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Design and Evaluation of ACAFiB-APP, a clinical decision support system for anticoagulant considerations in patients with atrial fibrillation

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Abstract

Background Patients with atrial fibrillation are at risk for various complications, including thromboembolic events. This study involves developing and evaluating a Clinical Decision Support System (CDSS) to select appropriate anticoagulant drug, considering comorbidities, laboratory data, and concurrent medications. The system is based on a streamlined interpretation of the most recent globally accepted clinical guidelines.

Methods Primarily a semi-structured interview regarding the challenges in the field of thromboprophylaxis for AF and clinical pharmacists and cardiologists' needs in practice was conducted. Then the required data were extracted from the latest guidelines and confirmed by the expert panel. Using Microsoft Visio software each scenario and its corresponding rules were modeled. Dart programming language, the Flutter framework, and the Visual Studio editor were used to develop the application. Finally, the uMARS questionnaire was used to evaluate the application quality.

Results The selection of the anticoagulants was reported to be the most challenging domain by 78.6% of the participants in the interview. According to the designed algorithms, the application was developed using Asp.net with the Microsoft SQL Server database platform. This CDSS is called ACAFiB-APP, which stands for Anticoagulant in AF Application. The user goes through various calculators and obtains the required data, moreover, the user will choose one or more comorbidities/clinical scenarios. Finally, ACAFiB-APP will represent the proper anticoagulant options with dosing and related considerations. All of the sections in the uMARS questionnaire received acceptable scores.

Conclusions The CDSS will facilitate the informed selection of anticoagulants for complicated AF cases by considering the patient clinical scenario.

Clinical trial number Not applicable.

Keywords Atrial fibrillation, Anticoagulant, Clinical decision support system, Digital health

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Background

Atrial Fibrillation (AF) as the most prevalent cardiac arrhythmia, may affect more than 6 million individuals in the USA by 2050 [1]. Stroke is the main leading cause of mortality in this population since patients with AF are 3–5 times more at risk of stroke. Moreover, AF is responsible for nearly one-third of all ischemic strokes globally. For Asian AF patients, the annual risk of ischemic stroke is around 3.0% [2].

It has been suggested that AF imposes a financial burden of 0.3 to 3.0% of the total health system in developed countries [3].

Thromboprophylaxis is one of the cornerstones of AF management. It has been shown that thromboprophylaxis reduces stroke by 64% and mortality by 26% in AF patients [4–6].

It has been reported that the regional age-standardized incidence rate and the standardized mortality rate of AF represent a slightly increasing trend from 1990 to 2019 in the Middle East [7].

There are several challenges in terms of thromboprophylaxis in this population leading to morbidity and mortality including identifying patients eligible for anticoagulant therapy, those eligible for thromboprophylaxis using non-pharmacologic approaches, administration of antiplatelet drugs instead of the anticoagulant, selection of improper anticoagulant drug as well as rationale dose and interval, neglecting regarding patients' comorbidities (including co-administered medications), etc [8–10].

The most common medical error in the field is considering no anticoagulant therapy in patients with a definite indication or considering lower standard dose anticoagulant in these patients mainly due to the concerns regarding bleeding [11–13].

Oral anticoagulant prescription rates for eligible AF patients show regional variation, with the highest administration in Europe (90.1%), followed by North America (78.3%) and Asia (55.2%) [14]. Results of a study on 2021 patients from the Middle East suggest that the thromboprophylaxis of nearly 55.0% of the patients was consistent with the A (Avoid stroke) strategy as part of the Atrial fibrillation Better Care (ABC) pathway [15]. Results of a study in Iran during 2018–2020 suggest that just 69.5% of AF individuals with definite indications received anticoagulants [11].

Implementing clinical guidelines is one of the main approaches to improving the Rational Use of Drugs (RUD) [16–18].

Several well-known clinical guidelines for AF management exist, including those published by the American Heart Association (AHA) [19], the American College of Cardiology (ACC) [20], the European Society of Cardiology (ESC) [21], and the European Heart Rhythm Association (EHRA) [22]. Non-adherence to clinical guidelines is common in AF management [2, 23].

Physician workloads and time limitations besides the exponential growth of data production globally could result in discrepancies between clinical guidelines and actual medical practice [8, 24].

Moreover, due to the increased life expectancy worldwide, more complicated clinical scenarios have arisen [25].

Implementing digital health technologies is a part of the multi-disciplinary approaches announced for AF management, as the World Health Organization (WHO) has considered a global digital health strategy from 2020 to 2025 [26, 27].

Implementing digital health technologies is common in cardiology including heart failure, hypertension, metabolic syndrome, AF, stroke, and acute coronary syndrome [28].

Clinical Decision Support Systems (CDSS) assist physicians in screening, diagnosis, management, and monitoring, besides educating patients and medical staff regarding the disease [29, 30]. The National Academy of Medicine (NAM) recommends using CDSSs to organize the delivery of clinical services. Any tool to support clinical decisions should be carefully evaluated, such as the rigorous evaluations of the development of new drugs and new medical methods [31, 32].

More than 500 mobile applications, emphasizing diagnostic aspects [23], have been developed worldwide regarding different aspects of AF to date.

To our knowledge, most of the currently available digital systems developed as a CDSS for healthcare professionals regarding thromboprophylaxis of AF patients, are limited to medical calculators considering patients' risk factors for estimating the risk of bleeding (HAS-BLED, ATRIA, HEMORR2HAGES), stroke (CHA2DS-2VASC, CHA2DS2), evaluating renal (Cockcroft-Gault) or liver function (Child-Pugh), and INR (International Normalized Ratio) calculators [33, 34]. Most of the current systems do not consider an individualized approach by considering patients' demographic data, laboratory results, comorbidities, and concurrent medications to recommend an anticoagulant drug with proper dosing.

AnticoagEvaluator developed by the ACC (active URL: https://www.acc.org/anticoagevaluator) is one of the systems in the field providing recommendations regarding the selection of anticoagulants. It should be noted that AnticoagEvaluator does not recommend a specific anticoagulant based on a special clinical scenario including patient clinical features, laboratory data, comorbidities, and concurrent medications. It is limited to several medical calculators and general/ fixed recommendations based on the data just from the guidelines released by the ACC [34, 35].

Since no comprehensive CDSS has been developed regarding the selection of anticoagulant drugs in AF patients so far, and due to the aforementioned challenges, in this study, we aimed to design, develop, and evaluate a CDSS for the selection of rational anticoagulant drugs including dosing interval, considering patients' comorbidities, laboratory data, concurrent medications, based on the simplification of the available data from the latest version of globally accepted clinical guidelines. Moreover, we considered developing monitoring calculators and related considerations for each anticoagulant drug.

Materials and methods

This is an applied-developmental study that was conducted in six steps.

First step: needs assessment

Fifteen Board-Certified Clinical Pharmacists (BCCPs) and fifteen cardiologists affiliated with the Tehran University of Medical Sciences (TUMS) participated in semi-structured interviews. All participants had at least two years of experience working in cardiology or Cardiac Care Unit (CCU) wards, or participating in consultations and medical rounds within those wards.

Based on the results of this step, the software design and development requirements were extracted. The sampling method at this stage was purposive sampling. The sample size was determined based on similar prior studies, which used equal or smaller sample sizes for the needs assessment phase of mobile application or CDSS development [36, 37].

Purposive (judgmental) sampling is a non-probability sampling method in which qualified people are selected as a sample based on specific assumptions. The application's functional and non-functional requirements were extracted during this stage. Some closed questions were asked from the experts, which were included in the design step. The experts also presented their needs regarding thromboprophylaxis for AF patients in clinical practice.

Second step: extracting data using guidelines and references

In the second step of the study, we extracted the data regarding anticoagulant therapy in AF from relevant references including:

i. 2020 ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease [38],
ii. 2021 ESC/EACTS Guidelines for the Management of Valvular Heart Disease [39],
iii. 2023 ESC Guidelines for the Management of Acute Coronary Syndromes [40],
iv. 2020 ESC Guidelines for the Diagnosis and Management of Atrial Fibrillation Developed in Collaboration with the European Association of Cardio-thoracic Surgery (EACTS) [41],
v. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation [20],
vi. 2019 AHA/ACC/HRS focused Update of the 2014 AHA/ ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation [19],
vii. 2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient with Cardiac Amyloidosis [42],
viii. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients with Chronic Coronary Disease [43],
ix. 2022 Version of Perioperative Management of Antithrombotic Therapy from the American College of Chest Physicians Clinical Practice Guideline [44],
x. 2021 European Heart Rhythm Association Practical Guide on the use of Non-vitamin K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation [22],
xi. 2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy [45],
xii. 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS) [6].

Furthermore, the Pharmacotherapy Handbook [46] and Braunwald Heart Disease [47] were considered during data extraction.

Third step: setting expert panels for content confirmation

During data extraction, when contraindications were observed between chosen references, an expert panel including 3 professors of clinical pharmacy, 3 professors of cardiologists, and 2 experts in medical bioinformatics (Eight experts) was held to make decisions regarding the issue. While consensus was not reached regarding an issue in the expert panel due to the strong evidence regarding each controversial recommendation, both recommendations would be reprinted to the user with relevant references and class/level of recommendation to be interpreted in the context of the physician's clinical judgment before making clinical decisions. The content of the application has been reviewed and confirmed by the cardiology department of Imam Khomeini Hospital Complex (IKHC), and the Clinical Pharmacy department of TUMS.

Fourth Step: developing rules and medical calculators

Based on these data, we prepared rule-based algorithms using Microsoft Visio, considering demographic, laboratory data, concurrent medications, and comorbidities. After gathering these data, the algorithms go through the selection of anticoagulant drug, dose, interval, and related considerations consequently. Moreover, several medical calculators have been implemented in these algorithms including CHA2DS2VA, HAS-BLED, Cockcroft-Gault, Child-Pugh, BMI (Body Mass Index), 4Ts score (for Unfractionated Heparin (UFH), and Enoxaparin), INR (for Warfarin), and aPTT (activated Partial Thromboplastin Time) (for UFH, and Enoxaparin) calculator. In this web-based decision support system, seven anticoagulant drugs have been defined to be recommended when indicated including UFH, Enoxaparin, Warfarin, Dabigatran, Rivaroxaban, Edoxaban, and Apixaban. In terms of evaluating drug interaction, medications would be evaluated based on the 2021 European Heart Rhythm Association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with AF [22], the 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS) [6], and absolute contraindications in Lexi-Comp [48] since there might be contraindications/ caution during co-administration of anticoagulants and these medications.

In the last section of the algorithms considerations regarding anticoagulant therapy in AF patients have been considered including management of the supratherapeutic INR, management of bleeding while on anticoagulant, pre/post-operative management of anticoagulant, considerations regarding concurrent AF and ischemic heart disease, acute coronary syndrome, peripheral artery disease, cardiac ablation, cardiac cardioversion, percutaneous intervention, coronary artery bypass graft, issues regarding modifiable risk factors and monitoring, recommendations regarding how to switch between anticoagulant when indicated, and how to manage missed dose or double dose in patients.

Fifth step: technical development of the application

Based on the confirmed content from the previous steps, standard algorithms were designed to develop this CDSS. The research team used Microsoft Visio design software to draw the rules coherently.

The research team took advantage of the Dart programming language in the Visual Studio (VS) Code editor. Dart is one of the most widely used and newest multi-purpose languages . It can be used for various tasks such as designing and developing website pages and creating mobile, desktop, and console applications. This language can adapt to all browsers and is very fast [49]. The application was developed using Asp.net with the Microsoft SQL Server database platform.

Flutter was used to develop this web application. Flutter is a mobile user interface framework and free open-source software development package (Software Development Kit| SDK). Flutter allows developers to create a native mobile application with only one codebase. A native application is used on a specific device and its operating system. The ability to develop a native application with only one source code in Flutter means that you can create two or more different applications for iOS and Android with only one programming language and one source code. For Flutter development, there are special Flutter and Dart plugins in VS code that make it easier for developers. This tool also provides debugging, project execution, and dependency management.

Sixth step: usability evaluation of the application

To evaluate the content and user experience of the system, Users- Mobile Application Rating Scale (uMARS) questionnaire was used. The uMARS has 23 items which are categorized into five sections: "A section: engagement (5 items), B section: functionality (4 items), C section: aesthetics (3 items), D section: information quality (7 items) and E section: subjective quality scale (4 items)." Scores of all items have a maximal possible value of five. Each section (A-B-C-D-E) is scored on a 5-point scale from one ("inadequate") to five ("excellent"), with more specific descriptors for the response options for each question. The distinct component of this questionnaire (F section), which consists of six questions, assesses the perceived influence of an application on the user's awareness, knowledge, orientation, attitudes, and intentions to alter the user's mode of operation, and aids the user in searching. Upon completion, seven scores are reported, including the mean scores for each subscale (A, B, C, D sections), a total mean score, a mean subjective quality score (E section), and a mean score of the app-specific subscale, perceived impact section of the application (F section). All items of the F section are ranked 1 ("strongly disagree") to 5 ("strongly agree") accordingly [50]. The Persian version of uMARS was used in this study, which has been translated and validated in a previous study [51].

In this step, 15 BCCPs, 15 cardiologists, and 15 experts in medical bioinformatics were requested to go through the application for at least 15 min during a week and then complete the uMARS questionnaire. Participants were informed that their answers would be confidential and there was no need to declare their identity in the questionnaire. Informed consent to participate was obtained from all participants.

Statistical analysis was conducted using IBM SPSS Statistics Version 20 (SPSS Inc., Chicago, IL, USA). The

mean ± SD was used to report the scores in each section of the uMARS. The Kruskal-Wallis test was used to compare the results among the three groups. Mann-Whitney test was used to compare the results among males and females. The significance value was set at p-*value* < 0.05.

The main steps of the conducted methodology are depicted in Fig. 1.

Results

Requirement analysis

The application's functional and non-functional requirements were extracted during a semi-structured interview with a panel of experts. Based on the results, some closed questions were asked from the experts, which were included in the design step. The experts also presented

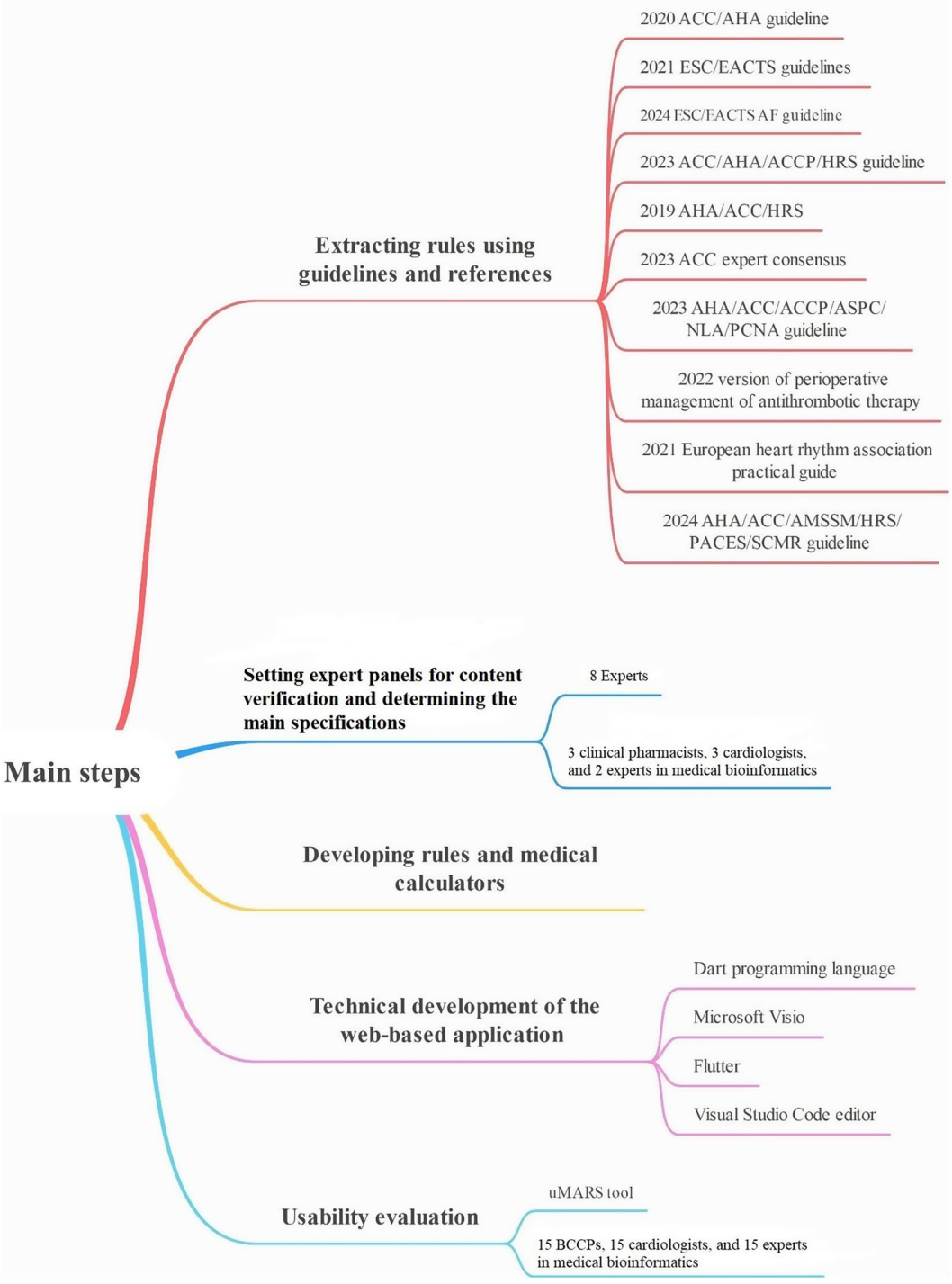

Fig. 1 A glance at the conducted methodology

their additional opinions in the following. The result of a semi-structured interview regarding the requirement extraction stage is provided in Table 1.

As presented in Table 1, more than 60% of the participants have previously used CDSS and more than 70% of the participants suggested that the design of a CDSS is highly (57.1%) and very highly (21.4%) necessary for the thromboprophylaxis of AF patients. Among experts who considered the necessity of designing a CDSS for the thromboprophylaxis of AF as low or middle, the financial burden and limitations regarding the ability of the CDSS to consider the exact clinical context of the clinical scenarios were the main concerns.

The selection of the anticoagulant drug was reported to be the most challenging domain declared by 78.6% of the participants.

Due to the importance of considering co-morbidities, laboratory data, and concurrent drug use in terms of thromboprophylaxis in AF patients, more than 85% of participants suggest that these aspects should be considered in a CDSS for AF. In terms of drug interaction, more than half of the participants prefer considering clinically reported interactions besides absolute contraindications since some of the interactions reported in the drug interaction references have just theoretical aspects without significance in practice. Another challenge in terms of AF prophylaxis is that disagreement between clinical guidelines exists in some clinical scenarios. In this aspect, most of the participants (92.9%) prefer to see the recommendations of all guidelines in view and decide based on the clinical texture of the patient, since each patient is a specific clinical scenario. While asking about preferred references for the development of the scientific content of the CDDS, the latest clinical guidelines (92.9%) followed by Up-to-date (64.3%) were reported.

As represented in Tables 1 and 14 clinical scenarios/comorbidities, 8 medical calculators, and 7 laboratory data were suggested to be considered in this CDDS. Since detailed recommendations from guidelines are sometimes too long incorporating the details of previous studies, participants were asked about the visual aspects of the application in this regard. More than 85% prefer to see a summary on the main page and the details on other pages based on the request from the users. More than 10 topics were recommended by the participants to be included in the section on considerations about anticoagulants. The first five top issues are represented in Table 1. Moreover, most of the participants (85.7%) suggest English as the language of the application and prefer to access the application through both PC and mobile phone (64.3%). On the other hand, email and foreign mobile applications are reported to be the preferred ways to contact the app- developers. Since CDSS are designed for medical staff more than 78% of participants prefer applying restrictions on the accessibility to the application. The findings from this stage characterized the application's content, language, accessibility limitations for the general population, including medical calculators and laboratory data, the types of drug interactions covered, and communication methods with the development team. These features are described in the following section.

Development of the application

We prepared the rules and statements extracted from guidelines and expert panel outputs in designs that are depicted in Microsoft Visio. Additionally, determined requirements and design specifications have been applied in this stage. Since the extracted rules are extensive, some of these rules and statements are given in the diagram below (See Diagram a).

Then, based on the developed algorithms, the application was created using Asp.net with a Microsoft SQL Server database platform (active URL: https://www.acafib.ir/#/login). The application could be used online via Personal Computer (PC) or mobile (Android or iOS).

Figure 2 displays the written Dart codes in the VS editor. Figure 3. Represent the workflow of ACAFiB-APP.

This CDSS named ACAFiB-APP which stands for Anticoagulant in AF Application. Healthcare professionals including cardiologists, internalists, and clinical pharmacists would be the main users of the system. The first page of this application is provided in Fig. 4. Based on a suggestion from the expert panel, the demo film was inserted into the home page of the application under the title *Guide to use ACAFiB* to assist the user in better understanding pathways existing in the ACAFiB.

After confirmation of the AF or atrial flutter by the users, definite indications of the anticoagulant therapy would be represented to the user. Moreover, the CHA2DS2VA calculator has been implemented in this section to be used while required. Besides each indication, the exact recommendations and references have been added with the class and level of recommendations while the user clicks on a question mark in the right corner of the page.

ACAFiB-APP would recommend non-pharmacologic strategies for scenarios while thromboprophylaxis is indicated but contraindications exist regarding anticoagulant administration.

After going through calculators and receiving data including sex, age, weight, height, platelet count, serum creatinine, and other items that exist in each calculator, the user will select one or more comorbidity/ clinical scenarios. Some of these comorbidity/ clinical scenarios are linked to the aforementioned calculators and would be selected automatically based on the information received from the users in the previous stages.

Table 1 Extracted requirements and specifications of the application

Question	Results
Have you ever used any Clinical decision support system?	• Yes (64.3%) • No (35. 7%)
To what extent do you consider the design of a clinical decision support system necessary to help the thromboprophylaxis process in atrial fibrillation patients?	• Very high (21.4%) • High (57.1%) • Middle (14.3%) • Low (7.1%) • Very low (0%)
Which of the following domains do you find most challenging in the thromboprophylaxis of atrial fibrillation patients?	• Selection of an anticoagulant (78.6%) • Determination of proper dosing (64.3%) • Considerations (management of bleeding on anticoagulant, preoperative management of anticoagulants, etc.) (50.0%) • Evaluating indications for anticoagulant (21.4%)
Which features do you consider necessary to be included in this system?	• Determination of the type of drug and dosage of the drug taking into account the clinical aspects, concomitant drugs, and laboratory data (85.7%) • The presence of calculators necessary to calculate and modify the dose of the drug to achieve the therapeutic goal (71.4%) • Provide necessary suggestions if there is a contraindication for anticoagulants (50.0%) • Providing the necessary considerations regarding the use of anticoagulants (50.0%) • Providing the list of drug interactions and checking the medications taken simultaneously (42.9%) • Providing the time intervals required for periodic assessments of risk of bleeding, liver assessment, kidney assessment, etc. (42.9%)
What kind of drug interactions would you prefer to be included in this system?	• clinically significant interactions that are mentioned in the clinical guidelines besides absolute contraindications reported for each drug in the drug interaction references (57.1%) • All drug interactions mentioned in the drug interaction references including theoretical and clinical interactions. (35.7%) • Just clinically significant interactions that are mentioned in the clinical guidelines. (7.1%)
In cases where there is a disagreement between guidelines about a clinical scenario, how do you prefer the information to be displayed?	• Providing a summary of the opinion of all guidelines along with evidence and level of recommendation. (92.9%) • Providing the opinion of the latest guideline (35.7%) • Providing the opinion of the expert panel who developed the system (7.1%)
In cases where the written text of the guidelines regarding a clinical scenario is too long, which method of displaying information do you prefer?	• Provide a summary of the results on the home page and references to other pages if more details are needed (85.7%) • Providing all details on a home page (7.1%) • Just provide a summary on the home page without a need for details. (7.1%)
Which resources do you consider necessary to include in to design of this system?	• Latest guidelines in the field (92.9%) • Up to date (64.3%) • Latest articles in the field (35.7%) • Cardiology and pharmacotherapy reference books (21.4%)
Which comorbidities/ clinical scenarios do you think are necessary to be included in this system in terms of drug selection, dosing, and considerations?	• Renal failure (85.7%) • Thrombocytopenia (78.6%) • Pregnancy and lactation (78.6%) • Hepatic failure (71.4%) • Overweight/underweight (64.3%) • Cardioversion (64.3%) • Acute Kidney Injury (57.1%) • History of revascularization (57.1%) • Cancer (50.0%) • History of bleeding (50.0%) • Cardiac ablation (42.9%) • Congenital heart disease (35.7%) • Amyloidosis (35.7%) • Cardiomyopathy (28.6%)
Which medical calculators do you think are necessary to be included in this system in terms of drug selection, dosing, and considerations?	• Cockcroft- Gault (92.9%) • CHA2DS2VASC (92.9%) • HAS-BLED (78.6%) • Child-Pugh (78.6%) • 4Ts Score (71.4%) • BMI Calculator (57.1%) • INR Calculator (50.0%) • aPTT Calculator (35.7%)

Table 1 (continued)

Question	Results
Which laboratory parameters do you think are necessary to be included in this system in terms of drug selection, dosing, and considerations?	• Serum creatinine (92.9%) • Platelet count (92.9%) • INR/aPTT (71.4%) • Bilirubin (64.3%) • AST/ALT (50.0%) • Albumin (50.0%) • Urea (35.7%) • Hemoglobin (35.7%)
Which considerations regarding anticoagulant drugs do you think are necessary to be included in this system?	• Preoperative management of anticoagulants (92.9%) • Switching between anticoagulants (85.7%) • Management of bleeding while on anticoagulant (71.4%) • Considerations regarding concurrent use of antiplatelets (71.4%) • Risk factor modification for AF patients (35.7%)
If a clinical decision support system is designed for thromboprophylaxis in patients with atrial fibrillation, what language would you prefer to be used in the program?	• English (85.7%) • Persian (14.3%)
How do you prefer to access a clinical decision support system for patients with atrial fibrillation?	• Through mobile phones (35.7%) • Through PC (0%) • Both mobile phone and PC (64.3%)
Since the beforementioned system is designed for medical staff only, do you consider it necessary to restrict access to information, for example, through defining passwords and usernames?	• Yes (78.6%) • No (21.4%)
Which way do you prefer to communicate with system developers if needed?	• Email (14.3%) • Phone (14.3%) • Foreign mobile applications (including Telegram, WhatsApp, etc.) (64.3%) • Persian mobile applications (including Bale, Rubika, etc.) (7.1%)

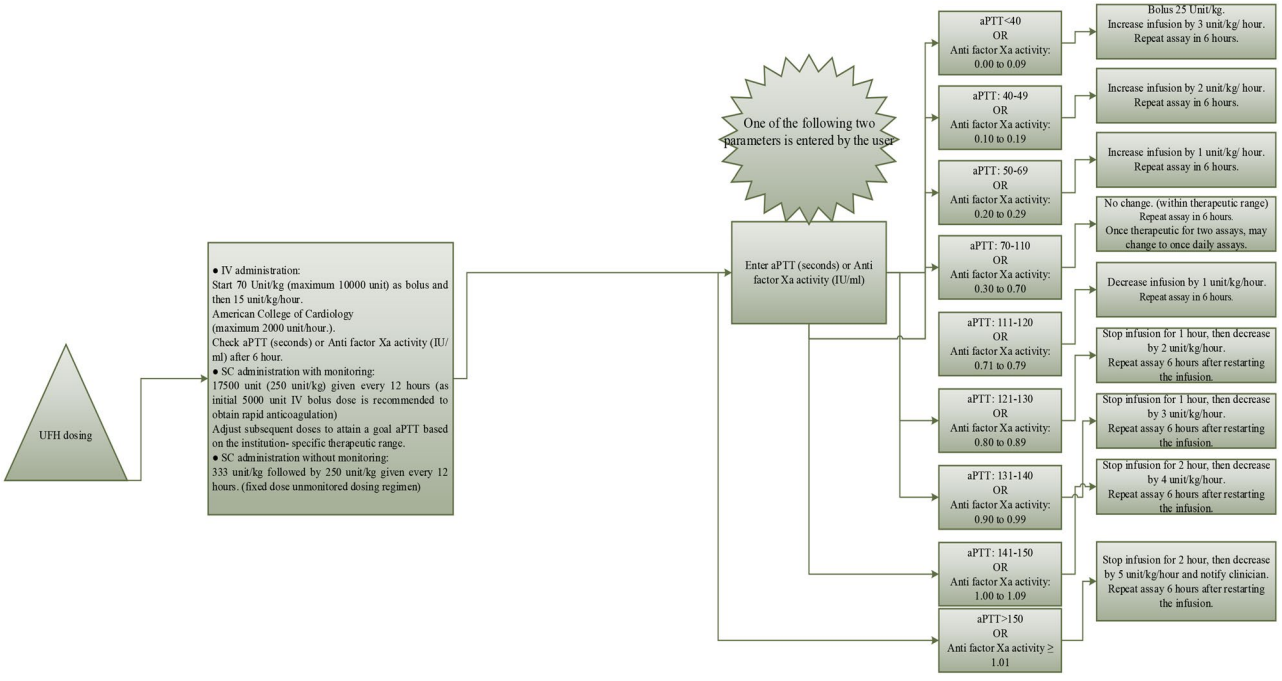

Diagram. 1 UFH dosing rules

```dart
import 'package:drtest/models/question/drug_interaction_model.dart';

List<DrugInteractionRowModel> drugInteractionData = [
  DrugInteractionRowModel(
    "Dronedarone",
    [
      DrugInteractionWithType(6, DrugInteractionEnum.red,
          calcType: DrugInteractionCalcType.crcfLess, value: 30),
      DrugInteractionWithType(6, DrugInteractionEnum.yellow,
          calcType: DrugInteractionCalcType.crcfMore, value: 29),
      DrugInteractionWithType(4, DrugInteractionEnum.yellow),
      DrugInteractionWithType(7, DrugInteractionEnum.red),
      DrugInteractionWithType(5, DrugInteractionEnum.yellow),
    ],
    id: 1,
  ),
  DrugInteractionRowModel(
    "HIV protease inhibitors (e.g., ritonavir)",
    [
      DrugInteractionWithType(6, DrugInteractionEnum.red),
      DrugInteractionWithType(4, DrugInteractionEnum.red),
      DrugInteractionWithType(7, DrugInteractionEnum.red),
      DrugInteractionWithType(5, DrugInteractionEnum.red),
    ],
    id: 2,
  ),
```

Fig. 2 Developmental Codes

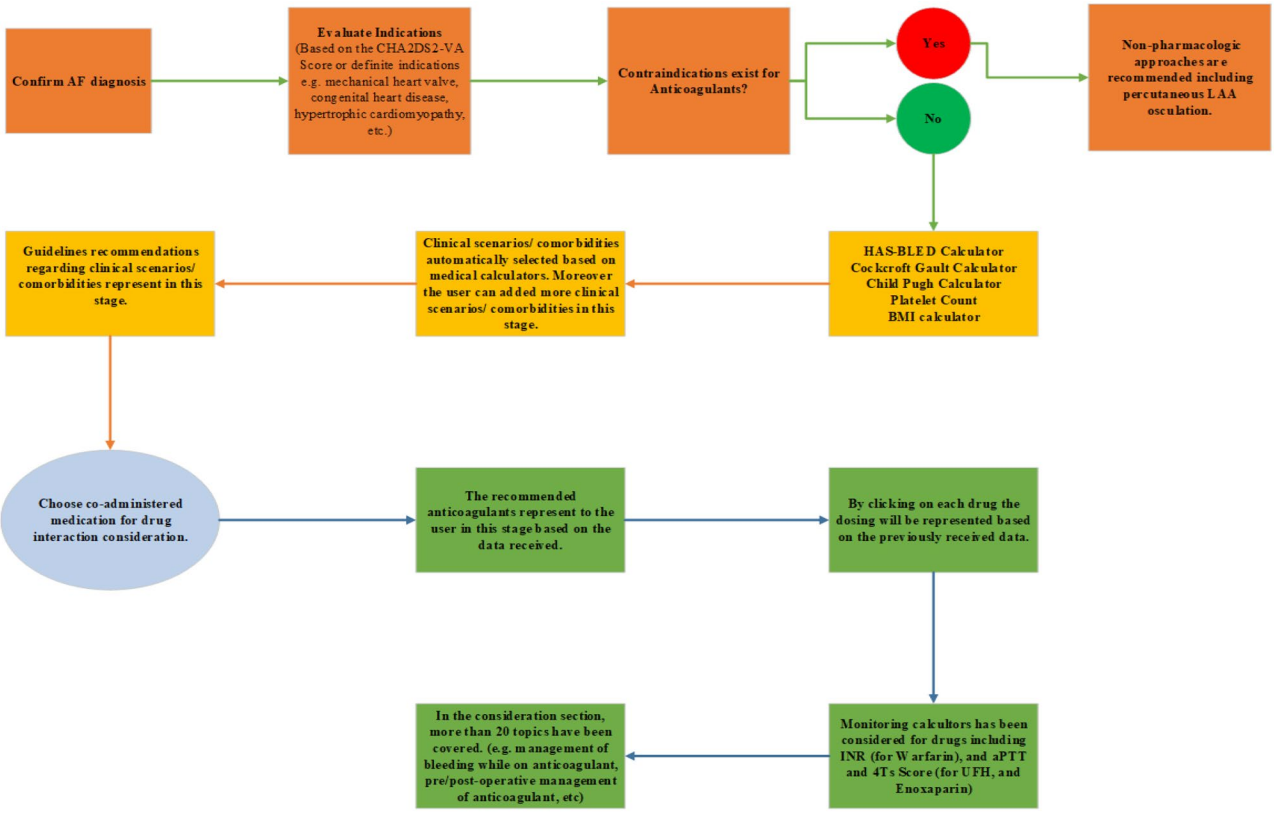

Fig. 3 The workflow of ACAFiB-APP

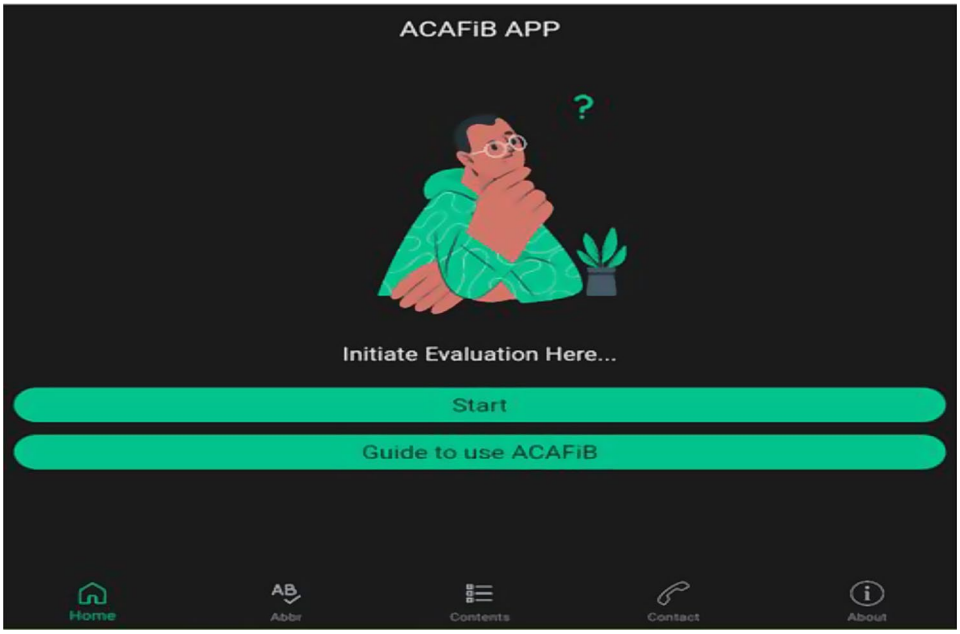

Fig. 4 The homepage of the ACAFiB-APP

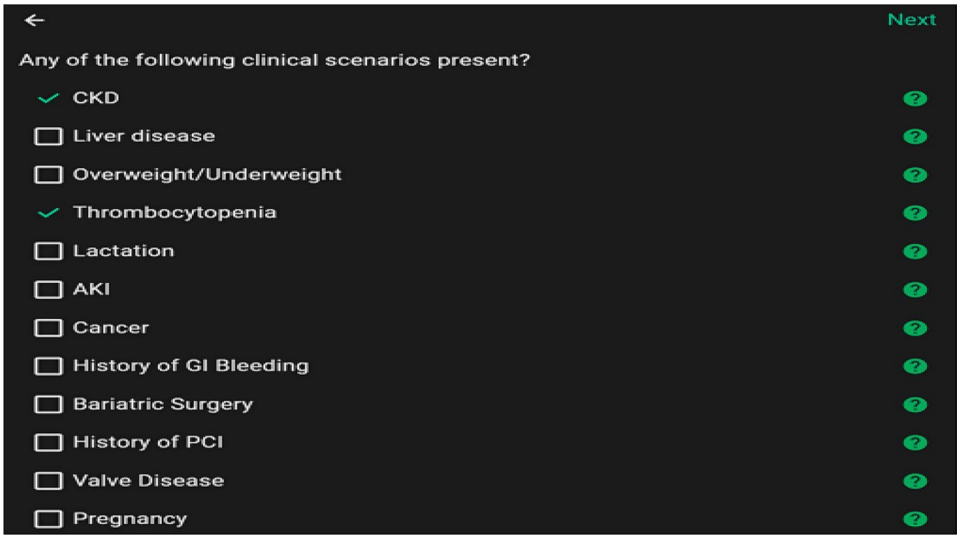

Fig. 5 Some of the Comorbidities/ clinical scenarios covered in ACAFiB-APP. (By clicking on (?) more detail regarding each scenario besides the class/ level of recommendation would be displayed.)

These comorbidities/ clinical scenarios include 1-hypertrophic cardiomyopathy, 2-mechanical heart valve implementation, 3-bioprosthetic heart valve implementation, 4-pregnancy, 5-lactation, 6-ablation, 7-cardioversion, 8-congenital heart disease, 9-cardiac amyloidosis, 10-moderate to severe mitral stenosis, 11-chronic kidney disease (based on the data from Cockcroft-Gault calculator), 12-hepatic failure (based on the data from Child-Pugh calculator), 13-thrombocytopenia, 14-cancer, 14-over/underweight (Based on the data from BMI calculator), 15-history of the gastrointestinal bleeding, and 16-history of the bariatric surgery (See Fig. 5).

When more than one comorbidity/ clinical scenario is selected by the users or automatically based on the data from calculators, the system would subscribe to similar drugs for each scenario and represent the final recommendations.

In the next step, concurrent medication would be evaluated for probable contraindication/ caution with co-administered anticoagulants. In this part, users would select co-administered drugs from a list and receive information regarding the drugs with contraindications marked as red or dark blue (due to the decrease and increased serum level respectively), those with caution

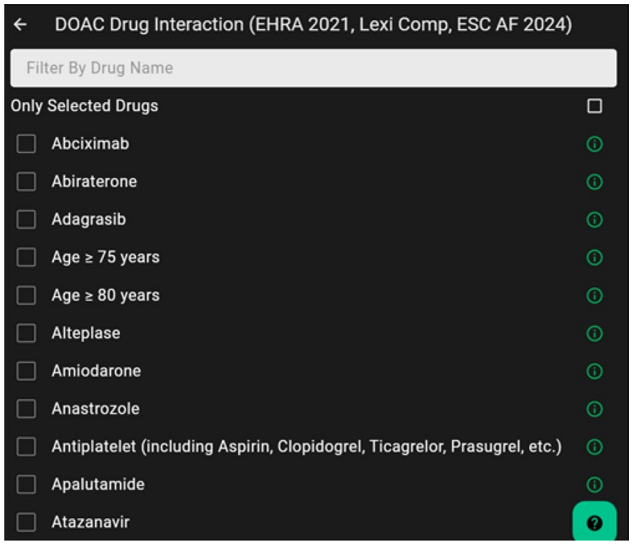

Fig. 6 List of the co-administered drugs for considering drug interactions in ACAFiB-APP

marked as yellow or light blue (due to the decreased and increased serum level respectively), and those requiring dose modification while being used concurrently (marked as purple) (See Fig. 6). Hints are inserted here to fully describe the clinical meaning behind each color. In this part, the final anticoagulant candidate for thromboprophylaxis based on the clinical context would be represented to the user. Anticoagulant represented by green has no contraindication based on the clinical context and drug interaction, those marked with red are contraindicated (due to increased or decreased serum level), those marked as yellow require caution during administration, and purple ones require dose modification (See Fig. 7).

By clicking on each drug in this part, users will go through several questions to determine the dose and interval of the anticoagulant. Several calculators have been inserted in the dosing section including, INR (for Warfarin), and aPTT (for UFH and Enoxaparin). Using these calculators' users could monitor the anticoagulant drug to identify whether it is required to modify the dose taken by the patient. 4Ts Score calculator has also been implemented in the dosing algorithms of UFH and Enoxaparin when a drop in platelet count is observed following the drug administration.

In the last section of the application considerations regarding relevant issues to anticoagulant therapy in AF patients have been considered including management of the supratherapeutic INR, management of bleeding while on anticoagulant, pre/post-operative management of anticoagulant, considerations regarding concurrent AF and ischemic heart disease, acute coronary syndrome, peripheral artery disease, cardiac ablation, cardiac cardioversion, percutaneous intervention, coronary artery bypass graft, issues regarding modifiable risk factors and monitoring, recommendations regarding how to switch between anticoagulant when indicated, and how to manage missed dose or double dose in patients. By selecting

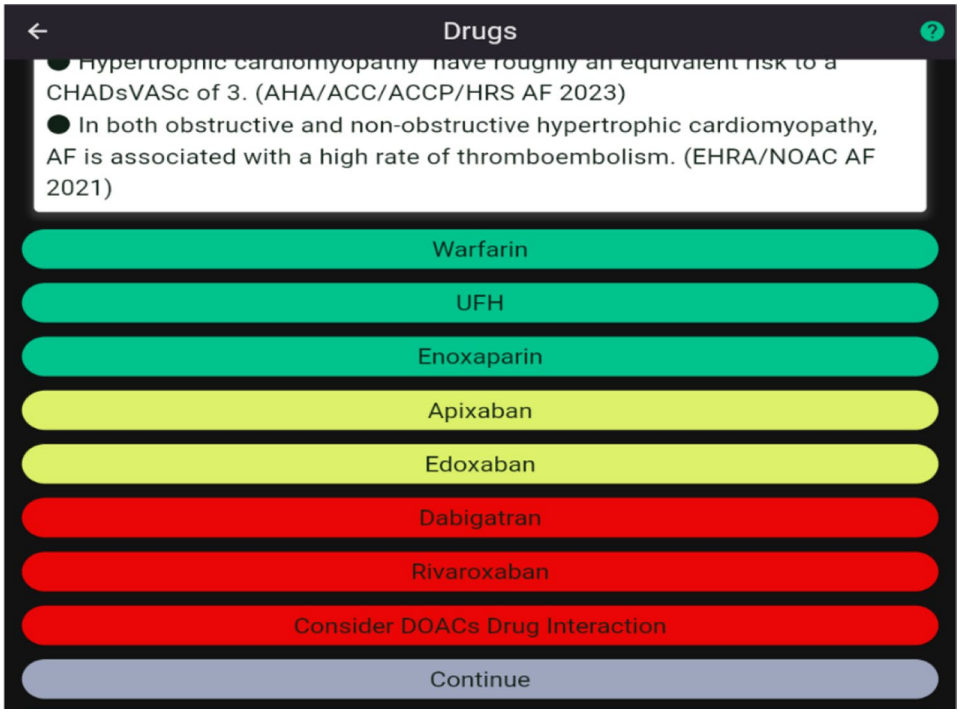

Fig. 7 Example of how ACAFiB-APP displayed results for the anticoagulant selection

each topic users will go through relevant algorithms and receive related information (See Fig. 8).

Usability evaluation

The averages obtained in each section are reported in Table 2. Items with an average score of three or more have good quality.

15 (33.33%) board-certified clinical pharmacists, 15 (33.33%) cardiologists, and 15 (33.33%) experts in medical informatics completed the questionnaire. In terms of sex distribution, 22 females (48.9%) and 23 males (51.1%) completed the questionnaire.

The minimum score among the fifth sections of uMARS was reported to be 3.54 ± 0.42 for section E regarding the application's subjective aspects, while the maximum mean score (3.84 ± 0.59) was reported for section B regarding the Functionality. Based on Table 2, all of the sections achieved acceptable scores. Moreover, the "application quality ratings" section of the application was reported to be 3.66 ± 0.52. Based on the results of a question from section E about paying for the application, 14 users (31.10%) declared willing to pay while 12 users were not (26.70%) willing to pay, and 19 users (42.20%) might pay. Moreover, more than 70% of the participants rated the overall score of application 4 or 5 from the range of 1 (minimum score) to 5 (maximum score).

Table 3 suggests that there were no statistically remarkable differences in none of the sections while considering the academic field of participants (Clinical Pharmacy, Cardiology, or Medical Bioinformatics) and sex.

Discussion

Health technologies affect cardiology more than other fields of medicine. A study that examined mobile health technologies in various fields showed that among the active platforms, most products are in cardiology (28.2%), ophthalmology and otolaryngology (16.1%), neurology (12.3%), general medicine (6.9%), and mother and child health (5.3%) [52].

Patient-centeredness, multidisciplinary teamwork, and the use of electronic health systems are the main pillars of an organized and coherent system for AF management [53]. CDSS may lead to an improvement in the rational use of anticoagulant drugs and an improvement in the prognosis of patients [54].

The use of digital technologies in the field of AF is widespread, including methods aimed at helping to diagnose the disease, educating patients and their companions and medical staff, remote patient care, assessing the risk of incidents such as bleeding and thrombosis, promoting the adherence of the patient to the drug, monitoring the effectiveness of the drug and helping to choose

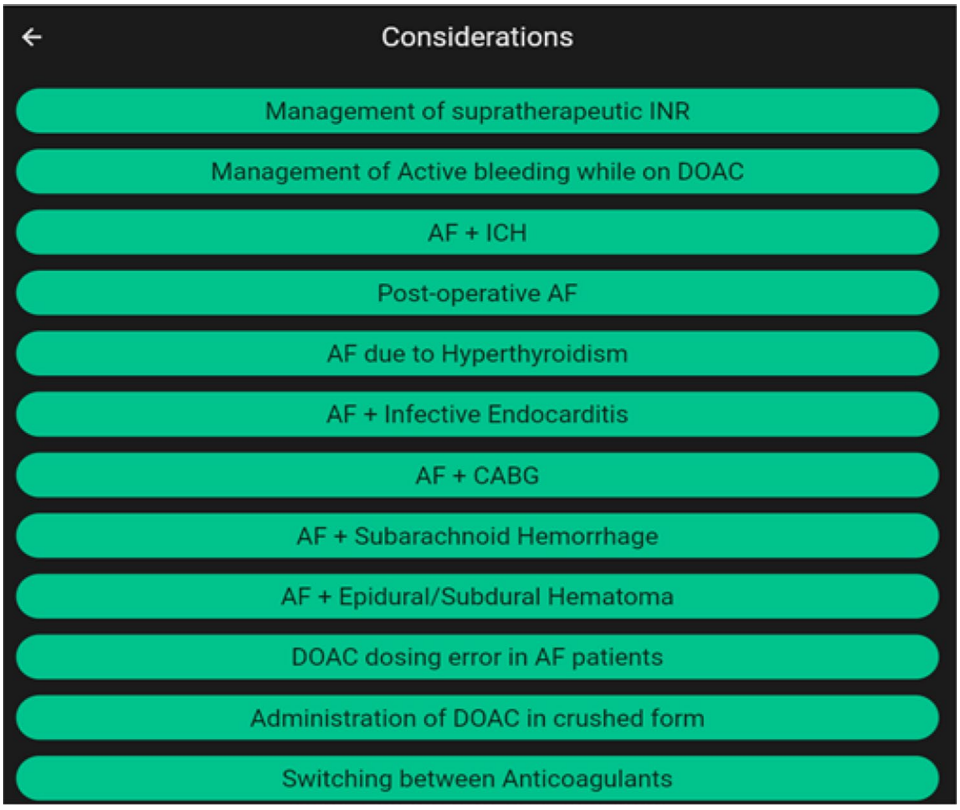

Fig. 8 Examples of topics covered in the consideration section of ACAFiB-APP

Table 2 Usability evaluation results

Sections	Number of items	Name of sub-section	Mean score	Quality
App quality ratings	**19**	A, B, C, D	**3.66 ± 0.52**	Good
A: Engagement	5	Entertainment; Interest; Customization; Interactivity; Target group	3.55 ± 0.50	Good
B: Functionality	4	Performance; Ease of use; Navigation; Gestural design	3.84 ± 0.59	Good
C: Aesthetics	3	Layout; Graphics; Visual appeal	3.62 ± 0.60	Good
D: Information	7	Accuracy of app; Goals; Quality of information; Quantity of information; Visual information; Credibility; Evidence base	3.65 ± 0.42	Good
App subjective quality	**4**	E	**3.54 ± 0.42**	Good
E: App subjective score	4	Recommendations; Usage; Pay; Rating	3.54 ± 0.42	Good
APP-specific	**6**	F	**3.67 ± 0.6**	Good
F: App perceived impact	6	Awareness; Knowledge; Attitudes; Intention to change; Help-seeking; Behavior change	3.67 ± 0.6	Good

the best treatment plan for the patient [55]. Digital technologies are now an integral part of everyday life [56]. Today, innovation, especially in the digital field, is happening on an unprecedented scale. However, despite its potential, its practical application in the field has been neglected to some extent [57].

Given the lack of a comprehensive CDSS for selecting anticoagulant drugs in AF patients, we aimed to develop a CDSS that takes into account patients' comorbidities, laboratory data, concurrent medications, and related considerations. The CDSS was designed to simplify the available data from the latest version of globally accepted clinical guidelines. In addition, we have considered the development of monitoring calculators and relevant considerations for every anticoagulant medication. In this regard, the developed application was evaluated by end-users and medical informaticians.

It is claimed that the use of these systems as an auxiliary tool for clinical decisions will help clinicians in terms of rational clinical judgment [58]. A study conducted with the presence of 15 physicians and 1493 AF patients showed that in more than 40% of patients, there was a discrepancy in the prescribed thromboprophylaxis process with the recommendations mentioned in the guidelines [59].

Results of a study involving 373 patients with AF demonstrated that a web-based CDSS for anticoagulant prescription significantly improved adherence to treatment guidelines, increasing compliance from 48 to 65.5% (P-*value* = 0.0001). The utilization of oral anticoagulant medications has risen markedly (P-*value* = 0.01). While reports highlight the positive impact of these technologies on thromboprophylaxis management, certain studies suggest that these systems may lack effectiveness [33, 60].

CDSSs can be utilized to prevent medication errors. A study was conducted to develop a CDSS in a hospital to prevent Anticoagulant Duplication (AD). The paper outlines the steps taken in this process, including the validation step that was completed [61].

Similar to this effort, the ACC developed an application known as AnticoagEvaluator [35], which is primarily accessible as a web-based system and a mobile application. This program gives the user basic recommendations regarding anticoagulant medicines after calculating the CHA2DS2-VASc score, HAS-BLED, and eGFR and obtaining some information to choose the anticoagulant drug in AF patients. In addition, it computes the risk of bleeding, thromboembolic events, and stroke for each anticoagulant and antiplatelet medication and provides broad information on the adverse effects of the medications. Unlike our study, this application simply produces basic and general pharmacological information and cannot account for the unique clinical situations of individuals, such as concurrent disorders and drugs that interfere with one another.

Researchers developed Anticoagulation Manager [62]; an intelligent clinical decision workflow management system designed for iOS-based mobile devices. The application assists clinicians in selecting the most suitable

Table 3 uMARS results based on the academic field and sex of experts

Section	Clinical Pharmacists	Cardiologists	Medical Informaticians	*P*-value	Male	Female	*P*-value
App quality ratings (A, B, C, D)	3.66 ± 0.36	3.73 ± 0.44	3.58 ± 0.40	0.60	3.66 ± 0.33	3.67 ± 0.43	0.88
A: Engagement	3.58 ± 0.56	3.68 ± 0.32	3.38 ± 0.64	0.39	3.58 ± 0.44	3.53 ± 0.74	0.23
B: Functionality	3.80 ± 0.59	3.84 ± 0.48	3.89 ± 0.78	0.73	3.74 ± 0.56	3.98 ± 0.80	0.35
C: Aesthetics	3.52 ± 0.71	3.72 ± 0.68	3.63 ± 0.51	0.61	3.65 ± 0.53	3.58 ± 0.71	0.80
D: Information	3.66 ± 0.63	3.88 ± 0.46	3.41 ± 0.32	0.20	3.67 ± 0.53	3.59 ± 0.48	0.36
E: App subjective score	3.67 ± 0.43	3.77 ± 0.32	3.19 ± 0.64	0.28	3.52 ± 0.48	3.58 ± 0.70	0.45
F: App perceived impact	3.77 ± 0.59	3.88 ± 0.40	3.36 ± 0.87	0.16	3.69 ± 0.75	3.65 ± 0.80	0.77

follow-up clotting tests. This application, in contrast to the aforementioned work, concentrates on clotting tests.

In line with this work, in [63], the "app quality score" section of the application was reported to be 3.45 ± 0.94. Same as ours, no relationship was found between sex and the median score of each section of the uMARS questionnaire. Notably, based on the results of the evaluation, section B regarding functionality has the highest score among various domains. This might be due to the development of a demo film regarding how the use of the application on the home page which might ease the usage. Another reason might be due to the development of a table of contents which makes it easier for the user to search through desired topics. It is concluded that setting a thorough usability evaluation is essential in system development. Conducting such an evaluation ensures that the system meets user needs effectively and enhances overall user experience [57].

On the other hand, section E regarding the application's subjective aspects received the lowest score. This section contains questions about recommending this application to others and the number of times to use the application in a year. Unlike cardiologists, not all clinical pharmacists work exclusively in cardiology wards. This can lead to the number of times the application use is less recommended.

No statistically remarkable differences were found between the sex and academic field of the participants who filled out the uMARS questionnaire in none of the items.

In the first section of uMARS, which is related to the interestingness and interactivity of the application, medical informatics experts gave a lower score. This could be due to differences in the way they interact with content. Because clinical pharmacists and cardiologists are familiar with the medical and clinical content, they are likely to better understand its application and importance. This might be the reason for higher but statistically insignificant scores reported by cardiologists in all domains, as this application might be used more by them as compared with clinical pharmacists and experts in bioinformatics.

This familiarity may make the application seem more attractive to them in terms of interaction and interestingness.

On the other hand, medical informatics professionals may focus more on the technical and structural aspects of the application, and if these aspects are not optimal for them, they may give a lower score to the interactivity and interesting part. For them, this criterion may be less important than the technical and functional dimensions.

ACAFiB is designed as a web-based application. An application software that is stored on a remote server and provided via the internet through a browser interface is referred to as a web application. The development cycles for web applications are often quite short, and the development teams are typically quite small [30]. Taking into consideration the benefits that both platforms offer, we decided to base our application on the web.

The process of identifying the indication, selecting the suitable medication, and establishing the correct dosage for thromboprophylaxis in patients with AF presents several challenges. Noncompliance with instructions and guidelines in the management of AF is a common problem, especially regarding thromboprophylaxis. Due to physicians' concerns about bleeding risks in this patient population, anticoagulant medications are often either not prescribed or administered at suboptimal doses. Patients often present with multiple underlying comorbidities which necessitate special considerations. As a result, opportunities to consider available resources for selecting the most suitable drug regimen for the patient, are often lacking.

To facilitate the dissemination of CDSSs and the advancement of new medical technologies, the development of a web-based CDSS capable of receiving patient information (including demographic information, tests, and underlying diseases) within a specified time frame is necessary. The introduction of the appropriate CDSS in the field contributes to the improvement of the health system and the well-being of society, as well as reducing treatment complications and costs. Recommendations from ACAFiB may pave the way for considering which options exist before shared decision-making and considering patients' preferences for finalizing a clinical decision.

Limitations and future directions

Although the majority of the world's authoritative guidelines were incorporated in this application leading to the comprehensiveness of the ACAFiB, it should be noted that there might be several clinical scenarios not incorporated in this application mainly due to the lack of enough clinical evidence to be incorporated in clinical guidelines. This might be considered one of the limitations of our work. While using ACAFiB it should be noted that each patient is a specific clinical scenario, so besides ACAFiB assistance the physician's clinical judgment should be the main source for clinical decisions. Another limitation might be the presence of varying recommendations within the content of some selected guidelines, necessitating a review by a panel of experts. However, in some cases, the experts could not reach a definite conclusion. In these cases, both results were displayed to the user with the relevant references and level/class of recommendation.

Future studies should evaluate the effectiveness of these CDSS based on the complicated clinical scenarios, and

patient-related outcomes. Considering the effect of these systems on the patients' safety, concordance of physicians' decisions to clinical guidelines, the confidence level of physicians during decision-making, and the time spent for decision-making regarding each clinical scenario considering physician workloads seems logical before widely being used in clinical practice.

Conclusion

ACAFiB has incorporated and simplified the latest guidelines in the field of thromboprophylaxis of AF besides considering patient-specific factors like comorbidities, lab results, and concurrent medications. In light of the development of novel medical technologies and the advancement of CDSSs, a web-based application that can quickly represent patient-specific recommendations was designed. Considering these aspects, ACAFiB may facilitate decision-making regarding the thromboprophylaxis of complicated AF clinical scenarios.

Abbreviations

CDSS	Clinical Decision Support System
AF	Atrial Fibrillation
DOAC	Direct Oral Anticoagulant
RUD	Rational Use of Drugs
AHA	American Heart Association
ACC	American College of Cardiology
ESC	European Society of Cardiology
EHRA	European Heart Rhythm Association
NAM	National Academy of Medicine
EACTS	European Association of Cardio-thoracic Surgery
UFH	Unfractionated Heparin
aPTT	activated Partial Thromboplastin Time
VS	Visual Studio
SDK	Software Development Kit
BMI	Body Mass Index
INR	International Normalized Ratio
AD	Anticoagulant Duplication

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04615-w.

Supplementary Material 1

Supplementary Material 2

Author contributions

S.N. and K.M. contributed to the study's conception and design. Material preparation and data collection were conducted by R.A. A A. S. and E.R. supervised the technical aspects of application development. S.N., K. M., and R.M. organized the expert panel for content confirmation. Analysis regarding application quality was performed by M.KM. The first draft of the manuscript was written by S.R. All authors read and approved the final manuscript.

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Data availability

You can access the application via the link: (http://www.acafib.ir) A username and password for log-in can be sent based on your request.

Declarations

Ethics approval and consent to participate

This study was conducted according to the guidelines of the Declaration of Helsinki. The methodology was approved by the Tehran University of Medical Sciences (Ethics approval number: IR.TUMS.TIPS. REC. 1402.052). Informed consent to participate was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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