

**ABC (Atrial fibrillation Better Care) pathway and healthcare costs in atrial fibrillation.  
The ATHERO-AF study.**

Daniele Pastori MD, PhD(1)\*, Alessio Farcomeni PhD(2)\*, Pasquale Pignatelli MD, PhD(1),

Francesco Violi MD(1)\*\*, Gregory YH Lip MD(3)\*\*.

[\*equal contribution; \*\*joint authorship]

**Running head: ABC pathway and health-related costs**

(1) Department of Internal Medicine and Medical Specialties, Sapienza University of Rome, Rome, Italy.

(2) Department of Public Health and Infectious Diseases, Sapienza University of Rome, Rome, Italy.

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

**Correspondence to:** Professor Gregory Y.H. Lip. Email address: [gregory.lip@liverpool.ac.uk](mailto:gregory.lip@liverpool.ac.uk).

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## Abstract

**BACKGROUND:** The Atrial fibrillation Better Care (ABC) pathway for the integrated approach to the management of patients with atrial fibrillation has been proposed to streamline patient management in an integrated, holistic manner, as follows: ‘A’ Avoid stroke with Anticoagulation; ‘B’ Better symptom management, with rate or rhythm control; ‘C’ Cardiovascular risk and comorbidity management, including lifestyle factors. ABC pathway compliance has been associated with a reduced rate of cardiovascular events compared to non-ABC compliant patients. However, the impact of the ABC pathway on health-related costs has not been evaluated.

**METHODS:** We performed an exploratory analysis of costs related to cardiovascular events in the ATHERO-AF study, which is a prospective single-center cohort study including atrial fibrillation patients treated with vitamin K antagonists. A Diagnosis-Related Group code provided by the Italian Ministry of Health was assigned to each cardiovascular event by event typology to estimate the relative cost. The analysis was performed by dividing patients according to ABC pathway components.

**RESULTS:** Overall, the 118 cardiovascular events in the cohort incurred a cost of 1,017,354 euros (1,149,610 USD). The mean total costs were 13,050 (14,747 USD) and 11,218 euros (12,676 USD) for a non-fatal cardiac event or ischaemic stroke, respectively. The highest costs were related to cardiac complications, followed by non-fatal ischaemic stroke and cardiovascular death. Based on the ABC pathway components, the cost-saving was 719 euros (813 USD) per patient-year for patients in group A vs non-A, 703 euros (794 USD) for B vs non-B, 480 euros (542 USD) for C vs non-C and 2776 euros (3,137 USD) for ABC vs non-ABC.

The cost per cardiovascular event increased with the number of uncontrolled ABC components: 0-1: 507 euros (573 USD), raising to 965 euros (1,091 USD) for 2 components and to 3,431 euros (3,877 USD) for patients not having any of the three components of the ABC.

**CONCLUSIONS:** Management of atrial fibrillation patients according to the ABC pathway was associated with significantly lower health-related costs. Application of the ABC pathway as a management strategy may help reduce healthcare costs related to cardiovascular events in this high-risk patient population.

**Keywords:** ABC, atrial fibrillation, healthcare costs, cardiovascular events, management.

## Introduction

Patients with atrial fibrillation are often elderly and have multiple comorbidities, leading to a high risk of cardiovascular events<sup>1 2, 3</sup>, despite the use of oral anticoagulants, whether with the vitamin K antagonists (VKAs) or non-vitamin K antagonist oral anticoagulants (NOACs).

While stroke prevention is an important priority in atrial fibrillation management<sup>4 5</sup>, only 1 in 10 deaths related to atrial fibrillation are stroke-related, while 7 in 10 deaths are cardiovascular-related<sup>6</sup>. The burden of cardiovascular events in atrial fibrillation patients is high, representing a frequent complication of the natural history of these patients<sup>7</sup>, also in those classified as ‘low-risk’<sup>8</sup>. Hospital admissions for episodes of atrial fibrillation with uncontrolled ventricular rate, or for atrial fibrillation -related symptoms or complications represent an important public health issue<sup>9</sup>, given the growing numbers of patients living with this arrhythmia<sup>10</sup>.

Such observations warrant a more holistic or integrated approach to the management of patients with atrial fibrillation, which should not be limited to the monitoring of the quality of anticoagulation in terms of time in therapeutic range for VKAs and adherence to treatment for NOACs, but should include optimizing the management of comorbidities, such as achieving a good blood pressure control, an adequate blood glucose level, and reaching LDL cholesterol targets thus proactively managing cardiovascular risk<sup>11</sup>.

The Atrial fibrillation Better Care (ABC) pathway for the integrated approach to the management of patients with atrial fibrillation has been proposed to streamline patient management in an integrated, holistic manner, as follows: ‘A’ Avoid stroke with Anticoagulation; ‘B’ Better symptom management, with rate or rhythm control; ‘C’ Cardiovascular risk and comorbidity management, including lifestyle factors<sup>12</sup>. ABC pathway compliance has been associated with a reduced rate of cardiovascular events compared to non-ABC compliant patients. when evaluated in post-hoc ancillary analysis of clinical trial<sup>13</sup>, and in a real-world cohort study of unselected patients

monitored for the prescription and management of VKAs, the ATHERO-AF study<sup>14</sup>. However, the impact of the ABC pathway on health-related costs has not been evaluated.

In the present analysis, we evaluated the costs related to cardiovascular events occurring in atrial fibrillation patients in the ATHERO-AF study who were managed or not in accordance with the ABC pathway.

## Methods

The definitions of the components included in the ABC pathway have been previously described<sup>14</sup>.

Briefly, the A, B and C components were defined as follows: “A” by the quality of anticoagulation, as assessed by the time in therapeutic range  $\geq 65\%$  calculated over the last year of follow-up and stopped at the time of the first cardiovascular event; “B” was defined as the presence of symptoms, classified by the recommended European Heart Rhythm Association (EHRA) symptom scale. Patients in EHRA I-II classes were considered as having well controlled symptoms (vs. EHRA III-IV). “C”: *Cardiovascular and other comorbidity risk optimisation*, including proactive management of associated lifestyle and cardio-metabolic risk factors, including optimized proactive management of uncontrolled blood pressure ( $\geq 160/90$  mmHg), diabetes mellitus, heart failure, and underlying ischemia (cardiac and/or cerebrovascular). To be defined as ‘C-compliant’, all these risk factors should have been well controlled and/or treated with appropriate cardiovascular prevention drugs.

To estimate health care costs, we assigned a Diagnosis-Related Group code to each of 118 cardiovascular events occurred in the ATHERO-AF study (**Table 1**)<sup>14</sup>. The Diagnosis-Related Group codes are provided by the Italian Ministry of Health and represent the official costs for medical reimbursement for outpatients and inpatients accessing the National Health System services.

These Diagnosis-Related Group codes are periodically updated, and last version was released on 28/01/2013 (supplement of <http://www.gazzettaufficiale.it/eli/gu/2013/01/28/23/sg/pdf>).

The costs for non-fatal events, such as myocardial infarction (MI), cardiac revascularization, ischaemic stroke, and transient ischaemic attack (TIA) were calculated including both cost for hospitalisation and rehabilitation, which is standardized at 30 and 60 days for cardiac and cerebrovascular events, respectively. Causes of cardiovascular death were divided into heart attack, heart failure/shock, fatal ischaemic stroke, fatal MI.

### *Statistical analysis*

We firstly performed a descriptive analysis of absolute costs by assigning a specific Diagnosis-Related Group code by typology of cardiovascular event. When more than one Diagnosis-Related Group code was applicable to a specific event, a mean cost of Diagnosis-Related Group code was calculated and applied. We then compared the cost of cardiovascular events according to each component of the ABC pathway, that is, the “non-A” vs. “A” group, “non-B” vs. “B” group, “non-C” vs. “C” group, and finally, the “non-ABC” vs. “ABC” group. We also calculated the cost of each cardiovascular event in relation to increasing number(s) of uncontrolled risk factors.

The expected costs were obtained by multiplying cause-specific one-year incidence rates by the price estimated for each event. To improve the generalizability of our results, we reported costs related to cardiovascular events both in euros and in US dollars (USD). Analyses were performed using SPSS Statistics, version 23.0 (IBM) and R version 3.4.2.

## Results

The study cohort was composed of 882 patients, of whom 198 (22.4%) were optimally managed according to the ABC pathway. Overall, the 118 cardiovascular events had a cost of 1,017,354 euros (1,149,610 USD) during the follow-up. A detailed description of cardiovascular events is reported in Table 2. The highest cost was related to cardiac complications, followed by non-fatal ischaemic stroke and cardiovascular death (**Table 2**). The mean cost for each cardiovascular event 8621,64 euros (9,742.45 USD). The mean total costs were 13,050 euros (14,747 USD) for non-fatal cardiac events, 11,218 euros (12,676 USD) for non-fatal ischaemic strokes, and 2,543 euros (2,874 USD) for TIAs (**Table 1**). The costs for specific causes of cardiovascular death is summarised in **Table 1**.

A detailed cost for each cardiovascular event according to ABC groups is shown in **Figure 1**. Cost-saving was 719 euros per patient-year for A vs non-A, 703 euros for B vs non-B, 480 euros for C vs non-C, and 2,776 euros for ABC vs non-ABC (**Figure 1, Panel A**).

Similar analysis was repeated using USD (**Figure 1, Panel B**), which showed a cost-saving of 813 USD per patient-year for A vs non-A, 794 USD for B vs non-B, 542 USD for C vs non-C, and 3,137 USD for ABC vs non-ABC.

The cost of each cardiovascular event increased with the number of uncontrolled ABC components, as follows: 0-1: 507 euros (573 USD), raising to 965 euros (1,091 USD) for 2 components and to 3,431 euros (3,877 USD) for patients not having any of the three components of the ABC pathway.

### *A simulation model of the application of the ABC pathway in the nationwide Italian population*

It is estimated that 22.6% of people living in Italy is aged >65 years resulting in 13,693,340 elderly subjects. In this elderly population, about 7.3% of subjects are affected by atrial fibrillation<sup>15</sup>, for a total of 999,614 patients. Taking into consideration data coming from the GLORIA-AF study<sup>16</sup>, we have to exclude 4% (n=39,985) of atrial fibrillation patients that are not receiving any oral

anticoagulant treatment. Of the remaining 959,629 atrial fibrillation patients, 42% is currently being treated with a VKA<sup>16</sup>, for a total sample of 403,044 atrial fibrillation patients treated with VKAs.

Assuming that the proportion of patients optimally managed in the ATHERO-AF study (22.4%) group would be representative of the Italian atrial fibrillation patients' population, we would have 90,282 patients managed according to the ABC strategy, and 312,762 having at least one component of the ABC pathway not well controlled.

The annual cost for fatal and non-fatal events in the group of ABC-compliant patients would be estimated at 14,010,841 euros (15,832,250 USD), as compared to 121,342,329 euros (137,116,832 USD) of ABC non-compliant patients. The optimization of management of patients according to ABC integrated care approach would translate into an annual cost-saving of 72,773,496 euros (82,234,051 USD).

## **Discussion**

In this exploratory analysis, we showed that management of atrial fibrillation patients according to the ABC pathway was associated with significantly lower health-related costs. Thus, application of the ABC pathway as a management strategy may help reduce healthcare costs related to cardiovascular events in this high-risk patient population.

While screening for atrial fibrillation has been demonstrated to be a cost-effective strategy in patients aged 65 years or older<sup>17</sup>, it is still unknown which is the optimal management for patients with atrial fibrillation to reduce cardiovascular complications and its related healthcare costs<sup>18</sup>. In Italy, the mean cost for a hospitalisation related to a cardiac complication was 5,540 euros, raising to 13,050 euros when considering cardiac rehabilitation. Similarly, the mean cost for an ischaemic stroke was 6,073 euros, raising to 11,218 euros including neurologic rehabilitation. The latter cost is substantially in line with findings from a Danish registry showing a cost for patients with atrial



fibrillation admitted with a first-incident stroke event, which was estimated at USD \$7,683 (\$6,863 in our study)<sup>19</sup>, and higher than another study from United States where the cost for a nonrepeat atrial fibrillation-related stroke was estimated at USD \$4905<sup>20</sup>.

The healthcare costs within each group of the ABC pathway was halved in adherent vs. non-adherent patients, as a consequence of the reduced rate of cardiovascular events. Moreover, amongst ABC-compliant patients, as compared to those with all uncontrolled components, the health care costs were reduced by 80%.

Modelling these figures into the nationwide population may lead to an annual cost-saving of 72,773,496 euros (82,234,051 USD). We therefore suggest that this approach may significantly impact positively on health costs of atrial fibrillation-related complications, representing a potential major cost-saving strategy for this high-risk patient population.

#### *Limitations.*

We may have underestimated the cost for non-fatal cardiovascular events, as we did not consider the severity of non-fatal MI and ischaemic stroke, which may lead to a longer hospital stay and need for extensive rehabilitation. We cannot exclude a further cost-saving in the group of patients with well-controlled symptoms related to a lower rate of admissions to the emergency department because of dyspnoea or chest pain. Furthermore, all patients in this study were treated with VKAs, and therefore healthcare costs may be different in patients treated with NOACs.

We included only Caucasian elderly patients referring to a hospital specialized clinic for the management of antithrombotic therapies. Thus, health-related costs for patients managed in other clinical settings (ie. primary care) may be different.

Finally, the specific way of assignment of cost to events in the Italian public health system may make difficult comparisons with other national health systems, especially for those countries where

a private insurance is needed. This may affect the management of patients with atrial fibrillation (i.e. reduced rate of hospitalisation and lower length of in-hospital stay).

In conclusion, optimising management of atrial fibrillation patients according to the ABC pathway was associated with significantly lower health-related costs. Compliance with the ABC pathway as a management strategy may help reduce healthcare costs related to cardiovascular events in this high-risk patient population.

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