**The Atrial fibrillation Better Care (ABC) pathway for managing atrial fibrillation: a review**

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**Introduction**

Atrial fibrillation (AF) is associated with a five-fold increase in the risk of stroke1 and a higher risk of cardiovascular and all-cause mortality.2 Current European Society of Cardiology (ESC) guidelines on AF management advocate the use of oral anticoagulants (OACs) to reduce stroke risk in patients with a CHA2DS2-VASc risk score of ≥1 for men and ≥2 for women.3

More recently, there has been a move towards recommending an integrated care approach to AF management.3-5 6-8 Three studies examining integrated care for the management of AF6-8 were analyzed in a meta-analysis, which showed a significant reduction in the risk of both mortality and hospitalisation9; however, this systematic review showed inconsistency in the populations recruited and the care provided between the studies.

In 2017, the Atrial Fibrillation Better Care (ABC) pathway was proposed as an integrated, structured approach to AF management,10 addressing three main components: “A” refers to “Avoid stroke”, by offering stroke prevention with appropriate oral anticoagulation to patients with a CHA2DS2-VAScscore of ≥1 for men and ≥2 for women,11 “B” refers to “Better symptom management” and involves a patient and symptom-focused approach to decisions on managing heart rate or rhythm. “C” refers to “Cardiovascular and comorbidity risk reduction”, comprising the management of risk factors for other cardiovascular outcomes.

Several studies12-23 have examined the impact of adherence/non-adherence to the ABC pathway. This review summarizes the definitions used for the ABC criteria in different datasets and evaluates the impact of adherence/non-adherence on clinical outcomes.

**Methods**

*Literature search*

Medline Ovid was searched from inception to 1st December 2020, using the following terms in the title or abstract of the article: ABC or “Atrial Fibrillation Better Care”, Pathway and Atrial Fibrillation. Additionally, studies were examined based on references cited in identified sources and communication with experts in the field.

*Study selection*

Papers were included if they defined criteria for ABC pathway adherence in an AF cohort. There were no restrictions based on study design. To be included, studies needed to compare groups of patients who were either ABC adherent or non-ABC adherent or which had an intervention that aimed to improve ABC adherence in one arm of a randomized clinical trial. Reviews and guidelines with no data were excluded. The first author screened the available titles and abstracts, and the potentially included papers were discussed and agreed with other authors.

*Data Extraction and Synthesis*

Data extracted from relevant publications included: first author, year of publication, number of participants, the proportion of males and females, mean (Standard deviation, SD)/median (Interquartile range, IQR) age, length of the follow-up period, criteria used for ABC adherence definitions, sample selection criteria, disease outcomes reported, the number of events in ABC adherent and non-ABC adherent groups and the covariates adjusted for. The first author completed the data extraction, and other authors were consulted to resolve any queries. Following extraction, this data was summarized in Tables. The variation in definitions and criteria included also precluded any attempts to combine the results of individual studies in a meta-analysis.

**Results**

The searches for this review returned 19 studies and after reviewing the titles and abstracts, 12 studies12-23 were reviewed as full-text and included. Reasons for exclusion included: reviews (n=2), guidelines (n=2), ABC criteria not defined (n=1), wrong population and no reference to ABC pathway (n=1), and wrong outcomes (i.e., costs) (n=1). The 12 included studies used data from seven different datasets. Three datasets were prospectively collected,12,15-18 two were retrospective post-hoc analyses of prospectively collected data19,21,22 and two were registries or electronic health records.13,14,20,23 Characteristics of the included studies are provided in **Table 1**. Studies used data from around the world: South Korea (n=3),13,14,23 China (n=2),17,18 the Middle East (n=2),15,16 Italy (n=1)19, Europe (n=1)20, the US and Canada (n=2)21,22 and the Balkans (n=1).12

Sample sizes varied from 603 in the Gulf Survey of Atrial Fibrillation Events (SAFE) Registry15 to over 260,000 in the Korea National Health Insurance Service database.13 Age varied considerably between studies, ranging from 56.716 to 73.1 years.19 Two studies had a difference of over 8 years in mean age between ABC adherent and non-ABC adherent patients.13,16 The proportion of women included in each study ranged from 37.5%14 to 52.2%.15

The follow-up times of six of the studies were relatively short, at only one to two years.15-20 Only the studies based on the Korean Nation Health Insurance Service database13,14,23 and the AFFIRM trial21,22 followed up patients for more than two years. There was no significant difference between the results of studies with longer and shorter follow-up. However, there was no indication that studies had tested that the risk reduction due to ABC adherence remained constant over time although they used models that assumed proportional hazards.

AF was denoted differently, with some studies based on AF trial cohorts where patients had AF confirmed by >30 seconds AF in ECG or 24h Holter,15-18 while others relied on an AF diagnosis recorded in their electronic health records.13,14,23 Seven studies12-14,16,19,20,23 included all available AF patients within their cohorts, while some only included patients who were already high risk of stroke21,22 with some requiring a CHA2DS2-VASc score ≥217,18 or for patients to have a specific comorbidity, such as diabetes mellitus.15 Thus, in five of these studies,15,17,18,21,22 all patients were eligible for OAC (based on CHA2DS2-VASc score). Five studies reported on stroke incidence,13,14,17,20,21 eight on all-cause mortality,13-17,20-22 two on cardiovascular mortality,20,21 five on bleeding,13,14,17,20,21 one on dementia,23 and three on hospitalisation.17,21,22 Composite outcomes considering combinations of these outcomes were considered in 10 studies.13-22

The different definitions for the individual components of the ABC pathway (**Figure 1**) used in the studies are shown in **Table 2**.

*‘A’ - Avoid stroke with oral anticoagulation*

All studies required OAC prescription for patients to be based on stroke risk identified with the CHA2DS2-VASc score. The definition of a high risk of stroke varied between studies. To meet the criteria for the ‘A’ component, one study considered OAC optional for patients with a CHA2DS2-VASc of 1 or 2 for men or women19, respectively, while others considered that OAC was required in these patients.13,16,20,23 Five studies only included patients that had a CHA2DS2-VASc score ≥1 or ≥2 for men or women, respectively, meaning that all patients were eligible for OAC.15,17,18,21,22

Each study defined OAC adherence using different criteria. For patients receiving warfarin or other vitamin K antagonists (VKAs), time in therapeutic range (TiTR) was utilized to indicate anticoagulation control by five papers. 17-19,21,22 For three studies17-19 the target TiTR was >65% and in two others21,22 the target was >70%. TiTR was not always available; alternatively, prescription days coverage >80%13,14,23 was used.

*‘B’ - Better symptom management*

Seven studies defined adherence to the ‘B’ criterion as symptom levels classified as European Heart Rhythm Association (EHRA) classes I-II.12,15-20 Studies using the AFFIRM trial data allowed ≤2 symptoms from their own list.21,22 The studies based on the Korea National Health Insurance Service database did not have data on symptoms, therefore the authors used the criteria of <5 outpatient visits per year as a proxy.13,14,23

*‘C’ - Cardiovascular and co-morbidity management*

Each study considered a different set of conditions when defining the ‘C’ criteria as shown in **Table 2**. All studies considered hypertension although it was defined in multiple ways. Nine studies required blood pressure (BP) to be controlled at <140/90 mm Hg12-16,20-23 although other cut-offs (e.g., 160/9019 or 140/85 17,18) were used17-19. Two studies looked for active treatment of hypertension with pharmacological treatment rather than BP control.12,19 Each study looked at a different selection of other conditions such as diabetes,12-14,16,19,20,23 heart failure,12-23 peripheral artery disease13-16,20-23 and coronary artery disease12,15,16,20-22; these were considered based on drugs used for prevention and/or treatment. BMI with a cut-off of 30 kg/m2 was considered in three studies.13,14,23

There was a wide-range in the proportion of participants assessed as ABC adherent in the included studies (7.0% to 43.8%),12,21,22 as shown in **Table 3**. Mean age varied among studies depending on the inclusion criteria. In three studies, those who were ABC adherent were over 10 years younger12-14 than those who were not ABC adherent; conversely in another study ABC-adherent patients were over 8 years older.16 In four studies a lower proportion of ABC adherent patients were women,14,20-22 while in two studies a higher proportion were women.12,19 Hypertension was more prevalent in ABC non-adherent patients although this was dependent on definitions.

**Table 4** presents the outcomes in ABC-adherent versus non-ABC adherent patients within each study. Each study adjusted for a different set of potential confounders, although age, sex and diabetes status were adjusted for in eight of the studies.13,14,17,18,20-23 Due to different data availability, both Cox proportional hazards models and logistic regression were used to estimate the effect of ABC adherence on clinical outcomes. Hazard ratios (HRs) and odds ratios varied due to differing definitions but consistently reported that ABC pathway adherent care was beneficial for lowering mortality (Figure 2, n=4 studies, HR 0.35 (95% Confidence Interval 0.17-0.75), HR 0.57 (0.43-0.78), HR 0.82 (0.78-0.86) and HR 0.93 (0.90-0.97)),13,14,20,21 cardiovascular mortality (Supplementary Figure 1, n=2 studies, HR 0.17 (0.04-0.70) and HR 0.52 (0.35-0.78)),20,21 major bleeding (Supplementary Figure 2, n=3 studies, HR 0.26 (0.08-0.81), HR 0.89 (0.84-0.94) and HR 0.99 (0.95-1.02)),13,14,21 stroke (n=1 study, HR 0.86 (0.83-0.89)),13,14 myocardial infarction (n=1 study, HR 0.76 (0.69-0.83)),13 hospitalization risk (n=1 study, HR 0.65 (0.53-0.80))21 and composites of these outcomes.

Four studies examined how the number of ABC criteria fulfilled impacted on the outcomes. 14,20-22 The risk of mortality was reduced by meeting one (n=3 studies, HR 0.70 (0.55-0.90), HR 0.69 (0.42-1.14) and HR 0.91 (0.88-0.94)), two (n=3 studies, HR 0.49 (0.35-0.67), HR 0.47 (0.29-0.76) and HR 0.86 (0.84-0.89)) and three (n=3 studies, HR 0.25 (0.12-0.55), HR 0.32 (0.18-0.54) and HR 0.80 (0.77-0.84)) ABC criteria compared with meeting no ABC criteria. 14,20,21 There was also a risk reduction for cardiovascular mortality20 and composite outcomes.14,20-22 There was a consistent dose-response effect with more ABC-adherent criteria fulfilled translating into a lower risk for all outcomes.14,20-22

**Discussion**

All nine studies that examined the risk of adverse outcomes among patients adherent to the ABC pathway reported a significant risk reduction of adverse events, with only one study showing a non-significant result for major bleeding.13 The risks of stroke, mortality, myocardial infarction, hospitalization and composites of these outcomes have all been shown to be lower in patient’s adherent to the ABC pathway. None of the studies suggested that there was any negative effect of being adherent to the ABC pathway.

The significant positive effect of ABC pathway adherence was robust amongst the different datasets. However, there was a relatively large variation in the strength of the risk reduction (e.g., HRs ranged from 0.35 to 0.93 for mortality), reflecting the differences between the datasets, and criteria used to denote A, B, and C adherence which may result in differences in the degree of risk reduction. Several factors could be driving variation, for example, some of the studies only included patients with other stroke risk factors (e.g. older age or diabetes) and some studies used more robust definitions for ABC adherence. Seven of the included studies conducted a retrospective analysis of pre-existing datasets.13,14,19-23 The various retrospective analyses led to variation between the studies examined within this review including differences in the inclusion/exclusion criteria, definitions of ABC-adherence employed and study design. Lack of appropriate data, such as TiTR, AF symptoms, and treatment data for each of the criteria of the ABC pathway included, led to some studies using less comprehensive definitions13,14,23 than others.12,15-22

Care is needed when defining the ‘A’, ‘B’ and ‘C’ criteria to be used in retrospective studies as there is also the potential for healthier patients to be selected rather than just those who have had ABC adherent management. Not all criteria can be modified quickly after AF diagnosis and some require patient involvement, such as adherence to prescriptions, increasing TiTR, and reducing risk factors such as obesity.

All studies only examined if the patient’s care was adherent to the ABC pathway at baseline. However, risk factors have the potential to change over time,24 especially in patients that were newly diagnosed with AF at baseline. In studies with longer follow-up, changes from baseline are more likely. There was a large variation in follow-up length in the studies in this review although all but two datasets had follow-up less than or equal to two years. 13,14,21-23 Although all studies adjusted for the patient’s age when analyzing the risk of adverse outcomes in patients adherent and non-adherent to the ABC pathway, only one stratified the results by different age groups.23 The results of this study suggested that there may be a greater risk reduction in older patients, but the study lacked power for this analysis.

Wagner et al first purported the idea of integrated care for chronic diseases in 1996.25 The key to integrated care is engaging the patient in the decision-making process and management of their condition. Also crucial is involving a multidisciplinary team from specialists to carers in the success of AF management. These strategies aim to improve treatment adherence, reduce perceived treatment burden and provide better outcomes for the patient.

While some of the individual components that comprise the ABC pathway have previously been included in guidelines,26 the ABC pathway has recently been incorporated into the 2020 ESC guidelines for the management of AF,3 bringing these together in an easy to follow structure. This review adds to the evidence supporting the inclusion of the ABC pathway in AF guidelines and implementation in practice to improve patient outcomes. The heterogeneity of the retrospective cohorts and the ABC pathway assessments based on available data and outcomes are intrinsic to the particular studies; this could be avoided by prospective studies. The mAFA-II cluster randomized trial compared usual care against app-based mobile health (mHealth) intervention based on the ABC pathway18 and showed a risk reduction for those using the app-based care of 61% for a composite outcome of stroke/thromboembolism, all-cause mortality and re-hospitalization and a risk reduction of 68% for re-hospitalization.

The long term mAFA-II cohort showed high adherence and persistence of use, and maintenance of improved clinical outcomes with ABC pathway adherent management.17

*Strengths and Limitations*

This review has summarized all available studies that have examined the impact of ABC adherent versus non-ABC adherent treatment in AF patients, showing a consistent clinically significant reduction in the risk of adverse outcomes for patients whose treatment is adherent to the ABC pathway. However, variation between the studies included in this review raises questions over the precise magnitude of the benefit of adherence to the ABC pathway in a general AF population using ideal definitions of ABC adherence. This variation in definitions and criteria included also precluded any attempts to combine the results of individual studies in a meta-analysis.

*Conclusion*

All studies consistently showed statistically significant reductions in the risk of stroke, myocardial infarction, and mortality among those with treatment adherent to the ABC pathway. The ABC pathway provides a simple decision-making framework to enable consistent equitable care from clinicians in both primary and secondary/tertiary care. Further research examining the impact of ABC pathway implementation in prospective cohorts where consistent inclusion criteria and definitions of ‘A’, ‘B’, and ‘C’ adherent care can be used is needed.

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**Table 1.** Summary of the characteristics of the included studies

| First author, year, country | Study Cohort | Cohort description, a N, b Mean ± SD or Median [IQR] age, c N (%) female, d ethnicity, e Mean ± SD or Median [IQR] CHA2DS2-VASc score, f Mean ± SD or Median [IQR] HAS-BLED score | Selection criteria | Length of follow-up Mean ± SD or Median [IQR] | Outcomes |
| --- | --- | --- | --- | --- | --- |
| Prospective |
| Domek (2020), Middle East15 | Gulf Survey of Atrial Fibrillation Events (SAFE) Registry | Consecutive patients admitted to ED in 23 hospitals in 6 Middle East countries independently from the primary reason for admission, a 603, b 63.42 ± 11.75, c 315 (52.2%), d Not reported, e 3.69 ± 1.58, f 1.56± 1.07 | **Inclusion criteria:** ≥ 18 years old, >30 seconds AF on 12-lead resting ECG, Diabetes | 12 months | **Primary:** ACM, Composite: stroke/systemic embolism, ACM, CV hospitalization |
| Gumprecht (2020), Middle East16 | Gulf Survey of Atrial Fibrillation Events (SAFE) Registry | Consecutive patients admitted to ED in 23 hospitals in 6 Middle East countries independently from the primary reason for admission, a 2021, b 56.74 ± 16.47, c 968 (47.9%), d Not reported, e 2.34 ± 1.78, f 1.13 ± 1.065 | **Inclusion criteria:** ≥18 years old, >30 seconds AF on 12-lead resting electrocardiogram **Exclusion criteria:** Insufficient data for calculating CHA2DS2-VASc score | 1 year | **Primary:** ACM, Composite of ischemic stroke or systemic embolism/all-cause mortality and CV hospitalization |
| Guo (2020) 1 year, China18 | mAFA II trial | 2 arm cluster-RCT. Clusters were 40 Chinese hospitals, a 3324, b mAFA: 67.0 ± 15.0 UC: 70.0 ± 12.0, c mAFA: 625 (38.0%) UC: 637 (38.0%), d Not reported, e mAFA: 3 [2-4] UC: 3 [2-4], f mAFA: 1 [1-2] UC: 1 [1-2] | **Inclusion criteria:** ≥18 years old, AF confirmed by ECG or 24-hr Holter, CHA2DS2-VASc ≥2 **Exclusion criteria:** Mechanical prosthetic value or moderate/severe mitral stenosis, Unable to provide informed consent, Unable to be followed up for 1 year for any reason | 12 months | **Primary:** Composite: stroke/ thromboembolism, ACM, and re-hospitalization |
| Guo (2020) Extension, China17 | mAFA II trial | 2 arm cluster-RCT. Clusters were 40 Chinese hospitals, a 2473, b mAFA: 67.8 ± 15.4 UC: 70.1 ± 12.0, c mAFA: 430 (34.1%) UC: 511 (42.1%), d Not reported, e mAFA: 3 [2-4] UC: 3 [2-4], f mAFA: 2 [1-3] UC: 2 [1-3] | **Inclusion criteria:** ≥18 years old, AF confirmed by ECG or 24-hr Holter, CHA2DS2-VASc ≥2, Over 1 year of follow-up **Exclusion criteria:** Mechanical prosthetic value or moderate/severe mitral stenosis, Unable to provide informed consent | mAFA: 687 ± 191; 701 [489-841] days, Usual care: 514 ± 167; 546 [394-632] days | **Primary:** Composite: stroke/ thromboembolism, ACM, and re-hospitalization **Secondary:** Ischemic stroke, Other thromboembolism, Intracranial bleeding, Extracranial bleeding, Recurrent AF or AF symptom, Heart Failure, ACM |
| Koziel (2020), Balkans12 | BALKAN-AF survey | Consecutive patients managed in hospitals and outpatient settings; 8 Balkan countries; 49 centers; 14-week observational survey recorded prospectively, a 2712, b ABC: 49 [41, 57] non-ABC: 64 [55,71], c ABC: 485 (47.9%) non-ABC: 557 (42.9%), d Not reported, e ABC: 3.4 ± 1.8 non-ABC: 3.4 ± 1.9, f ABC: 1.94 ± 1.2 non-ABC: 1.99 ± 1.2 | **Inclusion criteria:** ≥18 years old **Exclusion criteria:** Prosthetic mechanical heart valves, Moderate or severe mitral valve stenosis or any significant heart valve disease with indications for surgical treatment | None | **Primary:** ABC adherence |
| Retrospective – post-hoc |
| Proietti (2018, 2020), US and Canada21,22 | AFFIRM | Retrospective analysis of RCT comparing rate vs. rhythm control and OAC.; 200 sites in US and Canada, a 3169, b 70 [65-76], c 1237 (39.0%), d NR, e 3 [2-4], f Not reported | **Inclusion criteria:** On VKA - warfarin, Documented AF within last 6 weeks, Aged ≥65 years, or <65 years with ≥1 risk factor for stroke, AF episodes in last 6 months totaling ≥6 hrs, unless cardioversion within 6 hrs, Continuous AF <6 months, unless SR restored and maintained ≥24 hours, Eligible for rate and rhythm control, Eligible for ≥2 AADs (or 2 dose levels of amiodarone) and ≥2 rate-control drugs | 3.7 [2.8-4.6] | **Primary:** ACM, Composite: stroke/ major bleeding/CV mortality, hospitalization **Secondary:** Stroke, Major bleeding, CV mortality, CV hospitalization, Recurrent hospitalization, Total hospitalizations, Length of stay for first hospitalization, Total length of stay |
| Pastori (2019), Italy19 | ATHERO-AF | Single-center cohort study in Rome, Feb 2008 to Dec 2016; Retrospective analysis on prospective observational study, a 882, b 73.1±8.5, c 40.8%, d Not reported, e 3.50 ± 1.5, f Not reported | **Inclusion criteria:** ≥18 years old, AF, All patients on warfarin after risk stratification: CHA2DS2-VASc for men/women: 0/1 – maybe aspirin but no OAC, 1/2 maybe aspirin but preferably OAC, 2+/3+ OAC **Exclusion criteria:** Prosthetic heart valves or severe valvulopathies, Severe cognitive impairment, Chronic infections (HIV, hepatitis B or C), Systemic autoimmune disease, Active cancer, Liver insufficiency (e.g., cirrhosis)  | 36.9 [20.0-57.5] months | **Primary:** CV events |
| Retrospective – Registry or Electronic health records |
| Yoon (2019), South Korea14 | Korea National Health Insurance Service database | National cohort; Data from 2005 to 2015; Retrospective analysis, a 204842, b ABC: 52.9 ± 12.2 non-ABC: 64.9 ± 10.8, c ABC: 10129 (32.0%) non-ABC: 66778 (38.6%), d Not reported, e ABC: 0.91 ± 1.39 non-ABC: 2.97 ± 1.80, f Not reported | **Inclusion criteria:** Adult, Non-valvular AF, Baseline health check-up data within the year before enrolment, AF outpatient clinic visit during the follow-up period | 6.2 ± 3.5 years | **Primary:** ACM, Ischemic stroke, Major bleeding, Myocardial Infarction, Composite of other 4 outcomes |
| Proietti (2020) ESC-EHRA, Europe20 | ESC-EORP Atrial Fibrillation General Long-Term Registry | Multicenter observational registry held by the ESC and endorsed by the European Heart Rhythm Association (EHRA), a 9663, b ABC: 70 [61-76] non-ABC: 69 [61-76], c ABC: 741 (37.1%), non-ABC: 1926 (41.4%), d Not reported, e ABC: 2.68 ± 1.57; 3 [2-4] non-ABC: 3.07 ± 1.90; 3 [2-4], f ABC: 1.58 ± 1.12; 2 [1-2] non-ABC: 1.26 ± 0.93; 1 [1-2] | **Inclusion criteria:** ≥ 18 years old, AF documented within 12 months before enrolment based on objective electrocardiographic evaluation | 12 months | **Primary:** Composite: TE, ACS, CV mortality, CV mortality, ACM, Stroke, Any TE , Bleeding events, ICH, Any readmission, Any AF readmission, Any CV readmission, ACS |
| Yang (2020) Dementia, South Korea23 | Korea National Health Insurance Service database | National cohort; Data from 2005 to 2015, a 228026, b ABC: 68.8 ± 10.2 non-ABC: 69.7 ± 11.6, c ABC: 18016 (39.2%) non-ABC: 70218 (38.6%), d Not reported, e ABC: 0 [0-1] non-ABC: 2 [1-3], f ABC: 0 [0-1] non-ABC: 2 [1-3] | **Inclusion criteria:** ≥18 years old, Non-valvular AF, Have baseline health check-up data within the year before enrolment **Exclusion criteria:** Patients who had an ischemic stroke, Patients with a history of dementia, Patients with an ischemic stroke during the follow-up period | 6.0 [3.3-9.5] years | **Primary:** Dementia, **Secondary:** Alzheimer’s disease, Vascular dementia |
| Yang (2020) Frailty, South Korea13 | Korea National Health Insurance Service database | National cohort; Data from 2005 to 2015, a 262,987, b ABC: 50 [41, 58] non-ABC: 65 [56,72], c ABC: 39.4%, non-ABC: 38.6%, d Not reported, e ABC: 0 [0-1], non-ABC: 2 [1-3], f ABC: 0 [0-1], non-ABC: 2 [1-3] | **Inclusion criteria:** ≥18 years old, Non-valvular AF, Have baseline health check-up data within the year before enrolment **Exclusion criteria:** Patients who had an ischemic stroke | Mean 5.9 IQR [3.2, 9.4] | **Primary:** ACM, Ischemic stroke, Heart failure admission, Myocardial infarction, Major bleeding, Composite of other 5 outcomes |

Abbreviations: AADs – Anti-arrhythmic drugs, ABC – Atrial Fibrillation Better Care, ACM – All-cause mortality, ACS – Acute Coronary Syndrome, AF – Atrial Fibrillation, CV – Cardiovascular, ED – Emergency Department, EHRA - European Heart Rhythm Association, ESC – European Society of Cardiology, ICH – Intra-cranial hemorrhage, mAFA – mobile AF-App, RCT - randomized controlled trial, TE – Thromboembolism, UC – Usual Care

**Table 2.** Summary of criteria used by the included studies to define the A, B and C criteria of the Atrial fibrillation Better Care (ABC) pathway **10**

|  | Components of the Atrial fibrillation Better Care (ABC) pathway and definitions utilized |
| --- | --- |
| First author, year, country | Anticoagulation ‘A’ | Better symptom management ‘B’ | Cardiovascular and co-morbidity management ‘C’ |
| Prospective |
| Domek (2020) 15 | All high risk so OAC | EHRA classes I-II considered adherent | According to 2016 ESC AF guidelines 26: **Hypertension:** Controlled - < 140/90 mm Hg, **HF:** ACEi/ARB or BB, **PAD:** Statins or ACEi/ARB, **CAD:** Statins or ACEi/ARB, **Stroke/TIA:** Statins |
| Gumprecht (2020) 16 | CHA2DS2-VASc for men/women 0/1: no OAC, 1+/2+: OAC | EHRA classes I-II considered adherent | According to 2016 ESC AF guidelines 26: **Hypertension:** Controlled - < 140/90 mm Hg, **HF:** ACEi or ARB along with BB, digoxin and diuretic, **PAD:** Statins or ACEi/ARB, **CAD:** ACEi or ARB along with BB, aspirin or clopidogrel and LL drugs, **Stroke/TIA:** Withdraw OAC for short period depending on stroke severity and consider switching OAC if stroke while on OAC, **Diabetes:** Diet, Insulin therapy, oral antidiabetic drugs |
| Guo (2020) 1 year and extension 17,18 | CHA2DS2-VASc > 2/3 for men/women: OAC. If on Warfarin: weekly INR until stable and then monthly. Mean TiTR of 65% defined as good control | Evaluated using EHRA classification | **Hypertension:** <140/85mm Hg or ideally 130/80 mm Hg., **Vascular disease:** Statins, **Educational materials:** Hypertension, Heart failure, Acute Coronary Syndrome (ACS), Valvular disease, self-care |
| Koziel (2020) 12 | CHA2DS2-VASc for men/women: 0/1 no OAC, 1+/2+: OAC. Antiplatelet therapy should not be used concomitantly without clinical indications | EHRA classes II-IV considered adherent with rate or rhythm control strategy. EHRA class I not considered non- adherent but included in non-ABC adherent group | **Hypertension:** Treated ≥ 140/90 mm Hg ACEi, AT1 receptor antagonist, CCB, BB, thiazide diuretic 27, **HF:** ACEi, AT1 receptor antagonist, BB, thiazide diuretic, spironolactone, loop diuretic 28, **CAD:** ACEi, AT1 receptor antagonist, CCB, BB, aspirin, statins, other LL drugs 29, **Diabetes:** Lifestyle modifications, insulin therapy, oral antidiabetic drugs 30 |
| Retrospective – post hoc |
| Proietti (2018, 2020) 21,22 | All patients on warfarin (cohort only includes those ≥ 65 years or with ≥1 risk factors for stroke). TiTR >70%  | ≤2 symptoms from: chest pain, diaphoresis, diuresis, dizziness, dyspnea, oedema, fast heart rate, fatigue, orthopnea, palpitations, panic, paroxysmal nocturnal dyspnea, syncope, plus other symptoms | According to 2016 ESC guidelines 31: **Hypertension:** Treated appropriately, <140/90mm Hg, **HF:** ACEi + BB + diuretic, **PAD:** ACEi + LL drugs, **CAD:** ACEi + BB + LL drugs, **Stroke/TIA:** LL drugs |
| Pastori (2019) 19 | CHA2DS2-VASc for men/women: 0/1 no OAC, 1/2 preferably OAC maybe aspirin, 2+/3 OAC. Warfarin used exclusively with TiTR > 65% over last year calculated by the Rosendaal method | EHRA classes I-II considered adherent | **Hypertension:** Active management of ≥160/90 mm Hg with ARB, ACEi, BB or mineralocorticoid receptor antagonist 32, **HF:** ACEi or ARB along with BB along with further considerations 33, **Diabetes:** Lifestyle modification, glucose control, insulin and metformin first line therapy for T1D and T2D respectively 34 |
| Retrospective – Registry or Electronic health records |
| Yoon (2019) 14 | Use of OACs in accordance with the guidelines with high adherence (prescription covering >80% of days) - Does not reference which guidelines | < 5 outpatient visits per year considered adherent | According to unspecified guidelines: **Hypertension:** Controlled <140/90mm Hg, **HF:** ACEi or ARB along with BB, **MI:** ACEi or ARB along with BB and LL drugs, **PAD:** LL drugs, **Diabetes:** Oral anti-diabetics or insulin, **Obesity:** BMI < 30 kg/m^2 |
| Proietti (2020) ESC-EHRA 20 | CHA2DS2-VASc for men/women: 0/1 no OAC, 1+/2+: OAC | EHRA classes I-II considered adherent | **Hypertension:** ≤ 140/90 mm Hg, **CAD:** ACEi, BB and statins, **PAD:** statins, **Previous stroke/TIA:** statins, **HF:** ACEi/ARB and BB, **Diabetes:** Insulin or oral antidiabetics |
| Yang (2020) Frailty and Dementia 13,23  | CHA2DS2-VASc for men/women: 0/1 no OAC, 1+/2+ OAC with prescription covering 80% of days | < 5 visits per year considered adherent | According to 2016 ESC AF guidelines 26: **Hypertension:** Controlled <140/90 mm Hg, **MI:** Initially short period of triple therapy (OAC, aspirin and clopidogrel) reducing to double (OAC and aspirin or clopidogrel), **HF:** ACEi or ARB along with BB, digoxin and diuretic, **PAD:** Statins or ACEi/ARB, **Stroke/TIA:** Withdraw OAC for short period depending on stroke severity and consider switching OAC if stroke while on OAC, **Diabetes:** Diet, Insulin therapy, oral antidiabetic drugs, **Obesity:** BMI < 30 kg/m^2 |

Abbreviations: ABC – Atrial Fibrillation Better Care, ACEi - Angiotensin-converting-enzyme inhibitors, AF – Atrial Fibrillation, ARB - Angiotensin Receptor Blockers, BB – Beta Blocker, BMI – Body Mass Index, CAD – Coronary Artery Disease, ESC – European Society of Cardiology, EHRA – European Heart Rhythm Association, HF – Heart Failure, LL, MI – Myocardial Infarction, OAC – Oral Anticoagulant, PAD – Peripheral Artery Disease, TIA – Transient Ischemic Attack, TiTR – Time in Therapeutic Range

**Table 3**. Summary of baseline characteristics by ABC adherence status for the selected studies

| Paper | Grouped and overall | N (%) | Mean ± SD or Median [IQR] Age | Women (%) | Hypertension (%) | Mean ± SD or Median [IQR] CHA2DS2-VASc  |
| --- | --- | --- | --- | --- | --- | --- |
| Prospective |
| Domek (2020) 15 | **ABC:** | 86 (14.3%) | 64.8 ± 10.8 | 44 (51.2%) | 69 (80.2%) | 3.60 ± 1.27 |
|  | **Non-ABC:** | 517 (85.7%) | 63.2 ± 11.9 | 271 (52.4%) | 421 (81.4%) | 3.70 ± 1.63 |
|  | **All:** | 603 | 63.4 ± 11.8 | 315 (52.2%) | 490 (81.3%) | 3.69 ± 1.58 |
| Gumprecht (2020) 16 | **ABC:** | 168 (8.3%) | 64.5 ± 12.0  | 77 (45.7%)  | 117 (69.6%)  | 3.01 ± 1.53  |
|  | **Non-ABC:** | 1853 (91.7%) | 56.0 ± 16.7 | 891 (48.1%) | 948 (51.2%) | 2.28 ± 1.79 |
|  | **All:** | 2021 | 56.7 ± 16.47 | 968 (47.9%) | 1065 (52.7%) | 2.34 ± 1.78 |
| Guo (2020) 1 year 18 | **mAFA:** | 1646 (49.5%) | 67.0 ± 15.0 | 625 (38.0%) | 908 (55.2%) | 3 [2-4] |
|  | **Usual Care:** | 1678 (50.5%) | 70.0 ± 12.0 | 637 (38.0%) | 962 (57.3%) | 3 [2-4] |
|  | **All:** | 3324 | Not reported | 1262 | 1870 (56.3%) | Not reported |
| Guo (2020) Extension 17 | **mAFA:** | 1261 (51.0%) | 67.8 ± 15.4 | 34.1% | 797 (63.2%) | 3 [2-4] |
|  | **Usual Care:** | 1212 (49.0%) | 70.1 ± 12.0 | 42.1% | 776 (64.0%) | 3 [2-4] |
|  | **All:** | 2473 | Not reported | Not reported | Not reported | Not reported |
| Koziel (2020) 12 | **ABC:** | 1013 (43.8%) | 49 [41-57]  | 485 (47.9%)  | 898 (88.6%)  | 3.4 ± 1.8  |
|  | **Non-ABC:** | 1299 (56.2%) | 64 [55-71] | 557 (42.9%) | 882 (67.9%) | 3.4 ± 1.9 |
|  | **All:** | 2712 | Not reported | Not reported | Not reported | Not reported |
| Retrospective – post hoc |
| Proietti (2018, 2020) 21,22 | **ABC:** | 222 (7.0%) | 70 [65-75] | 60 (27.0%)  | 141 (63.5%)  | 3 [2-4]  |
|  | **Non-ABC:** | 2947 (93.0%) | 70 [65-76] | 1177 (39.9%) | 2102 (71.3%) | 2 [1-3] |
|  | **All:** | 3169 | 70 [65-76] | 1237 (39.0%) | 2243 (70.8%) | 3 [2-4] |
| Pastori (2019) 19 | **ABC:** | 198 (22.4%) | 71.7±9.0 | 48.2%  | 85.6%  | 2.56 ± 1.1  |
|  | **Non-ABC:** | 684 (77.6%) | 73.5±8.3 | 38.7% | 89.3% | 3.7 ± 1.5 |
|  | **All:** | 882 | 73.1±8.5 | 40.8% | 88.5% | 3.50 ± 1.5 |
| Retrospective – Registry or electronic health records |
| Yoon (2019) 14 | **ABC:** | 31674 (15.5%) | 52.9 ± 12.2 | 10129 (32.0%) | 5708 (18.0%) | 0.91 ± 1.39 |
|  | **Non-ABC:** | 173168 (84.5%) | 64.9 ± 10.8 | 66778 (38.6%) | 139411 (80.5%) | 2.97 ± 1.80 |
|  | **All:** | 204842 | Not reported | Not reported | Not reported | Not reported |
| Proietti (2020) ESC-EHRA 20 | **ABC:** | 1996 (30.0%) | 70 [61-76] | 741 (37.1%)  | 1184 (59.7%)  | 2.68 ± 1.57; 3 [2-4] |
|  | **Non-ABC:** | 4650 (70.0%) | 69 [61-76] | 1926 (41.4%) | 2693 (58.5%) | 3.07 ± 1.90; 3 [2-4] |
|  | **All:** | 6646 | Not reported | Not reported | Not reported | Not reported |
| Yang (2020) Dementia 23 | **ABC:** | 45994 (20.2%) | 68.8 ± 10.2  | 18016 (39.2%)  | 2425 (5.3%)  | 0 [0-1]  |
|  | **Non-ABC:** | 182052 (79.8%) | 69.7 ± 11.6 | 70218 (38.6%) | 117688 (64.7%) | 2 [1-3] |
|  | **All:** | 228026 | Not reported | Not reported | Not reported | Not reported |
| Yang (2020) Frailty 13 | **ABC:** | 49,533 (18.8%) | 50 [41, 58]  | 39.4% | 7.0%  | 0 [0-1]  |
|  | **Non-ABC:** | 213,454 (81.1%) | 65 [56,72] | 38.6% | 65.5% | 2 [1-3] |
|  | **All:** | 262,987 | Not reported | Not reported | Not reported | Not reported |

Abbreviations: ABC – Atrial Fibrillation Better Care, AF – Atrial Fibrillation, EHRA - European Heart Rhythm Association, ESC – European Society of Cardiology, mAFA – mobile AF-App

**Table 4.** Summary of the results and analysis by outcome among the included studies

| First author, year | Outcome | Adjustment variables | Adjusted Hazard Ratio/Odds Ratio |
| --- | --- | --- | --- |
| Prospective |
| Domek (2020) 15 | All-cause mortality | AF type, Renal dysfunction, Dyslipidemia, Aspirin use, Major bleeding | **ABC vs non-ABC at 6 months:** OR 0.18 (0.04-0.75) **ABC vs non-ABC at 1 year:** OR 0.29 (0.11-0.76) **AB vs non-ABC at 1 year:** OR 0.73 (0.44-1.19) **AC vs non-ABC at 1 year:** OR 0.72 (0.38-1.36) **BC vs non-ABC at 1 year:** OR 0.53 (0.28-1.01) |
|  | Composite: Stroke/systemic embolism, All-cause mortality, CV hospitalization |  | **ABC vs non-ABC at 6 months:** OR 0.54 (0.30-1.00) **ABC vs non-ABC at 1 year:** OR 0.57 (0.33-0.97) **AB vs non-ABC at 1 year:** OR 0.78 (0.54-1.12) **AC vs non-ABC at 1 year:** OR 1.15 (0.74-1.77) **BC vs non-ABC at 1 year:** OR 0.58 (0.37-0.91) |
| Gumprecht (2020) 16 | All-cause mortality | AF type, Renal dysfunction, Dyslipidemia, Aspirin use, Major bleeding | **ABC vs non-ABC at 6 months:** OR 0.31 (0.13-0.77) **ABC vs non-ABC at 1 year:** OR 0.46 (0.25-0.86) **Standard care vs AB vs BC vs AC at 1 year:** AB: OR 0.78 (0.58-1.06), AC: OR 0.95 (0.62-1.46), BC: OR 0.73 (0.47-1.13) |
|  | Composite: Ischemic stroke or systemic embolism, All-cause mortality, and CV hospitalization |  | **ABC vs non-ABC at 6 months:** OR 0.49 (0.31-0.79) **ABC vs non-ABC at 1 year:** OR 0.53 (0.36-0.80) **Standard care vs AB vs BC vs AC at 1 year:** AB: OR 0.75 (0.61-0.92), AC: OR 1.00 (0.74-1.36), BC: OR 0.68 (0.50-0.92) |
| Guo (2020) 1 year 18 | Composite: Stroke/ thromboembolism, All-cause mortality, and Re-hospitalization | Age, Sex, AF type, Prior AF rhythm control, hypertension, diabetes, CAD, OSA, HF, hyperthyroidism, ischemic stroke, dilated cardiomyopathy, HOCM | **mAFA vs Usual Care:** Overall: HR 0.39 (0.22-0.67), Female: HR 0.48 (0.22-1.04, Male: HR 0.34 (0.18-0.67), Age <75 years: HR 0.17 (0.08-0.36), Age ≥75 years: HR 0.63 (0.29-1.38), Paroxysmal AF: HR 0.49 (0.25-0.94), Persistent and permanent AF: HR 0.40 (0.17-0.94), CHA2DS2-VASc ≥2 in males, ≥3 in females: HR 0.57 (0.31-1.03), CHA2DS2-VASc 0-1 in males or 1-2 in females: HR 0.04 (0.01-0.27), HAS-BLED ≥3: HR 0.86 (0.35-2.16), HAS-BLED 0-2: HR 0.21 (0.12-0.37), Hypertension: HR 0.52 (0.26-1.03), No Hypertension: HR 0.11 (0.03-0.36), CAD: HR 0.53 (0.26-1.11), No CAD: HR 0.22 (0.11-0.44) |
|  | Re-hospitalization |  | **mAFA vs Usual Care:** Overall: HR 0.32 (0.17-0.60), Female: HR 0.27 (0.10-0.72, Male: HR 0.31 (0.15-0.64), Age <75 years: HR 0.17 (0.07-0.40), Age ≥75 years: HR 0.46 (0.19-1.12), Paroxysmal AF: HR 0.43 (0.19-0.94), Persistent and permanent AF: HR 0.34 (0.13-0.86), CHA2DS2-VASc ≥2 in males, ≥3 in females: HR 0.41 (0.21-0.80), CHA2DS2-VASc 0-1 in males or 1-2 in females: HR 0.07 (0.01-0.55), HAS-BLED ≥3: HR 0.78 (0.24-2.56), HAS-BLED 0-2: HR 0.18 (0.09-0.38), Hypertension: HR 0.33 (0.15-0.75), No Hypertension: HR 0.17 (0.05-0.58), CAD: HR 0.45 (0.21-1.00), No CAD: HR 0.13 (0.04-0.38) |
|  | Ischemic stroke |  | **mAFA vs Usual Care:** HR 1.31 (0.18-9.31) |
|  | Other thromboembolism |  | **mAFA vs Usual Care:** HR 1.02 (0.18-5.93) |
|  | Extracranial bleeding |  | **mAFA vs Usual Care:** HR 0.95 (0.54-1.66) |
|  | Recurrent AF or AF symptoms |  | **mAFA vs Usual Care:** HR 0.48 (0.29-0.79) |
|  | Heart failure |  | **mAFA vs Usual Care:** HR 0.99 (0.51-1.92) |
|  | Acute coronary syndrome |  | **mAFA vs Usual Care:** HR 0.21 (0.04-1.21) |
|  | All-cause mortality |  | **mAFA vs Usual Care:** HR 0.71 (0.26-1.91) |
| Guo (2020) Extension 17 | Composite: Stroke/ thromboembolism, All-cause mortality, and Re-hospitalization | Cluster effect, Age, Sex, CAD, Diabetes mellitus, Heart failure, PAD, Pulmonary disease, a Dilated cardiomyopathy, Prior ischemic stroke, thromboembolism, intracranial bleeding, other bleeding, Liver/renal dysfunction | **mAFA vs Usual Care:** HR 0.18 (0.13-0.25) |
|  | Ischemic stroke |  | **mAFA vs Usual Care:** HR 0.11 (0.05-0.27) |
|  | Other thromboembolism |  | **mAFA vs Usual Care:** HR 0.29 (0.09-0.94) |
|  | Extracranial bleeding |  | **mAFA vs Usual Care:** HR 0.37 (0.20-0.70) |
|  | Recurrent AF or AF symptoms |  | **mAFA vs Usual Care:** HR 0.33 (0.23-0.48) |
|  | Heart failure |  | **mAFA vs Usual Care:** HR 0.11 (0.24-0.66) |
|  | Re-hospitalization |  | **mAFA vs Usual Care:** HR 0.69 (0.49-0.97) |
|  | All-cause mortality |  | **mAFA vs Usual Care:** HR 0.94 (0.39-2.23) |
| Retrospective – post hoc |
| Proietti (2018) 21 | All-cause mortality | Age, Sex, Diabetes, Hepatic/renal disease, Pulmonary disease, First AF episode, Aspirin use | **ABC vs non-ABC:** HR 0.35 (0.17-0.75) **Standard care vs AB vs BC vs AC vs ABC:** AB: HR 0.72 (0.48-1.08), BC: HR 0.64 (0.37-1.09), AC: HR 0.42 (0.24-0.76), ABC: HR 0.31 (0.15-0.67) **0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.70 (0.55-0.90), 2 criteria: HR 0.49 (0.35-0.67), 3 criteria: HR 0.25 (0.12-0.55) |
|  | Composite: Stroke, Major bleeding, CV mortality and first hospitalization |  | **ABC vs non-ABC:** HR 0.35 (0.18-0.68) **Standard care vs AB vs BC vs AC vs ABC:** AB: HR 0.75 (0.53-1.07), BC: HR 0.68 (0.43-1.09), AC: HR 0.68 (0.43-1.09), ABC: HR 0.32 (0.16-0.62) **0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.73 (0.59-0.91), 2 criteria: HR 0.54 (0.40-0.71), 3 criteria: HR 0.26 (0.13-0.52) |
|  | Stroke |  | **ABC vs non-ABC:** HR 0.90 (0.39-2.06) |
|  | Major bleeding |  | **ABC vs non-ABC:** HR 0.26 (0.08-0.81) |
|  | CV mortality |  | **ABC vs non-ABC:** HR 0.17 (0.04-0.70) |
|  | First hospitalization |  | **ABC vs non-ABC:** HR 0.65 (0.53-0.80) |
|  | First CV hospitalization |  | **ABC vs non-ABC:** HR 0.57 (0.43-0.77) |
|  | Multiple hospitalizations |  | **ABC vs non-ABC:** OR 0.38 (0.26-0.56) |
|  | Total hospitalizations |  | **ABC vs non-ABC:** Beta **-**0.098 |
|  | Length of first hospital stay |  | **ABC vs non-ABC:** Beta -0.034 |
|  | Total length of all hospital stays |  | **ABC vs non-ABC:** Beta -0.061 |
| Pastori (2019) 19 | Composite of CV events including: Fatal/non-fatal ischemic stroke, MI, TIA, cardiac revascularization (stent placement or coronary artery bypass), and cardiovascular mortality | Age ≥75yrs, Sex, Paroxysmal AF | **ABC vs non-ABC:** HR0.44 (0.24-0.80) |
| Proietti (2020) 22 | Composite: All-cause hospitalization, All-cause mortality | Age, Sex, first AF episode **For Multimorbidity subgroup:** Aspirin use **For Polypharmacy subgroup:** Diabetes, Hepatic/renal disease, Pulmonary disease **For Hospitalization subgroup:** Diabetes, Hepatic/renal disease, Pulmonary disease, Aspirin use | **Multimorbidity subgroup ABC vs non-ABC:** HR 0.61 (0.44–0.85) **Polypharmacy subgroup ABC vs non-ABC:** HR 0.68 (0.47–1.00) **Hospitalization** **subgroup ABC vs non-ABC:** HR 0.59 (0.42–0.85) **Multimorbidity subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.73 (0.64-0.83), 2 criteria: HR 0.57 (0.49-0.82), 3 criteria: HR 0.47 (0.33-0.66) **Polypharmacy subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.70 (0.60-0.82), 2 criteria: HR 0.57 (0.47-0.69), 3 criteria: HR 0.51 (0.35-0.76) **Hospitalization** **subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.70 (0.60-0.81), 2 criteria: HR 0.64 (0.53-0.77), 3 criteria: HR 0.45 (0.31-0.65) |
|  | All-cause mortality |  | **Multimorbidity subgroup ABC vs non-ABC:** HR 0.23 (0.06–0.94) **Polypharmacy subgroup ABC vs non-ABC:** HR 0.49 (0.16–1.54) **Hospitalization** **subgroup ABC vs non-ABC:** HR 0.49 (0.18–1.33) **Multimorbidity subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.78 (0.59-1.02), 2 criteria: HR 0.50 (0.33-0.75), 3 criteria: HR 0.18 (0.05-0.75) **Polypharmacy subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.68 (0.48-0.94), 2 criteria: HR 0.51 (0.31-0.83), 3 criteria: HR 0.37 (0.12-1.18) **Hospitalization** **subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.61 (0.44-0.85), 2 criteria: HR 0.49 (0.31-0.76), 3 criteria: HR 0.36 (0.13-0.97) |
|  | Hospitalization |  | **Multimorbidity subgroup ABC vs non-ABC:** HR 0.62 (0.45–0.87) **Polypharmacy subgroup ABC vs non-ABC:** HR 0.69 (0.46–1.01) **Hospitalization** **subgroup ABC vs non-ABC:** HR 0.58 (0.40–0.84) **Multimorbidity subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.72 (0.63-0.82), 2 criteria: HR 0.57 (0.48-0.68), 3 criteria: HR 0.48 (0.34-0.67) **Polypharmacy subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.70 (0.60-0.82), 2 criteria: HR 0.57 (0.47-0.70), 3 criteria: HR 0.51 (0.35-0.76) **Hospitalization** **subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.70 (0.60-0.81), 2 criteria: HR 0.63 (0.53-0.76), 3 criteria: HR 0.44 (0.30-0.64) |
|  | CV events |  | **Multimorbidity subgroup ABC vs non-ABC:** HR 0.54 (0.35–0.84) **Polypharmacy subgroup ABC vs non-ABC:** HR 0.67 (0.41–1.08) **Hospitalization** **subgroup ABC vs non-ABC:** HR 0.48 (0.30–0.77) **Multimorbidity subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.71 (0.61-0.83), 2 criteria: HR 0.67 (0.55-0.81), 3 criteria: HR 0.43 (0.27-0.67) **Polypharmacy subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.61 (0.51-0.73), 2 criteria: HR 0.64 (0.51-0.79), 3 criteria: HR 0.49 (0.30-0.80)**Hospitalization** **subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.73 (0.61-0.87), 2 criteria: HR 0.75 (0.60-0.92), 3 criteria: HR 0.39 (0.24-0.63) |
|  | Any event |  | **Multimorbidity subgroup ABC vs non-ABC:** HR 0.60 (0.43–0.84) **Polypharmacy subgroup ABC vs non-ABC:** HR 0.68 (0.46–0.99) **Hospitalization** **subgroup ABC vs non-ABC:** HR 0.59 (0.41–0.84) **Multimorbidity subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.73 (0.64-0.83), 2 criteria: HR 0.59 (0.50-0.69), 3 criteria: HR 0.47 (0.33-0.65) **Polypharmacy subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.71 (0.61-0.82), 2 criteria: HR 0.58 (0.47-0.70), 3 criteria: HR 0.51 (0.34-0.75) **Hospitalization** **subgroup 0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.69 (0.60-0.80), 2 criteria: HR 0.66 (0.55-0.79), 3 criteria: HR 0.45 (0.45-0.64)  |
| Retrospective – Registry or electronic health records |
| Proietti (2020) ESC-EHRA 20 | Composite: Thromboembolism, Acute Coronary Syndrome, CV mortality | Type of AF, CHA2DS2-VASc score factors | **ABC vs non-ABC at 1 year:** OR 0.48 (0.37-0.62) |
|  | Stroke |  | **ABC vs non-ABC at 1 year:** OR 0.78 (0.40-1.50) |
|  | Any thromboembolism |  | **ABC vs non-ABC at 1 year:** OR 0.60 (0.36-1.02) |
|  | CV mortality |  | **ABC vs non-ABC at 1 year:** OR 0.38 (0.27-0.54) |
|  | All-cause mortality |  | **ABC vs non-ABC at 1 year:** OR 0.45 (0.34-0.59) |
|  | Acute coronary syndrome |  | **ABC vs non-ABC at 1 year:** OR 0.68 (0.42-1.10) |
|  | Any readmission |  | **ABC vs non-ABC at 1 year:** OR 0.80 (0.71-0.91) |
|  | Any AF readmission |  | **ABC vs non-ABC at 1 year:** OR 0.86 (0.72-1.02) |
|  | Any CV readmission |  | **ABC vs non-ABC at 1 year:** OR 0.81 (0.71-0.93) |
|  | Composite: Thromboembolism, Acute Coronary Syndrome, CV mortality |  | **ABC vs non-ABC:** HR 0.59 (0.44-0.79) **0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.68 (0.44-1.10), 2 criteria: HR 0.46 (0.29-0.74), 3 criteria: HR 0.31 (0.19-0.52) |
|  | CV mortality |  | **ABC vs non-ABC:** HR 0.52 (0.35-0.78) **0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.60 (0.33-0.94), 2 criteria: HR 0.40 (0.24-0.66), 3 criteria: HR 0.25 (0.14-0.45) |
|  | All-cause mortality |  | **ABC vs non-ABC:** HR 0.57 (0.43-0.78) **0 vs 1 vs 2 vs 3 criteria fulfilled:** 1 criteria: HR 0.69 (0.42-1.14), 2 criteria: HR 0.47 (0.29-0.76), 3 criteria: HR 0.32 (0.18-0.54) |
|  | Hemorrhagic Events | Type of AF, HAS-BLED score factors | **ABC vs non-ABC at 1 year:** OR 0.78 (0.40-1.50) |
|  | Intracranial Hemorrhage | Type of AF, HAS-BLED score factors, Sex | **ABC vs non-ABC at 1 year:** OR 0.64 (0.18-2.27) |
| Yoon (2019) 14 | All-cause mortality | Age, Sex, HF, Hypertension, Diabetes, Previous ischemic stroke/TIA | **ABC vs non-ABC:** HR 0.82 (0.78-0.86) **Number of ABC criteria fulfilled with 0 baseline:** 1 criteria: HR 0.91 (0.88-0.94), 2 criteria: HR 0.86 (0.84-0.89), 3 criteria: HR 0.80 (0.77-0.84) |
|  | Composite: Mortality, Ischemic stroke, Major bleeding, Myocardial Infarction |  | **ABC vs non-ABC:** HR 0.86 (0.83-0.89) **Number of ABC criteria fulfilled with 0 baseline:** 1 criteria: HR 0.73 (0.70-0.75), 2 criteria: HR 0.63 (0.60-0.65), 3 criteria: HR 0.57 (0.53-0.60) |
|  | Ischemic stroke |  | **ABC vs non-ABC:** HR 0.86 (0.82-0.91) |
|  | Major bleeding |  | **ABC vs non-ABC:** HR 0.89 (0.84-0.94) |
|  | Myocardial infarction |  | **ABC vs non-ABC:** HR 0.82 (0.72-0.90) |
| Yang (2020) Dementia 23 | Dementia | Age, Sex, HF, Hypertension, Diabetes mellitus, Previous MI, PAD, Economic status, CHA2DS2-VASc, HAS-BLED | **ABC vs non-ABC:** Overall: HR 0.80 (0.73–0.87), Female: HR 0.75 (0.66-0.86), Male: HR 0.84 (0.74-0.95), Non Heart failure: HR 0.84 (0.76-0.93), Heart failure: HR 0.63 (0.45-0.87), Non-Hypertension: HR 0.87 (0.77-0.97), Hypertension: HR 0.93 (0.86-1.01), Non-diabetes mellitus: HR 0.83 (0.75-0.91), Diabetes mellitus: HR 0.62 (0.45-0.86), CHA2DS2-VASc 0-1: HR 1.06 (0.90-1.24), CHA2DS2-VASc ≥2: HR 0.80 (0.69-0.93), Non-AF RFCA: HR 0.79 (0.72-0.87), AF RFCA: HR 1.40 (0.51-3.83), Age ≥ 70: HR 0.82 (0.69–0.98), Age 60-70: HR 0.93 (0.81–1.08), Age 50-60: HR 1.05 (0.84–1.30), Age <50: HR 0.94 (0.58–1.54) |
|  | Alzheimer’s Dementia |  | **ABC vs non-ABC:** HR 0.79 (0.71–0.88) |
|  | Vascular Dementia |  | **ABC vs non-ABC:** HR 0.76 (0.59–0.98) |
| Yang (2020) Frailty 13 | All-cause mortality |  | **ABC vs non-ABC:** Overall: HR 0.93 (0.90-0.97), Low frailty: HR 0.95 (0.91-0.99), Intermediate frailty: HR 0.89 (0.82-0.97), High frailty: HR 0.74 (0.56-0.97) |
|  | Ischemic stroke |  | **ABC vs non-ABC:** Overall: HR 0.86 (0.82-0.91), Low frailty: HR 0.88 (0.83-0.93), Intermediate frailty: HR 0.75 (0.62-0.92), High frailty: HR 1.03 (0.72-1.49) |
|  | Heart failure admission |  | **ABC vs non-ABC:** Overall: HR 0.84 (0.79-0.89), Low frailty: HR 0.84 (0.79-0.89), Intermediate frailty: HR 0.81 (0.68-0.95), High frailty: HR 0.89 (0.61-1.56) |
|  | Acute Myocardial Infarction |  | **ABC vs non-ABC:** Overall: HR 0.76 (0.69-0.83), Low frailty: HR 0.77 (0.69-0.85), Intermediate frailty: HR 0.72 (0.56-0.94), High frailty: HR 0.69 (0.32-1.47) |
|  | Major bleeding |  | **ABC vs non-ABC:** Overall: HR 0.99 (0.95-1.02), Low frailty: HR 1.04 (0.96-1.09), Intermediate frailty: HR 0.83 (0.75-0.91), High frailty: HR 0.72 (0.54-0.96) |
|  | Composite: All-cause mortality, Ischemic stroke, Heart failure admission, Acute Myocardial Infarction, Major bleeding |  | **ABC vs non-ABC:** Overall: HR 0.93 (0.90-0.97), Low frailty: HR 0.95 (0.91-0.99), Intermediate frailty: HR 0.89 (0.82-0.97), High frailty: HR 0.74 (0.56-0.97) |

Abbreviations: ABC – Atrial Fibrillation Better Care, AF – Atrial Fibrillation, CAD – coronary artery disease; CV - Cardiovascular, ESC – European Society of Cardiology, EHRA – European Heart Rhythm Association, HOCM -hypertrophic cardiomyopathy, HR – Hazard Ratio, mAFA – mobile AF-App, MI – Myocardial Infarction, OR – Odds Ratio, OSA – Obstructive Sleep Apnea, PAD – Peripheral Artery Disease, RFCA - radio frequency catheter ablation, TIA – transient ischemic attack

a Pulmonary disease includes chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, and pulmonary hypertension

**The Atrial Fibrillation Better Care (ABC) pathway** for integrated care management

**‘A’ Avoid stroke**

Optimize stroke prevention

**‘B’ Better symptom management**

Treat symptoms

**‘C’ Cardiovascular and other comorbidities**

Manage risk factors

Birmingham 3-step

**Step 1**

Identify low-risk patients

**Step 2**

* Offer stroke prevention to patients with one or more risk factors for stroke
* Assess bleeding risk

**Step 3**

Decide on OAC (either a VKA with well-managed TTR or a NOAC)

Patient-centered and symptom-directed decisions on rate versus rhythm control

* Manage hypertension, heart failure, diabetes mellitus, cardiac ischemia, and sleep apnea
* Lifestyle changes: obesity reduction, regular exercise, and reduction of alcohol and stimulant use
* Patient psychological morbidity
* Consider patient values and preferences

Figure 1: Flowchart of the steps in the Atrial Fibrillation Better Care (ABC) pathway adapted from 10

Abbreviations: OAC – Oral Anticoagulant, NOAC – Non-vitamin K antagonist Oral Anticoagulant, TTR – Time in Therapeutic Range, VKA – Vitamin K Antagonist

0

0.25

0.5

0.75

1

1.25

All-cause Mortality

Yang 2020 Frailty

Proietti 2020 ESC-EHRA

Proietti 2018

Yoon 2019

Proietti 2020 ESC-EHRA

Proietti 2018

Proietti 2020 ESC-EHRA

Gumprecht 2020

0.95 [0.90, 0.97]

0.57 [0.43, 0.78]

0.35 [0.17, 0.75]

0.82 [0.78, 0.86]

0.57 [0.43, 0.78]

0.35 [0.17, 0.75]

0.45 [0.34, 0.59]

0.46 [0.25, 0.86]

**Study**

**Estimate [95% CI]**

**a) Hazard ratios including Yang 2020 Frailty**

**b) Hazard ratios including Yoon 2019**

**c) Odds Ratios at 1 year**

**Figure 2:** Forest plot depicting hazard ratios (a and b) and odds ratios (c) for ABC adherence vs non-adherence for all-cause mortality

Yang 2020 and Yoon 2019 were analyses from subsets of the same dataset and were included separately in a) and b).

Abbreviations: EHRA, European Heart Rhythm Association; ESC, European Society of Cardiology