrillation: a systematic review and meta-analysis of evidence from randomized controlled trials. journal article. *Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing*. Jun 2018;52(1):9-18. doi:10.1007/s10840-018-0349-8

85. Packer DL, Mark DB, Robb RA, et al. Effect of Catheter Ablation vs Antiarrhythmic Drug Therapy on Mortality, Stroke, Bleeding, and Cardiac Arrest Among Patients With Atrial Fibrillation: The CABANA Randomized Clinical Trial. *JAMA*. 2019;321(13):1261-1274. doi:10.1001/jama.2019.0693

86. Mark DB, Anstrom KJ, Sheng S, et al. Effect of Catheter Ablation vs Medical Therapy on Quality of Life Among Patients With Atrial Fibrillation: The CABANA Randomized Clinical Trial. *JAMA*. 2019;321(13):1275-1285. doi:10.1001/jama.2019.0692

87. Blomstrom-Lundqvist C, Gizurarson S, Schwieler J, et al. Effect of Catheter Ablation vs Antiarrhythmic Medication on Quality of Life in Patients With Atrial Fibrillation: The CAPTAF Randomized Clinical Trial. *JAMA*. Mar 19 2019;321(11):1059-1068. doi:10.1001/jama.2019.0335

88. Teh AW, Kistler PM, Lee G, et al. Electroanatomic remodeling of the left atrium in paroxysmal and persistent atrial fibrillation patients without structural heart disease. *Journal of cardiovascular electrophysiology*. Mar 2012;23(3):232-8. doi:10.1111/j.1540-8167.2011.02178.x

89. D'Ascenzo F, Corleto A, Biondi-Zoccai G, et al. Which are the most reliable predictors of recurrence of atrial fibrillation after transcatheter ablation?: a meta-analysis. *Int J Cardiol*. Sep 1 2013;167(5):1984-9. doi:10.1016/j.ijcard.2012.05.008

90. Berruezo A, Tamborero D, Mont L, et al. Pre-procedural predictors of atrial fibrillation recurrence after circumferential pulmonary vein ablation. *Eur Heart J*. Apr 2007;28(7):836-41. doi:10.1093/eurheartj/ehm027

91. Nedios S, Kosiuk J, Koutalas E, et al. Comparison of left atrial dimensions in CT and echocardiography as predictors of long-term success after catheter ablation of atrial fibrillation. journal article. *Journal of interventional cardiac electrophysiology : an international journal of arrhythmias and pacing*. Sep 2015;43(3):237-44. doi:10.1007/s10840-015-0010-8

92. Njoku A, Kannabhiran M, Arora R, et al. Left atrial volume predicts atrial fibrillation recurrence after radiofrequency ablation: a meta-analysis. *Europace*. Jan 1 2018;20(1):33-42. doi:10.1093/europace/eux013

93. Costa FM, Ferreira AM, Oliveira S, et al. Left atrial volume is more important than the type of atrial fibrillation in predicting the long-term success of catheter ablation. *Int J Cardiol*. Apr 1 2015;184:56-61. doi:10.1016/j.ijcard.2015.01.060

94. Marrouche NF, Wilber D, Hindricks G, et al. Association of atrial tissue fibrosis identified by delayed enhancement MRI and atrial fibrillation catheter ablation: the DECAAF study. *JAMA*. Feb 5 2014;311(5):498-506. doi:10.1001/jama.2014.3

95. Natale A, Reddy VY, Monir G, et al. Paroxysmal AF catheter ablation with a contact force sensing catheter: results of the prospective, multicenter SMART-AF trial. *J Am Coll Cardiol*. Aug 19 2014;64(7):647-56. doi:10.1016/j.jacc.2014.04.072

96. Arbelo E, Guiu E, Ramos P, et al. Benefit of left atrial roof linear ablation in paroxysmal atrial fibrillation: a prospective, randomized study. *J Am Heart Assoc*. Sep 5 2014;3(5):e000877. doi:10.1161/JAHA.114.000877

97. McLellan AJ, Ling LH, Azzopardi S, et al. A minimal or maximal ablation strategy to achieve pulmonary vein isolation for paroxysmal atrial fibrillation: a prospective multi-centre randomized controlled trial (the Minimax study). *Eur Heart J*. Jul 21 2015;36(28):1812-21. doi:10.1093/eurheartj/ehv139

98. Verma A, Jiang CY, Betts TR, et al. Approaches to catheter ablation for persistent atrial fibrillation. *The New England journal of medicine*. May 7 2015;372(19):1812-22. doi:10.1056/NEJMoa1408288

99. Luik A, Radzewitz A, Kieser M, et al. Cryoballoon Versus Open Irrigated Radiofrequency Ablation in Patients With Paroxysmal Atrial Fibrillation: The Prospective, Randomized, Controlled, Noninferiority FreezeAF Study. *Circulation*. Oct 6 2015;132(14):1311-9. doi:10.1161/CIRCULATIONAHA.115.016871

100. Dukkipati SR, Cuoco F, Kutinsky I, et al. Pulmonary Vein Isolation Using the Visually Guided Laser Balloon: A Prospective, Multicenter, and Randomized Comparison to Standard Radiofrequency Ablation. *J Am Coll Cardiol*. Sep 22 2015;66(12):1350-60. doi:10.1016/j.jacc.2015.07.036

101. Reddy VY, Dukkipati SR, Neuzil P, et al. Randomized, Controlled Trial of the Safety and Effectiveness of a Contact Force-Sensing Irrigated Catheter for Ablation of Paroxysmal Atrial Fibrillation: Results of the TactiCath Contact Force Ablation Catheter Study for Atrial Fibrillation (TOCCASTAR) Study. *Circulation*. Sep 8 2015;132(10):907-15. doi:10.1161/CIRCULATIONAHA.114.014092

102. Scherr D, Khairy P, Miyazaki S, et al. Five-year outcome of catheter ablation of persistent atrial fibrillation using termination of atrial fibrillation as a procedural endpoint. *Circ Arrhythm Electrophysiol*. Feb 2015;8(1):18-24. doi:10.1161/CIRCEP.114.001943

103. Kuck KH, Hoffmann BA, Ernst S, et al. Impact of Complete Versus Incomplete Circumferential Lines Around the Pulmonary Veins During Catheter Ablation of Paroxysmal Atrial Fibrillation: Results From the Gap-Atrial Fibrillation-German Atrial Fibrillation Competence Network 1 Trial. *Circ Arrhythm Electrophysiol*. Jan 2016;9(1):e003337. doi:10.1161/CIRCEP.115.003337

104. Nery PB, Belliveau D, Nair GM, et al. Relationship Between Pulmonary Vein Reconnection and Atrial Fibrillation Recurrence: A Systematic Review and Meta-Analysis. *JACC Clin Electrophysiol*. Aug 2016;2(4):474-483. doi:10.1016/j.jacep.2016.02.003

105. Bassiouny M, Saliba W, Hussein A, et al. Randomized Study of Persistent Atrial Fibrillation Ablation: Ablate in Sinus Rhythm Versus Ablate Complex-Fractionated Atrial Electrograms in Atrial Fibrillation. *Circ Arrhythm Electrophysiol*. Feb 2016;9(2):e003596. doi:10.1161/CIRCEP.115.003596

106. Hindricks G, Sepehri Shamloo A, Lenarczyk R, et al. Catheter ablation of atrial fibrillation: current status, techniques, outcomes and challengesCatheter ablation of atrial fibrillation: current status, techniques, outcomes, and challenges. *Kardiologia polska*. 2018;76(12):1680-1686. doi:10.5603/KP.a2018.0216

107. Pathak RK, Middeldorp ME, Lau DH, et al. Aggressive risk factor reduction study for atrial fibrillation and implications for the outcome of ablation: the ARREST-AF cohort study. *J Am Coll Cardiol*. Dec 2 2014;64(21):2222-31. doi:10.1016/j.jacc.2014.09.028

108. Pathak RK, Elliott A, Middeldorp ME, et al. Impact of CARDIOrespiratory FITness on Arrhythmia Recurrence in Obese Individuals With Atrial Fibrillation: The CARDIO-FIT Study. *J Am Coll Cardiol*. Sep 01 2015;66(9):985-96. doi:10.1016/j.jacc.2015.06.488

109. Pathak RK, Middeldorp ME, Meredith M, et al. Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort: A Long-Term Follow-Up Study (LEGACY). *J Am Coll Cardiol*. May 26 2015;65(20):2159-69. doi:10.1016/j.jacc.2015.03.002

110. Donnellan E, Wazni OM, Kanj M, et al. Association between pre-ablation bariatric surgery and atrial fibrillation recurrence in morbidly obese patients undergoing atrial fibrillation ablation. *Europace*. Oct 1 2019;21(10):1476-1483. doi:10.1093/europace/euz183

111. Donnellan E, Aagaard P, Kanj M, et al. Association Between Pre-Ablation Glycemic Control and Outcomes Among Patients With Diabetes Undergoing Atrial Fibrillation Ablation. *JACC Clin Electrophysiol*. Aug 2019;5(8):897-903. doi:10.1016/j.jacep.2019.05.018

112. Voskoboinik A, Kalman JM, De Silva A, et al. Alcohol Abstinence in Drinkers with Atrial Fibrillation. *N Engl J Med*. Jan 2 2020;382(1):20-28. doi:10.1056/NEJMoa1817591

113. Elliott AD, Linz D, Mishima R, et al. Association between physical activity and risk of incident arrhythmias in 402 406 individuals: evidence from the UK Biobank cohort. *Eur Heart J*. Apr 14 2020;41(15):1479-1486. doi:10.1093/eurheartj/ehz897

114. Lau DH, Nattel S, Kalman JM, Sanders P. Modifiable Risk Factors and Atrial Fibrillation. *Circulation*. Aug 8 2017;136(6):583-596. doi:10.1161/CIRCULATIONAHA.116.023163

115. Abed HS, Wittert GA, Leong DP, et al. Effect of weight reduction and cardiometabolic risk factor management on symptom burden and severity in patients with atrial fibrillation: a randomized clinical trial. *JAMA*. Nov 20 2013;310(19):2050-60. doi:10.1001/jama.2013.280521

116. Lavie CJ, Thomas RJ, Squires RW, Allison TG, Milani RV. Exercise training and cardiac rehabilitation in primary and secondary prevention of coronary heart disease. *Mayo Clin Proc*. Apr 2009;84(4):373-83. doi:10.1016/S0025-6196(11)60548-X

117. Mont L. Arrhythmias and sport practice. *Heart*. Mar 2010;96(5):398-405. doi:10.1136/hrt.2008.160903

118. Menezes AR, Lavie CJ, De Schutter A, et al. Lifestyle modification in the prevention and treatment of atrial fibrillation. *Progress in cardiovascular diseases*. Sep-Oct 2015;58(2):117-25. doi:10.1016/j.pcad.2015.07.001

119. Conen D, Albert CM. Alcohol consumption and risk of atrial fibrillation: how much is too much? *J Am Coll Cardiol*. Jul 22 2014;64(3):290-2. doi:10.1016/j.jacc.2014.04.038

120. Larsson SC, Drca N, Wolk A. Alcohol consumption and risk of atrial fibrillation: a prospective study and dose-response meta-analysis. *J Am Coll Cardiol*. Jul 22 2014;64(3):281-9. doi:10.1016/j.jacc.2014.03.048

121. Pisters R, Lane DA, Marin F, Camm AJ, Lip GY. Stroke and thromboembolism in atrial fibrillation. *Circ J*. 2012;76(10):2289-304.

122. Freedman B, Camm J, Calkins H, et al. Screening for Atrial Fibrillation: A Report of the AF-SCREEN International Collaboration. *Circulation*. May 9 2017;135(19):1851-1867. doi:10.1161/CIRCULATIONAHA.116.026693

123. Epstein LJ, Kristo D, Strollo PJ, Jr., et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine*. Jun 15 2009;5(3):263-76.

124. Linz D, McEvoy RD, Cowie MR, et al. Associations of Obstructive Sleep Apnea With Atrial Fibrillation and Continuous Positive Airway Pressure Treatment: A Review. *JAMA cardiology*. Jun 1 2018;3(6):532-540. doi:10.1001/jamacardio.2018.0095

125. Lip GYH, Coca A, Kahan T, et al. Hypertension and cardiac arrhythmias: a consensus document from the European Heart Rhythm Association (EHRA) and ESC Council on Hypertension, endorsed by the Heart Rhythm Society (HRS), Asia-Pacific Heart Rhythm Society (APHRS) and Sociedad Latinoamericana de Estimulacion Cardiaca y Electrofisiologia (SOLEACE). *Europace*. Jun 1 2017;19(6):891-911. doi:10.1093/europace/eux091

126. Hobbs FD, Fitzmaurice DA, Mant J, et al. A randomised controlled trial and cost-effectiveness study of systematic screening (targeted and total population screening) versus routine practice for the detection of atrial fibrillation in people aged 65 and over. The SAFE study. *Health Technol Assess*. Oct 2005;9(40):iii-iv, ix-x, 1-74.

127. Pallisgaard JL, Schjerning AM, Lindhardt TB, et al. Risk of atrial fibrillation in diabetes mellitus: A nationwide cohort study. *Eur J Prev Cardiol*. Apr 2016;23(6):621-7. doi:10.1177/2047487315599892

128. Wynn GJ, Todd DM, Webber M, et al. The European Heart Rhythm Association symptom classification for atrial fibrillation: validation and improvement through a simple modification. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology*. Jul 2014;16(7):965-72. doi:10.1093/europace/eut395

129. Friberg L, Rosenqvist M, Lip GYH. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. *European Heart Journal*. 2012;33(12):1500-1510. doi:10.1093/eurheartj/ehr488

130. Schulman S, Kearon C. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. *Journal of thrombosis and haemostasis : JTH*. Apr 2005;3(4):692-4. doi:10.1111/j.1538-7836.2005.01204.x

131. Schulman S, Angeras U, Bergqvist D, et al. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in surgical patients. *Journal of Thrombosis and Haemostasis*. 2010;8(1):202-204. doi:10.1111/j.1538-7836.2009.03678.x

132. Calvert M, Kyte D, Price G, Valderas JM, Hjollund NH. Maximising the impact of patient reported outcome assessment for patients and society. *BMJ (Clinical research ed)*. Jan 24 2019;364:k5267. doi:10.1136/bmj.k5267

133. Rotenstein LS, Huckman RS, Wagle NW. Making Patients and Doctors Happier - The Potential of Patient-Reported Outcomes. *The New England journal of medicine*. Oct 5 2017;377(14):1309-1312. doi:10.1056/NEJMp1707537

134. Steinberg BA, Dorian P, Anstrom KJ, et al. Patient-Reported Outcomes in Atrial Fibrillation Research: Results of a Clinicaltrials.gov Analysis. *JACC Clinical electrophysiology*. May 2019;5(5):599-605. doi:10.1016/j.jacep.2019.03.008

135. Aliot E, Botto GL, Crijns HJ, Kirchhof P. Quality of life in patients with atrial fibrillation: how to assess it and how to improve it. *Europace : European pacing, arrhythmias, and cardiac electrophysiology : journal of the working groups on cardiac pacing, arrhythmias, and cardiac cellular electrophysiology of the European Society of Cardiology*. Jun 2014;16(6):787-96. doi:10.1093/europace/eut369

136. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Medical care*. Mar 1996;34(3):220-33. doi:10.1097/00005650-199603000-00003

137. Kotecha D, Ahmed A, Calvert M, Lencioni M, Terwee CB, Lane DA. Patient-Reported Outcomes for Quality of Life Assessment in Atrial Fibrillation: A Systematic Review of Measurement Properties. *PloS one*. 2016;11(11):e0165790. doi:10.1371/journal.pone.0165790

138. Spertus J, Dorian P, Bubien R, et al. Development and validation of the Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) Questionnaire in patients with atrial fibrillation. *Circulation Arrhythmia and electrophysiology*. Feb 2011;4(1):15-25. doi:10.1161/circep.110.958033

139. Singh SN, Tang XC, Singh BN, et al. Quality of Life and Exercise Performance in Patients in Sinus Rhythm Versus Persistent Atrial Fibrillation: A Veterans Affairs Cooperative Studies Program Substudy. *Journal of the American College of Cardiology*. 2006/08/15/ 2006;48(4):721-730. doi:<https://doi.org/10.1016/j.jacc.2006.03.051>

140. Dorian P, Guerra PG, Kerr CR, et al. Validation of a New Simple Scale to Measure Symptoms in Atrial Fibrillation. *Circulation: Arrhythmia and Electrophysiology*. 2009;2(3):218-224. doi:doi:10.1161/CIRCEP.108.812347

141. Dorian P, Jung W, Newman D, et al. The impairment of health-related quality of life in patients with intermittent atrial fibrillation: implications for the assessment of investigational therapy. *Journal of the American College of Cardiology*. 2000/10/01/ 2000;36(4):1303-1309. doi:[https://doi.org/10.1016/S0735-1097(00)00886-X](https://doi.org/10.1016/S0735-1097%2800%2900886-X)

142. Seligman WH, Das-Gupta Z, Jobi-Odeneye AO, et al. Development of an international standard set of outcome measures for patients with atrial fibrillation: a report of the International Consortium for Health Outcomes Measurement (ICHOM) atrial fibrillation working group. *European heart journal*. Mar 7 2020;41(10):1132-1140. doi:10.1093/eurheartj/ehz871

143. *Crossing the Quality Chasm: A New Health System for the 21st Century*. National Academies Press (US); 2001.

144. Benjamin EJ, Muntner P, Alonso A, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation*. Mar 5 2019;139(10):e56-e528. doi:10.1161/CIR.0000000000000659

145. Gorin L, Fauchier L, Nonin E, Charbonnier B, Babuty D, Lip GYH. Prognosis and Guideline-Adherent Antithrombotic Treatment in Patients With Atrial Fibrillation and Atrial Flutter: Implications of Undertreatment and Overtreatment in Real-life Clinical Practice; the Loire Valley Atrial Fibrillation Project. *Chest*. 2011/10/01/ 2011;140(4):911-917. doi:<https://doi.org/10.1378/chest.10-2436>

146. Nielsen PB, Larsen TB, Skjøth F, Overvad TF, Lip GYH. Stroke and thromboembolic event rates in atrial fibrillation according to different guideline treatment thresholds: A nationwide cohort study. *Scientific Reports*. 2016/06/06 2016;6(1):27410. doi:10.1038/srep27410

147. Lip GYH, Laroche C, Dan G-A, et al. A prospective survey in European Society of Cardiology member countries of atrial fibrillation management: baseline results of EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry. Journal Article. *Europace*. 2014-03-01 00:00:00 2014;16(3):308-319. doi:10.1093/europace/eut373

148. Lip GYH, Laroche C, Dan G-A, et al. ‘Real-World’ Antithrombotic Treatment in Atrial Fibrillation: The EORP-AF Pilot Survey. *American Journal of Medicine*. 2014;127(6):519-529.e1. doi:<http://dx.doi.org/10.1016/j.amjmed.2013.12.022>

149. Lip GYH, Laroche C, Popescu MI, et al. Improved outcomes with European Society of Cardiology guideline-adherent antithrombotic treatment in high-risk patients with atrial fibrillation: a report from the EORP-AF General Pilot Registry. *EP Europace*. 2015;17(12):1777-1786. doi:10.1093/europace/euv269

150. Lip GYH, Laroche C, Boriani G, et al. Regional differences in presentation and treatment of patients with atrial fibrillation in Europe: a report from the EURObservational Research Programme Atrial Fibrillation (EORP-AF) Pilot General Registry. *Europace*. 2015-02-01 00:00:00 2015;17(2):194-206. doi:10.1093/europace/euu201

151. Fumagalli S, Said SAM, Laroche C, et al. Age-Related Differences in Presentation, Treatment, and Outcome of Patients With Atrial Fibrillation in Europe: The EORP-AF General Pilot Registry (EURObservational Research Programme-Atrial Fibrillation). *JACC: Clinical Electrophysiology*. 2015/08/01/ 2015;1(4):326-334. doi:<https://doi.org/10.1016/j.jacep.2015.02.019>

152. Boriani G, Laroche C, Diemberger I, et al. Asymptomatic Atrial Fibrillation: Clinical Correlates, Management, and Outcomes in the EORP-AF Pilot General Registry. *American Journal of Medicine*. 2015/05/01/ 2015;128(5):509-518.e2. doi:<http://dx.doi.org/10.1016/j.amjmed.2014.11.026>

153. Boriani G, Laroche C, Diemberger I, et al. ‘Real-world’ management and outcomes of patients with paroxysmal vs. non-paroxysmal atrial fibrillation in Europe: the EURObservational Research Programme–Atrial Fibrillation (EORP-AF) General Pilot Registry. *EP Europace*. 2016;18(5):648-657. doi:10.1093/europace/euv390

154. Proietti M, Laroche C, Opolski G, Maggioni AP, Boriani G, Lip GYH. ‘Real-world’ atrial fibrillation management in Europe: observations from the 2-year follow-up of the EURObservational Research Programme-Atrial Fibrillation General Registry Pilot Phase. *Europace*. 2016-05-18 00:00:00 2016;doi:10.1093/europace/euw112

155. Boriani G, Glotzer TV, Ziegler PD, et al. Detection of new atrial fibrillation in patients with cardiac implanted electronic devices and factors associated with transition to higher device-detected atrial fibrillation burden. *Heart Rhythm*. 2018;15(3):376-383. doi:10.1016/j.hrthm.2017.11.007

156. Arbelo E, Brugada J, Hindricks G, et al. The Atrial Fibrillation Ablation Pilot Study: an European Survey on Methodology and results of catheter ablation for atrial fibrillation conducted by the European Heart Rhythm Association. *European Heart Journal*. June 7, 2014 2014;35(22):1466-1478. doi:10.1093/eurheartj/ehu001

157. Arbelo E, Brugada J, Lundqvist CB, et al. Contemporary management of patients undergoing atrial fibrillation ablation: in-hospital and 1-year follow-up findings from the ESC-EHRA atrial fibrillation ablation long-term registry. 10.1093/eurheartj/ehw564. *European Heart Journal*. 2017;

158. Riahi S, Arbelo E, Brugada J, et al. Regional differences in referral, procedures, and outcome after ablation for atrial fibrillation in Europe: a report from the Atrial Fibrillation Ablation Pilot Registry of the European Society of Cardiology. *Europace*. 2016-02-01 00:00:00 2016;18(2):191-200. doi:10.1093/europace/euv386

159. Barnett AS, Kim S, Fonarow GC, et al. Treatment of Atrial Fibrillation and Concordance With the American Heart Association/American College of Cardiology/Heart Rhythm Society Guidelines. *Circulation: Arrhythmia and Electrophysiology*. 2017;10(11):e005051. doi:doi:10.1161/CIRCEP.117.005051

160. Potpara TS, Lip GYH, Dagres N, et al. Cohort profile The ESC EURObservational Research Programme Atrial Fibrillation III (AF III) Registry. *European Heart Journal - Quality of Care and Clinical Outcomes*. 2020;doi:10.1093/ehjqcco/qcaa050

161. McNamara RL, Brass LM, Drozda JP, et al. ACC/AHA key data elements and definitions for measuring the clinical management and outcomes of patients with atrial fibrillation. A report of the American College of Cardiology/American Heart Association Task Force on clinical data standards (writing commitee to develop data standards on atrial fibrillation). *Journal of the American College of Cardiology*. 2004;44(2):475-495. doi:10.1016/j.jacc.2004.06.041

162. McGlynn EA. Introduction and overview of the conceptual framework for a national quality measurement and reporting system. *Med Care*. Jan 2003;41(1 Suppl):I1-7. doi:10.1097/00005650-200301001-00001

163. Staerk L, Lip GY, Olesen JB, et al. Stroke and recurrent haemorrhage associated with antithrombotic treatment after gastrointestinal bleeding in patients with atrial fibrillation: nationwide cohort study. *BMJ (Clinical research ed)*. Nov 16 2015;351:h5876. doi:10.1136/bmj.h5876

164. Van Gelder IC, Groenveld HF, Crijns HJGM, et al. Lenient versus Strict Rate Control in Patients with Atrial Fibrillation. *New England Journal of Medicine*. 2010;362(15):1363-1373. doi:doi:10.1056/NEJMoa1001337

165. Seligman WH, Das-Gupta Z, Jobi-Odeneye AO, et al. Development of an international standard set of outcome measures for patients with atrial fibrillation: a report of the International Consortium for Health Outcomes Measurement (ICHOM) atrial fibrillation working group. *European Heart Journal*. 2020;doi:10.1093/eurheartj/ehz871

166. Calvert M, Blazeby J, Altman DG, et al. Reporting of patient-reported outcomes in randomized trials: The consort pro extension. *JAMA*. 2013;309(8):814-822. doi:10.1001/jama.2013.879

167. Wallentin L, Gale CP, Maggioni A, Bardinet I, Casadei B. EuroHeart: European Unified Registries On Heart Care Evaluation and Randomized Trials: An ESC project to develop a new IT registry system which will encompass multiple features of cardiovascular medicine. *European Heart Journal*. 2019;40(33):2745-2749. doi:10.1093/eurheartj/ehz599

168. Bunting KV, Van Gelder IC, Kotecha D. STEEER-AF: a cluster-randomized education trial from the ESC: The STEEER-AF trial is designed by the European Society of Cardiology (ESC) to see if better education for healthcare professionals can improve how patients are treated and how AF is managed. *European Heart Journal*. 2020;41(21):1952-1954. doi:10.1093/eurheartj/ehaa421