BEYOND Pooled – part of the BEYOND study program

(BEnefit of NOACs studY of nOn-valvular AF patieNts in NorDic countries)

AARHUS UNIVERSITY

Department of Clinical Epidemiology
Aarhus University Hospital
Olof Palmes Allé 43 -45
8200 Aarhus N
DENMARK

UNIVERSITY OF BERGEN
Department of Global Public Health and Primary Care
University of Bergen
Kalfarveien 31
5018 Bergen
NORWAY

Karolinska Institutet

Centre for Pharmacoepidemiology
Karolinska Institutet
Karolinska University Hospital
SE 171 76 Stockholm
SWEDEN

FINAL REPORT

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Title	Beyond Pooled –Part of the BEYOND study program (BEnefit of NOACs studY of nOn-valvular AF patieNts in NorDic countries)
Protocol number	B0661103
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Medicinal product	Warfarin Pradaxa® - dabigatran Xarelto® - rivaroxaban Eliquis® - apixaban
Product reference	EU/1/11/691/001 -015
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Marketing Authorisation Holder (MAH)	Bristol -Myers Squibb/Pfizer European Economic Interest Group (EEIG)
Joint PASS	No
Research question and objectives	The overall aim of this study is to evaluate effectiveness and safety of each NOAC compared with warfarin in treatment-naïve initiators of anticoagulants with NVAF in routine clinical practice in Denmark, Norway and Sweden. The study used pooled data from nationwide registries in Denmark, Norway and Sweden.
Author	Vera Ehrenstein, MPH, DSc Grethe S. Tell, MD, MPH, PhD Marie Linder, PhD

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1. ABSTRACT (STAND -ALONE DOCUMENT)

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AF	Atrial fibrillation
ACE	Angiotensin converting enzyme
ATC	Anatomical Therapeutic Chemical
BEYOND	**BE**nefit of NOACs stud**Y** of n**On-valv**ular AF patie**N**ts in Nor**D**ics
CAD	Coronary artery disease
CCI	Charlson Comorbidity Index
CDM	Common data model
$CHADS_2$	Congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke [double weight]
CHA_2DS_2VASc	Congestive heart failure/LV dysfunction, Hypertension, Age≥75 years, Diabetes mellitus, Stroke, Vascular disease, Age 65 -74 years, Sex category
CI	Confidence interval
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
DVT	Deep vein thrombosis
EMA	European Medicines Agency
GI	Gastrointestinal
GPP	Good Pharmacoepidemiology Practices
GVP	Good Pharmacovigilance Practice
HAS-BLED	Hypertension, Abnormal renal and liver function, Stroke, Bleeding, Labile INR, Elderly, Drugs or alcohol
HF	Heart failure
HR	Hazard ratio
ICMJE	International Committee of Medical Journal Editors
ICD-10	International Classification of Diseases, Tenth Revision
IEC	Independent Ethics Committee
INR	International normalised ratio
IQR	Interquartile range
IRB	Institutional Review Board
ISPE	International Society for Pharmacoepidemiology
ITT	Intention-to-treat
MAH	Marketing Authorisation Holder

MI	Myocardial infarction
NI	Non-interventional
NOAC	Non-vitamin K oral anticoagulants
NSAID	Non-steroidal anti-inflammatory drug
NVAF	Non-valvular atrial fibrillation
OAC	Oral anticoagulant
PAD	Peripheral arterial disease
PAS	Post -authorisation study
PASS	Post -authorisation safety study
PE	Pulmonary embolism
PS	Propensity score
RCT	Randomised controlled trial
SAP	Statistical Analysis Plan
SD	Standard deviation
SMD	Standardised mean difference
SE	Systemic embolism
SSRI	Selective serotonin reuptake inhibitor
TIA	Transient ischaemic attack
US	United States
VKA	Vitamin K antagonist

3. INVESTIGATORS

Principal Investigator(s) of the Protocol

Name, degree(s)	Title	Affiliation
Henrik Toft Sørensen, MD, PhD, DMSc	Professor, legally responsible investigator	Department of Clinical Epidemiology, Aarhus University, Aarhus, Denmark
Aaron Jenkins, PhD	Outcomes and Evidence Director, Pfizer NI study lead	Pfizer Inc.

Lead Country Investigator(s) of the Protocol

Name, degree(s)	Title	Affiliation	Address
Helle Kieler, MD, PhD	Professor, Principal Investigator, Sweden	Centre for Pharmacoepidemiology Karolinska Institutet	Karolinska Universitetssjukhuset Solna, Centrum för läkemedelsepidemiologi T2 171 76 Stockholm, Sweden http://ki.se/en/meds/centre-for-pharmacoepidemiology
Grethe S. Tell, MD, MPH, PhD	Professor, Principal Investigator, Norway	Department of Global Public Health and Primary Care University of Bergen	Kalfarveien 31, NO-5018 Bergen, Norway http://www.uib.no/en/globpub
Vera Ehrenstein, MPH, DSc	Professor, Lead Investigator, Denmark	Department of Clinical Epidemiology Aarhus University	Olof Palmes Allé 43-45 DK-8200 Aarhus N, Denmark, http://www.kea.au.dk/en/index.html

4. OTHER RESPONSIBLE PARTIES

Responsible Party name and affiliation	Role in the study
Morten Madsen, MSc	Statistician, Denmark Department of Clinical Epidemiology Aarhus University Olof Palmes Allé 43-45 DK-8200 Aarhus N, Denmark
Astrid Lunde, MSc, PhD	Statistician, Norway Department of Global Public Health and Primary Care University of Bergen Kalfarveien 31, NO-5018 Bergen, Norway
Marie Linder, PhD	Statistician, Sweden Centre for Pharmacoepidemiology Karolinska Institutet Karolinska Universitetssjukhuset Solna Centrum för läkemedelsepidemiologi T2 171 76 Stockholm, Sweden
Søren Paaske Johnsen, MD, PhD	Co-investigator, Denmark (through October 2018) Department of Clinical Epidemiology Aarhus University Hospital Olof Palmes Allé 43-45 DK-8200 Aarhus N, Denmark
Morten Schmidt, MD, PhD	Clinical expert, Denmark (from November 2018) Registrar, Department of Clinical Epidemiology Aarhus University Hospital Olof Palmes Allé 43-45 DK-8200 Aarhus N, Denmark
Gerhard Sulo, MD, PhD	Clinical expert, Norway Department of Global Public Health and Primary Care University of Bergen Kalfarveien 31, NO-5018 Bergen, Norway
Zoltan Thinsz	Project manager, Sweden Centre for Pharmacoepidemiology Karolinska Institutet Karolinska Universitetssjukhuset Solna Centrum för läkemedelsepidemiologi T2 171 76 Stockholm, Sweden
Anna Ingemarsdotter	Project administrator, Sweden Centre for Pharmacoepidemiology Karolinska Institutet Karolinska Universitetssjukhuset Solna Centrum för läkemedelsepidemiologi T2 171 76 Stockholm, Sweden

List of Steering Committee members

Name, degree(s)	Title/Role	Affiliation	Address
Denmark			
Søren Paaske Johnsen, MD, PhD	Professor Member of Steering Committee*	Center for Clinical Health Services Research, Aalborg University	Sdr. Skovvej 15, 9000 Aalborg, Denmark
Gunnar Gislason, MD, PhD	Professor Cardiologist Member of Steering Committee*	Department of Cardiology, Gentofte University Hospital	Herlev-Gentofte Hospital-Gentofte, Kildegårdsvej 28, 2900 Hellerup
Norway			
Sigrun Halvorsen MD, Ph.D	Professor Cardiologist Member of Steering Committee*	Department of Cardiology, Oslo University Hospital, Ullevål, Oslo	Oslo University Hospital, Ullevål NO-0424 Oslo Norway
Waleed Ghanima, MD, PhD	Professor, Haematologist Member of Steering Committee*	Østfold Hospital Trust Fredrikstad	Sigrid Undset v 12 1619 FREDRIKSTAD
Sweden			
Faris Al-Khalili, MD	Senior Consultant Cardiologist Member of Steering Committee	Sophiahemmet Hospital,, Stockholm –Sweden	HLA-mottagningen Sophiahemmet Valhallavägen 91,E1 Stockholm Sweden
Germany			
Stefan Hohnloser, MD	Professor Cardiologist Chair of Steering Committee*	Dep. of Cardiology J. W. Goethe University	J. W. Goethe University Dep. of Cardiology Div. of Clinical Electrophysiology Building 23 c Theodor Stern Kai 7 60590 Frankfurt Germany
Steering Committee provides advice on study design, review of study results and may act as publication authors in accordance with International Committee of Medical Journal Editors (ICMJE) criteria.			

5. MILESTONES

Milestone	Planned date	Actual date
Start of data collection	17 August 2018	17 August 2018
End of data collection	22 September 2018	22 September 2018
Registration in the EU PAS register	06 October 2017	5 October, 2017
Final study report	15 March 2019	25 July 2019

6. RATIONALE AND BACKGROUND

Atrial fibrillation (AF) is the most common cardiac rhythm disorder. AF is a disturbance of cardiac rhythm that results from dysfunction of the electrophysiological conduction system in the upper chambers of the heart. It is marked by disorganised, rapid, and irregular atrial activation. The ventricular response is also irregular. Symptoms of AF vary substantially. Many patients are asymptomatic and have no apparent haemodynamic consequences from AF. Other patients experience only minor palpitations or sense of irregularity of the pulse. However, haemodynamic effect in patients with AF can be dramatic, depending on the need of normal atrial contractivity and ventricular response. Hypotension, pulmonary congestion and angina symptoms may be severe in some patients (1-3).

In contrast to other cardiac diseases, such as acute myocardial infarction or stroke, the prevalence of AF is rising. In the last several decades, incidence of hospital-diagnosed AF has been increasing, on average, by 4% annually, owing, among other things, to diagnostic-advances driven improved detection and to population aging (1-3). Risk of AF increases with age, and affects 5% of persons 75 years or older. AF is more prevalent in men than in women. In addition to sex and age, risk factors for AF include hypothyroidism, hypertension, anaemia, ischaemic heart disease, and valvular heart disease (1). AF is associated with a five-fold increase in the risk of stroke and a two-fold increase in mortality (2).

AF treatment strategies include acute rate control, including termination; chronic rate control; and catheter and surgical ablation therapy for prevention of AF recurrence. AF is of particular importance in patients with risk factors for stroke. In patients not adequately anticoagulated and AF is lasting longer than 24-48 hours, a trans-oesophageal electrocardiogram can be performed to rule out the presence of left atrial thrombus that may dislodge, with attempted restoration of sinus rhythm with either non-pharmacologic or non-pharmacologic therapy.

Most AF patients require long-term pharmacologic treatment with oral anticoagulants (OACs), for which, until recently, vitamin K antagonists (VKAs), primarily warfarin, have been the standard care (4). When optimally dosed, VKAs are effective in stroke prevention. Challenges of treatment with VKAs include the need for close monitoring (via the international normalised ratio [INR] measures) to maintain the optimal anticoagulation level; dietary restrictions to allow for constant dosing; and concerns about drug interactions. Bleeding, especially intracranial bleeding, is the main safety concern associated with VKAs use (5).

Non-vitamin K oral anticoagulants (NOACs) are an alternative treatment option for patients with non-valvular AF (NVAF), since they allow for a more convenient anticoagulation regimen than VKAs, with comparable efficacy and safety (4). Current guidelines in the United States (US) (6) and in Europe (7) recommend NOACs as the first-line treatment strategy for stroke prevention in patients with AF. In Denmark, dabigatran was first introduced in August 2011, rivaroxaban in February 2012, and apixaban in December 2012 (8). The respective dates were July 2008, December 2008, and October 2011 in Norway (9-11); and March 2008, September 2008, and May 2011, in Sweden (12, 13). The NVAF indication was approved in Europe in August 2011 for dabigatran (14), in December 2011 for rivaroxaban (15), and in November 2012 for apixaban (16, 17).

In randomised controlled trials (RCTs) of individual NOACs vs. warfarin among patients with NVAF (the ARISTOTLE trial [apixaban] (18); the RE-LY trial [dabigatran] (19); and the ROCKET-AF trial [rivaroxaban] (20)), apixaban was the only NOAC with lower rate of discontinuation or major bleeding compared with warfarin (18-20). In two network meta-analyses of the trial data (adjusted indirect comparisons of each NOAC against warfarin), apixaban was safer and more efficacious than dabigatran or rivaroxaban as measured by

bleeding or discontinuation and bleeding outcomes (21, 22). A subsequent meta-analysis, which also included RCTs evaluating edoxaban and ximelagatran in addition to apixaban, dabigatran and rivaroxaban, showed no evidence for superiority of any NOAC drug class of once vs. twice daily regimen (23).

Many previous observational studies that examined safety and effectiveness of NOACs in routine clinical practice generally found apixaban, dabigatran and rivaroxaban to have a positive benefit to risk balance when comparing each NOAC with warfarin (8, 24-29). Among the limitations affecting many of the previous studies are the relatively short follow-up, concerns about unmeasured confounding, and low precision of results, especially in subgroup analyses. The current study aims to use individually pooled routinely collected data from three Scandinavian countries to assess effectiveness and safety of apixaban, rivaroxaban, dabigatran, each compared with warfarin, among patients with NVAF, and to describe characteristics and health care utilisation level among the NOAC users. The specific projected contribution of this study will be to obtain precise estimates of association overall and in clinically important subgroups, while taking advantage of a longer follow-up, and applying previously used analytic strategy (26, 27) to facilitate comparison of results across studies. Other important advantages of the Scandinavian countries include universal access to health care, similar clinical practice, uniform recording practices, comparable patterns of hospitalisation and referral to specialist care, and high overall quality of care, including high quality of warfarin therapy (30-40).

This non-interventional study is designated as a Post-Authorisation Safety Study (PASS) and is conducted voluntarily by the MAH.

7. RESEARCH QUESTION AND OBJECTIVES

The overall aim of this study was to evaluate effectiveness and safety of each NOAC compared with warfarin in treatment-naïve adult initiators of anticoagulants with NVAF in routine clinical practice in Denmark, Norway and Sweden. The primary, secondary, and exploratory objectives are listed below.

7.1. Primary objectives

- To compare risks of the composite endpoint of ischaemic or haemorrhagic stroke (hereafter, any stroke) or systemic embolism (SE) at an acute hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare risks of intracranial, gastrointestinal (GI) or other (hereafter any bleeding) at an acute hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin

7.2. Secondary objectives

- To compare risks of ischaemic stroke at an acute hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare risks of haemorrhagic stroke at an acute hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare risks of intracranial bleeding at an acute hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin

- To compare risks of GI bleeding at an acute hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare risks of acute myocardial infarction (MI) at an acute hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare risks of systemic embolism at an acute hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare all-cause mortality among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare risks of the composite endpoint of ischaemic stroke at an acute hospitalisation with an overnight stay, SE at an acute hospitalisation with an overnight stay, acute MI at an acute hospitalisation with an overnight stay, or all-cause mortality among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare risks of any bleeding at an acute or planned hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare risks of any bleeding occurring at an acute hospital contact without an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin
- To compare risks of bleeding (intracranial, GI, other) recorded as the primary diagnosis at an acute hospitalisation with an overnight stay among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin (sensitivity analysis)
- To describe demographic, clinical, and socioeconomic (to the extent possible) characteristics for OAC treatment naïve patients with NVAF who initiate apixaban, dabigatran, rivaroxaban, or warfarin

7.3. Exploratory objective

To describe bleeding- and stroke-related acute hospital care resource utilisation among the OAC-treatment naïve NVAF patients who initiate apixaban, dabigatran, rivaroxaban, or warfarin, as measured by the number of hospitalisations and bed days, number of planned and acute outpatient hospital visits, and to assess, to the extent possible, associated costs.

8. AMENDMENTS AND UPDATES

Table 1. Amendments to the Protocol

Amendment number	Date	Substantial or administrative amendment	Protocol section(s) changed	Summary of amendment(s)	Reason
1.1	26th June 2018	Administrative	2 (Responsible parties)	Update of names for responsible parties, and clarification of roles as principle investigators, steering committee and other responsible parties.	Change of personnel, and provision of additional clarification

		Administrative	3 (Abstract)	Abstract updated to be consistent with changes in other section of the protocol and statistical analysis plan (SAP).	Review of SAP resulted in a number of further clarifications and amendments (see entries below).
		Administrative	5 (Milestones)	End of data collection and date of final study report updated to reflect new timelines.	New timelines for availability of data from Norway has meant study timelines were required to be updated.
		Administrative	7 (Research question and objectives)	Primary objectives to clarify definition of any stroke to include ischaemic or haemorrhagic stroke. Primary and secondary endpoints updated to require acute hospitalisation with an overnight stay .Additional secondary endpoint added to provide full breakdown of composite primary endpoint. Update of description of exploratory endpoints.	Provide clarity to study objectives, and select most robust endpoint definition for analysis. Secondary endpoints added to provide full breakdown of composite endpoints, capture safety events not requiring an overnight stay in hospital .Details on exploratory endpoints added to reflect outpatient hospital visits.
		Administrative	8 (Research methods)	Updated to reflect availability of data from Sweden until 2016, so this is now in line with other countries in the study. Clarification of patient population as treatment naïve. Clarification of exclusion criteria look back periods (5 years for mitral stenosis or mechanical heart valves; 9 months for pregnancy).Definition of primary and secondary endpoints clarified to reflect updates in section 7.Additional subgroup analyses added and clarified. Additional section in 8 added for Record retention. Definition of cumulative incidence updated to incorporate data over full follow up period.	Changes made to be consistent with greater data availability in Sweden, provide clarification on definition of patients as treatment naïve and clarify exclusion criteria. Endpoints updated to reflect clarified definitions in other sections. Further subgroup analyses added after discussion with steering committee. Additional sub-sections in section 8 added as required by Pfizer Clinical and Medical Controlled Document (CMCD) communication on the Global Standard Operating Procedure (GSOP) Clinical Trial 24 (CT24-GSOP) protocol and

					informed consent document templates 25-JUN-2018, as required by the General Data Protection Regulation.

9. RESEARCH METHODS

Study Protocol version 1.1 (Appendix 2), amended 5 July 2018, describes the research methods in detail. Key elements of the research methods are presented below.

9.1. Study design

This was a cohort study based on routinely and prospectively collected data from population-based health and administrative registries and databases in Denmark, Norway, and Sweden. The primary study endpoints were serious medical conditions requiring hospitalisation and are therefore expected to be well captured in the available data sources. Furthermore, this study used the active comparator new user design to maximise alignment of the start of follow-up with the start of treatment, thus reducing healthy adherer bias, which might potentially preclude identification of early adverse events (41). Propensity score (PS) matching was used to balance multiple measured covariates in each NOAC vs. warfarin contrasts.

9.2. Setting

This study was set in the three Scandinavian countries, each of which has tax-funded universal health care (42); routine recording of prescription dispensings, hospital diagnoses, migrations and deaths; and individual-level data linkage, thus enabling nearly complete follow-up of the entire populations and virtually no loss to follow-up (34, 36).

The source population of this study consisted of adults (persons ages 18 years or older) alive and residents of Denmark, Norway, or Sweden on 01 January 2013. During the relevant period, the adult population was 4.4 million in Denmark (www.statistikbanken.dk); 3.9 million Norway (https://www.ssb.no/en/befolkning); and 7.7 million in Sweden (http://www.scb.se).

9.3. Subjects

The study population were treatment-naïve adults in the source population diagnosed with AF, with a dispensing of apixaban, rivaroxaban or dabigatran (‘the NOACs’) or warfarin during the study population identification period. The study population identification period was from 01 January 2013 to 31 December 2016, with follow-up through 31 December 2016. The maximum baseline period was 5 years pre-index date, and was shorter for selected covariates, such as cancer (Appendix 4). For each patient included in the study, the date of dispensing of the first study OAC (apixaban, dabigatran, rivaroxaban, or warfarin) during the study population identification period was the index date. In the main analyses of the primary

and secondary endpoints (Section 9.4.2), patients were followed from the index date until a given endpoint, death, OAC treatment switch or discontinuation, emigration, or 31 December 2016, whichever came first. In the intention-to-treat (ITT)-like sensitivity analyses of the primary endpoints and the secondary composite endpoint, follow-up was not censored by treatment switch or discontinuation, i.e., patients were followed from the index date until a given endpoint, death, emigration, or 31 December 2016, whichever came first.

9.3.1. Inclusion criteria

Patients had to meet all of the following inclusion criteria on the index date:

- Be alive and of age 18 years or older;
- A dispensing of apixaban, dabigatran, rivaroxaban, or warfarin between 01 January 2013 and 31 December 2016;
- Diagnosis of AF recorded up to 5 years before or up to 60 days after the index date.

9.3.2. Exclusion criteria

Patients meeting any of the following criteria were ineligible and therefore excluded:

- A diagnosis of mitral stenosis or presence of mechanical heart valves recorded up to 5 years before and including the index date, to rule out non-NVAF indication of OAC use;
- A diagnosis of pulmonary embolism (PE) or deep vein thrombosis (DVT) recorded up to 6 months before and including the index date, to rule out non-NVAF indication of OAC use;
- A record of knee arthroplasty or hip arthroplasty 6 weeks before and including the index date, to rule out non-NVAF indication of OAC use;
- A dispensing, within the 12 months before the index date, of any VKAs, direct thrombin inhibitors, or direct factor Xa inhibitors;
- Dispensing of more than one different OACs on index date;
- Residence in a given country for less than 5 years before index date;
- A record of pregnancy within 9 months before index date.

9.4. Variables

9.4.1. Exposure

Initiation of an OAC was measured by a dispensing at a community pharmacy, as recorded in the nationwide prescription registries of the three Scandinavian countries (see Section 9.5).

9.4.2. Endpoints

Primary, secondary, and exploratory endpoints were defined.

9.4.2.1. Primary endpoints

- Composite endpoint of any stroke or SE at an acute hospitalisation with an overnight stay;
- Any bleeding at an acute hospitalisation with an overnight stay.

9.4.2.2. Secondary endpoints

- Ischaemic stroke at an acute hospitalisation with an overnight stay;

- Haemorrhagic stroke at an acute hospitalisation with an overnight stay;
- Intracranial bleeding at an acute hospitalisation with an overnight stay;
- GI bleeding at an acute hospitalisation with an overnight stay;
- Acute MI at an acute hospitalisation with an overnight stay;
- SE at an acute hospitalisation with an overnight stay;
- Death of any cause;
- The composite endpoint of ischaemic stroke at an acute hospitalisation with an overnight stay, SE at an acute hospitalisation with an overnight stay, acute MI at an acute hospitalisation with an overnight stay, or all-cause mortality;
- Any bleeding at an acute or planned hospitalisation with an overnight stay;
- Any bleeding occurring at an acute hospital contact without an overnight stay;
- Any bleeding recorded as the primary diagnosis at an acute hospitalisation with an overnight stay (sensitivity analysis).

9.4.2.3. Exploratory endpoints

In an exploratory analysis, bleeding- and stroke-related health care resource utilisation among the patients treated with the study OACs (number of hospitalisations and bed days) and the associated costs were assessed descriptively in the PS-matched population.

9.4.3. Covariates

Baseline characteristics of the study population were ascertained during up to 5-year baseline before and including the index date: age at index date (in groups and as a continuous variable), sex, overall comorbidity (using the Charlson Comorbidity Index [CCI]), the CHA_2DS_2VASc score, $CHADS_2$ score, the HAS-BLED score, major bleeding, ischaemic stroke, transient ischaemic attack (TIA), history of heart failure (HF), cancer, diabetes, chronic obstructive pulmonary disease (COPD), hypertension, chronic kidney disease (CKD), liver disease, MI, alcohol abuse, peripheral arterial disease (PAD), coronary artery disease (CAD), dementia, cancer, and cardioversion. Baseline concomitant medication use was assessed using dispensings records within 90 days of index date for angiotensin converting enzyme (ACE) inhibitors, amiodarone, dronedarone, beta-blockers, H2-receptor antagonists, proton pump inhibitors, antidiabetics, anti-platelets, statins, aspirin, selective serotonin reuptake inhibitors (SSRIs), and non-steroidal anti-inflammatory drugs (NSAIDs). Health care utilisation level at baseline was measured by inpatient and outpatient hospital encounters. Available socioeconomic characteristics varied by country. Denmark: household income in 3 years pre-index date, highest achieved education, and employment status. Sweden: personal income in 3 years pre-index date, and highest achieved education. Data on socioeconomic characteristics were not available in Norway for this analysis.

9.4.4. Subgroups

Consistency of the results for the primary endpoints and of the composite secondary endpoint were evaluated according to the following subgroups:

- In each country (Denmark, Norway, Sweden);
- By age on the index date (<65; 65-<75 years, ≥75-<85 years; and in patients ≥85 years old);
- By sex;

- According to CHA_2DS_2VASc score category in the baseline;
- According to $CHADS_2$ score category in the baseline;
- According to HAS-BLED score category in the baseline;
- According to initial dosage in the baseline (any licensed dose for AF vs reduced dose);
- In patients with/without CKD in the baseline;
- In patients with/without HF in the baseline;
- In patients with/without CAD in the baseline;
- In patients with/without PAD in the baseline;
- In patients with/without prior ischaemic stroke in the baseline;
- In patients with/without prior any stroke in the baseline;
- In patients with/without prior haemorrhagic stroke in the baseline;
- In patients with/without prior TIA in the baseline;
- In patients with/without prior SE at baseline;
- In patients with/without prior GI bleeding at baseline;
- In patients with/without prior intracranial bleeding at baseline;
- In patients with/without diabetes in the baseline.

9.5. Data sources and measurement

Data for this study originated from selected population-based health and administrative registries in Denmark, Norway and Sweden, summarised in Table 2. In each country, data from all registries are individually linkable via a unique personal identifier (34, 36). The Statistical Analysis Plan (SAP, Appendix 4) provides operational definitions for all variables.

Data in the Scandinavian national registries have been validated and the validity has in general been found to be high in all countries (27, 43-52). For example, the positive predictive value of the combined diagnosis of AF and/or atrial/flutter and other cardiovascular diagnoses typically exceeds 95% in Denmark (53-55), Norway (27) and Sweden (52). Other hospital diagnoses have also been validated (56), including the conditions included in the CCI (50, 57). For drugs used chronically, there is also high level of agreement between general practitioner reported use and dispensing records (58). Furthermore, the CHA_2DS_2VASc, $CHADS_2$ and the HAS-BLED scores can be constructed based on registry data (the HAS-BLED version does not require information regarding INR) (59, 60).

Table 2. National registries in Denmark, Norway and Sweden and type of data available from each registry

Variable	Role	Data source(s)
AF and inclusion/exclusion criteria based on hospital diagnoses and procedures	Definition of the study population	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50)
Initiation of an OAC (apixaban, dabigatran, rivaroxaban, warfarin)	Exposure	Danish National Health Services Prescription Database (38, 62), Norwegian Prescription Database (38), Swedish Prescribed Drug Register (38)

Variable	Role	Data source(s)
Any stroke/SE	Endpoint	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50)
Ischaemic stroke	Endpoint	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50)
Haemorrhagic stroke	Endpoint	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50)
Any bleeding	Endpoint	Danish National Patient Registry(56), Norwegian Patient Registry(61), Swedish National Patient Register (37, 50)
Intracranial bleeding	Endpoint	Danish National Patient Registry(56), Norwegian Patient Registry(61), Swedish National Patient Register (37, 50)
GI bleeding	Endpoint	Danish National Patient Registry(56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50)
Other bleeding	Endpoint	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50)
Acute MI	Endpoint	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50)
Death of all causes	Endpoint	Danish Civil Registration System (36), National Population Register of Norway, Swedish Total Population Register (34), National Registry (Norway) (63), Swedish Cause of Death Register (64)
Emigration	Censoring variable	Danish Civil Registration System (36), National Population Register of Norway, Swedish Total Population Register (34), National Registry (Norway) (63), Swedish Population Register (34)
Sex	Covariate	Danish Civil Registration System (36), National Population Register of Norway, Swedish Total Population Register (34), National Registry (Norway) (63), Swedish Population Register (34)
Age, years	Covariate/subgroup variable	Danish Civil Registration System (36), National Population Register of Norway, Swedish Total Population Register (34), National Registry (Norway) (63), Swedish Population Register (34)
CHA_2DS_2VASc score (65, 66)	Covariate/subgroup variable	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50), Danish National Health Services Prescription Database (38, 62), Norwegian Prescription Database (38), Swedish Prescribed Drug Register (38)
$CHADS_2$ score	Covariate/subgroup variable	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50), Danish National Health Services Prescription Database (38, 62), Norwegian Prescription Database (38), Swedish Prescribed Drug Register (38)
HAS-BLED score (65, 66)	Covariate/subgroup variable	Danish National Patient Registry (56), Norwegian Patient Registry (41), Swedish National Patient Register (31, 42), Danish National Health Services Prescription Database (38, 62), Norwegian Prescription Database (38), Swedish Prescribed Drug Register (38)
Concomitant medication	Covariate	Danish National Health Services Prescription Database (38, 62), Norwegian Prescription Database (38), Swedish Prescribed Drug Register (38)
Comorbidities	Covariates	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50)

Variable	Role	Data source(s)
Health care utilisation	Descriptive characteristic, exploratory endpoint	Danish National Patient Registry (56), Norwegian Patient Registry (61), Swedish National Patient Register (37, 50)
Household income	Covariate	Statistics Denmark, Statistics Sweden
Education	Covariate	Statistics Denmark, Statistics Sweden
Employment	Covariate	Statistics Denmark, Statistics Sweden
Health care costs	Exploratory endpoint	Published data on mean health care costs for specific types of visit

9.6. Bias

An important source of bias is confounding by indication, *i.e.*, prognostically informative prescribing of NOACs vs. warfarin, which is expected to be absent when treatment is randomised (67). Confounding by indication will occur if physicians prescribe NOAC vs. warfarin based on patients' characteristics predictive of the study endpoints (e.g., sex, age, comorbidity, risk scores). In this study, covariates were balanced using 1-to-1 PS matching of members of each NOAC cohort to with members of warfarin cohort. Another important source of bias is Berkson's bias, whereby endpoints' detection rate varies by treatment (68). Because warfarin-treated patients require closer monitoring than NOAC-treated patients, the risks of endpoints may be inflated compared with NOAC-treated patients. In this study, treatment-specific sensitivity of ascertainment of the study endpoints is not known. Potential sources of information bias include misclassification of treatment status by dispensing records or interruptions during hospital stays, misclassification of treatment-naïve status by a 12-month washout period, and potentially differential according to treatment type ascertainment of absolute risks of the study endpoints by hospital encounters. At the same time, specificity of the events' recording is high and relative estimates are therefore expected to be unbiased due to outcome misclassification. Nor can severity of most comorbidities be established, potentially causing misclassification of treatment duration or covariates; the latter will result in residual confounding. Finally, routinely collected data contain no information on the quality of warfarin treatment control or dose for individual patients.

9.7. Study size

Detailed computations of study size and precision are presented in the Study Protocol (Appendix 2). Briefly, it was estimated that the number of patients across the three countries would be sufficient to detect a risk ratio (RR) of 0.8 with a power of 90% and an alpha of 0.05 in a population with a background annual bleeding risk of 2% if there are at least 17,307 apixaban users (assumed to be the smallest group). Similar computations apply to the other primary endpoint of stroke/SE.

9.8. Data transformation

The analyses were conducted on an individual-level dataset from the three countries, prepared according to a common data model (CDM) (69). Statisticians at the investigators' institutions in Denmark, Norway and Sweden completed all data management and quality control required to convert the raw data into the pre-specified CDM. Within each country, the CDM input data files were linked on individual level via a unique study identifier, which replaced the true personal identifier for the purposes of analysis. The completed input datasets from all countries were transferred for analysis to a secure server at Statistics Denmark, where all data were kept in accordance to the rules and regulations governing protection of personal data.

9.9. Statistical methods

9.9.1. Main summary measures

Continuous variables were summarised using either means and standard deviations (SDs) or medians and interquartile ranges (IQRs), or categorised as appropriate. Categorical variables were summarised using frequencies and proportions or percentages. Risk scores were computed using the definitions of the source covariates, as described in the SAP (Appendix 4).

For all primary and secondary endpoints, crude cumulative incidences over the available follow-up and 95% confidence intervals (CIs) within each OAC cohort were computed while treating death as a competing risk (70). Crude rate of each primary and secondary endpoint was computed as a ratio of a first-recorded endpoint-defining event during the follow-up divided by the total amount of person-time in a given cohort. The follow-up for computation of cumulative incidences and rates was censored by death, emigration, treatment switch or discontinuation, or 31 December 2016. Individual outcomes in non-composite endpoints did not censor one another's follow-up.

9.9.2. Main statistical methods

To compare risks of the primary and secondary endpoints among initiators of each NOAC vs warfarin, Cox's proportional-hazards regression was used. Crude and adjusted (via PS-matching) hazard ratios (HRs) and 95% CIs for all primary and secondary endpoints were estimated for initiators of each NOAC vs. propensity-score matched initiators of warfarin. For each patient, a PS was estimated, separately in each country, via logistic regression, as the probability of receiving the given NOAC vs. warfarin, given the covariates, entered into the model as first-order terms. The variables measuring health care utilisation were log-transformed. For each initiator of a given NOAC, initiators of warfarin were matched 1-to-1, without replacement, on the logit of the PS, using caliper of width equal to 0.2 of the standard deviation of the logit of the PS (71). Three NOAC-warfarin PS-matched populations were constructed, for apixaban, dabigatran, and rivaroxaban. Within each matched population, the balance of the measured covariates was assessed by examining standardised mean differences (SMDs) before and after the matching. A SMD <0.1 was considered to be indicative of balance of a given covariate. Members of NOAC cohorts without a match were excluded from the PS-matched analyses. To enable inclusion of all patients in the analysis, in a sensitivity analysis of the primary and composite secondary endpoints, confounding was controlled using conventional adjustment using Cox proportional-hazards regression.

Treatment duration was defined as described by Halvorsen et al (27): for each dispensing, the OAC days of supply was computed using information on date of dispensing, the number of packages, and the pack-size dispensed. For NOAC initiators, a patient was considered on-treatment from the index date and for the subsequent number of days corresponding to the number of tablets in all dispensed packages for rivaroxaban (used once daily) or half the number of tablets in all dispensed packages for dabigatran or apixaban (used twice daily).

For each patient, the on-treatment period was defined as index date + the estimated days supplied + 30-day grace period to account for incomplete adherence. To approximate the on-treatment period for warfarin in the absence of data on INR, first age-group-specific (age at index date <55 years, 55-<65 years, 65-<75 years, 75-<85 years, ≥85 years) mean daily dose was computed for all patients initiating warfarin in the study period by dividing the total amount dispensed during the follow-up by the follow-up length. For each patient in a given age group and country, median daily dose was used as the assumed warfarin daily dose in computing duration of warfarin use. A patient switched treatment if an OAC different from the index OAC was dispensed within 30 days after the estimated end of supply; the patient

discontinued the index OAC treatment if next OAC dispensing was more than 30 days after the estimated end of supply.

The subgroup analyses of the primary and the composite secondary endpoints were carried out within the subgroups of patients included in the overall pairwise PS-matched analysis sets. A Cox's proportional-hazards regression model was fit including, in addition to the treatment variable, a subgroup-by-treatment interaction term. Within each subgroup, covariate balance was evaluated as described above and covariates with a SMD ≥0.1 were included in the regression model to estimate the subgroup-specific adjusted HRs and 95% CIs. Subgroup-specific adjusted HRs with fewer than 10 events per degree of freedom were not estimated, to avoid unstable estimates.

9.9.3. Missing values

There were 258 patients from Denmark and 37 patients from Sweden with missing data on income (a variable included in PS-estimation). To avoid automatic exclusion of these patients from the PS computation, median income value was imputed for these patients.

9.9.4. Sensitivity analyses

The following sensitivity analyses were performed overall, for the primary endpoints and the composite secondary endpoint:

- The ITT-like analyses: the overall PS-matched analyses to estimate HRs of the primary endpoints and the composite secondary endpoint were repeated without censoring by treatment switch or discontinuation;
- The overall comparative analyses of the primary endpoints and the composite secondary endpoint in the PS-matched population were repeated using an alternative definition of warfarin discontinuation, based on maximum likelihood estimation of a parametric two-component mixture model for the waiting time distribution, as recently described in a similar setting and using data on the percentiles of the waiting time distribution previously reported for Danish patients (72, 73);
- The overall comparative analyses of the primary endpoints and the composite secondary endpoint was repeated in the full analysis dataset using conventional adjustment instead of PS matching to avoid exclusion of non-matched patients from the analyses;
- For the analyses stratified on the initial dose, de-novo PS matching within the initial dose defined subgroups were performed.

To provide context to the findings, in a series of post-hoc analyses, computed crude cumulative incidences of treatment discontinuation and treatment switch were computed in each cohort.

9.9.5. Exploratory analyses

All analyses of the exploratory endpoints were conducted in the PS-matched population, separately in each country. Health care utilisation costs assumed for this analysis were based on published estimates are shown in Table 3. Costs are presented separately for patients with index dates at least one year and for patients with index dates at least two years of before the end of the study. The mean values were computed across all patients included in that year.

Table 3. Assumed costs for the selected health care resource utilisation indicators

	DENMARK* (74)	NORWAY (75)	SWEDEN (76)

Mean cost in 2016	Local currency (DKK)	2016 EURO exchange rate, mean*	EURO	Local currency (NOK)	2016 EURO exchange rate, mean*	EURO	Local currency (SEK)	2016 EURO exchange rate, mean*	EURO
Per hospital bed-day	4,000.00	7.4452	537.26	15,125.00	9.2906	1,627.99	9,562.00	9.4689	1,009.83
Planned outpatient visit	702.00	7.4452	94.29	502.00	9.2906	54.03	349.10	9.4689	36.87
Acute outpatient visit	702.00	7.4452	94.29	502.00	9.2906	54.03	349.10	9.4689	36.87

*https://www.ecb.europa.eu/stats/policy_and_exchange_rates/euro_reference_exchange_rates/html/eurofxref-graph-dkk.en.html (European Central Bank) Costs where local published data could not be obtained are based on the latest data from the World Health Organisation WHO unit costs (77)
Norway: https://statistikk.helsedirektoratet.no/bi/Dashboard/be512ba0-a6e6-4e8f-900a-bbee3f50cc29?e=false&vo=viewonly (75)
Sweden: https://skl.se/tjanster/englishpages.411.html (76)

Data were analysed using SAS Software version 9.4 (SAS Inc., Cary, NC, USA). The detailed methodology is documented in the SAP, dated 05 June 2018 (Appendix 4).

9.9.6. Amendments to the statistical analysis plan

There were the following deviations from the SAP:

- Calendar year was not included in the computation of apixaban-warfarin propensity scores, as that would result in a substantial depletion of the PS-matched population; instead, calendar year was used as an adjustment variable in regression model.
- Stratification by unspecified stroke was not conducted as unspecified stroke could not be separated in the coded data from ischaemic stroke.
- In a post-hoc analysis, crude rates and HRs of treatment switch and treatment discontinuation were estimated, in addition to the planned analyses, to help inform interpretation of the results.

9.10. Quality control

Data management and analyses were carried out according to each investigator's institutional standard procedures. All study documents were reviewed by the entire research team and by clinicians with relevant expertise. A senior epidemiologist in each institution reviewed the report before submission to the MAH.

9.11. Protection of human subjects

Subject information and consent

Not applicable.

Independent Ethics Committee (IEC)/Institutional Review Board (IRB)

In Denmark, this study was approved by the Danish Data Protection Agency (journal number 2014-54-0922/KEA-2015-17). In Norway, the study was approved by the Regional Committee for Medical and Health Research Ethics, Region West (ref no. 2015/1503)) and the Norwegian Data Protection Agency (ref no. 17/01153). In Sweden, this study was approved by the regional ethical board in Stockholm, Sweden, on 20 November 2013 (record number 2013/1850-31/1), and two supplements that was approved on 17 July 2014 (record number 2014/1214-32) and 15 July 2016 (record number 2016/2218-32).

Ethical conduct of the study

The study was conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and follow generally accepted research practices described in in Guidelines for Good Pharmacoepidemiology Practices (GPP) issued by the International Society for Pharmacoepidemiology (ISPE), European Medicines Agency (EMA) Guideline for Good Pharmacovigilance Practice (GVP).

Regulations specific to Statistics Denmark

Data analysis for this study has been conducted in the servers of Statistics Denmark and therefore reporting must comply with Statistics Denmark's requirements in place to prevent inadvertent identification of individuals. These requirements include full anonymisation of the data; inability of the analysis to download individual data on own PC, and ban on reporting any cells with <5 individuals, including any complementary aggregate statistics that may potentially allow re-computation of such cells from the existing results. All results of this study are reported according to the regulations set by Statistics Denmark. To comply with data protection regulation of Statistics Denmark, 'clouding' was used in situations in which the number of events in a given cell was between 1 and 5 or could be computed from adjacent data. In such instances (e.g., computation of rates), numbers of events was rounded to the nearest 10. The rates and the CIs were based on the observed (i.e., unrounded) event counts.

10. RESULTS

10.1. Participants

Between 01 January 2013 and 31 December 2016, in Denmark, Norway and Sweden, there were 781,093 adults with a dispensing of apixaban, dabigatran, rivaroxaban, or warfarin. Among them, 450,969 (58%) patients had a diagnosis of AF. Among those, 197,515 (44%) patients had a dispensing of a VKA, a direct thrombin inhibitor or a direct factor Xa inhibitor in the 12 months before the index date did not fulfil eligibility criteria and were excluded. The second largest exclusion (21,591 patients, 5%) was due to history of mitral stenosis or a mechanical heart valve. After applying the inclusion and exclusion criteria, 219,545 patients were included in the total study population (Table 15.1, Figure 15.1): 71,585 patients entered the apixaban cohort; 31,209 patients entered the dabigatran cohort; 37,580 patients entered the rivaroxaban cohort and 79,171 patients entered the warfarin cohort (Figure 15.1). The country-specific inclusion and exclusion of patients are summarised in Figure 15.2 (Denmark), Figure 15.3 (Norway), and Figure 15.4 (Sweden). The apixaban cohort was the largest NOAC cohort in each country, and the largest OAC cohort in Norway (Figure 15.3).

10.2. Descriptive data

Table 15.1 shows distribution of the baseline characteristics of the study cohorts in the three countries combined. The OAC cohorts differed with respect to the year of OAC initiation, with most apixaban and rivaroxaban cohort members initiating the OAC in 2016 and most warfarin and dabigatran cohort members initiating the OAC in 2013. Patients in the apixaban cohort had a greater proportion of persons ≥85 years old than patients in all other cohorts, and, related to age, patients in the apixaban cohort had a greater prevalence of overall comorbidity burden (CCI ≥3) than the patients in the other NOACs cohorts). Patients in the apixaban cohort also had higher prevalence of prior intracranial bleeding, stroke, TIA,

diabetes, COPD, and dementia than patients in the other NOAC cohorts. Patients in the apixaban cohort had greater prevalence of high risk scores than patients in either the dabigatran or the rivaroxaban cohort. At the same time, patients in the apixaban cohort had lower prevalence of high risk scores than patients in the warfarin cohort. All cohorts had comparable prevalence of alcoholism, and 6-month baseline prevalence of cancer. Between one-quarter and one-third of the NOAC initiators started with a reduced dose. The country-specific distributions of the baseline characteristics by cohort are shown in Table 15.2 (Denmark), Table 15.3 (Norway), and Table 15.4 (Sweden).

10.3. Outcome data

The median (IQR) follow-up time for death in main/ITT-like sensitivity analyses and until the two primary endpoints (main analysis), in the full population, are shown, by country and/or cohort in Table 4.

Table 4. Median follow-up time, months, for death and primary endpoints, by country and/or cohort

Country	Cohort	Follow-up until a primary endpoint or death, median (interquartile range), months			
		Until death, main analysis	Until death, ITT-like analysis	Until primary endpoint stroke/SE, main analysis	Until primary endpoint any bleeding, main analysis
Overall	All	9.88 (3.94- 21.72)	21.42 (9.95 - 34.07)	9.72 (3.91 - 21.49)	9.59 (3.78 - 21.32)
All	Apixaban	9.26 (3.75 - 17.84)	12.75 (5.88 - 21.19)	9.13 (3.75 - 17.64)	9.10 (3.75 - 17.61)
All	Dabigatran	11.53 (3.94 - 29.67)	31.34 (19.42 - 39.16)	11.20 (3.94 - 29.34)	11.14 (3.94 - 29.21)
All	Rivaroxaban	10.84 (4.21 - 21.95)	17.41 (8.34 - 29.54)	10.74 (4.21 - 21.75)	10.64 (4.21 - 21.52)
All	Warfarin	9.58 (4.14 - 24.41)	30.72 (17.81 - 39.62)	9.47 (3.81 - 23.99)	9.47 (3.58 - 23.69)
Denmark	All	8.77 (3.14 - 20.76)	20.40 (9.20 - 33.45)	8.54 (3.09 - 20.53)	8.42 (3.02 - 20.30)
Norway	All	9.49 (3.94 - 21.13)	21.85 (10.25 - 34.53)	9.33 (3.88 - 20.86)	9.13 (3.75 - 20.60)
Sweden	All	10.70 (4.34 - 22.37)	21.65 (10.22 - 34.14)	10.51 (4.27 - 22.16)	10.45 (4.21 - 22.08)
Denmark	Apixaban	9.18 (3.52 - 18.40)	13.47 (6.01 - 22.41)	8.87 (3.38 - 18.04)	8.84 (3.35 - 18.04)
	Dabigatran	12.91 (3.94 - 31.08)	32.10 (21.42 - 39.39)	12.48 (3.94 - 30.72)	12.29 (3.94 - 30.49)
	Rivaroxaban	8.25 (3.09 - 18.04)	13.37 (5.65 - 25.40)	8.13 (3.02 - 17.74)	7.92 (2.92 - 17.51)
	Warfarin	7.46 (2.97 - 18.87)	24.77 (12.65 - 36.90)	7.39 (2.97 - 18.66)	7.16 (2.97 - 18.27)
Norway	Apixaban	8.74 (3.75 - 16.69)	12.55 (5.91 - 21.19)	8.61 (3.75 - 16.53)	8.51 (3.75 - 16.36)
	Dabigatran	10.91 (3.94 - 30.37)	33.81 (23.75 - 41.07)	10.84 (3.94 - 30.14)	10.56 (3.83 - 29.86)
	Rivaroxaban	12.02 (4.27 - 24.71)	21.39 (11.14 - 34.10)	11.83 (4.21 - 24.44)	11.56 (4.21 - 23.82)
	Warfarin	8.21 (3.43 - 20.83)	31.80 (18.99 - 40.44)	8.06 (3.43 - 20.57)	7.82 (3.43 - 20.01)
Sweden	Apixaban	9.56 (3.84 - 18.07)	12.58 (5.85 - 20.73)	9.46 (3.75 - 17.87)	9.46 (3.75 - 17.87)
	Dabigatran	10.78 (3.94 - 27.17)	27.17 (12.68 - 36.86)	10.51 (3.94 - 26.84)	10.61 (3.94 - 26.84)
	Rivaroxaban	12.58 (4.40 - 23.13)	18.50 (9.33 - 28.09)	12.45 (4.27 - 22.90)	12.29 (4.27 - 22.77)
	Warfarin	11.40 (4.75 - 27.20)	32.53 (20.37 - 40.28)	11.16 (4.53 - 26.81)	11.03 (4.51 - 26.61)

Table 15.5 – Table 15.17 show crude rates and crude pairwise NOAC-warfarin HRs with 95% CIs of the primary and secondary endpoints, overall and by country.

Crude rates (95% CI), per 100 person-years of any stroke or SE were 2.1 (2.0 - 2.2) in the apixaban cohort, 1.4 (1.3 - 1.5) in the dabigatran cohort, 1.9 (1.8 - 2.1) in the rivaroxaban cohort, and 1.9 (1.8 - 2.0) in the warfarin cohort (Table 15.5). Crude rates (95% CI) for any bleeding at an acute hospitalisation with an overnight stay were 3.0 (2.9 - 3.2) in the apixaban cohort, 2.5 (2.3 - 2.6) in the dabigatran cohort, 3.9 (3.7 - 4.1) in the rivaroxaban cohort, and

3.5 (3.4 - 3.6) in the warfarin cohort (Table 15.6). Crude rates (95% CI) for intracranial bleeding at an acute hospitalisation with an overnight stay were 0.6 (0.6 - 0.7) in the apixaban cohort, 0.3 (0.3 - 0.4) in the dabigatran cohort, 0.7 (0.6 - 0.8) in the rivaroxaban cohort, and 0.9 (0.8 - 0.9) in the warfarin cohort (Table 15.9). Crude rates (95% CI) for GI bleeding at an acute hospitalisation with an overnight stay were 1.2 (1.1 - 1.3) in the apixaban cohort, 1.3 (1.2 - 1.4) in the dabigatran cohort, 1.7 (1.6 - 1.8) in the rivaroxaban cohort, and 1.3 (1.2 - 1.4) in the warfarin cohort (Table 15.10). Crude rates (95% CI) for acute MI at an acute hospitalisation with an overnight stay were 1.4 (1.3 - 1.5) in the apixaban cohort, 0.9 (0.8 - 1.0) in the dabigatran cohort, 1.1 (1.0 - 1.2) in the rivaroxaban cohort, and 1.4 (1.3 - 1.4) in the warfarin cohort (Table 15.11). Crude rates (95% CI) for SE at an acute hospitalisation with an overnight stay were 0.1 (0.1 - 0.1) in the apixaban cohort, 0.1 (0.0 - 0.1) in the dabigatran cohort, 0.1 (0.0 - 0.1) in the rivaroxaban cohort, and 0.1 (0.1 - 0.1) in the warfarin cohort (Table 15.12) Crude all-cause mortality (95% CI) was 7.6 (7.4 - 7.8) in the apixaban cohort, 3.6 (3.4 - 3.8) in the dabigatran cohort, 6.9 (6.6 - 7.1) in the rivaroxaban cohort, and 5.6 (5.4 - 5.7) in the warfarin cohort (Table 15.13). Crude rates (95% CI) for the secondary composite endpoint were 10.2 (9.9 - 10.4) in the apixaban cohort, 5.4 (5.2 - 5.6) in the dabigatran cohort, 8.9 (8.6 - 9.2) in the rivaroxaban cohort, and 7.9 (7.7 - 8.1) in the warfarin cohort (Table 15.14). Crude rates (95% CI) for any bleeding at an acute or planned hospitalisation with an overnight stay were 3.4 (3.2 - 3.5) in the apixaban cohort, 2.7 (2.5 - 2.9) in the dabigatran cohort, 4.3 (4.1 - 4.5) in the rivaroxaban cohort, and 3.8 (3.7 - 3.9) in the warfarin cohort (Table 15.15). Crude rates (95% CI) for any bleeding at an acute hospital contact without an overnight stay were 1.9 (1.8 - 2.0) in the apixaban cohort, 1.0 (0.9 - 1.1) in the dabigatran cohort, 2.6 (2.5 - 2.8) in the rivaroxaban cohort, and 2.4 (2.3 - 2.5) in the warfarin cohort (Table 15.16). Crude rates (95% CI) for any bleeding recorded as the primary diagnosis at an acute hospitalisation with an overnight stay (sensitivity endpoint) were 1.9 (1.8 - 2.0) in the apixaban cohort, 1.7 (1.6 - 1.8) in the dabigatran cohort, 2.7 (2.6 - 2.9) in the rivaroxaban cohort, and 2.5 (2.4 - 2.6) in the warfarin cohort (Table 15.17).

Figure 15.5 – Figure 15.17 display crude cumulative incidences of the primary and secondary endpoints, overall and by country, while treating death as a competing risk. Table 15.18 – Table 15.30 show corresponding numeric cumulative incidences (95% CIs) over 12, 24, 36 and 48 months of follow-up. Figure 15.5 and Table 15.18 show crude cumulative incidence for any stroke or SE at an acute hospitalisation with an overnight stay; Figure 15.6 and Table 15.19 show crude cumulative incidence for any bleeding at an acute hospitalisation with an overnight stay; Figure 15.7 and Table 15.20 show crude cumulative incidence of ischaemic stroke at an acute hospitalisation with an overnight stay; Figure 15.8 and Table 15.21 show crude cumulative incidence for haemorrhagic stroke at an acute hospitalisation with an overnight stay; Figure 15.9 and Table 15.22 shows crude cumulative incidence for intracranial bleeding at an acute hospitalisation with an overnight stay; Figure 15.10 and Table 15.23 show crude cumulative incidence for GI bleeding at an acute hospitalisation with an overnight stay; Figure 15.11 and Table 15.24 show crude cumulative incidence for acute MI at an acute hospitalisation with an overnight stay; Figure 15.12 and Table 15.25 show crude cumulative incidence for SE at an acute hospitalisation with an overnight stay; Figure 15.13 and Table 15.26 show crude cumulative mortality; Figure 15.14 and Table 15.27 show crude cumulative incidence for composite endpoint of ischaemic stroke at an acute hospitalisation with an overnight stay, SE at an acute hospitalisation with an overnight stay, acute MI at an acute hospitalisation with an overnight stay, or death of any cause; Figure 15.15 and Table 15.28 show crude cumulative incidence for any bleeding at an acute or planned hospitalisation with an overnight stay; Figure 15.16 and Table 15.29 show crude cumulative incidence for any bleeding occurring at an acute hospital contact without an overnight stay; and Figure 15.17 and Table 15.30 show crude cumulative incidence for any

bleeding recorded as the primary diagnosis at an acute hospitalisation with an overnight stay (sensitivity analysis).

10.4. Main results

10.4.1. Primary and secondary endpoints: crude analyses

Table 15.5 – Table 15.17 show crude pairwise HRs (95% CIs) of the primary and secondary endpoints, overall and by country, comparing each NOAC vs. warfarin. Crude HR (95% CI) for any stroke or SE were 0.99 (0.92 - 1.06) for apixaban, 0.76 (0.69 - 0.83) for dabigatran, and 1.01 (0.93 - 1.09) for rivaroxaban. There were differences between countries: with higher crude rates for apixaban and rivaroxaban in Denmark vs. lower in Norway or Sweden (Table 15.5).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for any bleeding at an acute hospitalisation with an overnight stay were 0.79 (0.75 - 0.84) for apixaban, 0.72 (0.67 - 0.77) for dabigatran, and 1.10 (1.03 - 1.16) for rivaroxaban (Table 15.6).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for ischaemic stroke at an acute hospitalisation with an overnight stay 1.07 (0.99 - 1.15) for apixaban, 0.86 (0.78 - 0.95) for dabigatran, and 1.04 (0.95 - 1.14) for rivaroxaban (Table 15.7).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for haemorrhagic stroke at an acute hospitalisation with an overnight stay were 0.86 (0.74 - 1.01) for apixaban, 0.41 (0.32 - 0.53) for dabigatran, and 1.06 (0.89 - 1.26) for rivaroxaban (Table 15.8).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for intracranial bleeding at an acute hospitalisation with an overnight stay were 0.70 (0.63 - 0.79) for apixaban, 0.39 (0.33 - 0.47) for dabigatran, and 0.79 (0.70 - 0.90) for rivaroxaban (Table 15.9).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for GI bleeding at an acute hospitalisation with an overnight stay were 0.84 (0.77 - 0.91) for apixaban, 1.06 (0.96 - 1.17) for dabigatran, and 1.25 (1.14 - 1.37) for rivaroxaban (Table 15.10).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for acute MI at an acute hospitalisation with an overnight stay were 0.96 (0.88 - 1.04) for apixaban, 0.67 (0.60 - 0.75) for dabigatran, and 0.80 (0.72 - 0.89) for rivaroxaban (Table 15.11).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for SE at an acute hospitalisation with an overnight stay were 0.59 (0.43 - 0.83) for apixaban, 0.60 (0.40 - 0.92) for dabigatran, and 0.56 (0.37 - 0.85) for rivaroxaban (Table 15.12).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for death of all causes were 1.28 (1.23 - 1.33) for apixaban, 0.67 (0.63 - 0.70) for dabigatran, and 1.22 (1.17 - 1.28) for rivaroxaban (Table 15.13). Mortality rates differed among the three countries.

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for the secondary composite endpoint were 1.19 (1.16 - 1.23) for apixaban, 0.71 (0.68 - 0.75) for dabigatran, and 1.12 (1.08 - 1.16) for rivaroxaban (Table 15.14).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for any bleeding at an acute or planned hospitalisation with an overnight stay were 0.81 (0.77 - 0.85) for

apixaban, 0.73 (0.69 - 0.78) for dabigatran, and 1.10 (1.05 - 1.17) for rivaroxaban (Table 15.15).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for any bleeding at an acute hospital contact without an overnight stay were 0.78 (0.73 - 0.84) for apixaban, 0.42 (0.37 - 0.46) for dabigatran, and 1.11 (1.03 - 1.19) for rivaroxaban (Table 15.16).

In a pairwise comparison of each NOAC with warfarin, crude HR (95% CI) for any bleeding recorded as the primary diagnosis at an acute hospitalisation with an overnight stay (sensitivity analysis) were 0.70 (0.66 - 0.75) for apixaban, 0.70 (0.64 - 0.76) for dabigatran, and 1.07 (1.00 - 1.15) for rivaroxaban (Table 15.17).

10.4.2. Primary and secondary endpoints: analyses in PS-matched population

Table 5 summarises the initial size of each NOAC cohort available for matching, the sizes of the cohorts after exclusion of patients without a suitable match from the warfarin cohort, and SMDs before and after matching. Overall, proportions of the NOAC cohorts with a match were 78% for apixaban, 91% for dabigatran, and 81% for rivaroxaban. The proportion of NOAC patients with a successful warfarin match was the lowest in Norway.

Table 5. NOAC initiators included in the full population and in the PS-matched populations, overall, by cohort, and by country

	Apixaban vs. warfarin	Dabigatran vs. warfarin	Rivaroxaban vs. warfarin
All countries combined			
NOAC initiators in the full population	71,585	31,209	37,580
NOAC initiators successfully matched	55,581 (78%)	28,428 (91%)	30,599 (81%)
Maximum SMD before/after matching	0.23/0.02	0.47/0.03	0.58/0.04
Source output	Table 15.31	Table 15.35	Table 15.39
Denmark			
NOAC initiators in the full population	14,980	12,446	12,682
NOAC initiators successfully matched	13,173 (89%)	11,465 (92%)	10,537 (83%)
Maximum SMD before/after matching	0.27/0.06	0.33/0.03	0.52/0.06
Source output	Table 15.32	Table 15.36	Table 15.40
Norway			
NOAC initiators in the full population	17,780	8,684	10,565
NOAC initiators successfully matche	10,598 (60%)	7,205 (83%)	7,268 (69%)
Maximum SMD before/after matching	0.37/0.05	0.43/0.05	0.49/0.06
Source output	Table 15.33	Table 15.37	Table 15.41
Sweden			
NOAC initiators in the full population	38,825	10,079	14,333
NOAC initiators successfully matched	31,810 (82%)	9,758 (97%)	12,794 (89%)
Maximum SMD before/after matching	0.42/0.03	0.43/0.03	0.80/0.04
Source output	Table 15.34	Table 15.38	Table 15.42

Figure 15.18 – Figure 15.29 show adjusted HRs for each NOAC vs. warfarin pairwise comparison of the primary endpoints overall and in the prespecified subgroups (additionally adjusted within each subgroup for variables for which balance was not achieved, per SAP, Appendix 4).

Among patients initiating apixaban vs. warfarin in the three countries combined, the adjusted HR (95% CI) were 0.96 (0.87 - 1.06) for any stroke or SE at an acute hospitalisation with an overnight stay; 0.73 (0.67 - 0.78) for any bleeding at an acute hospitalisation with an overnight stay; and 1.12 (1.07 - 1.17) for the secondary composite endpoint. For the primary bleeding endpoint, there was no appreciable variability of HRs in any of the subgroups examined (Figure 15.18). The adjusted apixaban vs. warfarin HRs for the primary endpoints overall and subgroups for Denmark are in Figure 15.21, for Norway in Figure 15.24 and for Sweden in Figure 15.27.

Among patients initiating dabigatran vs. warfarin in the three countries combined, the adjusted HR (95% CI) were 0.89 (0.80 - 1.00) for any stroke or SE at an acute hospitalisation with an overnight stay; 0.89 (0.82 - 0.97) for any bleeding at an acute hospitalisation with an overnight stay; and 1.03 (0.97 - 1.10) for the secondary composite endpoint. Estimable HRs did not vary in a clinically important way in most subgroups, except by prior HF, age (for bleeding), and certain comorbidities (Figure 15.19). The adjusted dabigatran vs. warfarin HRs for the primary endpoints overall and subgroups for Denmark are in Figure 15.22 for Norway in Figure 15.25 and for Sweden in Figure 15.28.

Among patients initiating rivaroxaban vs. warfarin in the three countries combined, the adjusted HR (95% CI) were 1.03 (0.92 - 1.14) for any stroke or SE at an acute hospitalisation with an overnight stay; 1.15 (1.07 - 1.25) for any bleeding at an acute hospitalisation with an overnight stay; and 1.20 (1.14 - 1.26) for the secondary composite endpoint. Estimable HRs did not vary in clinically important way in any of the subgroups (Figure 15.20). The adjusted rivaroxaban vs. warfarin HRs for the primary endpoints overall and subgroups for Denmark are in Figure 15.23 for Norway in Figure 15.26, and for Sweden in Figure 15.29.

Death, as the most common event within the secondary composite endpoint, accounted for most of the observed results for this endpoint.

Figure 15.30 – Figure 15.33 show combined across all countries and country-specific adjusted HRs for the secondary endpoints using pairwise comparisons of apixaban vs. warfarin: ischaemic stroke and haemorrhagic stroke (Figure 15.30); intracranial bleeding and GI bleeding (Figure 15.31); the three definitions of any bleeding (Figure 15.32); and acute MI, SE and death of any cause (Figure 15.33). Apixaban compared with warfarin was associated with similar rates of ischaemic stroke, acute MI, and SE, higher rates of all-cause death, and lower rates of haemorrhagic stroke, and all bleeding endpoints.

Figure 15.34 – Figure 15.37 show combined across all countries and country-specific adjusted HRs for the secondary endpoints using pairwise comparisons of dabigatran vs. warfarin: ischaemic stroke and haemorrhagic stroke (Figure 15.34); intracranial bleeding and GI bleeding (Figure 15.35); the three definitions of any bleeding (Figure 15.36); and acute MI, SE and death of any cause (Figure 15.37). Dabigatran compared with warfarin was associated with similar rates of ischaemic stroke, acute MI, SE, and all-cause death, higher rates GI bleeding, and lower rates of haemorrhagic stroke, and the bleeding endpoints other than GI bleeding.

Figure 15.38 – Figure 15.41 show combined across all countries and country-specific adjusted (via PS-matching) HRs and 95% CIs for the secondary endpoints using pairwise comparisons of rivaroxaban vs. warfarin: ischaemic stroke and haemorrhagic stroke (Figure 15.38); intracranial bleeding and GI bleeding (Figure 15.39); the three definitions of any bleeding (Figure 15.40); and acute MI, SE and death of any cause (Figure 15.41). Rivaroxaban compared with warfarin was associated with similar rates of ischaemic stroke, haemorrhagic stroke and acute MI, higher rates of all bleeding endpoints except intracranial bleeding, and death of any cause, and lower rates of intracranial bleeding and SE.

10.5. Other analyses

10.5.1. Post-hoc analyses

Cumulative incidence of treatment switch was highest in the dabigatran cohort and lowest in the apixaban cohort. At the end of the follow-up, treatment switch occurred for approximately one-third of the dabigatran cohort and for slightly less than one-tenth of the apixaban cohort (Figure 1). Cumulative incidence of treatment discontinuation was the highest in the warfarin cohort and lowest in the apixaban cohort and in the rivaroxaban cohort. By the end of the follow-up, treatment discontinuation occurred in close to 60% of the warfarin cohort and in about one-quarter of the apixaban cohort or the rivaroxaban cohort (Figure 2).

Figure 1. Cumulative incidence of treatment switch, by country and cohort

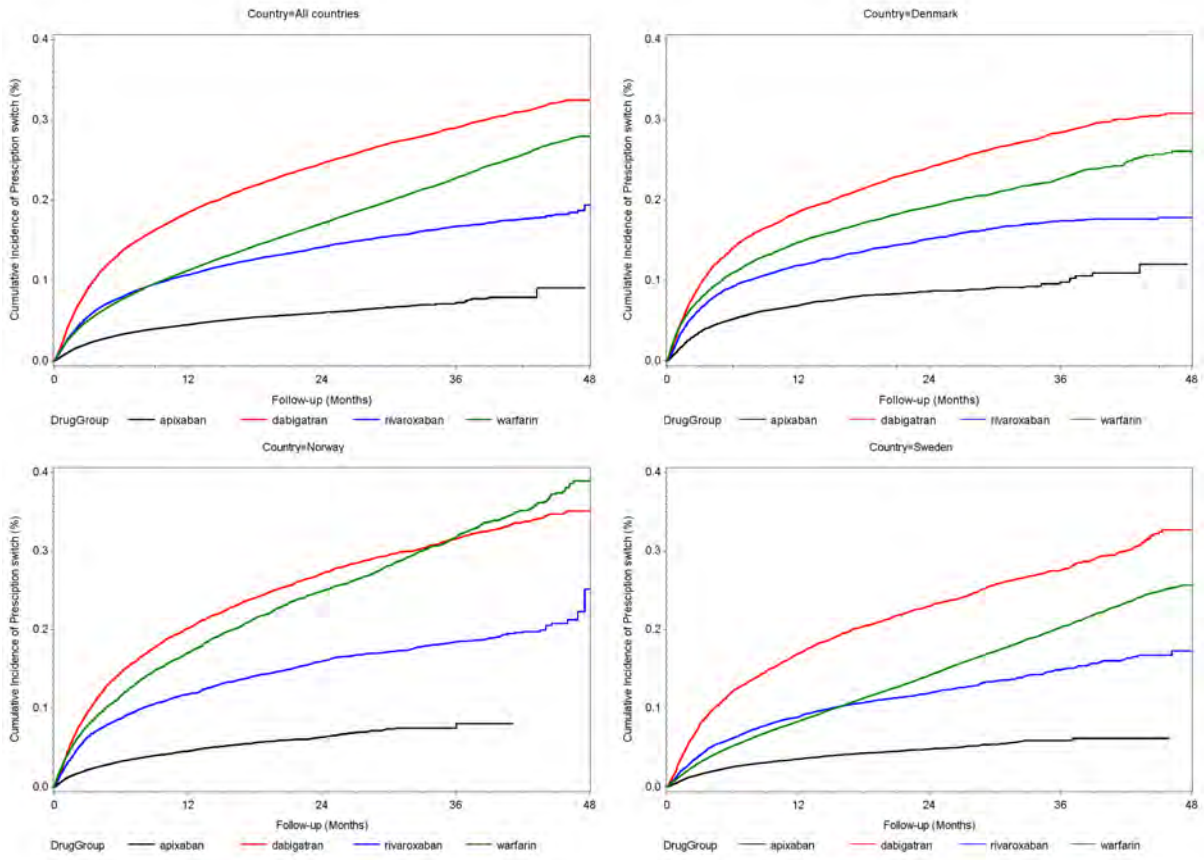
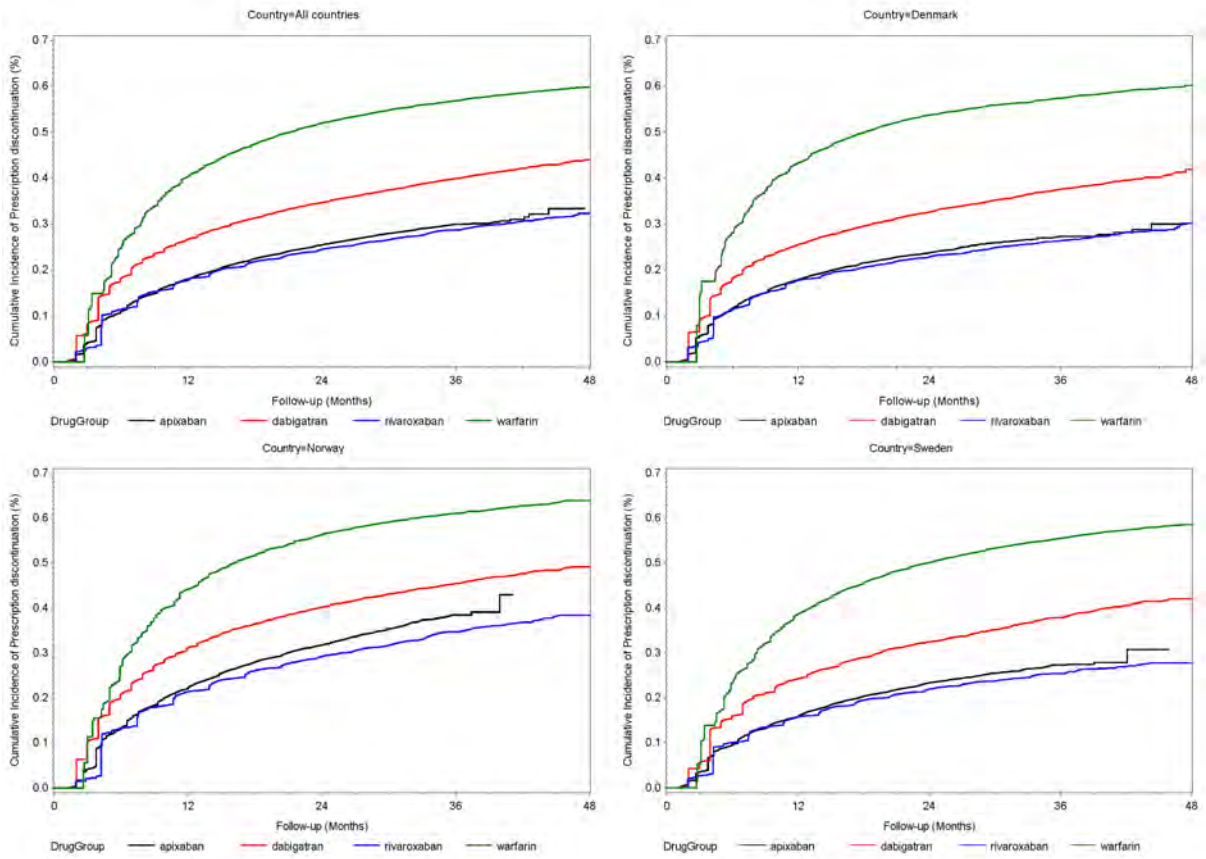


Figure 2. Cumulative incidence of treatment discontinuation, by country and cohort



10.5.2. Sensitivity analyses

10.5.2.1. Conventional adjustment

Figure 15.48 – Figure 15.50 show adjusted HRs for the primary endpoints and the composite secondary endpoints, whereby conventional adjustment is used in the Cox's proportional hazards regression using the entire study population available.

Among the 150,756 patients initiating apixaban vs. warfarin, conventionally adjusted HRs (95% CI) were 0.90 (0.83 – 0.99) for any stroke or SE at an acute hospitalisation with an overnight stay; and 0.73 (0.69 – 0.78) for any bleeding at an acute hospitalisation with an overnight stay (Figure 15.48 displays country-specific results).

Among the N=110,380 patients initiating dabigatran vs. warfarin, conventionally adjusted HRs (95% CI) were 0.88 (0.80 – 0.97) for any stroke or SE at an acute hospitalisation with an overnight stay; and 0.86 (0.80 - 0.93) for any bleeding at an acute hospitalisation with an overnight stay (Figure 15.49 displays country-specific results).

Among the 116,751 patients initiating rivaroxaban vs. warfarin, conventionally adjusted HR (95% CI) was 0.96 (0.88 - 1.05) for any stroke or SE at an acute hospitalisation with an overnight stay; and 1.10 (1.03 - 1.17) for any bleeding at an acute hospitalisation with an overnight stay (Figure 15.50 displays country-specific results).

10.5.2.2. ITT-like analyses

The ITT-like analyses of the primary and the composite secondary endpoints in the PS -score matched populations are presented, overall and stratified by country in Figure 15.42 for apixaban vs. warfarin contrast; in Figure 15.43 for the dabigatran vs. warfarin contrast and in

Figure 15.44 for the rivaroxaban vs. warfarin contrast. The HR estimates from the main analysis are presented for comparison.

10.5.2.3. Alternative definition of warfarin discontinuation

The analyses for the primary and composite secondary endpoints using the previously reported 80% percentile of the waiting time distribution to estimate the time of warfarin discontinuation are shown in Figure 15.45 for apixaban; in Figure 15.46 for dabigatran; and in Figure 15.47 for rivaroxaban.

Table 6 summarises HRs for the primary and the composite secondary endpoints obtained, using data combined from all three countries, using the different approaches: crude, conventionally adjusted (sensitivity analysis), PS-matched main analysis, and PS-matched ITT-like sensitivity analysis.

Table 6. Hazard ratios for the primary endpoints obtained from different analytic approaches

Primary endpoint	Hazard ratio (95% CI)				
	Crude*	Conventionally adjusted*	**PS-matched* MAIN ANALYSIS**	PS-matched** ITT-like	PS-matched* Alternative definition of warfarin discontinuation
Apixaban vs. warfarin					
Any stroke or SE at an acute hospitalisation with an overnight stay	0.99 (0.92 - 1.06)	0.90 (0.83 - 0.99)	0.96 (0.87 - 1.06)	0.96 (0.88 - 1.04)	0.96 (0.86 - 1.06)
Any bleeding at an acute hospitalisation with an overnight stay	0.79 (0.75 - 0.84)	0.73 (0.69 - 0.78)	0.73 (0.67 - 0.78)	0.75 (0.70 - 0.80)	0.74 (0.68 - 0.80)
Source output	Table 15.5/Table 15.6	Figure 15.48	Figure 15.18	Figure 15.42	Figure 15.45
Dabigatran vs. warfarin					
Any stroke or SE at an acute hospitalisation with an overnight stay	0.76 (0.69 - 0.83)	0.88 (0.80 - 0.97)	0.89 (0.80 - 1.00)	0.90 (0.83 - 0.98)	0.89 (0.78 - 1.00)
Any bleeding at an acute hospitalisation with an overnight stay	0.72 (0.67 - 0.77)	0.86 (0.80 - 0.93)	0.89 (0.82 - 0.97)	0.88 (0.82 - 0.94)	0.88 (0.80 - 0.97)
Source output	Table 15.5/Table 15.6	Figure 15.49	Figure 15.19	Figure 15.43	Figure 15.46
Rivaroxaban vs. warfarin					
Any stroke or SE at an acute hospitalisation with an overnight stay	1.01 (0.93 - 1.09)	0.96 (0.88 - 1.05)	1.03 (0.92 - 1.14)	1.03 (0.95 - 1.12)	1.04 (0.93 - 1.16)
Any bleeding at an acute hospitalisation with an overnight stay	1.10 (1.03 - 1.16)	1.10 (1.03 - 1.17)	1.15 (1.07 - 1.25)	1.08 (1.01 - 1.15)	1.17 (1.07 - 1.27)
Source output	Table 15.5/Table 15.6	Figure 15.50	Figure 15.20	Figure 15.44	Figure 15.47

*Censored by death, emigration, discontinuation or switch.
**Censored by death or emigration.

10.5.2.4. Analyses in subgroups defined by initial NOAC dose with de-novo PS matching

The overall results of the PS-matching within the subgroups of initial dose (standard/reduced) for the apixaban cohort are presented in Table 15.43 and Table 15.44 (country specific results are in Table 15.45/Table 15.46 [Denmark]; Table 15.47/Table 15.48 [Norway]; Table 15.49/Table 15.50 [Sweden]).

The overall results of the PS-matching within the subgroups of initial dose (standard/reduced) for the dabigatran cohort are presented in Table 15.51 and Table 15.52 (country-specific results are in Table 15.53/Table 15.54 [Denmark]; Table 15.55/Table 15.56 [Norway]; Table 15.57/Table 15.58 [Sweden]).

The overall results of the PS-matching within the subgroups of initial dose (standard/reduced) for the rivaroxaban cohort are presented in Table 15.59 and Table 15.60 (country-specific results are in Table 15.61/Table 15.62 [Denmark]; Table 15.63/Table 15.64 [Norway]; Table 15.65/Table 15.66 [Sweden]).

The HRs for apixaban for the primary endpoint any stroke or SE at an acute hospitalisation with an overnight stay were associated with similar or slightly lower risk compared with warfarin in both initial dose subgroups, and the magnitude of the HR varied slightly by country. For the primary endpoint any bleeding at an acute hospitalisation with an overnight stay, apixaban was associated with a lower than warfarin risk in both standard and reduce initial dose subgroups. The estimates were consistent across the countries (Table 15.67).

The HRs for dabigatran for the primary endpoint any stroke or SE at an acute hospitalisation with an overnight stay were associated with no difference in risk compared with warfarin, in both initial dose subgroups and across the three countries. For the primary endpoint any bleeding at an acute hospitalisation with an overnight stay, dabigatran was associated with a lower than warfarin risk in the standard initial dose subgroup, but not in reduced initial dose subgroup, with this result being consistent across the countries (Table 15.68).

The HRs for rivaroxaban the primary endpoint any stroke or SE at an acute hospitalisation with an overnight stay were associated with no difference in risk compared with warfarin, in both initial dose subgroups and across the three countries, although the risks were numerically higher in Norway. For the primary endpoint any bleeding at an acute hospitalisation with an overnight stay, rivaroxaban was associated with a similar with warfarin risk for the standard dose and higher than warfarin in the reduced dose (Table 15.69).

Table 7 summarises initial -dose stratified analyses for each of the NOACs combined across the three countries for the primary endpoints.

Table 7. Hazard ratios for the primary endpoints, overall and stratified on initial dose after de-novo PS-matching within each subgroup of initial NOAC dose.

Group/subgroup			Hazard ratio (95% CI) after de-novo PS matching within each subgroup of initial NOAC dose	
	Successfully matched NOAC initiators/total NOAC initiators (%)	Maximum SMD before matching/after matching	Any stroke or SE at an acute hospitalisation with an overnight stay	Any bleeding at an acute hospitalisation with an overnight stay
	Apixaban vs. warfarin			
All*			0.92 (0.84 - 1.01)	0.73 (0.68 - 0.78)
Standard dose	42,672/50,310 (85%)	0.29/0.02	0.88 (0.78 - 1.00)	0.75 (0.69 - 0.83)
Reduced dose	18,794/21,275 (88%)	1.07/0.02	0.96 (0.83 - 1.10)	0.69 (0.61 - 0.76)
	Dabigatran vs. warfarin			

Group/subgroup			Hazard ratio (95% CI) after de-novo PS matching within each subgroup of initial NOAC dose	
	Successfully matched NOAC initiators/total NOAC initiators (%)	Maximum SMD before matching/after matching	Any stroke or SE at an acute hospitalisation with an overnight stay	Any bleeding at an acute hospitalisation with an overnight stay
All**			0.93 (0.83 - 1.04)	0.87 (0.80 - 0.94)
Standard dose	18,701/20,478 (91%)	0.78/0.03	0.95 (0.80 - 1.12)	0.75 (0.66 - 0.85)
Reduced dose	10,669/10,731 (99%)	0.62/0.03	0.90 (0.76 - 1.05)	0.95 (0.85 - 1.07)
	Rivaroxaban vs. warfarin			
All***			0.97 (0.88 - 1.07)	1.11 (1.03 - 1.20)
Standard dose	23,703/28,366 (84%)	0.62/0.04	0.96 (0.85 - 1.09)	1.09 (0.99 - 1.20)
Reduced dose	9,088/9,214 (99%)	0.74/0.04	0.98 (0.83 - 1.16)	1.15 (1.02 - 1.29)

*Combined population of the successfully matched patients within each category of initial apixaban dose; country-specific results in Table 15.67
**Combined population of the successfully matched patients within each category of initial dabigatran dose; country-specific results in Table 15.68
***Combined population of the successfully matched patients within each category of initial rivaroxaban dose; country-specific results in Table 15.69

10.5.3. Analyses of the exploratory endpoints

10.5.3.1. Denmark

Results of the exploratory endpoints for Denmark are presented in Table 15.70 (apixaban and warfarin), Table 15.71 (dabigatran and warfarin), and Table 15.72 (rivaroxaban and warfarin).

10.5.3.2. Norway

Results of the exploratory endpoints for Norway are presented in Table 15.73 (dabigatran and warfarin), Table 15.74 (dabigatran and warfarin), and Table 15.75 (rivaroxaban and warfarin).

10.5.3.3. Sweden

Results of the exploratory endpoints for Sweden are presented in Table 15.76 (apixaban and warfarin) Table 15.77 (dabigatran and warfarin), and Table 15.78 (rivaroxaban and warfarin).

10.6. Adverse events/adverse reactions

Not applicable.

11. DISCUSSION

11.1. Key results

This population-based cohort study used combined individual-level data from Denmark, Norway, and Sweden and included 219,545 adult patients with NVAF initiating apixaban (N=71,585), dabigatran (N=31,209), rivaroxaban (N=37,580), or warfarin (N=79,171) in 2013 -2016. Patients initiating apixaban tended to be older and to have greater comorbidity indicators than patients initiating OACs. Between one-fourth and one-third of patients initiating the NOACs were started on a reduced initial dose.

In the PS-matched population, patients in the apixaban cohort (N=55,581, 78% of all apixaban initiators) had similar rates of any stroke or SE at an acute hospitalisation with an overnight stay compared with patients in the warfarin cohort (HR 0.96, 95% CI: 0.87 - 1.06), with similar results for standard (HR 0.88 95% CI: 0.78 - 1.00) and reduced (HR 0.96, 95% CI: 0.83 - 1.10) initial dose of apixaban. Patients in the apixaban cohort had a lower rate of any bleeding at an acute hospitalisation with an overnight stay than patients in the warfarin

cohort (adjusted HR 0.73, 95% CI: 0.67 - 0.78), with similar results for standard (HR 0.75, 95% CI 0.69 - 0.83) and reduced (HR 0.69, 95% CI: 0.61 - 0.76) initial apixaban dose. Patients in the apixaban cohort had similar with patients in the warfarin cohort rates of ischaemic stroke and acute MI, and had lower rates of haemorrhagic stroke, all bleeding endpoints, or SE. Treatment with apixaban was associated with a slightly higher all-cause mortality than treatment with warfarin. The rate of the secondary composite endpoint was higher in the low dose apixaban group than in the warfarin group.

In the PS-matched population, patients in the dabigatran cohort (N=28,428, 91% of all eligible) compared with patients in the warfarin cohort had a similar rate of any stroke or SE at an acute hospitalisation with an overnight stay (HR 0.89, 95% CI: 0.80 - 1.00), with similar results for standard (HR 0.95 (0.80 - 1.12)) and reduced (HR 0.90 (0.76 - 1.05)) initial dabigatran dose. Patients in the dabigatran cohort compared with warfarin had a lower rate of any bleeding at an acute hospitalisation with an overnight stay (HR 0.89 95% CI: 0.82 - 0.97). The association was more pronounced in patients with standard initial dabigatran dose (HR 0.75, 95% CI: 0.66 - 0.85) than in patients with reduced initial dabigatran dose (HR 0.95, 95% CI: 0.85 - 1.07). Patients in the dabigatran cohort had similar with patients in the warfarin cohort rates of ischaemic stroke, SE, acute MI, or death of any cause, had lower rates of haemorrhagic stroke, and of intracranial bleeding, but had a substantially higher rate of GI bleeding.

In the PS-matched population, patients in the rivaroxaban cohort (N=30,599, 81% of all initiators) had similar rates of any stroke or SE as compared with patients in the warfarin cohort (HR 1.03, 95% CI: 0.92 - 1.14), similar estimates in patients with standard initial rivaroxaban dose (HR 0.96, 95% CI: 0.85 - 1.09) and patients with reduced initial rivaroxaban dose (HR 0.98, 95% CI: 0.83 - 1.16). Patients in the rivaroxaban cohort had a higher rate of any bleeding at acute hospitalisation with an overnight stay compared with patients in the warfarin cohort (HR 1.15, 95% CI: 1.07 - 1.25), seen both in patients with standard (HR 1.09, 95% CI: 0.99 - 1.20) and reduced (HR 1.15, 95% CI: 1.02 - 1.29) initial rivaroxaban dose. Patients in the rivaroxaban cohort had similar with patients in the warfarin cohort rates of ischaemic stroke, or acute MI, but substantially higher rate of type of any bleeding except intracranial bleeding. Rates of GI bleeding were substantially higher in the rivaroxaban cohort than in the warfarin cohort.

The estimates for the primary and secondary endpoints were robust to changes in analytic approaches, and there was no evidence of strong measured confounding in the data.

Patients with NVAF in the apixaban cohort or in the rivaroxaban cohort were substantially less likely than their matched warfarin cohort to switch or discontinue treatment, resulting in shorter follow-up available in patients treated with warfarin, with potentially fewer endpoint events captured in the main (on-treatment) analysis. Initiators of dabigatran were more likely than their matched initiators of warfarin to switch to another OAC during the follow-up. High treatment/discontinuation rates in dabigatran and warfarin cohorts is consistent with findings from with another Danish study based on the BEYOND Protocol (26).

The uptake of NOACs in the Scandinavian countries has been high (78, 79). In this study, contrary to the expectation of apixaban initiators being the smallest group, apixaban cohort was the largest NOAC cohort and the largest cohort in Norway, which may partially explain smaller proportion of patients for whom a suitable warfarin match was available. The three countries have uniform health care system and high level of adherence to existing guidelines

(80). Sweden is the largest country among the three, and Swedish results likely drive most of the analyses.

Many previous observational studies in the US and Europe have examined the safety and effectiveness of NOACs in real world settings. In three recent Danish cohort studies, whose data overlap with the present dataset, NOACs and warfarin were associated with similar risks of ischaemic stroke, but apixaban and dabigatran conferred lower risks of death (24) and bleeding (24-26) compared with warfarin. In the current study, apixaban and rivaroxaban were associated with a greater risk of death compared with warfarin in all countries except Norway, while dabigatran was associated with a slightly lower risk of death. In a Norwegian study, apixaban and dabigatran each was associated with a lower than warfarin risk of major or clinically relevant non-major bleeding, with the exception of GI bleeding, which was higher with dabigatran or rivaroxaban (27) than with warfarin. This observation is likewise consistent with the present study. Similar findings have been reported from the US (28). A study among patients treated with reduced-dose OACs in Denmark found generally comparable rates of thromboembolic and bleeding events in all groups, noting a trend towards a higher rate of thromboembolic events associated with a reduced dose of apixaban (29). Another Danish study, which conducted a head-to-head inter-NOAC comparison, concluded that the three NOACs had comparable positive benefit-risk balance (8).

11.2. Strengths and limitations

Scandinavian countries have a nearly 100% completeness of out of hospital dispensings, person-level linkage to data from other high-quality registries with national coverage, and complete follow-up, making Scandinavian countries an optimal setting to address comparative effectiveness of anticoagulants in routine clinical practice. Other advantages of the Scandinavian countries for pharmacoepidemiologic research include universal access to health care, similar clinical practice, as well as uniform recording practices, comparable patterns of hospitalisation and referral to specialist care, and high overall quality of care, including high quality of warfarin therapy (30-34, 36-38, 42, 53, 56), an aspect that is unique among all published evidence.

Limitations of this study include small number of events in some subgroups, despite the large study size, and the associated loss in precision. Furthermore, SMD often exceeded the balance threshold of <0.1 in the subgroups, necessitating additional adjustment. Another limitation of this approach is potential loss of generalisability (by the necessary exclusion of patients for whom a match cannot be found and who may differ from the included patients). Furthermore, there was no data on OAC treatment during the hospital stay, and patients may change this medication upon discharge. ICD-10 code used for AF do not distinguish between AF and atrial flutter, so that up to 10% of patients with a diagnosis of AF may in fact have atrial flutter (81). Results of the primary endpoint component of ‘any stroke’ are difficult to interpret in terms of clinical implications, since prevention of ischaemic stroke is the intended treatment goal, when haemorrhagic stroke is a feared side effect. Furthermore, daily dose of warfarin is only crudely estimate because of the lack of data on INR.

Confounding by indication and detection bias are important potential limitations. Patients initiating apixaban were older and had higher comorbidity burdens than patients initiating dabigatran or rivaroxaban, but had lower prevalence of high risk scores than patients initiating warfarin. At the same time ascertainment of the endpoints is likely to be inflated in warfarin compared with NOAC-treated patients due to closer contact with the health care system. These two biases would drive relative estimates in the opposite directions. Potential sources of information bias include misclassification of treatment status by dispensing

records or interruptions during hospital stays, misclassification of treatment-naïve status by a 12-month washout period, and potentially differential according to treatment type ascertainment of absolute risks of the study endpoints by hospital encounters. At the same time, specificity of the events' recording is high and relative estimates are therefore expected to be unbiased due to outcome misclassification. Nor can severity of most comorbidities be established, potentially causing misclassification of treatment duration or covariates; the latter will result in residual confounding. Finally, routinely collected data contain no information on the quality of warfarin treatment control or dose for individual patients.

11.3. Interpretation

Relative to warfarin, apixaban and dabigatran were associated with lower rates of bleeding whereas rivaroxaban was associated with a higher rate. The three NOACs had comparable rates of stroke and systemic embolism relative to warfarin.

Treatment discontinuation and switch occurred more frequently in patients taking dabigatran or warfarin than in patients taking apixaban or rivaroxaban.

11.4. Generalisability

Generalisability of PS-matched analysis is limited because, by design, patients without a match are excluded from the analyses. Thus, results from the PS-matched population may not be fully generalisable to all patients treated with NOACs. Specifically, patients who are highly likely or highly unlikely to be treated with one or the other treatment based on unusual constellation of risk factors would be excluded from PS-score matched analysis. Finally, this study focussed on OACs initiators with a hospital diagnosis of AF and its results are not necessarily generalisable to patients who are not treatment-naïve or those treated exclusively in primary care. Any lack of generalisability is not a concern if the observed effects are biologically determined (82). Furthermore, HRs may still be generalisable to larger populations even if the underlying absolute risks of the endpoints in the study population are different from those in the source population. In this study, just under 60% of the NOAC - treated patients had a hospital diagnosis of AF within 5 years of treatment start during the study period, and, in this study of initiators, most patients' diagnosis was recent. In a recent study of apixaban utilisation in Denmark and Sweden close to 80% of apixaban initiators (both treatment naïve and switchers) had NVAF (83, 84).

12. OTHER INFORMATION

Not applicable.

13. CONCLUSIONS

Among patients with NVAF initiating OACs, compared with warfarin, apixaban and dabigatran were associated with lower rates of bleeding whereas rivaroxaban was associated with a higher rate. The three NOACs had comparable rates of stroke and systemic embolism relative to warfarin. The uptake of NOACs in the Scandinavian countries is high, and large studies with NOAC-NOAC comparisons are needed to help clinicians choose NOACs in comparable patient populations.

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15. LIST OF SOURCE TABLES AND FIGURES

15.1. List of tables

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Table 15.1 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban, dabigatran, rivaroxaban or warfarin (Denmark, Norway, Sweden, 2013 -2016)

Characteristic	Apixaban (N= 71,585)	Dabigatran (N= 31,209)	Rivaroxaban (N= 37,580)	Warfarin (N= 79,171)	Total (N=219,545)
Country					
All countries	71,585 (100%)	31,209 (100%)	37,580 (100%)	79,171 (100%)	219,545 (100%)
Year of OAC initiation					
2013	1,840 (2.57%)	12,566 (40.3%)	6,948 (18.5%)	34,996 (44.2%)	56,350 (25.7%)
2014	13,102 (18.3%)	10,468 (33.5%)	8,284 (22.0%)	23,333 (29.5%)	55,187 (25.1%)
2015	25,920 (36.2%)	4,218 (13.5%)	11,095 (29.5%)	13,387 (16.9%)	54,620 (24.9%)
2016	30,723 (42.9%)	3,957 (12.7%)	11,253 (29.9%)	7,455 (9.42%)	53,388 (24.3%)
Time form most recent relative to index date hospital AF diagnosis, median (IQR), months	0.2 (0.0 - 3.1)	0.2 (0.0 - 10.0)	0.3 (0.0 - 12.1)	0.4 (0.1 - 15.5)	0.3 (0.0 - 9.3)
Time from AF diagnosis to index					
3 - 60 months	17,980 (25.1%)	9,275 (29.7%)	11,859 (31.6%)	26,198 (33.1%)	65,312 (29.7%)
< 3 months	53,605 (74.9%)	21,934 (70.3%)	25,721 (68.4%)	52,973 (66.9%)	154,233 (70.3%)
Sex					
Female	32,911 (46.0%)	12,261 (39.3%)	16,676 (44.4%)	32,984 (41.7%)	94,832 (43.2%)
Male	38,674 (54.0%)	18,948 (60.7%)	20,904 (55.6%)	46,187 (58.3%)	124,713 (56.8%)
Age, median (IQR), years	75.5 (68.2 - 83.5)	71.0 (64.6 - 78.7)	74.2 (67.3 - 82.0)	75.0 (67.5 - 82.2)	74.4 (67.2 - 82.2)
Age group					
< 55years	3,323 (4.64%)	2,434 (7.80%)	1,772 (4.72%)	4,481 (5.66%)	12,010 (5.47%)
55-<65 years	8,416 (11.8%)	5,737 (18.4%)	4,961 (13.2%)	10,103 (12.8%)	29,217 (13.3%)
65-<75 years	22,884 (32.0%)	11,793 (37.8%)	13,028 (34.7%)	25,057 (31.6%)	72,762 (33.1%)
75-<85 years	22,328 (31.2%)	8,077 (25.9%)	11,463 (30.5%)	26,704 (33.7%)	68,572 (31.2%)
≥ 85 years	14,634 (20.4%)	3,168 (10.2%)	6,356 (16.9%)	12,826 (16.2%)	36,984 (16.8%)
Initial dose **					
Reduced	21,275 (29.7%)	10,731 (34.4%)	9,214 (24.5%)		
Standard	50,310 (70.3%)	20,478 (65.6%)	28,366 (75.5%)		
Baseline comorbidity 5 years before and including index date					
Charlson Comorbidity Index score					
0	28,413 (39.7%)	15,333 (49.1%)	16,044 (42.7%)	29,605 (37.4%)	89,395 (40.7%)
1 -2	24,544 (34.3%)	10,286 (33.0%)	12,756 (33.9%)	25,602 (32.3%)	73,188 (33.3%)
≥3	18,628 (26.0%)	5,590 (17.9%)	8,780 (23.4%)	23,964 (30.3%)	56,962 (25.9%)
Baseline comorbidity 5 years before and including index date					
Prior bleeding (any)	8,016 (11.2%)	2,811 (9.01%)	3,863 (10.3%)	8,865 (11.2%)	23,555 (10.7%)
Prior gastrointestinal bleeding	670 (0.94%)	243 (0.78%)	327 (0.87%)	821 (1.04%)	2,061 (0.94%)
Prior intracranial bleeding	899 (1.26%)	284 (0.91%)	417 (1.11%)	710 (0.90%)	2,310 (1.05%)
Prior stroke (any)	10,044 (14.0%)	3,379 (10.8%)	4,857 (12.9%)	9,610 (12.1%)	27,890 (12.7%)
Prior ischaemic stroke	9,741 (13.6%)	3,297 (10.6%)	4,720 (12.6%)	9,404 (11.9%)	27,162 (12.4%)
Prior haemorrhagic stroke	695 (0.97%)	202 (0.65%)	296 (0.79%)	521 (0.66%)	1,714 (0.78%)
Prior systemic embolism	395 (0.55%)	133 (0.43%)	223 (0.59%)	760 (0.96%)	1,511 (0.69%)
Prior transient ischaemic attack	3,092 (4.32%)	1,157 (3.71%)	1,466 (3.90%)	3,117 (3.94%)	8,832 (4.02%)
Chronic kidney disease	3,509 (4.90%)	555 (1.78%)	1,322 (3.52%)	6,529 (8.25%)	11,915 (5.43%)
Heart failure	13,650 (19.1%)	4,332 (13.9%)	6,160 (16.4%)	18,006 (22.7%)	42,148 (19.2%)
Coronary artery disease	15,580 (21.8%)	5,511 (17.7%)	7,533 (20.0%)	21,453 (27.1%)	50,077 (22.8%)
Peripheral arterial disease	4,842 (6.76%)	1,630 (5.22%)	2,459 (6.54%)	6,031 (7.62%)	14,962 (6.82%)
Cardioversion	4,396 (6.14%)	2,537 (8.13%)	2,112 (5.62%)	6,886 (8.70%)	15,931 (7.26%)
Hypertension	47,785 (66.8%)	18,972 (60.8%)	24,334 (64.8%)	54,106 (68.3%)	145,197 (66.1%)
Diabetes	11,785 (16.5%)	4,291 (13.7%)	5,988 (15.9%)	14,676 (18.5%)	36,740 (16.7%)
Chronic obstructive pulmonary disease	9,151 (12.8%)	3,264 (10.5%)	4,622 (12.3%)	10,116 (12.8%)	27,153 (12.4%)
Liver disease	608 (0.85%)	261 (0.84%)	325 (0.86%)	816 (1.03%)	2,010 (0.92%)
Alcoholism	1,772 (2.48%)	857 (2.75%)	1,026 (2.73%)	1,785 (2.25%)	5,440 (2.48%)
Dementia	1,821 (2.54%)	416 (1.33%)	897 (2.39%)	1,216 (1.54%)	4,350 (1.98%)
Cancer 6 months before and including index date	1,847 (2.58%)	878 (2.81%)	1,242 (3.30%)	2,135 (2.70%)	6,102 (2.78%)
Prescription medication dispensed in 90 days before and including index date					
Platelet inhibitors (excluding heparin)	26,854 (37.5%)	10,354 (33.2%)	14,113 (37.6%)	30,838 (39.0%)	82,159 (37.4%)
Low -dose aspirin	23,583 (32.9%)	9,175 (29.4%)	12,328 (32.8%)	27,177 (34.3%)	72,263 (32.9%)
ADP receptor blockers	4,860 (6.79%)	1,645 (5.27%)	2,374 (6.32%)	7,098 (8.97%)	15,977 (7.28%)
Renin -angiotensin system inhibitors	33,264 (46.5%)	13,043 (41.8%)	16,481 (43.9%)	38,067 (48.1%)	100,855 (45.9%)

Angiotensin -converting enzyme inhibitors	15,888 (22.2%)	5,969 (19.1%)	7,312 (19.5%)	20,500 (25.9%)	49,669 (22.6%)
Angiotensin II antagonists, plain	11,222 (15.7%)	3,962 (12.7%)	5,318 (14.2%)	11,854 (15.0%)	32,356 (14.7%)
Angiotensin II antagonists, combinations	5,821 (8.13%)	2,722 (8.72%)	3,424 (9.11%)	5,212 (6.58%)	17,179 (7.82%)
Beta-blockers	51,522 (72.0%)	21,754 (69.7%)	25,190 (67.0%)	56,980 (72.0%)	155,446 (70.8%)
Proton pump inhibitors	15,636 (21.8%)	5,180 (16.6%)	7,502 (20.0%)	17,349 (21.9%)	45,667 (20.8%)
H2-receptor antagonists	379 (0.53%)	128 (0.41%)	214 (0.57%)	379 (0.48%)	1,100 (0.50%)
Non-steroidal anti-inflammatory drugs	5,624 (7.86%)	2,995 (9.60%)	3,109 (8.27%)	5,861 (7.40%)	17,589 (8.01%)
Statins	24,550 (34.3%)	9,851 (31.6%)	12,533 (33.4%)	28,743 (36.3%)	75,677 (34.5%)
Antidiabetic agents	8,226 (11.5%)	3,066 (9.82%)	4,283 (11.4%)	10,408 (13.1%)	25,983 (11.8%)
Loop diuretics	16,494 (23.0%)	5,372 (17.2%)	7,835 (20.8%)	22,174 (28.0%)	51,875 (23.6%)
Non-loop diuretics	901 (1.26%)	374 (1.20%)	448 (1.19%)	1,229 (1.55%)	2,952 (1.34%)
Alpha adrenergic blockers	12,537 (17.5%)	4,611 (14.8%)	6,158 (16.4%)	15,809 (20.0%)	39,115 (17.8%)
Amiodarone	1,691 (2.36%)	638 (2.04%)	727 (1.93%)	2,561 (3.23%)	5,617 (2.56%)
Dronedarone	678 (0.95%)	95 (0.30%)	158 (0.42%)	597 (0.75%)	1,528 (0.70%)
Antihypertensive, combination drugs	7,933 (11.1%)	3,807 (12.2%)	4,683 (12.5%)	7,700 (9.73%)	24,123 (11.0%)
Calcium channel blockers	16,995 (23.7%)	6,710 (21.5%)	8,599 (22.9%)	19,675 (24.9%)	51,979 (23.7%)
Selective serotonin reuptake inhibitors	4,615 (6.45%)	1,546 (4.95%)	2,310 (6.15%)	4,793 (6.05%)	13,264 (6.04%)
Drugs used in alcohol dependence	112 (0.16%)	82 (0.26%)	73 (0.19%)	120 (0.15%)	387 (0.18%)
Risk scores					
CHA2DS2-VASc score, mean (SD)	3.4 (1.7)	2.8 (1.7)	3.2 (1.7)	3.4 (1.8)	3.3 (1.7)
0 -1	10,417 (14.6%)	7,481 (24.0%)	6,152 (16.4%)	11,520 (14.6%)	35,570 (16.2%)
2 -3	28,435 (39.7%)	13,783 (44.2%)	16,023 (42.6%)	30,326 (38.3%)	88,567 (40.3%)
≥4	32,733 (45.7%)	9,945 (31.9%)	15,405 (41.0%)	37,325 (47.1%)	95,408 (43.5%)
CHADS2 score, mean (SD)	2.3 (1.5)	1.7 (1.4)	2.0 (1.5)	2.4 (1.5)	2.2 (1.5)
0	8,006 (11.2%)	6,303 (20.2%)	5,430 (14.4%)	8,298 (10.5%)	28,037 (12.8%)
1	15,830 (22.1%)	9,436 (30.2%)	9,770 (26.0%)	15,842 (20.0%)	50,878 (23.2%)
≥2	47,749 (66.7%)	15,470 (49.6%)	22,380 (59.6%)	55,031 (69.5%)	140,630 (64.1%)
HAS-BLED score, mean (SD)	2.0 (1.0)	1.8 (1.1)	2.0 (1.0)	2.0 (1.1)	2.0 (1.0)
<3	51,368 (71.8%)	23,531 (75.4%)	27,055 (72.0%)	56,153 (70.9%)	158,107 (72.0%)
≥3	20,217 (28.2%)	7,678 (24.6%)	10,525 (28.0%)	23,018 (29.1%)	61,438 (28.0%)
Health care utilisation in 12 months before the index date					
Hospitalisations, median (IQR)	1.0 (1.0 - 2.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 2.0)	1.0 (0.0 - 2.0)
Planned non-acute outpatient visits, median (IQR)	2.0 (0.0 - 4.0)	2.0 (0.0 - 4.0)	2.0 (1.0 - 4.0)	2.0 (0.0 - 4.0)	2.0 (0.0 - 4.0)
Emergency/acute outpatient visits, median (IQR)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)

*Set to zero if AF diagnosed after index date (maximum 60 days)
**Initial dose equals the strength of one tablet in the initial dispensing for rivaroxaban (used once daily) and to twice the strength of one in the initial dispensing for apixaban or dabigatran (used twice daily).
Available socioeconomic characteristics vary by country and are reported in country-specific tables.

Table 15.2 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban, dabigatran, rivaroxaban or warfarin (Denmark, 2013 -2016)

Characteristic	Apixaban (N= 14,980)	Dabigatran (N= 12,446)	Rivaroxaban (N= 12,682)	Warfarin (N= 20,070)	Total (N= 60,178)
Country					
Denmark	14,980 (100%)	12,446 (100%)	12,682 (100%)	20,070 (100%)	60,178 (100%)
Year of OAC initiation					
2013	711 (4.75%)	5,381 (43.2%)	2,348 (18.5%)	6,808 (33.9%)	15,248 (25.3%)
2014	3,136 (20.9%)	4,376 (35.2%)	1,881 (14.8%)	5,398 (26.9%)	14,791 (24.6%)
2015	5,385 (35.9%)	1,625 (13.1%)	3,508 (27.7%)	4,582 (22.8%)	15,100 (25.1%)
2016	5,748 (38.4%)	1,064 (8.55%)	4,945 (39.0%)	3,282 (16.4%)	15,039 (25.0%)
Time form most recent relative to index date hospital AF diagnosis, median (IQR), months	0.2 (0.1 - 1.9)	0.2 (0.0 - 3.5)	0.2 (0.1 - 3.8)	0.3 (0.1 - 6.1)	0.3 (0.1 - 3.6)
Time from AF diagnosis to index					
3 - 60 months	3,321 (22.2%)	3,202 (25.7%)	3,361 (26.5%)	5,787 (28.8%)	15,671 (26.0%)
< 3 month	11,659 (77.8%)	9,244 (74.3%)	9,321 (73.5%)	14,283 (71.2%)	44,507 (74.0%)
Sex					
Female	7,111 (47.5%)	4,990 (40.1%)	5,710 (45.0%)	7,954 (39.6%)	25,765 (42.8%)
Male	7,869 (52.5%)	7,456 (59.9%)	6,972 (55.0%)	12,116 (60.4%)	34,413 (57.2%)
Age, median (IQR), years	75.8 (68.4 - 83.8)	71.2 (64.6 - 78.9)	74.1 (67.2 - 82.1)	73.3 (66.1 - 80.6)	73.6 (66.5 - 81.4)
Age group					
< 55years	656 (4.38%)	945 (7.59%)	633 (4.99%)	1,524 (7.59%)	3,758 (6.24%)
55-<65 years	1,712 (11.4%)	2,298 (18.5%)	1,696 (13.4%)	2,869 (14.3%)	8,575 (14.2%)
65-<75 years	4,748 (31.7%)	4,600 (37.0%)	4,365 (34.4%)	6,820 (34.0%)	20,533 (34.1%)
75-<85 years	4,611 (30.8%)	3,288 (26.4%)	3,765 (29.7%)	6,275 (31.3%)	17,939 (29.8%)
≥ 85 years	3,253 (21.7%)	1,315 (10.6%)	2,223 (17.5%)	2,582 (12.9%)	9,373 (15.6%)
Initial dose **					
Reduced	5,271 (35.2%)	4,593 (36.9%)	3,123 (24.6%)		
Standard	9,709 (64.8%)	7,853 (63.1%)	9,559 (75.4%)		
Baseline comorbidity 5 years before and including index date					
Charlson Comorbidity Index score					
0	6,030 (40.3%)	6,446 (51.8%)	5,748 (45.3%)	8,598 (42.8%)	26,822 (44.6%)
1 -2	5,337 (35.6%)	3,951 (31.7%)	4,281 (33.8%)	6,004 (29.9%)	19,573 (32.5%)
≥3	3,613 (24.1%)	2,049 (16.5%)	2,653 (20.9%)	5,468 (27.2%)	13,783 (22.9%)
Baseline comorbidity 5 years before and including index date					
Prior bleeding (any)	1,526 (10.2%)	998 (8.02%)	1,097 (8.65%)	1,941 (9.67%)	5,562 (9.24%)
Prior gastrointestinal bleeding	198 (1.32%)	110 (0.88%)	129 (1.02%)	273 (1.36%)	710 (1.18%)
Prior intracranial bleeding	200 (1.34%)	100 (0.80%)	125 (0.99%)	141 (0.70%)	566 (0.94%)
Prior stroke (any)	2,542 (17.0%)	1,272 (10.2%)	1,741 (13.7%)	1,976 (9.85%)	7,531 (12.5%)
Prior ischaemic stroke	2,493 (16.6%)	1,250 (10.0%)	1,707 (13.5%)	1,944 (9.69%)	7,394 (12.3%)
Prior haemorrhagic stroke	132 (0.88%)	54 (0.43%)	77 (0.61%)	85 (0.42%)	348 (0.58%)
Prior systemic embolism	64 (0.43%)	32 (0.26%)	45 (0.35%)	107 (0.53%)	248 (0.41%)
Prior transient ischaemic attack	611 (4.08%)	426 (3.42%)	421 (3.32%)	604 (3.01%)	2,062 (3.43%)
Chronic kidney disease	599 (4.00%)	171 (1.37%)	358 (2.82%)	1,690 (8.42%)	2,818 (4.68%)
Heart failure	2,376 (15.9%)	1,596 (12.8%)	1,848 (14.6%)	3,567 (17.8%)	9,387 (15.6%)
Coronary artery disease	2,712 (18.1%)	2,043 (16.4%)	2,135 (16.8%)	4,588 (22.9%)	11,478 (19.1%)
Peripheral arterial disease	1,040 (6.94%)	622 (5.00%)	776 (6.12%)	1,628 (8.11%)	4,066 (6.76%)
Cardioversion	553 (3.69%)	852 (6.85%)	608 (4.79%)	1,387 (6.91%)	3,400 (5.65%)
Hypertension	9,507 (63.5%)	7,443 (59.8%)	7,822 (61.7%)	12,265 (61.1%)	37,037 (61.5%)
Diabetes	2,516 (16.8%)	1,690 (13.6%)	1,965 (15.5%)	3,488 (17.4%)	9,659 (16.1%)
Chronic obstructive pulmonary disease	1,976 (13.2%)	1,249 (10.0%)	1,540 (12.1%)	2,570 (12.8%)	7,335 (12.2%)
Liver disease	157 (1.05%)	99 (0.80%)	110 (0.87%)	237 (1.18%)	603 (1.00%)
Alcoholism	481 (3.21%)	406 (3.26%)	410 (3.23%)	590 (2.94%)	1,887 (3.14%)
Dementia	443 (2.96%)	203 (1.63%)	312 (2.46%)	220 (1.10%)	1,178 (1.96%)
Cancer 6 months before and including index date	588 (3.93%)	388 (3.12%)	507 (4.00%)	926 (4.61%)	2,409 (4.00%)
Prescription medication dispensed in 90 days before and including index date					
Platelet inhibitors (excluding heparin)	4,863 (32.5%)	3,611 (29.0%)	3,960 (31.2%)	6,764 (33.7%)	19,198 (31.9%)
Low -dose aspirin	3,417 (22.8%)	2,810 (22.6%)	2,912 (23.0%)	5,109 (25.5%)	14,248 (23.7%)
ADP receptor blockers	1,683 (11.2%)	985 (7.91%)	1,199 (9.45%)	2,256 (11.2%)	6,123 (10.2%)
Renin -angiotensin system inhibitors	6,285 (42.0%)	5,023 (40.4%)	5,167 (40.7%)	8,422 (42.0%)	24,897 (41.4%)
Angiotensin -converting enzyme inhibitors	3,095 (20.7%)	2,493 (20.0%)	2,550 (20.1%)	4,512 (22.5%)	12,650 (21.0%)

Angiotensin II antagonists, plain	1,920 (12.8%)	1,330 (10.7%)	1,404 (11.1%)	2,217 (11.0%)	6,871 (11.4%)
Angiotensin II antagonists, combinations	974 (6.50%)	881 (7.08%)	914 (7.21%)	1,214 (6.05%)	3,983 (6.62%)
Beta-blockers	9,395 (62.7%)	8,150 (65.5%)	7,884 (62.2%)	12,424 (61.9%)	37,853 (62.9%)
Proton pump inhibitors	3,436 (22.9%)	2,116 (17.0%)	2,620 (20.7%)	4,508 (22.5%)	12,680 (21.1%)
Non-steroidal anti-inflammatory drugs	1,402 (9.36%)	1,340 (10.8%)	1,274 (10.0%)	1,980 (9.87%)	5,996 (9.96%)
Statins	5,044 (33.7%)	3,908 (31.4%)	4,168 (32.9%)	6,991 (34.8%)	20,111 (33.4%)
Antidiabetic agents	1,884 (12.6%)	1,305 (10.5%)	1,504 (11.9%)	2,651 (13.2%)	7,344 (12.2%)
Loop diuretics	3,975 (26.5%)	2,499 (20.1%)	3,019 (23.8%)	5,797 (28.9%)	15,290 (25.4%)
Non-loop diuretics	175 (1.17%)	163 (1.31%)	154 (1.21%)	345 (1.72%)	837 (1.39%)
Alpha adrenergic blockers	2,663 (17.8%)	2,135 (17.2%)	2,275 (17.9%)	3,668 (18.3%)	10,741 (17.8%)
Amiodarone	560 (3.74%)	392 (3.15%)	368 (2.90%)	974 (4.85%)	2,294 (3.81%)
Dronedarone	10 (0.07%)	9 (0.07%)	17 (0.13%)	25 (0.12%)	61 (0.10%)
Antihypertensive, combination drugs	1,603 (10.7%)	1,455 (11.7%)	1,474 (11.6%)	2,112 (10.5%)	6,644 (11.0%)
Calcium channel blockers	3,431 (22.9%)	2,812 (22.6%)	2,936 (23.2%)	4,789 (23.9%)	13,968 (23.2%)
Selective serotonin reuptake inhibitors	1,065 (7.11%)	686 (5.51%)	825 (6.51%)	1,151 (5.73%)	3,727 (6.19%)
Drugs used in alcohol dependence	29 (0.19%)	43 (0.35%)	31 (0.24%)	49 (0.24%)	152 (0.25%)
Risk scores					
CHA2DS2-VASc score, mean (SD)	3.4 (1.7)	2.8 (1.6)	3.2 (1.7)	3.1 (1.7)	3.1 (1.7)
0 -1	1,982 (13.2%)	2,750 (22.1%)	2,001 (15.8%)	3,581 (17.8%)	10,314 (17.1%)
2 -3	5,861 (39.1%)	5,644 (45.3%)	5,477 (43.2%)	8,413 (41.9%)	25,395 (42.2%)
≥4	7,137 (47.6%)	4,052 (32.6%)	5,204 (41.0%)	8,076 (40.2%)	24,469 (40.7%)
CHADS2 score, mean (SD)	1.9 (1.3)	1.5 (1.2)	1.7 (1.2)	1.6 (1.2)	1.7 (1.2)
0	2,002 (13.4%)	2,510 (20.2%)	2,024 (16.0%)	3,468 (17.3%)	10,004 (16.6%)
1	4,278 (28.6%)	4,480 (36.0%)	4,040 (31.9%)	6,320 (31.5%)	19,118 (31.8%)
≥2	8,700 (58.1%)	5,456 (43.8%)	6,618 (52.2%)	10,282 (51.2%)	31,056 (51.6%)
HAS-BLED score, mean (SD)	2.2 (1.1)	2.0 (1.1)	2.1 (1.1)	2.1 (1.2)	2.1 (1.1)
<3	9,065 (60.5%)	8,684 (69.8%)	8,237 (65.0%)	12,664 (63.1%)	38,650 (64.2%)
≥3	5,915 (39.5%)	3,762 (30.2%)	4,445 (35.0%)	7,406 (36.9%)	21,528 (35.8%)
Health care utilisation in 12 months before the index date					
Hospitalisations, median (IQR)	1.0 (1.0 - 2.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 2.0)	1.0 (0.0 - 1.0)
Planned non-acute outpatient visits, median (IQR)	2.0 (0.0 - 5.0)	1.0 (0.0 - 4.0)	2.0 (0.0 - 4.0)	2.0 (0.0 - 6.0)	2.0 (0.0 - 5.0)
Emergency/acute outpatient visits, median (IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)
Socioeconomic characteristics					
Standardised household income during 3 full calendar years preceding the index date, median (IQR), thousand Euros	40 (29 - 62)	46 (32 - 76)	41 (29 - 65)	41 (30 - 63)	42 (30 - 66)
Highest education achieved					
Secondary compulsory	5,814 (38.8%)	4,398 (35.3%)	5,000 (39.4%)	8,430 (42.0%)	23,642 (39.3%)
Vocational / High school	5,913 (39.5%)	5,251 (42.2%)	4,982 (39.3%)	8,140 (40.6%)	24,286 (40.4%)
Higher education	2,626 (17.5%)	2,404 (19.3%)	2,256 (17.8%)	2,979 (14.8%)	10,265 (17.1%)
Unknown	627 (4.19%)	393 (3.16%)	444 (3.50%)	521 (2.60%)	1,985 (3.30%)
Employment status in calendar year before index date					
Employed or self -employed	2,331 (15.6%)	3,068 (24.7%)	2,242 (17.7%)	3,716 (18.5%)	11,357 (18.9%)
Unemployed	602 (4.02%)	708 (5.69%)	591 (4.66%)	1,194 (5.95%)	3,095 (5.14%)
Retired	11,935 (79.7%)	8,576 (68.9%)	9,765 (77.0%)	15,012 (74.8%)	45,288 (75.3%)
Unknown	112 (0.75%)	94 (0.76%)	84 (0.66%)	148 (0.74%)	438 (0.73%)

*Set to zero if AF diagnosed after index date (maximum 60 days)
**Initial dose equals the strength of one tablet in the initial dispensing for rivaroxaban (used once daily) and to twice the strength of one in the initial dispensing for apixaban or dabigatran (used twice daily).
IQR interquartile range; OAC oral anticoagulant; SD standard deviation

Table 15.3 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban, dabigatran, rivaroxaban or warfarin (Norway, 2013 -2016)

Characteristic	Apixaban (N= 17,780)	Dabigatran (N= 8,684)	Rivaroxaban (N= 10,565)	Warfarin (N= 11,949)	Total (N= 48,978)
Country					
Norway	17,780 (100%)	8,684 (100%)	10,565 (100%)	11,949 (100%)	48,978 (100%)
Year of OAC initiation					
2013	336 (1.89%)	4,164 (48.0%)	2,705 (25.6%)	5,805 (48.6%)	13,010 (26.6%)
2014	3,192 (18.0%)	2,852 (32.8%)	2,593 (24.5%)	3,447 (28.8%)	12,084 (24.7%)
2015	6,307 (35.5%)	928 (10.7%)	2,848 (27.0%)	1,764 (14.8%)	11,847 (24.2%)
2016	7,945 (44.7%)	740 (8.52%)	2,419 (22.9%)	933 (7.81%)	12,037 (24.6%)
Time form most recent relative to index date hospital AF diagnosis, median (IQR), months	0.2 (0.0 - 1.7)	0.2 (0.0 - 16.3)	0.3 (0.0 - 16.1)	0.7 (0.1 - 23.2)	0.3 (0.0 - 11.3)
Time from AF diagnosis to index					
3 - 60 months	3,998 (22.5%)	2,834 (32.6%)	3,487 (33.0%)	4,641 (38.8%)	14,960 (30.5%)
< 3 month	13,782 (77.5%)	5,850 (67.4%)	7,078 (67.0%)	7,308 (61.2%)	34,018 (69.5%)
Sex					
Female	7,901 (44.4%)	3,310 (38.1%)	4,513 (42.7%)	4,740 (39.7%)	20,464 (41.8%)
Male	9,879 (55.6%)	5,374 (61.9%)	6,052 (57.3%)	7,209 (60.3%)	28,514 (58.2%)
Age, median (IQR), years	74.7 (67.5 - 83.0)	70.7 (64.6 - 78.8)	73.4 (66.7 - 81.5)	75.3 (66.7 - 83.2)	73.8 (66.5 - 82.0)
Age group					
< 55years	935 (5.26%)	719 (8.28%)	553 (5.23%)	832 (6.96%)	3,039 (6.20%)
55-<65 years	2,259 (12.7%)	1,598 (18.4%)	1,524 (14.4%)	1,692 (14.2%)	7,073 (14.4%)
65-<75 years	5,835 (32.8%)	3,299 (38.0%)	3,756 (35.6%)	3,355 (28.1%)	16,245 (33.2%)
75-<85 years	5,408 (30.4%)	2,171 (25.0%)	3,085 (29.2%)	3,856 (32.3%)	14,520 (29.6%)
≥ 85 years	3,343 (18.8%)	897 (10.3%)	1,647 (15.6%)	2,214 (18.5%)	8,101 (16.5%)
Initial dose **					
Reduced	4,817 (27.1%)	3,054 (35.2%)	2,649 (25.1%)		
Standard	12,963 (72.9%)	5,630 (64.8%)	7,916 (74.9%)		
Baseline comorbidity 5 years before and including index date					
Charlson Comorbidity Index score					
0	6,276 (35.3%)	3,872 (44.6%)	4,043 (38.3%)	3,336 (27.9%)	17,527 (35.8%)
1 -2	6,089 (34.2%)	3,009 (34.6%)	3,747 (35.5%)	3,813 (31.9%)	16,658 (34.0%)
≥3	5,415 (30.5%)	1,803 (20.8%)	2,775 (26.3%)	4,800 (40.2%)	14,793 (30.2%)
Baseline comorbidity 5 years before and including index date					
Prior bleeding (any)	2,312 (13.0%)	904 (10.4%)	1,255 (11.9%)	1,779 (14.9%)	6,250 (12.8%)
Prior gastrointestinal bleeding	196 (1.10%)	79 (0.91%)	122 (1.15%)	191 (1.60%)	588 (1.20%)
Prior intracranial bleeding	222 (1.25%)	76 (0.88%)	110 (1.04%)	160 (1.34%)	568 (1.16%)
Prior stroke (any)	2,133 (12.0%)	813 (9.36%)	1,261 (11.9%)	1,435 (12.0%)	5,642 (11.5%)
Prior ischaemic stroke	2,080 (11.7%)	793 (9.13%)	1,225 (11.6%)	1,380 (11.5%)	5,478 (11.2%)
Prior haemorrhagic stroke	136 (0.76%)	51 (0.59%)	67 (0.63%)	106 (0.89%)	360 (0.74%)
Prior systemic embolism	87 (0.49%)	46 (0.53%)	56 (0.53%)	140 (1.17%)	329 (0.67%)
Prior transient ischaemic attack	715 (4.02%)	301 (3.47%)	434 (4.11%)	463 (3.87%)	1,913 (3.91%)
Chronic kidney disease	1,330 (7.48%)	252 (2.90%)	579 (5.48%)	1,560 (13.1%)	3,721 (7.60%)
Heart failure	3,280 (18.4%)	1,221 (14.1%)	1,603 (15.2%)	3,110 (26.0%)	9,214 (18.8%)
Coronary artery disease	4,615 (26.0%)	1,847 (21.3%)	2,512 (23.8%)	4,409 (36.9%)	13,383 (27.3%)
Peripheral arterial disease	1,733 (9.75%)	564 (6.49%)	968 (9.16%)	1,371 (11.5%)	4,636 (9.47%)
Cardioversion	1,021 (5.74%)	682 (7.85%)	550 (5.21%)	900 (7.53%)	3,153 (6.44%)
Hypertension	10,534 (59.2%)	4,904 (56.5%)	6,258 (59.2%)	7,267 (60.8%)	28,963 (59.1%)
Diabetes	2,627 (14.8%)	1,088 (12.5%)	1,485 (14.1%)	2,103 (17.6%)	7,303 (14.9%)
Chronic obstructive pulmonary disease	2,626 (14.8%)	1,058 (12.2%)	1,425 (13.5%)	1,850 (15.5%)	6,959 (14.2%)
Liver disease	153 (0.86%)	78 (0.90%)	107 (1.01%)	154 (1.29%)	492 (1.00%)
Alcoholism	343 (1.93%)	162 (1.87%)	247 (2.34%)	170 (1.42%)	922 (1.88%)
Dementia	356 (2.00%)	104 (1.20%)	183 (1.73%)	226 (1.89%)	869 (1.77%)
Cancer 6 months before and including index date	1,037 (5.83%)	429 (4.94%)	639 (6.05%)	807 (6.75%)	2,912 (5.95%)
Prescription medication dispensed in 90 days before and including index date					
Platelet inhibitors (excluding heparin)	7,472 (42.0%)	3,332 (38.4%)	4,450 (42.1%)	5,395 (45.2%)	20,649 (42.2%)
Low -dose aspirin	7,080 (39.8%)	3,236 (37.3%)	4,273 (40.4%)	5,062 (42.4%)	19,651 (40.1%)
ADP receptor blockers	896 (5.04%)	229 (2.64%)	331 (3.13%)	1,134 (9.49%)	2,590 (5.29%)
Renin -angiotensin system inhibitors	7,966 (44.8%)	3,545 (40.8%)	4,434 (42.0%)	5,502 (46.0%)	21,447 (43.8%)
Angiotensin -converting enzyme inhibitors	2,927 (16.5%)	1,221 (14.1%)	1,391 (13.2%)	2,497 (20.9%)	8,036 (16.4%)

Angiotensin II antagonists, plain	2,609 (14.7%)	1,126 (13.0%)	1,458 (13.8%)	1,635 (13.7%)	6,828 (13.9%)
Angiotensin II antagonists, combinations	2,542 (14.3%)	1,214 (14.0%)	1,600 (15.1%)	1,454 (12.2%)	6,810 (13.9%)
Beta-blockers	12,344 (69.4%)	5,952 (68.5%)	6,727 (63.7%)	8,409 (70.4%)	33,432 (68.3%)
Proton pump inhibitors	3,807 (21.4%)	1,297 (14.9%)	1,987 (18.8%)	2,694 (22.5%)	9,785 (20.0%)
H2-receptor antagonists	228 (1.28%)	105 (1.21%)	152 (1.44%)	165 (1.38%)	650 (1.33%)
Non-steroidal anti-inflammatory drugs	1,612 (9.07%)	885 (10.2%)	957 (9.06%)	907 (7.59%)	4,361 (8.90%)
Statins	6,800 (38.2%)	2,932 (33.8%)	3,802 (36.0%)	5,018 (42.0%)	18,552 (37.9%)
Antidiabetic agents	1,754 (9.87%)	727 (8.37%)	1,001 (9.47%)	1,403 (11.7%)	4,885 (9.97%)
Loop diuretics	3,575 (20.1%)	1,229 (14.2%)	1,755 (16.6%)	3,392 (28.4%)	9,951 (20.3%)
Non-loop diuretics	284 (1.60%)	125 (1.44%)	151 (1.43%)	230 (1.92%)	790 (1.61%)
Alpha adrenergic blockers	1,152 (6.48%)	479 (5.52%)	610 (5.77%)	959 (8.03%)	3,200 (6.53%)
Amiodarone	688 (3.87%)	170 (1.96%)	226 (2.14%)	702 (5.87%)	1,786 (3.65%)
Dronedarone	262 (1.47%)	34 (0.39%)	71 (0.67%)	132 (1.10%)	499 (1.02%)
Antihypertensive, combination drugs	2,954 (16.6%)	1,410 (16.2%)	1,850 (17.5%)	1,740 (14.6%)	7,954 (16.2%)
Calcium channel blockers	3,835 (21.6%)	1,596 (18.4%)	2,194 (20.8%)	2,642 (22.1%)	10,267 (21.0%)
Selective serotonin reuptake inhibitors	795 (4.47%)	329 (3.79%)	486 (4.60%)	533 (4.46%)	2,143 (4.38%)
Drugs used in alcohol dependence	26 (0.15%)	20 (0.23%)	20 (0.19%)	15 (0.13%)	81 (0.17%)
Risk scores					
CHA2DS2-VASc score, mean (SD)	3.1 (1.7)	2.6 (1.7)	2.9 (1.7)	3.3 (1.9)	3.0 (1.8)
0 -1	3,289 (18.5%)	2,474 (28.5%)	2,215 (21.0%)	2,237 (18.7%)	10,215 (20.9%)
2 -3	7,757 (43.6%)	3,867 (44.5%)	4,690 (44.4%)	4,372 (36.6%)	20,686 (42.2%)
≥4	6,734 (37.9%)	2,343 (27.0%)	3,660 (34.6%)	5,340 (44.7%)	18,077 (36.9%)
CHADS2 score, mean (SD)	1.5 (1.3)	1.2 (1.2)	1.4 (1.3)	1.7 (1.4)	1.5 (1.3)
0	4,151 (23.3%)	2,811 (32.4%)	2,769 (26.2%)	2,526 (21.1%)	12,257 (25.0%)
1	5,860 (33.0%)	2,917 (33.6%)	3,466 (32.8%)	3,481 (29.1%)	15,724 (32.1%)
≥2	7,769 (43.7%)	2,956 (34.0%)	4,330 (41.0%)	5,942 (49.7%)	20,997 (42.9%)
HAS-BLED score, mean (SD)	2.0 (1.2)	1.8 (1.1)	2.0 (1.2)	2.1 (1.3)	2.0 (1.2)
<3	11,940 (67.2%)	6,470 (74.5%)	7,354 (69.6%)	7,412 (62.0%)	33,176 (67.7%)
≥3	5,840 (32.8%)	2,214 (25.5%)	3,211 (30.4%)	4,537 (38.0%)	15,802 (32.3%)
Health care utilisation in 12 months before the index date					
Hospitalisations, median (IQR)	1.0 (1.0 - 2.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 2.0)	1.0 (1.0 - 2.0)	1.0 (1.0 - 2.0)
Planned non-acute outpatient visits, median (IQR)	3.0 (1.0 - 5.0)	2.0 (1.0 - 5.0)	3.0 (1.0 - 5.0)	3.0 (1.0 - 5.0)	3.0 (1.0 - 5.0)
Emergency/acute outpatient visits, median (IQR)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)

*Set to zero if AF diagnosed after index date (maximum 60 days)
**Initial dose equals the strength of one tablet in the initial dispensing for rivaroxaban (used once daily) and to twice the strength of one in the initial dispensing for apixaban or dabigatran (used twice daily).
IQR interquartile range; OAC oral anticoagulant; SD standard deviation
Data on socioeconomic characteristics not available for Norway.

Table 15.4 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban, dabigatran, rivaroxaban or warfarin (Sweden, 2013 -2016)

Characteristic	Apixaban (N= 38,825)	Dabigatran (N= 10,079)	Rivaroxaban (N= 14,333)	Warfarin (N= 47,152)	Total (N=110,389)
Country					
Sweden	38,825 (100%)	10,079 (100%)	14,333 (100%)	47,152 (100%)	110,389 (100%)
Year of OAC initiation					
2013	793 (2.04%)	3,021 (30.0%)	1,895 (13.2%)	22,383 (47.5%)	28,092 (25.4%)
2014	6,774 (17.4%)	3,240 (32.1%)	3,810 (26.6%)	14,488 (30.7%)	28,312 (25.6%)
2015	14,228 (36.6%)	1,665 (16.5%)	4,739 (33.1%)	7,041 (14.9%)	27,673 (25.1%)
2016	17,030 (43.9%)	2,153 (21.4%)	3,889 (27.1%)	3,240 (6.87%)	26,312 (23.8%)
Time form most recent relative to index date hospital AF diagnosis, median (IQR), months	0.2 (0.0 - 6.1)	0.2 (0.0 - 16.3)	0.4 (0.0 - 20.7)	0.4 (0.1 - 18.0)	0.3 (0.0 - 14.0)
Time from AF diagnosis to index					
3 - 60 months	10,661 (27.5%)	3,239 (32.1%)	5,011 (35.0%)	15,770 (33.4%)	34,681 (31.4%)
< 3 month	28,164 (72.5%)	6,840 (67.9%)	9,322 (65.0%)	31,382 (66.6%)	75,708 (68.6%)
Sex					
Female	17,899 (46.1%)	3,961 (39.3%)	6,453 (45.0%)	20,290 (43.0%)	48,603 (44.0%)
Male	20,926 (53.9%)	6,118 (60.7%)	7,880 (55.0%)	26,862 (57.0%)	61,786 (56.0%)
Age, median (IQR), years	75.7 (68.5 - 83.6)	71.1 (64.7 - 78.4)	74.9 (67.8 - 82.5)	75.6 (68.4 - 82.6)	75.1 (67.9 - 82.6)
Age group					
< 55years	1,732 (4.46%)	770 (7.64%)	586 (4.09%)	2,125 (4.51%)	5,213 (4.72%)
55-<65 years	4,445 (11.4%)	1,841 (18.3%)	1,741 (12.1%)	5,542 (11.8%)	13,569 (12.3%)
65-<75 years	12,301 (31.7%)	3,894 (38.6%)	4,907 (34.2%)	14,882 (31.6%)	35,984 (32.6%)
75-<85 years	12,309 (31.7%)	2,618 (26.0%)	4,613 (32.2%)	16,573 (35.1%)	36,113 (32.7%)
≥ 85 years	8,038 (20.7%)	956 (9.49%)	2,486 (17.3%)	8,030 (17.0%)	19,510 (17.7%)
Initial dose **					
Reduced	11,187 (28.8%)	3,084 (30.6%)	3,442 (24.0%)		
Standard	27,638 (71.2%)	6,995 (69.4%)	10,891 (76.0%)		
Baseline comorbidity 5 years before and including index date					
Charlson Comorbidity Index score					
0	16,107 (41.5%)	5,015 (49.8%)	6,253 (43.6%)	17,671 (37.5%)	45,046 (40.8%)
1 -2	13,118 (33.8%)	3,326 (33.0%)	4,728 (33.0%)	15,785 (33.5%)	36,957 (33.5%)
≥3	9,600 (24.7%)	1,738 (17.2%)	3,352 (23.4%)	13,696 (29.0%)	28,386 (25.7%)
Baseline comorbidity 5 years before and including index date					
Prior bleeding (any)	4,178 (10.8%)	909 (9.02%)	1,511 (10.5%)	5,145 (10.9%)	11,743 (10.6%)
Prior gastrointestinal bleeding	276 (0.71%)	54 (0.54%)	76 (0.53%)	357 (0.76%)	763 (0.69%)
Prior intracranial bleeding	477 (1.23%)	108 (1.07%)	182 (1.27%)	409 (0.87%)	1,176 (1.07%)
Prior stroke (any)	5,369 (13.8%)	1,294 (12.8%)	1,855 (12.9%)	6,199 (13.1%)	14,717 (13.3%)
Prior ischaemic stroke	5,168 (13.3%)	1,254 (12.4%)	1,788 (12.5%)	6,080 (12.9%)	14,290 (12.9%)
Prior haemorrhagic stroke	427 (1.10%)	97 (0.96%)	152 (1.06%)	330 (0.70%)	1,006 (0.91%)
Prior systemic embolism	244 (0.63%)	55 (0.55%)	122 (0.85%)	513 (1.09%)	934 (0.85%)
Prior transient ischaemic attack	1,766 (4.55%)	430 (4.27%)	611 (4.26%)	2,050 (4.35%)	4,857 (4.40%)
Chronic kidney disease	1,580 (4.07%)	132 (1.31%)	385 (2.69%)	3,279 (6.95%)	5,376 (4.87%)
Heart failure	7,994 (20.6%)	1,515 (15.0%)	2,709 (18.9%)	11,329 (24.0%)	23,547 (21.3%)
Coronary artery disease	8,253 (21.3%)	1,621 (16.1%)	2,886 (20.1%)	12,456 (26.4%)	25,216 (22.8%)
Peripheral arterial disease	2,069 (5.33%)	444 (4.41%)	715 (4.99%)	3,032 (6.43%)	6,260 (5.67%)
Cardioversion	2,822 (7.27%)	1,003 (9.95%)	954 (6.66%)	4,599 (9.75%)	9,378 (8.50%)
Hypertension	27,744 (71.5%)	6,625 (65.7%)	10,254 (71.5%)	34,574 (73.3%)	79,197 (71.7%)
Diabetes	6,642 (17.1%)	1,513 (15.0%)	2,538 (17.7%)	9,085 (19.3%)	19,778 (17.9%)
Chronic obstructive pulmonary disease	4,549 (11.7%)	957 (9.49%)	1,657 (11.6%)	5,696 (12.1%)	12,859 (11.6%)
Liver disease	298 (0.77%)	84 (0.83%)	108 (0.75%)	425 (0.90%)	915 (0.83%)
Alcoholism	948 (2.44%)	289 (2.87%)	369 (2.57%)	1,025 (2.17%)	2,631 (2.38%)
Dementia	1,022 (2.63%)	109 (1.08%)	402 (2.80%)	770 (1.63%)	2,303 (2.09%)
Cancer 6 months before and including index date	222 (0.57%)	61 (0.61%)	96 (0.67%)	402 (0.85%)	781 (0.71%)
Prescription medication dispensed in 90 days before and including index date					
Platelet inhibitors (excluding heparin)	14,519 (37.4%)	3,411 (33.8%)	5,703 (39.8%)	18,679 (39.6%)	42,312 (38.3%)
Low -dose aspirin	13,086 (33.7%)	3,129 (31.0%)	5,143 (35.9%)	17,006 (36.1%)	38,364 (34.8%)
ADP receptor blockers	2,281 (5.88%)	431 (4.28%)	844 (5.89%)	3,708 (7.86%)	7,264 (6.58%)
Renin -angiotensin system inhibitors	19,013 (49.0%)	4,475 (44.4%)	6,880 (48.0%)	24,143 (51.2%)	54,511 (49.4%)

Angiotensin -converting enzyme inhibitors	9,866 (25.4%)	2,255 (22.4%)	3,371 (23.5%)	13,491 (28.6%)	28,983 (26.3%)
Angiotensin II antagonists, plain	6,693 (17.2%)	1,506 (14.9%)	2,456 (17.1%)	8,002 (17.0%)	18,657 (16.9%)
Angiotensin II antagonists, combinations	2,305 (5.94%)	627 (6.22%)	910 (6.35%)	2,544 (5.40%)	6,386 (5.78%)
Beta-blockers	29,783 (76.7%)	7,652 (75.9%)	10,579 (73.8%)	36,147 (76.7%)	84,161 (76.2%)
Proton pump inhibitors	8,393 (21.6%)	1,767 (17.5%)	2,895 (20.2%)	10,147 (21.5%)	23,202 (21.0%)
H2-receptor antagonists	151 (0.39%)	22 (0.22%)	61 (0.43%)	212 (0.45%)	446 (0.40%)
Non-steroidal anti-inflammatory drugs	2,610 (6.72%)	770 (7.64%)	878 (6.13%)	2,974 (6.31%)	7,232 (6.55%)
Statins	12,706 (32.7%)	3,011 (29.9%)	4,563 (31.8%)	16,734 (35.5%)	37,014 (33.5%)
Antidiabetic agents	4,588 (11.8%)	1,034 (10.3%)	1,778 (12.4%)	6,354 (13.5%)	13,754 (12.5%)
Loop diuretics	8,944 (23.0%)	1,644 (16.3%)	3,061 (21.4%)	12,985 (27.5%)	26,634 (24.1%)
Non-loop diuretics	442 (1.14%)	86 (0.85%)	143 (1.00%)	654 (1.39%)	1,325 (1.20%)
Alpha adrenergic blockers	8,722 (22.5%)	1,997 (19.8%)	3,273 (22.8%)	11,182 (23.7%)	25,174 (22.8%)
Amiodarone	443 (1.14%)	76 (0.75%)	133 (0.93%)	885 (1.88%)	1,537 (1.39%)
Dronedarone	406 (1.05%)	52 (0.52%)	70 (0.49%)	440 (0.93%)	968 (0.88%)
Antihypertensive, combination drugs	3,376 (8.70%)	942 (9.35%)	1,359 (9.48%)	3,848 (8.16%)	9,525 (8.63%)
Calcium channel blockers	9,729 (25.1%)	2,302 (22.8%)	3,469 (24.2%)	12,244 (26.0%)	27,744 (25.1%)
Selective serotonin reuptake inhibitors	2,755 (7.10%)	531 (5.27%)	999 (6.97%)	3,109 (6.59%)	7,394 (6.70%)
Drugs used in alcohol dependence	57 (0.15%)	19 (0.19%)	22 (0.15%)	56 (0.12%)	154 (0.14%)
Risk scores					
CHA2DS2-VASc score, mean (SD)	3.5 (1.7)	2.9 (1.8)	3.4 (1.7)	3.6 (1.8)	3.5 (1.8)
0 -1	5,146 (13.3%)	2,257 (22.4%)	1,936 (13.5%)	5,702 (12.1%)	15,041 (13.6%)
2 -3	14,817 (38.2%)	4,272 (42.4%)	5,856 (40.9%)	17,541 (37.2%)	42,486 (38.5%)
≥4	18,862 (48.6%)	3,550 (35.2%)	6,541 (45.6%)	23,909 (50.7%)	52,862 (47.9%)
CHADS2 score, mean (SD)	2.8 (1.5)	2.4 (1.5)	2.7 (1.5)	2.9 (1.5)	2.8 (1.5)
0	1,853 (4.77%)	982 (9.74%)	637 (4.44%)	2,304 (4.89%)	5,776 (5.23%)
1	5,692 (14.7%)	2,039 (20.2%)	2,264 (15.8%)	6,041 (12.8%)	16,036 (14.5%)
≥2	31,280 (80.6%)	7,058 (70.0%)	11,432 (79.8%)	38,807 (82.3%)	88,577 (80.2%)
HAS-BLED score, mean (SD)	1.9 (0.9)	1.7 (0.9)	1.9 (0.9)	1.9 (0.9)	1.9 (0.9)
<3	30,363 (78.2%)	8,377 (83.1%)	11,464 (80.0%)	36,077 (76.5%)	86,281 (78.2%)
≥3	8,462 (21.8%)	1,702 (16.9%)	2,869 (20.0%)	11,075 (23.5%)	24,108 (21.8%)
Health care utilisation in 12 months before the index date					
Hospitalisations, median (IQR)	1.0 (0.0 - 2.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 2.0)	1.0 (0.0 - 2.0)
Planned non-acute outpatient visits, median (IQR)	1.0 (0.0 - 3.0)	1.0 (0.0 - 3.0)	1.0 (0.0 - 3.0)	1.0 (0.0 - 3.0)	1.0 (0.0 - 3.0)
Emergency/acute outpatient visits, median (IQR)	1.0 (0.0 - 2.0)	1.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)	0.0 (0.0 - 1.0)	1.0 (0.0 - 1.0)
Socioeconomic characteristics					
Standardised personal income during 3 full calendar years preceding the index date, median (IQR), thousand Euros	17 (14 - 26)	20 (15 - 32)	17 (14 - 26)	17 (13 - 24)	17 (14 - 26)
Highest education achieved					
Secondary compulsory	14,643 (37.7%)	2,962 (29.4%)	5,346 (37.3%)	18,846 (40.0%)	41,797 (37.9%)
Vocational / High school	14,787 (38.1%)	3,994 (39.6%)	5,472 (38.2%)	18,479 (39.2%)	42,732 (38.7%)
Higher education	8,970 (23.1%)	3,014 (29.9%)	3,338 (23.3%)	9,335 (19.8%)	24,657 (22.3%)
Unknown	408 (1.05%)	101 (1.00%)	167 (1.17%)	482 (1.02%)	1,158 (1.05%)

*Set to zero if AF diagnosed after index date (maximum 60 days)
**Initial dose equals the strength of one tablet in the initial dispensing for rivaroxaban (used once daily) and to twice the strength of one in the initial dispensing for apixaban or dabigatran (used twice daily).
IQR interquartile range; OAC oral anticoagulant; SD standard deviation
Data on employment not available in Sweden.

Table 15.5 Crude rates, and crude pairwise hazard ratios of any stroke or systemic embolism at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin in Denmark, Norway, and Sweden

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	1430	68,651.7	2.1 (2.0 - 2.2)	0.99 (0.92 - 1.06)
All	Dabigatran	31,209	610	43,462.8	1.4 (1.3 - 1.5)	0.76 (0.69 - 0.83)
All	Rivaroxaban	37,580	870	44,813.4	1.9 (1.8 - 2.1)	1.01 (0.93 - 1.09)
All	Warfarin	79,171	1890	98,817.3	1.9 (1.8 - 2.0)	Ref.
Denmark	Apixaban	14,980	390	14,541.7	2.6 (2.4 - 2.9)	1.34 (1.16 - 1.54)
Denmark	Dabigatran	12,446	280	18,021.7	1.6 (1.4 - 1.7)	0.90 (0.77 - 1.05)
Denmark	Rivaroxaban	12,682	280	13,011.1	2.2 (1.9 - 2.4)	1.14 (0.98 - 1.32)
Denmark	Warfarin	20,070	400	21,053.4	1.9 (1.7 - 2.1)	Ref.
Norway	Apixaban	17,780	330	16,312.5	2.0 (1.8 - 2.2)	0.93 (0.79 - 1.10)
Norway	Dabigatran	8,684	130	12,180.5	1.1 (0.9 - 1.3)	0.58 (0.47 - 0.71)
Norway	Rivaroxaban	10,565	270	13,870.0	2.0 (1.7 - 2.2)	1.01 (0.85 - 1.19)
Norway	Warfarin	11,949	270	13,466.2	2.0 (1.8 - 2.3)	Ref.
Sweden	Apixaban	38,825	710	37,797.5	1.9 (1.7 - 2.0)	0.88 (0.80 - 0.97)
Sweden	Dabigatran	10,079	190	13,260.7	1.5 (1.3 - 1.7)	0.77 (0.66 - 0.90)
Sweden	Rivaroxaban	14,333	320	17,932.3	1.8 (1.6 - 2.0)	0.91 (0.80 - 1.03)
Sweden	Warfarin	47,152	1210	64,316.1	1.9 (1.8 - 2.0)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.6 Crude rates, and crude pairwise hazard ratios of any bleeding at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin in Denmark, Norway, and Sweden

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	2080	68,479.0	3.0 (2.9 - 3.2)	0.79 (0.75 - 0.84)
All	Dabigatran	31,209	1070	43,270.0	2.5 (2.3 - 2.6)	0.72 (0.67 - 0.77)
All	Rivaroxaban	37,580	1740	44,309.3	3.9 (3.7 - 4.1)	1.10 (1.03 - 1.16)
All	Warfarin	79,171	3460	97,816.2	3.5 (3.4 - 3.6)	Ref.
Denmark	Apixaban	14,980	510	14,533.5	3.5 (3.2 - 3.8)	0.84 (0.75 - 0.94)
Denmark	Dabigatran	12,446	480	17,909.6	2.7 (2.4 - 2.9)	0.74 (0.66 - 0.83)
Denmark	Rivaroxaban	12,682	540	12,861.5	4.2 (3.8 - 4.5)	1.04 (0.94 - 1.16)
Denmark	Warfarin	20,070	820	20,778.2	4.0 (3.7 - 4.2)	Ref.
Norway	Apixaban	17,780	610	16,175.6	3.8 (3.5 - 4.1)	0.71 (0.64 - 0.79)
Norway	Dabigatran	8,684	330	12,101.0	2.7 (2.4 - 3.0)	0.59 (0.51 - 0.67)
Norway	Rivaroxaban	10,565	610	13,638.9	4.5 (4.1 - 4.8)	0.94 (0.84 - 1.05)
Norway	Warfarin	11,949	650	13,210.9	4.9 (4.6 - 5.3)	Ref.
Sweden	Apixaban	38,825	960	37,770.0	2.6 (2.4 - 2.7)	0.76 (0.70 - 0.82)
Sweden	Dabigatran	10,079	260	13,259.4	2.0 (1.8 - 2.2)	0.64 (0.56 - 0.73)
Sweden	Rivaroxaban	14,333	590	17,808.9	3.3 (3.1 - 3.6)	1.05 (0.96 - 1.16)
Sweden	Warfarin	47,152	1980	63,868.0	3.1 (3.0 - 3.2)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.7 Crude rates, and crude pairwise hazard ratios of ischaemic stroke at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	1160	68,713.5	1.7 (1.6 - 1.8)	1.07 (0.99 - 1.15)
All	Dabigatran	31,209	520	43,498.3	1.2 (1.1 - 1.3)	0.86 (0.78 - 0.95)
All	Rivaroxaban	37,580	680	44,859.1	1.5 (1.4 - 1.6)	1.04 (0.95 - 1.14)
All	Warfarin	79,171	1420	98,992.0	1.4 (1.4 - 1.5)	Ref.
Denmark	Apixaban	14,980	320	14,553.7	2.2 (2.0 - 2.4)	1.42 (1.21 - 1.66)
Denmark	Dabigatran	12,446	240	18,035.7	1.3 (1.2 - 1.5)	1.00 (0.85 - 1.19)
Denmark	Rivaroxaban	12,682	230	13,021.8	1.8 (1.5 - 2.0)	1.18 (1.00 - 1.40)
Denmark	Warfarin	20,070	310	21,076.5	1.5 (1.3 - 1.7)	Ref.
Norway	Apixaban	17,780	260	16,331.5	1.6 (1.4 - 1.8)	1.06 (0.88 - 1.27)
Norway	Dabigatran	8,684	110	12,193.7	0.9 (0.7 - 1.1)	0.66 (0.52 - 0.84)
Norway	Rivaroxaban	10,565	200	13,889.1	1.4 (1.2 - 1.6)	1.05 (0.86 - 1.28)
Norway	Warfarin	11,949	190	13,493.4	1.4 (1.2 - 1.6)	Ref.
Sweden	Apixaban	38,825	580	37,828.3	1.5 (1.4 - 1.7)	0.94 (0.85 - 1.05)
Sweden	Dabigatran	10,079	170	13,268.9	1.3 (1.1 - 1.5)	0.88 (0.75 - 1.04)
Sweden	Rivaroxaban	14,333	250	17,948.3	1.4 (1.2 - 1.6)	0.94 (0.81 - 1.08)
Sweden	Warfarin	47,152	920	64,442.9	1.4 (1.3 - 1.5)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.8 Crude rates, and crude pairwise hazard ratios of haemorrhagic stroke at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	260	69,377.1	0.4 (0.3 - 0.4)	0.86 (0.74 - 1.01)
All	Dabigatran	31,209	70	43,889.8	0.2 (0.1 - 0.2)	0.41 (0.32 - 0.53)
All	Rivaroxaban	37,580	200	45,265.8	0.4 (0.4 - 0.5)	1.06 (0.89 - 1.26)
All	Warfarin	79,171	400	99,781.8	0.4 (0.4 - 0.4)	Ref.
Denmark	Apixaban	14,980	70	14,762.8	0.5 (0.4 - 0.6)	1.09 (0.79 - 1.50)
Denmark	Dabigatran	12,446	30	18,227.7	0.2 (0.1 - 0.3)	0.48 (0.32 - 0.71)
Denmark	Rivaroxaban	12,682	50	13,163.7	0.4 (0.3 - 0.5)	0.99 (0.70 - 1.39)
Denmark	Warfarin	20,070	90	21,205.9	0.4 (0.3 - 0.5)	Ref.
Norway	Apixaban	17,780	70	16,449.5	0.4 (0.3 - 0.5)	0.74 (0.53 - 1.03)
Norway	Dabigatran	8,684	20	12,276.3	0.2 (0.1 - 0.3)	0.33 (0.20 - 0.54)
Norway	Rivaroxaban	10,565	70	13,990.1	0.5 (0.4 - 0.6)	0.98 (0.71 - 1.36)
Norway	Warfarin	11,949	70	13,586.8	0.5 (0.4 - 0.7)	Ref.
Sweden	Apixaban	38,825	120	38,164.7	0.3 (0.3 - 0.4)	0.79 (0.63 - 0.99)
Sweden	Dabigatran	10,079	20	13,385.8	0.1 (0.1 - 0.2)	0.34 (0.21 - 0.55)
Sweden	Rivaroxaban	14,333	70	18,111.9	0.4 (0.3 - 0.5)	1.01 (0.77 - 1.32)
Sweden	Warfarin	47,152	240	65,010.8	0.4 (0.3 - 0.4)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.9 Crude rates, and crude pairwise hazard ratios of intracranial bleeding at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	450	69,327.6	0.6 (0.6 - 0.7)	0.70 (0.63 - 0.79)
All	Dabigatran	31,209	150	43,856.7	0.3 (0.3 - 0.4)	0.39 (0.33 - 0.47)
All	Rivaroxaban	37,580	320	45,217.2	0.7 (0.6 - 0.8)	0.79 (0.70 - 0.90)
All	Warfarin	79,171	870	99,578.9	0.9 (0.8 - 0.9)	Ref.
Denmark	Apixaban	14,980	120	14,751.1	0.8 (0.6 - 0.9)	1.02 (0.80 - 1.30)
Denmark	Dabigatran	12,446	60	18,218.6	0.3 (0.3 - 0.4)	0.47 (0.35 - 0.63)
Denmark	Rivaroxaban	12,682	90	13,151.8	0.7 (0.6 - 0.8)	0.93 (0.72 - 1.20)
Denmark	Warfarin	20,070	160	21,179.0	0.7 (0.6 - 0.9)	Ref.
Norway	Apixaban	17,780	110	16,437.3	0.7 (0.5 - 0.8)	0.67 (0.52 - 0.87)
Norway	Dabigatran	8,684	40	12,264.6	0.3 (0.2 - 0.4)	0.38 (0.27 - 0.54)
Norway	Rivaroxaban	10,565	100	13,972.7	0.7 (0.6 - 0.9)	0.81 (0.63 - 1.06)
Norway	Warfarin	11,949	120	13,564.4	0.9 (0.8 - 1.1)	Ref.
Sweden	Apixaban	38,825	230	38,139.2	0.6 (0.5 - 0.7)	0.63 (0.54 - 0.73)
Sweden	Dabigatran	10,079	50	13,373.5	0.3 (0.3 - 0.5)	0.38 (0.28 - 0.52)
Sweden	Rivaroxaban	14,333	120	18,092.6	0.7 (0.6 - 0.8)	0.75 (0.62 - 0.91)
Sweden	Warfarin	47,152	580	64,858.7	0.9 (0.8 - 1.0)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.10 Crude rates, and crude pairwise hazard ratios of gastrointestinal bleeding at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	830	69,056.4	1.2 (1.1 - 1.3)	0.84 (0.77 - 0.91)
All	Dabigatran	31,209	580	43,577.0	1.3 (1.2 - 1.4)	1.06 (0.96 - 1.17)
All	Rivaroxaban	37,580	750	44,872.5	1.7 (1.6 - 1.8)	1.25 (1.14 - 1.37)
All	Warfarin	79,171	1300	99,117.7	1.3 (1.2 - 1.4)	Ref.
Denmark	Apixaban	14,980	220	14,677.2	1.5 (1.3 - 1.7)	0.83 (0.70 - 0.99)
Denmark	Dabigatran	12,446	270	18,057.5	1.5 (1.3 - 1.7)	0.99 (0.85 - 1.16)
Denmark	Rivaroxaban	12,682	250	13,029.6	1.9 (1.7 - 2.1)	1.11 (0.95 - 1.31)
Denmark	Warfarin	20,070	360	21,032.5	1.7 (1.5 - 1.9)	Ref.
Norway	Apixaban	17,780	210	16,366.5	1.3 (1.1 - 1.5)	0.72 (0.60 - 0.87)
Norway	Dabigatran	8,684	170	12,197.0	1.4 (1.2 - 1.6)	0.88 (0.72 - 1.08)
Norway	Rivaroxaban	10,565	260	13,850.4	1.8 (1.6 - 2.1)	1.16 (0.97 - 1.39)
Norway	Warfarin	11,949	220	13,468.4	1.6 (1.4 - 1.9)	Ref.
Sweden	Apixaban	38,825	410	38,012.7	1.1 (1.0 - 1.2)	0.87 (0.77 - 0.99)
Sweden	Dabigatran	10,079	140	13,322.5	1.1 (0.9 - 1.3)	0.97 (0.81 - 1.16)
Sweden	Rivaroxaban	14,333	250	17,992.5	1.4 (1.2 - 1.5)	1.20 (1.04 - 1.39)
Sweden	Warfarin	47,152	720	64,652.7	1.1 (1.0 - 1.2)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.11 Crude rates, and crude pairwise hazard ratios of acute myocardial infarction at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	990	68,930.6	1.4 (1.3 - 1.5)	0.96 (0.88 - 1.04)
All	Dabigatran	31,209	380	43,669.3	0.9 (0.8 - 1.0)	0.67 (0.60 - 0.75)
All	Rivaroxaban	37,580	500	45,029.6	1.1 (1.0 - 1.2)	0.80 (0.72 - 0.89)
All	Warfarin	79,171	1340	98,840.2	1.4 (1.3 - 1.4)	Ref.
Denmark	Apixaban	14,980	150	14,707.2	1.0 (0.9 - 1.2)	0.94 (0.77 - 1.16)
Denmark	Dabigatran	12,446	140	18,119.0	0.8 (0.7 - 0.9)	0.85 (0.69 - 1.06)
Denmark	Rivaroxaban	12,682	100	13,128.4	0.8 (0.6 - 0.9)	0.75 (0.59 - 0.95)
Denmark	Warfarin	20,070	220	21,070.7	1.0 (0.9 - 1.2)	Ref.
Norway	Apixaban	17,780	310	16,329.0	1.9 (1.7 - 2.1)	0.81 (0.69 - 0.96)
Norway	Dabigatran	8,684	150	12,205.0	1.2 (1.0 - 1.4)	0.59 (0.49 - 0.72)
Norway	Rivaroxaban	10,565	200	13,879.3	1.5 (1.3 - 1.7)	0.71 (0.59 - 0.85)
Norway	Warfarin	11,949	290	13,399.0	2.1 (1.9 - 2.4)	Ref.
Sweden	Apixaban	38,825	530	37,894.3	1.4 (1.3 - 1.5)	0.96 (0.86 - 1.07)
Sweden	Dabigatran	10,079	100	13,345.3	0.7 (0.6 - 0.9)	0.54 (0.44 - 0.67)
Sweden	Rivaroxaban	14,333	200	18,021.9	1.1 (0.9 - 1.2)	0.81 (0.69 - 0.94)
Sweden	Warfarin	47,152	840	64,395.4	1.3 (1.2 - 1.4)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.12 Crude rates, and crude pairwise hazard ratios of systemic embolism at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	50	69,404.1	0.1 (0.1 - 0.1)	0.59 (0.43 - 0.83)
All	Dabigatran	31,209	30	43,894.7	0.1 (0.0 - 0.1)	0.60 (0.40 - 0.92)
All	Rivaroxaban	37,580	30	45,290.2	0.1 (0.0 - 0.1)	0.56 (0.37 - 0.85)
All	Warfarin	79,171	110	99,819.2	0.1 (0.1 - 0.1)	Ref.
Denmark	Apixaban	14,980	10	14,771.9	0.0 (0.0 - 0.1)	0.64 (0.26 - 1.57)
Denmark	Dabigatran	12,446	10	18,228.6	0.0 (0.0 - 0.1)	0.79 (0.34 - 1.81)
Denmark	Rivaroxaban	12,682	0	13,170.5	0.0 (0.0 - 0.1)	0.32 (0.09 - 1.10)
Denmark	Warfarin	20,070	20	21,223.8	0.1 (0.0 - 0.1)	Ref.
Norway	Apixaban	17,780	10	16,461.1	0.1 (0.0 - 0.1)	0.45 (0.20 - 0.99)
Norway	Dabigatran	8,684	10	12,277.1	0.1 (0.0 - 0.1)	0.55 (0.23 - 1.33)
Norway	Rivaroxaban	10,565	10	13,998.5	0.1 (0.0 - 0.1)	0.84 (0.40 - 1.74)
Norway	Warfarin	11,949	20	13,593.1	0.1 (0.1 - 0.2)	Ref.
Sweden	Apixaban	38,825	40	38,171.1	0.1 (0.1 - 0.1)	0.65 (0.43 - 0.97)
Sweden	Dabigatran	10,079	10	13,389.0	0.1 (0.0 - 0.1)	0.73 (0.40 - 1.35)
Sweden	Rivaroxaban	14,333	10	18,121.2	0.1 (0.0 - 0.1)	0.57 (0.32 - 1.02)
Sweden	Warfarin	47,152	80	65,022.5	0.1 (0.1 - 0.1)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.13 Crude rates, and crude pairwise hazard ratios of death of any cause among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	5280	69,427.6	7.6 (7.4 - 7.8)	1.28 (1.23 - 1.33)
All	Dabigatran	31,209	1590	43,910.4	3.6 (3.4 - 3.8)	0.67 (0.63 - 0.70)
All	Rivaroxaban	37,580	3110	45,303.9	6.9 (6.6 - 7.1)	1.22 (1.17 - 1.28)
All	Warfarin	79,171	5570	99,891.9	5.6 (5.4 - 5.7)	Ref.
Denmark	Apixaban	14,980	1620	14,774.3	10.9 (10.4 - 11.5)	1.68 (1.56 - 1.81)
Denmark	Dabigatran	12,446	900	18,235.3	4.9 (4.6 - 5.2)	0.84 (0.77 - 0.91)
Denmark	Rivaroxaban	12,682	1350	13,172.8	10.2 (9.7 - 10.8)	1.61 (1.49 - 1.73)
Denmark	Warfarin	20,070	1350	21,227.2	6.4 (6.0 - 6.7)	Ref.
Norway	Apixaban	17,780	920	16,467.0	5.6 (5.2 - 6.0)	0.91 (0.83 - 1.00)
Norway	Dabigatran	8,684	320	12,283.5	2.6 (2.3 - 2.9)	0.46 (0.40 - 0.52)
Norway	Rivaroxaban	10,565	660	14,005.5	4.7 (4.3 - 5.1)	0.82 (0.74 - 0.91)
Norway	Warfarin	11,949	800	13,604.8	5.9 (5.5 - 6.3)	Ref.
Sweden	Apixaban	38,825	2740	38,186.3	7.2 (6.9 - 7.4)	1.28 (1.22 - 1.35)
Sweden	Dabigatran	10,079	370	13,391.6	2.8 (2.5 - 3.1)	0.53 (0.48 - 0.59)
Sweden	Rivaroxaban	14,333	1110	18,125.6	6.1 (5.7 - 6.5)	1.15 (1.07 - 1.23)
Sweden	Warfarin	47,152	3400	65,082.2	5.2 (5.1 - 5.4)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.14 Crude rates, and crude pairwise hazard ratios of composite endpoint of ischaemic stroke at an acute hospitalisation with an overnight stay, systemic embolism at an acute hospitalisation with an overnight stay, acute myocardial infarction at an acute hospitalisation with an overnight stay or death of any cause among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	6930	68,209.9	10.2 (9.9 - 10.4)	1.19 (1.16 - 1.23)
All	Dabigatran	31,209	2350	43,247.9	5.4 (5.2 - 5.6)	0.71 (0.68 - 0.75)
All	Rivaroxaban	37,580	3970	44,588.7	8.9 (8.6 - 9.2)	1.12 (1.08 - 1.16)
All	Warfarin	79,171	7720	97,901.3	7.9 (7.7 - 8.1)	Ref.
Denmark	Apixaban	14,980	1970	14,486.4	13.6 (13.0 - 14.2)	1.57 (1.47 - 1.67)
Denmark	Dabigatran	12,446	1200	17,918.0	6.7 (6.3 - 7.1)	0.87 (0.81 - 0.94)
Denmark	Rivaroxaban	12,682	1580	12,977.6	12.1 (11.5 - 12.7)	1.44 (1.35 - 1.55)
Denmark	Warfarin	20,070	1760	20,924.6	8.4 (8.0 - 8.8)	Ref.
Norway	Apixaban	17,780	1380	16,193.1	8.5 (8.1 - 9.0)	0.90 (0.84 - 0.98)
Norway	Dabigatran	8,684	550	12,108.9	4.5 (4.1 - 4.9)	0.54 (0.49 - 0.60)
Norway	Rivaroxaban	10,565	970	13,765.0	7.0 (6.6 - 7.5)	0.82 (0.75 - 0.89)
Norway	Warfarin	11,949	1180	13,279.9	8.9 (8.4 - 9.4)	Ref.
Sweden	Apixaban	38,825	3590	37,530.4	9.6 (9.3 - 9.9)	1.17 (1.12 - 1.22)
Sweden	Dabigatran	10,079	600	13,221.0	4.5 (4.2 - 4.9)	0.61 (0.56 - 0.66)
Sweden	Rivaroxaban	14,333	1430	17,846.2	8.0 (7.6 - 8.4)	1.05 (0.99 - 1.11)
Sweden	Warfarin	47,152	4770	63,718.0	7.5 (7.3 - 7.7)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.15 Crude rates, and crude pairwise hazard ratios of <u>any bleeding</u> at an acute or planned hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	2300	68,348.7	3.4 (3.2 - 3.5)	0.81 (0.77 - 0.85)
All	Dabigatran	31,209	1170	43,190.4	2.7 (2.5 - 2.9)	0.73 (0.69 - 0.78)
All	Rivaroxaban	37,580	1890	44,185.4	4.3 (4.1 - 4.5)	1.10 (1.05 - 1.17)
All	Warfarin	79,171	3730	97,592.7	3.8 (3.7 - 3.9)	Ref.
Denmark	Apixaban	14,980	550	14,504.8	3.8 (3.5 - 4.1)	0.86 (0.77 - 0.96)
Denmark	Dabigatran	12,446	510	17,884.0	2.8 (2.6 - 3.1)	0.73 (0.66 - 0.82)
Denmark	Rivaroxaban	12,682	580	12,823.5	4.5 (4.2 - 4.9)	1.06 (0.95 - 1.17)
Denmark	Warfarin	20,070	890	20,722.3	4.3 (4.0 - 4.6)	Ref.
Norway	Apixaban	17,780	710	16,116.0	4.4 (4.1 - 4.7)	0.75 (0.67 - 0.83)
Norway	Dabigatran	8,684	380	12,060.7	3.1 (2.8 - 3.4)	0.61 (0.53 - 0.69)
Norway	Rivaroxaban	10,565	680	13,581.0	5.0 (4.6 - 5.4)	0.94 (0.85 - 1.05)
Norway	Warfarin	11,949	720	13,160.5	5.5 (5.1 - 5.9)	Ref.
Sweden	Apixaban	38,825	1040	37,727.8	2.7 (2.6 - 2.9)	0.76 (0.71 - 0.82)
Sweden	Dabigatran	10,079	280	13,245.7	2.1 (1.9 - 2.4)	0.65 (0.57 - 0.73)
Sweden	Rivaroxaban	14,333	630	17,781.0	3.5 (3.3 - 3.8)	1.05 (0.96 - 1.14)
Sweden	Warfarin	47,152	2110	63,754.2	3.3 (3.2 - 3.5)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.16 Crude rates, and crude pairwise hazard ratios of any bleeding at an acute hospital contact without an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	1320	68,601.6	1.9 (1.8 - 2.0)	0.78 (0.73 - 0.84)
All	Dabigatran	31,209	420	43,587.4	1.0 (0.9 - 1.1)	0.42 (0.37 - 0.46)
All	Rivaroxaban	37,580	1170	44,337.3	2.6 (2.5 - 2.8)	1.11 (1.03 - 1.19)
All	Warfarin	79,171	2320	97,841.1	2.4 (2.3 - 2.5)	Ref.
Denmark	Apixaban	14,980	160	14,662.3	1.1 (1.0 - 1.3)	0.79 (0.65 - 0.96)
Denmark	Dabigatran	12,446	80	18,162.1	0.5 (0.4 - 0.6)	0.36 (0.28 - 0.45)
Denmark	Rivaroxaban	12,682	220	12,983.9	1.7 (1.5 - 2.0)	1.26 (1.05 - 1.50)
Denmark	Warfarin	20,070	290	21,005.6	1.4 (1.2 - 1.5)	Ref.
Norway	Apixaban	17,780	130	16,379.5	0.8 (0.7 - 0.9)	0.56 (0.45 - 0.71)
Norway	Dabigatran	8,684	70	12,224.1	0.6 (0.4 - 0.7)	0.45 (0.34 - 0.60)
Norway	Rivaroxaban	10,565	190	13,829.2	1.3 (1.2 - 1.5)	1.04 (0.84 - 1.27)
Norway	Warfarin	11,949	180	13,435.0	1.3 (1.1 - 1.5)	Ref.
Sweden	Apixaban	38,825	1030	37,559.9	2.7 (2.6 - 2.9)	0.89 (0.83 - 0.97)
Sweden	Dabigatran	10,079	270	13,201.2	2.0 (1.8 - 2.3)	0.69 (0.61 - 0.79)
Sweden	Rivaroxaban	14,333	760	17,524.2	4.4 (4.1 - 4.7)	1.47 (1.35 - 1.60)
Sweden	Warfarin	47,152	1870	63,405.9	2.9 (2.8 - 3.1)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.17 Crude rates, and crude pairwise hazard ratios of any bleeding recorded as the primary diagnosis at an acute hospitalisation with an overnight stay (sensitivity analysis) among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

Country	Cohort	n	Number of events (rounded)	Person-years	Crude rate per 100 person-years (95% CI)	Crude hazard ratio (95% CI)
All	Apixaban	71,585	1320	68,835.5	1.9 (1.8 - 2.0)	0.70 (0.66 - 0.75)
All	Dabigatran	31,209	740	43,461.7	1.7 (1.6 - 1.8)	0.70 (0.64 - 0.76)
All	Rivaroxaban	37,580	1220	44,602.5	2.7 (2.6 - 2.9)	1.07 (1.00 - 1.15)
All	Warfarin	79,171	2470	98,420.0	2.5 (2.4 - 2.6)	Ref.
Denmark	Apixaban	14,980	400	14,579.5	2.7 (2.5 - 3.0)	0.80 (0.70 - 0.90)
Denmark	Dabigatran	12,446	390	17,979.6	2.2 (2.0 - 2.4)	0.73 (0.64 - 0.82)
Denmark	Rivaroxaban	12,682	460	12,902.1	3.6 (3.3 - 3.9)	1.07 (0.95 - 1.21)
Denmark	Warfarin	20,070	690	20,839.4	3.3 (3.1 - 3.6)	Ref.
Norway	Apixaban	17,780	290	16,332.2	1.8 (1.6 - 2.0)	0.64 (0.55 - 0.75)
Norway	Dabigatran	8,684	180	12,173.5	1.5 (1.3 - 1.7)	0.61 (0.51 - 0.74)
Norway	Rivaroxaban	10,565	340	13,808.7	2.4 (2.2 - 2.7)	0.97 (0.84 - 1.13)
Norway	Warfarin	11,949	340	13,405.8	2.6 (2.3 - 2.8)	Ref.
Sweden	Apixaban	38,825	630	37,923.8	1.7 (1.5 - 1.8)	0.69 (0.63 - 0.76)
Sweden	Dabigatran	10,079	170	13,308.5	1.3 (1.1 - 1.5)	0.57 (0.48 - 0.66)
Sweden	Rivaroxaban	14,333	430	17,891.7	2.4 (2.2 - 2.6)	1.04 (0.93 - 1.16)
Sweden	Warfarin	47,152	1430	64,209.8	2.2 (2.1 - 2.3)	Ref.

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.18 Crude cumulative incidence of any stroke or systemic embolism at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	1430	0.021 (0.020 - 0.023)	0.032 (0.030 - 0.034)	0.043 (0.039 - 0.048)	0.065 (0.046 - 0.089)
All	Dabigatran	31,210	610	0.016 (0.015 - 0.018)	0.025 (0.023 - 0.027)	0.034 (0.031 - 0.037)	0.043 (0.035 - 0.053)
All	Rivaroxaban	37,580	870	0.020 (0.019 - 0.022)	0.034 (0.032 - 0.037)	0.044 (0.040 - 0.047)	0.051 (0.046 - 0.057)
All	Warfarin	79,170	1890	0.022 (0.020 - 0.023)	0.033 (0.031 - 0.034)	0.043 (0.040 - 0.045)	0.051 (0.048 - 0.055)
Denmark	Apixaban	14,980	390	0.026 (0.023 - 0.030)	0.039 (0.035 - 0.044)	0.054 (0.045 - 0.065)	0.073 (0.052 - 0.100)
Denmark	Dabigatran	12,450	280	0.018 (0.015 - 0.021)	0.028 (0.024 - 0.032)	0.037 (0.033 - 0.042)	0.055 (0.037 - 0.077)
Denmark	Rivaroxaban	12,680	280	0.021 (0.018 - 0.024)	0.036 (0.031 - 0.041)	0.048 (0.041 - 0.055)	0.054 (0.046 - 0.064)
Denmark	Warfarin	20,070	400	0.020 (0.018 - 0.023)	0.031 (0.028 - 0.035)	0.037 (0.033 - 0.042)	0.048 (0.039 - 0.058)
Norway	Apixaban	17,780	330	0.021 (0.018 - 0.024)	0.032 (0.028 - 0.037)	0.043 (0.032 - 0.057)	0.043 (0.032 - 0.057)
Norway	Dabigatran	8,680	130	0.013 (0.011 - 0.016)	0.020 (0.016 - 0.024)	0.026 (0.022 - 0.032)	0.030 (0.024 - 0.037)
Norway	Rivaroxaban	10,570	270	0.022 (0.019 - 0.025)	0.035 (0.030 - 0.040)	0.048 (0.041 - 0.055)	0.059 (0.049 - 0.071)
Norway	Warfarin	11,950	270	0.021 (0.018 - 0.024)	0.033 (0.029 - 0.038)	0.050 (0.043 - 0.057)	0.054 (0.046 - 0.063)
Sweden	Apixaban	38,830	710	0.020 (0.018 - 0.021)	0.029 (0.027 - 0.032)	0.038 (0.033 - 0.044)	0.061 (0.033 - 0.102)
Sweden	Dabigatran	10,080	190	0.017 (0.014 - 0.020)	0.025 (0.021 - 0.029)	0.036 (0.030 - 0.042)	0.039 (0.032 - 0.047)
Sweden	Rivaroxaban	14,330	320	0.019 (0.017 - 0.022)	0.032 (0.029 - 0.036)	0.037 (0.032 - 0.042)	0.042 (0.035 - 0.050)
Sweden	Warfarin	47,150	1210	0.022 (0.021 - 0.024)	0.033 (0.031 - 0.035)	0.043 (0.040 - 0.046)	0.051 (0.047 - 0.055)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.19 Crude cumulative incidence of any bleeding at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	2080	0.030 (0.029 - 0.032)	0.050 (0.047 - 0.052)	0.064 (0.060 - 0.070)	0.071 (0.062 - 0.080)
All	Dabigatran	31,210	1070	0.028 (0.026 - 0.030)	0.045 (0.042 - 0.048)	0.060 (0.056 - 0.064)	0.077 (0.070 - 0.085)
All	Rivaroxaban	37,580	1740	0.042 (0.039 - 0.044)	0.068 (0.064 - 0.071)	0.087 (0.082 - 0.092)	0.108 (0.098 - 0.120)
All	Warfarin	79,170	3460	0.038 (0.037 - 0.040)	0.062 (0.059 - 0.064)	0.080 (0.077 - 0.083)	0.095 (0.091 - 0.100)
Denmark	Apixaban	14,980	510	0.034 (0.031 - 0.037)	0.055 (0.050 - 0.061)	0.074 (0.064 - 0.084)	0.079 (0.065 - 0.094)
Denmark	Dabigatran	12,450	480	0.030 (0.027 - 0.034)	0.049 (0.044 - 0.054)	0.063 (0.057 - 0.070)	0.080 (0.070 - 0.090)
Denmark	Rivaroxaban	12,680	540	0.041 (0.037 - 0.045)	0.067 (0.060 - 0.073)	0.087 (0.078 - 0.097)	0.101 (0.089 - 0.114)
Denmark	Warfarin	20,070	820	0.043 (0.040 - 0.047)	0.064 (0.059 - 0.069)	0.076 (0.070 - 0.083)	0.092 (0.082 - 0.102)
Norway	Apixaban	17,780	610	0.038 (0.035 - 0.042)	0.062 (0.056 - 0.068)	0.077 (0.066 - 0.089)	0.105 (0.069 - 0.149)
Norway	Dabigatran	8,680	330	0.030 (0.026 - 0.035)	0.049 (0.043 - 0.056)	0.068 (0.060 - 0.076)	0.083 (0.072 - 0.096)
Norway	Rivaroxaban	10,570	610	0.049 (0.045 - 0.054)	0.083 (0.076 - 0.090)	0.105 (0.096 - 0.115)	0.140 (0.106 - 0.180)
Norway	Warfarin	11,950	650	0.051 (0.047 - 0.056)	0.081 (0.074 - 0.088)	0.105 (0.095 - 0.114)	0.120 (0.108 - 0.132)
Sweden	Apixaban	38,830	960	0.026 (0.024 - 0.028)	0.043 (0.040 - 0.046)	0.055 (0.048 - 0.062)	0.055 (0.048 - 0.062)
Sweden	Dabigatran	10,080	260	0.022 (0.019 - 0.025)	0.035 (0.030 - 0.040)	0.049 (0.043 - 0.057)	0.071 (0.051 - 0.094)
Sweden	Rivaroxaban	14,330	590	0.036 (0.033 - 0.040)	0.057 (0.052 - 0.062)	0.072 (0.065 - 0.080)	0.095 (0.081 - 0.111)
Sweden	Warfarin	47,150	1980	0.033 (0.031 - 0.035)	0.055 (0.053 - 0.058)	0.075 (0.072 - 0.079)	0.091 (0.086 - 0.097)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.20 Cumulative incidence of ischaemic stroke at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	1160	0.017 (0.016 - 0.018)	0.026 (0.024 - 0.027)	0.034 (0.030 - 0.038)	0.057 (0.038 - 0.081)
All	Dabigatran	31,210	520	0.014 (0.013 - 0.016)	0.021 (0.019 - 0.023)	0.028 (0.026 - 0.031)	0.036 (0.028 - 0.046)
All	Rivaroxaban	37,580	680	0.016 (0.015 - 0.018)	0.026 (0.024 - 0.029)	0.033 (0.030 - 0.036)	0.039 (0.035 - 0.044)
All	Warfarin	79,170	1420	0.016 (0.015 - 0.017)	0.024 (0.023 - 0.025)	0.031 (0.030 - 0.033)	0.037 (0.034 - 0.040)
Denmark	Apixaban	14,980	320	0.022 (0.019 - 0.024)	0.033 (0.029 - 0.037)	0.043 (0.035 - 0.052)	0.065 (0.043 - 0.092)
Denmark	Dabigatran	12,450	240	0.016 (0.014 - 0.018)	0.024 (0.021 - 0.027)	0.031 (0.027 - 0.036)	0.046 (0.029 - 0.069)
Denmark	Rivaroxaban	12,680	230	0.018 (0.015 - 0.021)	0.029 (0.025 - 0.033)	0.037 (0.031 - 0.043)	0.043 (0.035 - 0.053)
Denmark	Warfarin	20,070	310	0.016 (0.014 - 0.018)	0.024 (0.021 - 0.027)	0.028 (0.025 - 0.033)	0.036 (0.028 - 0.044)
Norway	Apixaban	17,780	260	0.017 (0.014 - 0.019)	0.025 (0.022 - 0.029)	0.036 (0.025 - 0.050)	0.036 (0.025 - 0.050)
Norway	Dabigatran	8,680	110	0.010 (0.008 - 0.013)	0.016 (0.013 - 0.020)	0.022 (0.018 - 0.027)	0.023 (0.019 - 0.029)
Norway	Rivaroxaban	10,570	200	0.016 (0.013 - 0.019)	0.025 (0.021 - 0.030)	0.034 (0.029 - 0.041)	0.042 (0.034 - 0.052)
Norway	Warfarin	11,950	190	0.015 (0.013 - 0.018)	0.023 (0.019 - 0.027)	0.036 (0.030 - 0.043)	0.039 (0.033 - 0.047)
Sweden	Apixaban	38,830	580	0.016 (0.015 - 0.018)	0.023 (0.021 - 0.025)	0.030 (0.026 - 0.034)	0.053 (0.026 - 0.095)
Sweden	Dabigatran	10,080	170	0.015 (0.012 - 0.018)	0.021 (0.018 - 0.025)	0.030 (0.025 - 0.036)	0.034 (0.028 - 0.041)
Sweden	Rivaroxaban	14,330	250	0.015 (0.013 - 0.017)	0.025 (0.022 - 0.029)	0.029 (0.025 - 0.033)	0.030 (0.025 - 0.036)
Sweden	Warfarin	47,150	920	0.017 (0.016 - 0.018)	0.024 (0.023 - 0.026)	0.032 (0.029 - 0.034)	0.037 (0.034 - 0.040)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.21 Crude cumulative incidence of haemorrhagic stroke at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	260	0.004 (0.003 - 0.004)	0.007 (0.006 - 0.008)	0.009 (0.007 - 0.012)	0.009 (0.007 - 0.012)
All	Dabigatran	31,210	70	0.002 (0.001 - 0.002)	0.003 (0.002 - 0.004)	0.004 (0.003 - 0.006)	0.006 (0.004 - 0.008)
All	Rivaroxaban	37,580	200	0.004 (0.004 - 0.005)	0.008 (0.007 - 0.009)	0.011 (0.009 - 0.013)	0.013 (0.011 - 0.017)
All	Warfarin	79,170	400	0.004 (0.004 - 0.005)	0.008 (0.007 - 0.008)	0.010 (0.009 - 0.011)	0.013 (0.011 - 0.015)
Denmark	Apixaban	14,980	70	0.004 (0.003 - 0.006)	0.007 (0.006 - 0.010)	0.012 (0.007 - 0.019)	0.012 (0.007 - 0.019)
Denmark	Dabigatran	12,450	30	0.002 (0.001 - 0.003)	0.003 (0.002 - 0.005)	0.005 (0.004 - 0.008)	0.007 (0.004 - 0.011)
Denmark	Rivaroxaban	12,680	50	0.003 (0.002 - 0.005)	0.007 (0.005 - 0.010)	0.011 (0.008 - 0.015)	0.011 (0.008 - 0.015)
Denmark	Warfarin	20,070	90	0.004 (0.003 - 0.006)	0.007 (0.006 - 0.009)	0.009 (0.007 - 0.012)	0.012 (0.009 - 0.017)
Norway	Apixaban	17,780	70	0.005 (0.004 - 0.006)	0.008 (0.006 - 0.011)	0.008 (0.006 - 0.011)	0.008 (0.006 - 0.011)
Norway	Dabigatran	8,680	20	0.002 (0.001 - 0.003)	0.003 (0.002 - 0.005)	0.004 (0.003 - 0.007)	0.007 (0.004 - 0.012)
Norway	Rivaroxaban	10,570	70	0.006 (0.004 - 0.008)	0.010 (0.007 - 0.012)	0.014 (0.010 - 0.018)	0.017 (0.011 - 0.025)
Norway	Warfarin	11,950	70	0.005 (0.004 - 0.007)	0.010 (0.007 - 0.013)	0.014 (0.011 - 0.018)	0.014 (0.011 - 0.018)
Sweden	Apixaban	38,830	120	0.003 (0.002 - 0.004)	0.006 (0.005 - 0.007)	0.008 (0.005 - 0.013)	0.008 (0.005 - 0.013)
Sweden	Dabigatran	10,080	20	0.002 (0.001 - 0.003)	0.003 (0.002 - 0.004)	0.003 (0.002 - 0.004)	0.003 (0.002 - 0.004)
Sweden	Rivaroxaban	14,330	70	0.004 (0.003 - 0.005)	0.007 (0.005 - 0.009)	0.009 (0.006 - 0.012)	0.013 (0.008 - 0.020)
Sweden	Warfarin	47,150	240	0.004 (0.003 - 0.005)	0.007 (0.006 - 0.008)	0.010 (0.008 - 0.011)	0.013 (0.010 - 0.015)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.22 Crude cumulative incidence of intracranial bleeding at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	450	0.007 (0.006 - 0.007)	0.011 (0.010 - 0.013)	0.015 (0.012 - 0.018)	0.015 (0.012 - 0.018)
All	Dabigatran	31,210	150	0.003 (0.003 - 0.004)	0.006 (0.005 - 0.008)	0.009 (0.007 - 0.011)	0.014 (0.011 - 0.018)
All	Rivaroxaban	37,580	320	0.007 (0.006 - 0.008)	0.013 (0.011 - 0.015)	0.017 (0.015 - 0.019)	0.025 (0.018 - 0.035)
All	Warfarin	79,170	870	0.009 (0.009 - 0.010)	0.016 (0.015 - 0.018)	0.022 (0.020 - 0.024)	0.027 (0.024 - 0.029)
Denmark	Apixaban	14,980	120	0.008 (0.006 - 0.009)	0.012 (0.010 - 0.015)	0.019 (0.013 - 0.026)	0.019 (0.013 - 0.026)
Denmark	Dabigatran	12,450	60	0.003 (0.002 - 0.004)	0.006 (0.004 - 0.008)	0.009 (0.006 - 0.012)	0.015 (0.010 - 0.021)
Denmark	Rivaroxaban	12,680	90	0.007 (0.005 - 0.008)	0.012 (0.010 - 0.016)	0.018 (0.014 - 0.023)	0.018 (0.014 - 0.023)
Denmark	Warfarin	20,070	160	0.008 (0.007 - 0.010)	0.013 (0.011 - 0.016)	0.016 (0.013 - 0.019)	0.019 (0.015 - 0.024)
Norway	Apixaban	17,780	110	0.007 (0.006 - 0.009)	0.012 (0.010 - 0.015)	0.014 (0.010 - 0.018)	0.014 (0.010 - 0.018)
Norway	Dabigatran	8,680	40	0.004 (0.002 - 0.006)	0.007 (0.005 - 0.009)	0.008 (0.006 - 0.012)	0.013 (0.008 - 0.020)
Norway	Rivaroxaban	10,570	100	0.008 (0.006 - 0.010)	0.014 (0.011 - 0.017)	0.019 (0.015 - 0.024)	0.042 (0.015 - 0.091)
Norway	Warfarin	11,950	120	0.009 (0.007 - 0.011)	0.017 (0.014 - 0.020)	0.022 (0.018 - 0.027)	0.026 (0.020 - 0.033)
Sweden	Apixaban	38,830	230	0.006 (0.005 - 0.007)	0.011 (0.009 - 0.012)	0.014 (0.010 - 0.018)	0.014 (0.010 - 0.018)
Sweden	Dabigatran	10,080	50	0.004 (0.002 - 0.005)	0.007 (0.005 - 0.009)	0.010 (0.007 - 0.014)	0.016 (0.010 - 0.025)
Sweden	Rivaroxaban	14,330	120	0.007 (0.006 - 0.009)	0.013 (0.010 - 0.015)	0.015 (0.012 - 0.018)	0.025 (0.017 - 0.034)
Sweden	Warfarin	47,150	580	0.010 (0.009 - 0.011)	0.017 (0.016 - 0.019)	0.023 (0.021 - 0.026)	0.029 (0.026 - 0.032)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.23 Crude cumulative incidence of gastrointestinal bleeding at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	830	0.012 (0.011 - 0.013)	0.020 (0.019 - 0.022)	0.027 (0.024 - 0.031)	0.032 (0.025 - 0.041)
All	Dabigatran	31,210	580	0.015 (0.014 - 0.017)	0.024 (0.022 - 0.026)	0.032 (0.030 - 0.035)	0.041 (0.035 - 0.047)
All	Rivaroxaban	37,580	750	0.018 (0.017 - 0.020)	0.029 (0.026 - 0.031)	0.037 (0.034 - 0.040)	0.045 (0.039 - 0.051)
All	Warfarin	79,170	1300	0.015 (0.014 - 0.016)	0.023 (0.021 - 0.024)	0.029 (0.027 - 0.031)	0.034 (0.032 - 0.037)
Denmark	Apixaban	14,980	220	0.014 (0.012 - 0.016)	0.023 (0.020 - 0.027)	0.034 (0.027 - 0.043)	0.040 (0.028 - 0.054)
Denmark	Dabigatran	12,450	270	0.018 (0.015 - 0.021)	0.028 (0.024 - 0.031)	0.036 (0.031 - 0.041)	0.043 (0.036 - 0.051)
Denmark	Rivaroxaban	12,680	250	0.019 (0.016 - 0.022)	0.030 (0.026 - 0.035)	0.039 (0.033 - 0.045)	0.047 (0.038 - 0.056)
Denmark	Warfarin	20,070	360	0.019 (0.017 - 0.021)	0.026 (0.023 - 0.029)	0.031 (0.027 - 0.035)	0.041 (0.033 - 0.049)
Norway	Apixaban	17,780	210	0.013 (0.011 - 0.015)	0.022 (0.019 - 0.026)	0.026 (0.020 - 0.033)	0.037 (0.019 - 0.066)
Norway	Dabigatran	8,680	170	0.015 (0.012 - 0.018)	0.025 (0.021 - 0.029)	0.034 (0.028 - 0.040)	0.040 (0.033 - 0.048)
Norway	Rivaroxaban	10,570	260	0.021 (0.018 - 0.024)	0.034 (0.030 - 0.039)	0.044 (0.038 - 0.050)	0.055 (0.042 - 0.070)
Norway	Warfarin	11,950	220	0.018 (0.015 - 0.021)	0.028 (0.024 - 0.032)	0.032 (0.028 - 0.038)	0.035 (0.030 - 0.041)
Sweden	Apixaban	38,830	410	0.011 (0.009 - 0.012)	0.018 (0.016 - 0.020)	0.024 (0.020 - 0.029)	0.024 (0.020 - 0.029)
Sweden	Dabigatran	10,080	140	0.013 (0.010 - 0.015)	0.018 (0.015 - 0.021)	0.027 (0.022 - 0.032)	0.041 (0.024 - 0.065)
Sweden	Rivaroxaban	14,330	250	0.016 (0.014 - 0.018)	0.023 (0.020 - 0.026)	0.030 (0.025 - 0.035)	0.036 (0.027 - 0.046)
Sweden	Warfarin	47,150	720	0.012 (0.011 - 0.014)	0.020 (0.018 - 0.022)	0.027 (0.025 - 0.030)	0.032 (0.029 - 0.035)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.24 Crude cumulative incidence of acute myocardial infarction at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	990	0.014 (0.013 - 0.015)	0.022 (0.021 - 0.024)	0.029 (0.026 - 0.032)	0.029 (0.026 - 0.032)
All	Dabigatran	31,210	380	0.010 (0.008 - 0.011)	0.017 (0.015 - 0.019)	0.021 (0.019 - 0.024)	0.026 (0.022 - 0.031)
All	Rivaroxaban	37,580	500	0.012 (0.010 - 0.013)	0.019 (0.017 - 0.021)	0.027 (0.024 - 0.030)	0.029 (0.026 - 0.033)
All	Warfarin	79,170	1340	0.015 (0.014 - 0.016)	0.023 (0.021 - 0.024)	0.030 (0.028 - 0.032)	0.037 (0.034 - 0.041)
Denmark	Apixaban	14,980	150	0.010 (0.008 - 0.012)	0.015 (0.013 - 0.018)	0.021 (0.016 - 0.026)	0.021 (0.016 - 0.026)
Denmark	Dabigatran	12,450	140	0.009 (0.007 - 0.011)	0.016 (0.013 - 0.019)	0.019 (0.016 - 0.022)	0.020 (0.016 - 0.024)
Denmark	Rivaroxaban	12,680	100	0.008 (0.006 - 0.010)	0.013 (0.010 - 0.016)	0.018 (0.014 - 0.023)	0.018 (0.014 - 0.023)
Denmark	Warfarin	20,070	220	0.011 (0.010 - 0.013)	0.016 (0.014 - 0.019)	0.020 (0.017 - 0.023)	0.022 (0.018 - 0.027)
Norway	Apixaban	17,780	310	0.019 (0.017 - 0.021)	0.030 (0.026 - 0.034)	0.036 (0.029 - 0.043)	0.036 (0.029 - 0.043)
Norway	Dabigatran	8,680	150	0.012 (0.010 - 0.015)	0.023 (0.019 - 0.027)	0.029 (0.024 - 0.035)	0.039 (0.029 - 0.052)
Norway	Rivaroxaban	10,570	200	0.015 (0.013 - 0.018)	0.026 (0.022 - 0.031)	0.039 (0.033 - 0.045)	0.043 (0.035 - 0.051)
Norway	Warfarin	11,950	290	0.023 (0.020 - 0.027)	0.035 (0.030 - 0.039)	0.045 (0.039 - 0.052)	0.054 (0.045 - 0.065)
Sweden	Apixaban	38,830	530	0.014 (0.013 - 0.015)	0.022 (0.020 - 0.024)	0.029 (0.025 - 0.034)	0.029 (0.025 - 0.034)
Sweden	Dabigatran	10,080	100	0.008 (0.006 - 0.010)	0.013 (0.010 - 0.016)	0.018 (0.014 - 0.022)	0.023 (0.016 - 0.031)
Sweden	Rivaroxaban	14,330	200	0.012 (0.010 - 0.014)	0.018 (0.016 - 0.022)	0.024 (0.020 - 0.029)	0.026 (0.022 - 0.032)
Sweden	Warfarin	47,150	840	0.015 (0.013 - 0.016)	0.022 (0.021 - 0.024)	0.030 (0.028 - 0.033)	0.039 (0.034 - 0.044)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.25 Crude cumulative incidence of systemic embolism at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	50	0.001 (0.001 - 0.001)	0.001 (0.001 - 0.001)	0.001 (0.001 - 0.002)	0.001 (0.001 - 0.002)
All	Dabigatran	31,210	30	0.001 (0.000 - 0.001)	0.001 (0.001 - 0.002)	0.002 (0.001 - 0.002)	0.002 (0.001 - 0.005)
All	Rivaroxaban	37,580	30	0.001 (0.000 - 0.001)	0.001 (0.001 - 0.002)	0.001 (0.001 - 0.002)	0.001 (0.001 - 0.002)
All	Warfarin	79,170	110	0.001 (0.001 - 0.002)	0.002 (0.002 - 0.002)	0.002 (0.002 - 0.003)	0.003 (0.002 - 0.004)
Denmark	Apixaban	14,980	10	0.001 (0.000 - 0.001)	0.001 (0.000 - 0.001)	0.001 (0.000 - 0.003)	0.001 (0.000 - 0.003)
Denmark	Dabigatran	12,450	10	0.001 (0.000 - 0.001)	0.001 (0.000 - 0.002)	0.001 (0.000 - 0.002)	0.003 (0.001 - 0.010)
Denmark	Rivaroxaban	12,680	0	0.000 (0.000 - 0.001)	0.001 (0.000 - 0.002)	0.001 (0.000 - 0.002)	0.001 (0.000 - 0.002)
Denmark	Warfarin	20,070	20	0.001 (0.000 - 0.001)	0.001 (0.001 - 0.003)	0.001 (0.001 - 0.003)	0.001 (0.001 - 0.003)
Norway	Apixaban	17,780	10	0.001 (0.000 - 0.001)	0.001 (0.000 - 0.001)	0.001 (0.000 - 0.001)	0.001 (0.000 - 0.001)
Norway	Dabigatran	8,680	10	0.001 (0.000 - 0.002)	0.001 (0.000 - 0.002)	0.001 (0.000 - 0.002)	0.001 (0.000 - 0.002)
Norway	Rivaroxaban	10,570	10	0.001 (0.000 - 0.002)	0.002 (0.001 - 0.004)	0.002 (0.001 - 0.004)	0.002 (0.001 - 0.004)
Norway	Warfarin	11,950	20	0.001 (0.001 - 0.002)	0.002 (0.001 - 0.003)	0.002 (0.001 - 0.003)	0.003 (0.001 - 0.006)
Sweden	Apixaban	38,830	40	0.001 (0.001 - 0.001)	0.001 (0.001 - 0.002)	0.001 (0.001 - 0.002)	0.001 (0.001 - 0.002)
Sweden	Dabigatran	10,080	10	0.001 (0.000 - 0.001)	0.002 (0.001 - 0.003)	0.003 (0.002 - 0.006)	0.003 (0.002 - 0.006)
Sweden	Rivaroxaban	14,330	10	0.001 (0.000 - 0.002)	0.001 (0.001 - 0.002)	0.001 (0.001 - 0.002)	0.001 (0.001 - 0.002)
Sweden	Warfarin	47,150	80	0.002 (0.001 - 0.002)	0.002 (0.002 - 0.003)	0.003 (0.002 - 0.003)	0.003 (0.002 - 0.004)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.26 Crude cumulative mortality among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	5280	0.075 (0.073 - 0.077)	0.128 (0.124 - 0.132)	0.175 (0.167 - 0.184)	0.187 (0.174 - 0.200)
All	Dabigatran	31,210	1590	0.041 (0.038 - 0.043)	0.069 (0.065 - 0.073)	0.093 (0.088 - 0.098)	0.138 (0.108 - 0.171)
All	Rivaroxaban	37,580	3110	0.072 (0.069 - 0.075)	0.120 (0.115 - 0.124)	0.169 (0.162 - 0.176)	0.211 (0.195 - 0.228)
All	Warfarin	79,170	5570	0.061 (0.059 - 0.063)	0.098 (0.095 - 0.101)	0.133 (0.129 - 0.137)	0.171 (0.163 - 0.179)
Denmark	Apixaban	14,980	1620	0.110 (0.104 - 0.116)	0.173 (0.164 - 0.182)	0.242 (0.224 - 0.260)	0.252 (0.230 - 0.275)
Denmark	Dabigatran	12,450	900	0.056 (0.052 - 0.061)	0.091 (0.085 - 0.098)	0.121 (0.113 - 0.130)	0.205 (0.134 - 0.286)
Denmark	Rivaroxaban	12,680	1350	0.101 (0.095 - 0.108)	0.168 (0.158 - 0.178)	0.237 (0.222 - 0.252)	0.282 (0.258 - 0.307)
Denmark	Warfarin	20,070	1350	0.066 (0.062 - 0.070)	0.103 (0.097 - 0.110)	0.139 (0.130 - 0.148)	0.163 (0.150 - 0.176)
Norway	Apixaban	17,780	920	0.056 (0.052 - 0.060)	0.093 (0.087 - 0.101)	0.124 (0.110 - 0.138)	0.138 (0.115 - 0.164)
Norway	Dabigatran	8,680	320	0.031 (0.027 - 0.036)	0.050 (0.044 - 0.057)	0.068 (0.060 - 0.076)	0.085 (0.073 - 0.099)
Norway	Rivaroxaban	10,570	660	0.048 (0.043 - 0.053)	0.087 (0.080 - 0.095)	0.126 (0.115 - 0.137)	0.173 (0.132 - 0.219)
Norway	Warfarin	11,950	800	0.061 (0.056 - 0.067)	0.105 (0.097 - 0.113)	0.144 (0.133 - 0.156)	0.184 (0.163 - 0.206)
Sweden	Apixaban	38,830	2740	0.070 (0.067 - 0.073)	0.125 (0.120 - 0.131)	0.167 (0.156 - 0.178)	0.173 (0.159 - 0.187)
Sweden	Dabigatran	10,080	370	0.028 (0.025 - 0.033)	0.056 (0.050 - 0.062)	0.075 (0.067 - 0.084)	0.095 (0.082 - 0.110)
Sweden	Rivaroxaban	14,330	1110	0.065 (0.061 - 0.070)	0.107 (0.101 - 0.114)	0.150 (0.139 - 0.161)	0.184 (0.165 - 0.203)
Sweden	Warfarin	47,150	3400	0.058 (0.056 - 0.060)	0.095 (0.091 - 0.098)	0.127 (0.122 - 0.132)	0.170 (0.159 - 0.181)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.27 Crude cumulative incidence of composite outcome of ischaemic stroke at an acute hospitalisation with an overnight stay, systemic embolism at an acute hospitalisation with an overnight stay, acute myocardial infarction at an acute hospitalisation with an overnight stay, or death of any cause among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	6930	0.099 (0.097 - 0.102)	0.163 (0.158 - 0.167)	0.219 (0.210 - 0.228)	0.244 (0.223 - 0.266)
All	Dabigatran	31,210	2350	0.061 (0.058 - 0.064)	0.100 (0.096 - 0.105)	0.133 (0.127 - 0.139)	0.186 (0.155 - 0.220)
All	Rivaroxaban	37,580	3970	0.093 (0.089 - 0.096)	0.152 (0.147 - 0.158)	0.208 (0.200 - 0.216)	0.251 (0.235 - 0.267)
All	Warfarin	79,170	7720	0.086 (0.083 - 0.088)	0.134 (0.130 - 0.137)	0.177 (0.173 - 0.181)	0.220 (0.212 - 0.228)
Denmark	Apixaban	14,980	1970	0.133 (0.126 - 0.139)	0.207 (0.197 - 0.217)	0.284 (0.266 - 0.303)	0.310 (0.280 - 0.340)
Denmark	Dabigatran	12,450	1200	0.077 (0.072 - 0.083)	0.123 (0.116 - 0.130)	0.160 (0.151 - 0.170)	0.253 (0.180 - 0.333)
Denmark	Rivaroxaban	12,680	1580	0.119 (0.113 - 0.126)	0.198 (0.187 - 0.209)	0.268 (0.253 - 0.284)	0.313 (0.289 - 0.337)
Denmark	Warfarin	20,070	1760	0.087 (0.082 - 0.092)	0.132 (0.125 - 0.139)	0.174 (0.164 - 0.184)	0.203 (0.188 - 0.218)
Norway	Apixaban	17,780	1380	0.084 (0.079 - 0.089)	0.136 (0.128 - 0.145)	0.179 (0.161 - 0.198)	0.193 (0.167 - 0.222)
Norway	Dabigatran	8,680	550	0.052 (0.047 - 0.058)	0.085 (0.077 - 0.093)	0.112 (0.102 - 0.123)	0.137 (0.120 - 0.154)
Norway	Rivaroxaban	10,570	970	0.074 (0.068 - 0.080)	0.126 (0.117 - 0.135)	0.176 (0.164 - 0.189)	0.229 (0.188 - 0.272)
Norway	Warfarin	11,950	1180	0.093 (0.086 - 0.099)	0.148 (0.138 - 0.157)	0.201 (0.189 - 0.215)	0.249 (0.226 - 0.271)
Sweden	Apixaban	38,830	3590	0.093 (0.090 - 0.097)	0.157 (0.151 - 0.163)	0.207 (0.195 - 0.219)	0.219 (0.202 - 0.236)
Sweden	Dabigatran	10,080	600	0.049 (0.044 - 0.054)	0.084 (0.077 - 0.092)	0.115 (0.105 - 0.126)	0.138 (0.123 - 0.154)
Sweden	Rivaroxaban	14,330	1430	0.086 (0.081 - 0.091)	0.139 (0.131 - 0.146)	0.186 (0.175 - 0.198)	0.216 (0.198 - 0.234)
Sweden	Warfarin	47,150	4770	0.083 (0.081 - 0.086)	0.131 (0.127 - 0.135)	0.173 (0.167 - 0.178)	0.218 (0.208 - 0.228)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.28 Crude cumulative incidence of <u>any bleeding at an acute or planned hospitalisation with an overnight stay</u> among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	2300	0.034 (0.032 - 0.035)	0.055 (0.052 - 0.058)	0.071 (0.066 - 0.077)	0.078 (0.069 - 0.088)
All	Dabigatran	31,210	1170	0.030 (0.028 - 0.032)	0.049 (0.045 - 0.052)	0.066 (0.062 - 0.071)	0.084 (0.077 - 0.092)
All	Rivaroxaban	37,580	1890	0.045 (0.043 - 0.048)	0.073 (0.070 - 0.077)	0.095 (0.090 - 0.100)	0.117 (0.106 - 0.129)
All	Warfarin	79,170	3730	0.042 (0.040 - 0.043)	0.066 (0.064 - 0.068)	0.086 (0.083 - 0.089)	0.103 (0.099 - 0.108)
Denmark	Apixaban	14,980	550	0.037 (0.034 - 0.041)	0.062 (0.056 - 0.068)	0.080 (0.070 - 0.091)	0.085 (0.071 - 0.100)
Denmark	Dabigatran	12,450	510	0.031 (0.028 - 0.035)	0.052 (0.047 - 0.057)	0.068 (0.062 - 0.075)	0.085 (0.075 - 0.095)
Denmark	Rivaroxaban	12,680	580	0.044 (0.040 - 0.049)	0.073 (0.066 - 0.080)	0.096 (0.086 - 0.106)	0.112 (0.099 - 0.125)
Denmark	Warfarin	20,070	890	0.047 (0.043 - 0.051)	0.069 (0.064 - 0.074)	0.082 (0.076 - 0.089)	0.099 (0.089 - 0.111)
Norway	Apixaban	17,780	710	0.044 (0.040 - 0.048)	0.070 (0.064 - 0.076)	0.090 (0.078 - 0.102)	0.117 (0.081 - 0.160)
Norway	Dabigatran	8,680	380	0.034 (0.030 - 0.039)	0.055 (0.049 - 0.062)	0.077 (0.069 - 0.086)	0.096 (0.084 - 0.109)
Norway	Rivaroxaban	10,570	680	0.056 (0.051 - 0.061)	0.091 (0.084 - 0.099)	0.116 (0.107 - 0.126)	0.151 (0.116 - 0.190)
Norway	Warfarin	11,950	720	0.056 (0.052 - 0.062)	0.088 (0.081 - 0.096)	0.117 (0.107 - 0.127)	0.135 (0.122 - 0.148)
Sweden	Apixaban	38,830	1040	0.028 (0.026 - 0.030)	0.046 (0.043 - 0.049)	0.060 (0.053 - 0.068)	0.060 (0.053 - 0.068)
Sweden	Dabigatran	10,080	280	0.024 (0.020 - 0.027)	0.038 (0.034 - 0.044)	0.053 (0.046 - 0.061)	0.074 (0.055 - 0.098)
Sweden	Rivaroxaban	14,330	630	0.039 (0.035 - 0.042)	0.060 (0.055 - 0.066)	0.078 (0.071 - 0.086)	0.100 (0.085 - 0.116)
Sweden	Warfarin	47,150	2110	0.036 (0.034 - 0.038)	0.059 (0.056 - 0.062)	0.080 (0.076 - 0.083)	0.097 (0.092 - 0.103)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.29 Crude cumulative incidence of any bleeding occurring at an acute hospital contact without an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	1320	0.019 (0.018 - 0.020)	0.032 (0.030 - 0.034)	0.043 (0.039 - 0.047)	0.049 (0.041 - 0.059)
All	Dabigatran	31,210	420	0.010 (0.009 - 0.011)	0.018 (0.016 - 0.020)	0.025 (0.023 - 0.028)	0.031 (0.027 - 0.036)
All	Rivaroxaban	37,580	1170	0.028 (0.026 - 0.030)	0.046 (0.043 - 0.049)	0.060 (0.056 - 0.064)	0.073 (0.067 - 0.081)
All	Warfarin	79,170	2320	0.024 (0.023 - 0.025)	0.041 (0.039 - 0.043)	0.059 (0.056 - 0.062)	0.078 (0.073 - 0.083)
Denmark	Apixaban	14,980	160	0.010 (0.009 - 0.012)	0.018 (0.015 - 0.022)	0.022 (0.018 - 0.027)	0.031 (0.020 - 0.047)
Denmark	Dabigatran	12,450	80	0.005 (0.004 - 0.006)	0.009 (0.007 - 0.011)	0.011 (0.009 - 0.014)	0.015 (0.011 - 0.019)
Denmark	Rivaroxaban	12,680	220	0.017 (0.015 - 0.020)	0.030 (0.025 - 0.035)	0.038 (0.032 - 0.044)	0.047 (0.038 - 0.058)
Denmark	Warfarin	20,070	290	0.015 (0.013 - 0.017)	0.023 (0.020 - 0.027)	0.030 (0.026 - 0.035)	0.035 (0.029 - 0.041)
Norway	Apixaban	17,780	130	0.008 (0.007 - 0.010)	0.012 (0.010 - 0.015)	0.019 (0.014 - 0.026)	0.031 (0.013 - 0.062)
Norway	Dabigatran	8,680	70	0.006 (0.004 - 0.008)	0.011 (0.008 - 0.015)	0.015 (0.012 - 0.020)	0.018 (0.013 - 0.025)
Norway	Rivaroxaban	10,570	190	0.015 (0.012 - 0.018)	0.025 (0.021 - 0.029)	0.033 (0.027 - 0.039)	0.040 (0.031 - 0.051)
Norway	Warfarin	11,950	180	0.015 (0.012 - 0.018)	0.023 (0.019 - 0.027)	0.031 (0.026 - 0.037)	0.039 (0.030 - 0.048)
Sweden	Apixaban	38,830	1030	0.026 (0.025 - 0.028)	0.046 (0.043 - 0.050)	0.062 (0.055 - 0.069)	0.062 (0.055 - 0.069)
Sweden	Dabigatran	10,080	270	0.020 (0.017 - 0.023)	0.037 (0.032 - 0.042)	0.055 (0.047 - 0.063)	0.068 (0.056 - 0.082)
Sweden	Rivaroxaban	14,330	760	0.045 (0.042 - 0.049)	0.073 (0.067 - 0.079)	0.099 (0.090 - 0.108)	0.124 (0.108 - 0.140)
Sweden	Warfarin	47,150	1870	0.030 (0.028 - 0.032)	0.052 (0.049 - 0.054)	0.074 (0.070 - 0.078)	0.099 (0.092 - 0.106)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.30 Crude cumulative incidence of <u>any bleeding recorded as the primary diagnosis at an acute hospitalisation with an overnight stay (sensitivity analysis)</u> among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

Country	Cohort	Number of initiators - rounded	cases - rounded	Cumulative incidence after 12 m (95% CI)	Cumulative incidence after 24 m (95% CI)	Cumulative incidence after 36 m (95% CI)	Cumulative incidence after 48 m (95% CI)
All	Apixaban	71,590	1320	0.019 (0.018 - 0.020)	0.032 (0.030 - 0.035)	0.042 (0.038 - 0.047)	0.047 (0.039 - 0.056)
All	Dabigatran	31,210	740	0.019 (0.018 - 0.021)	0.031 (0.029 - 0.034)	0.042 (0.038 - 0.045)	0.053 (0.047 - 0.060)
All	Rivaroxaban	37,580	1220	0.029 (0.028 - 0.031)	0.047 (0.045 - 0.050)	0.060 (0.056 - 0.064)	0.078 (0.068 - 0.088)
All	Warfarin	79,170	2470	0.028 (0.026 - 0.029)	0.045 (0.043 - 0.047)	0.057 (0.055 - 0.060)	0.070 (0.066 - 0.074)
Denmark	Apixaban	14,980	400	0.027 (0.024 - 0.030)	0.043 (0.039 - 0.048)	0.057 (0.049 - 0.066)	0.062 (0.050 - 0.076)
Denmark	Dabigatran	12,450	390	0.025 (0.022 - 0.028)	0.041 (0.036 - 0.045)	0.052 (0.046 - 0.057)	0.064 (0.056 - 0.074)
Denmark	Rivaroxaban	12,680	460	0.035 (0.031 - 0.039)	0.058 (0.052 - 0.065)	0.074 (0.066 - 0.083)	0.088 (0.076 - 0.100)
Denmark	Warfarin	20,070	690	0.036 (0.033 - 0.040)	0.055 (0.050 - 0.059)	0.065 (0.059 - 0.071)	0.080 (0.070 - 0.090)
Norway	Apixaban	17,780	290	0.018 (0.016 - 0.021)	0.032 (0.028 - 0.036)	0.039 (0.031 - 0.049)	0.050 (0.030 - 0.078)
Norway	Dabigatran	8,680	180	0.017 (0.014 - 0.021)	0.027 (0.023 - 0.032)	0.036 (0.031 - 0.043)	0.044 (0.036 - 0.053)
Norway	Rivaroxaban	10,570	340	0.027 (0.024 - 0.031)	0.045 (0.040 - 0.051)	0.059 (0.052 - 0.067)	0.085 (0.053 - 0.127)
Norway	Warfarin	11,950	340	0.027 (0.023 - 0.030)	0.044 (0.039 - 0.050)	0.054 (0.048 - 0.061)	0.062 (0.054 - 0.072)
Sweden	Apixaban	38,830	630	0.017 (0.015 - 0.018)	0.029 (0.026 - 0.031)	0.038 (0.032 - 0.044)	0.038 (0.032 - 0.044)
Sweden	Dabigatran	10,080	170	0.014 (0.011 - 0.017)	0.022 (0.019 - 0.026)	0.033 (0.027 - 0.039)	0.049 (0.031 - 0.073)
Sweden	Rivaroxaban	14,330	430	0.027 (0.024 - 0.030)	0.041 (0.037 - 0.046)	0.049 (0.044 - 0.055)	0.068 (0.055 - 0.083)
Sweden	Warfarin	47,150	1430	0.024 (0.023 - 0.026)	0.041 (0.038 - 0.043)	0.054 (0.051 - 0.058)	0.067 (0.063 - 0.072)

CI confidence interval; NVAF non-valvular atrial fibrillation

Table 15.31 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin in Denmark, Norway, and Sweden and standardised mean differences before and after matching

Characteristic	Apixaban (rounded) before matching N=71585	Warfarin (rounded) before matching N=79171	Apixaban (rounded) after matching N=55581	Warfarin (rounded) after matching N=55581	Standardised mean difference before matching (max= 0.23)	Standardised mean difference after matching (max= 0.02)
Time from AF diag:< 1 month	49,240 (68.8%)	47,550 (60.1%)	35,990 (64.8%)	36,040 (64.8%)	0.183	0.002
Time from AF diag:1 - 6 month	6,180 (8.6%)	7,970 (10.1%)	5,200 (9.4%)	5,140 (9.3%)	0.049	0.004
Time from AF diag:6 - 60 months	16,170 (22.6%)	23,650 (29.9%)	14,390 (25.9%)	14,400 (25.9%)	0.166	0.000
Sex:Female	32,910 (46.0%)	32,980 (41.7%)	24,440 (44.0%)	24,410 (43.9%)	0.087	0.001
Sex:Male	38,670 (54.0%)	46,190 (58.3%)	31,140 (56.0%)	31,170 (56.1%)	0.087	0.001
Age, median(IQR)	75.5 (68.2 - 83.5)	75.0 (67.5 - 82.2)	75.1 (67.8 - 82.8)	75.1 (67.8 - 82.8)	0.098	0.004
Age -group:< 55 years	3,320 (4.6%)	4,480 (5.7%)	2,840 (5.1%)	2,740 (4.9%)	0.046	0.008
Age -group:55-<65 years	8,420 (11.8%)	10,100 (12.8%)	6,850 (12.3%)	7,010 (12.6%)	0.031	0.009
Age -group:65-<75 years	22,880 (32.0%)	25,060 (31.6%)	17,840 (32.1%)	17,790 (32.0%)	0.007	0.002
Age -group:75-<85 years	22,330 (31.2%)	26,700 (33.7%)	17,980 (32.3%)	17,860 (32.1%)	0.054	0.004
Age -group:>= 85 years	14,630 (20.4%)	12,830 (16.2%)	10,080 (18.1%)	10,170 (18.3%)	0.110	0.004
CCI-group:0	28,410 (39.7%)	29,610 (37.4%)	22,000 (39.6%)	22,160 (39.9%)	0.047	0.006
CCI-group:1-2	24,540 (34.3%)	25,600 (32.3%)	18,790 (33.8%)	18,290 (32.9%)	0.041	0.019
CCI-group:>=3	18,630 (26.0%)	23,960 (30.3%)	14,800 (26.6%)	15,130 (27.2%)	0.095	0.014
Prior bleeding (any)	8,020 (11.2%)	8,870 (11.2%)	6,110 (11.0%)	6,050 (10.9%)	0.000	0.003
Prior gastrointestinal bleeding	670 (0.9%)	820 (1.0%)	540 (1.0%)	550 (1.0%)	0.010	0.002
Prior intracranial bleeding	900 (1.3%)	710 (0.9%)	590 (1.1%)	570 (1.0%)	0.035	0.003
Prior stroke (any)	10,040 (14.0%)	9,610 (12.1%)	7,200 (13.0%)	7,190 (12.9%)	0.056	0.001
Prior ischaemic stroke	9,740 (13.6%)	9,400 (11.9%)	7,000 (12.6%)	7,000 (12.6%)	0.052	0.000
Prior haemorrhagic stroke	700 (1.0%)	520 (0.7%)	460 (0.8%)	430 (0.8%)	0.035	0.006
Prior systemic embolism	400 (0.6%)	760 (1.0%)	370 (0.7%)	360 (0.7%)	0.047	0.001
Prior transient ischaemic attack	3,090 (4.3%)	3,120 (3.9%)	2,310 (4.2%)	2,260 (4.1%)	0.019	0.005
Chronic kidney disease	3,510 (4.9%)	6,530 (8.2%)	3,170 (5.7%)	3,210 (5.8%)	0.135	0.003
Heart failure	13,650 (19.1%)	18,010 (22.7%)	11,220 (20.2%)	11,270 (20.3%)	0.090	0.003
Coronary artery disease	15,580 (21.8%)	21,450 (27.1%)	13,040 (23.5%)	13,110 (23.6%)	0.124	0.003
Peripheral arterial disease	4,840 (6.8%)	6,030 (7.6%)	3,840 (6.9%)	3,930 (7.1%)	0.033	0.006
Hypertension	47,790 (66.8%)	54,110 (68.3%)	37,340 (67.2%)	37,410 (67.3%)	0.034	0.003
Diabetes	11,790 (16.5%)	14,680 (18.5%)	9,520 (17.1%)	9,570 (17.2%)	0.055	0.002
Chronic obstructive	9,150 (12.8%)	10,120 (12.8%)	7,020 (12.6%)	6,970 (12.5%)	0.000	0.002

pulmonary disease						
Liver disease	610 (0.8%)	820 (1.0%)	510 (0.9%)	530 (0.9%)	0.019	0.004
Alcoholism	1,770 (2.5%)	1,790 (2.3%)	1,320 (2.4%)	1,310 (2.4%)	0.015	0.001
Dementia	1,820 (2.5%)	1,220 (1.5%)	1,110 (2.0%)	1,050 (1.9%)	0.071	0.008
Cancer 6 months before and including index date	1,850 (2.6%)	2,140 (2.7%)	1,440 (2.6%)	1,480 (2.7%)	0.007	0.005
Platelet inhibitors (excluding heparin)	26,850 (37.5%)	30,840 (39.0%)	21,020 (37.8%)	21,110 (38.0%)	0.030	0.003
Low -dose aspirin	23,580 (32.9%)	27,180 (34.3%)	18,430 (33.2%)	18,550 (33.4%)	0.029	0.005
ADP receptor blockers	4,860 (6.8%)	7,100 (9.0%)	4,180 (7.5%)	4,150 (7.5%)	0.081	0.002
Renin - angiotensin system inhibitors	33,260 (46.5%)	38,070 (48.1%)	26,110 (47.0%)	26,120 (47.0%)	0.032	0.000
Angiotensin - converting enzyme inhibitors	15,890 (22.2%)	20,500 (25.9%)	13,190 (23.7%)	13,250 (23.8%)	0.087	0.002
Angiotensin II antagonists, plain	11,220 (15.7%)	11,850 (15.0%)	8,490 (15.3%)	8,450 (15.2%)	0.020	0.002
Angiotensin II antagonists, combinations	5,820 (8.1%)	5,210 (6.6%)	4,080 (7.3%)	4,070 (7.3%)	0.059	0.000
Beta-blockers	51,520 (72.0%)	56,980 (72.0%)	40,010 (72.0%)	39,970 (71.9%)	0.000	0.002
Proton pump inhibitors	15,640 (21.8%)	17,350 (21.9%)	12,040 (21.7%)	12,040 (21.7%)	0.002	0.000
Non-steroidal anti-inflammatory drugs	5,620 (7.9%)	5,860 (7.4%)	4,260 (7.7%)	4,250 (7.6%)	0.017	0.001
Statins	24,550 (34.3%)	28,740 (36.3%)	19,250 (34.6%)	19,370 (34.9%)	0.042	0.004
Antidiabetic agents	8,230 (11.5%)	10,410 (13.1%)	6,710 (12.1%)	6,740 (12.1%)	0.050	0.002
Loop diuretics	16,490 (23.0%)	22,170 (28.0%)	13,760 (24.8%)	13,650 (24.5%)	0.114	0.005
Non-loop diuretics	900 (1.3%)	1,230 (1.6%)	730 (1.3%)	720 (1.3%)	0.025	0.003
Alpha adrenergic blockers	12,540 (17.5%)	15,810 (20.0%)	10,390 (18.7%)	10,440 (18.8%)	0.063	0.002
Amiodarone	1,690 (2.4%)	2,560 (3.2%)	1,480 (2.7%)	1,520 (2.7%)	0.053	0.004
Dronedarone	680 (0.9%)	600 (0.8%)	450 (0.8%)	450 (0.8%)	0.021	0.001
Antihypertensive, combination drugs	7,930 (11.1%)	7,700 (9.7%)	5,820 (10.5%)	5,800 (10.4%)	0.044	0.001
Calcium channel blockers	17,000 (23.7%)	19,680 (24.9%)	13,390 (24.1%)	13,410 (24.1%)	0.026	0.001
Selective serotonin reuptake inhibitors	4,620 (6.4%)	4,790 (6.1%)	3,460 (6.2%)	3,450 (6.2%)	0.016	0.001
Drugs used in alcohol dependence	110 (0.2%)	120 (0.2%)	90 (0.2%)	80 (0.1%)	0.001	0.005
CHA2DS2-VASc, mean(SD)	3.4 (1.74)	3.4 (1.76)	3.4 (1.74)	3.4 (1.74)	0.017	0.001
CHA2DS2-VASc:0 -1	10,420 (14.6%)	11,520 (14.6%)	8,210 (14.8%)	8,230 (14.8%)	0.000	0.001
CHA2DS2-VASc:2 -3	28,440 (39.7%)	30,330 (38.3%)	22,050 (39.7%)	21,800 (39.2%)	0.029	0.009
CHA2DS2-VASc:>=4	32,730 (45.7%)	37,330 (47.1%)	25,320 (45.6%)	25,550 (46.0%)	0.028	0.008
CHADS2, mean(SD)	2.3 (1.50)	2.4 (1.51)	2.3 (1.49)	2.3 (1.49)	0.056	0.002

CHADS2:0	8,010 (11.2%)	8,300 (10.5%)	5,810 (10.5%)	6,090 (11.0%)	0.023	0.016
CHADS2:1	15,830 (22.1%)	15,840 (20.0%)	12,090 (21.7%)	11,620 (20.9%)	0.052	0.021
CHADS2:>=2	47,750 (66.7%)	55,030 (69.5%)	37,680 (67.8%)	37,870 (68.1%)	0.060	0.007
HAS-BLED, mean(SD)	2.0 (1.03)	2.0 (1.05)	2.0 (1.04)	2.0 (1.04)	0.017	0.002
HAS-BLED:<3	51,370 (71.8%)	56,150 (70.9%)	40,000 (72.0%)	40,050 (72.1%)	0.018	0.002
HAS-BLED:>=3	20,220 (28.2%)	23,020 (29.1%)	15,580 (28.0%)	15,530 (27.9%)	0.018	0.002
log_n_hosp, median(IQR)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.025	0.008
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.7 (0.0 - 1.6)	0.038	0.004
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.229	0.006

Table 15.32 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin and standardised mean differences before and after matching, Denmark

Characteristic	Apixaban (rounded) before matching N=14980	Warfarin (rounded) before matching N=20070	Apixaban (rounded) after matching N=13173	Warfarin (rounded) after matching N=13173	Standardised mean difference before matching (max= 0.27)	Standardised mean difference after matching (max= 0.06)
Time from AF diag:< 1 month	10,490 (70.0%)	12,620 (62.9%)	9,090 (69.0%)	9,120 (69.3%)	0.152	0.005
Time from AF diag:1 - 6 month	1,660 (11.1%)	2,410 (12.0%)	1,490 (11.3%)	1,480 (11.2%)	0.028	0.004
Time from AF diag:6 - 60 months	2,830 (18.9%)	5,040 (25.1%)	2,590 (19.6%)	2,570 (19.5%)	0.152	0.003
Sex:Female	7,110 (47.5%)	7,950 (39.6%)	5,900 (44.8%)	5,920 (44.9%)	0.159	0.003
Sex:Male	7,870 (52.5%)	12,120 (60.4%)	7,270 (55.2%)	7,250 (55.1%)	0.159	0.003
Age, median(IQR)	75.8 (68.4 - 83.8)	73.3 (66.1 - 80.6)	74.5 (67.6 - 82.0)	74.6 (67.8 - 82.1)	0.270	0.001
Age -group:< 55 years	660 (4.4%)	1,520 (7.6%)	650 (5.0%)	630 (4.8%)	0.136	0.007
Age -group:55-<65 years	1,710 (11.4%)	2,870 (14.3%)	1,670 (12.6%)	1,640 (12.4%)	0.086	0.006
Age -group:65-<75 years	4,750 (31.7%)	6,820 (34.0%)	4,470 (33.9%)	4,490 (34.1%)	0.049	0.004
Age -group:75-<85 years	4,610 (30.8%)	6,280 (31.3%)	4,210 (31.9%)	4,160 (31.6%)	0.010	0.008
Age -group:>= 85 years	3,250 (21.7%)	2,580 (12.9%)	2,180 (16.5%)	2,250 (17.1%)	0.236	0.014
CCI-group:0	6,030 (40.3%)	8,600 (42.8%)	5,610 (42.5%)	5,770 (43.8%)	0.053	0.025
CCI-group:1-2	5,340 (35.6%)	6,000 (29.9%)	4,570 (34.7%)	4,180 (31.8%)	0.122	0.062
CCI-group:>=3	3,610 (24.1%)	5,470 (27.2%)	3,000 (22.8%)	3,220 (24.5%)	0.072	0.040
Prior bleeding (any)	1,530 (10.2%)	1,940 (9.7%)	1,250 (9.5%)	1,270 (9.6%)	0.017	0.003
Prior gastrointestinal bleeding	200 (1.3%)	270 (1.4%)	170 (1.3%)	170 (1.3%)	0.003	0.001
Prior intracranial bleeding	200 (1.3%)	140 (0.7%)	120 (0.9%)	120 (0.9%)	0.063	0.006
Prior stroke (any)	2,540 (17.0%)	1,980 (9.8%)	1,720 (13.1%)	1,730 (13.1%)	0.210	0.001
Prior ischaemic stroke	2,490 (16.6%)	1,940 (9.7%)	1,700 (12.9%)	1,700 (12.9%)	0.207	0.001
Prior haemorrhagic stroke	130 (0.9%)	90 (0.4%)	70 (0.6%)	80 (0.6%)	0.057	0.003
Prior systemic embolism	60 (0.4%)	110 (0.5%)	60 (0.4%)	70 (0.5%)	0.015	0.011
Prior transient ischaemic attack	610 (4.1%)	600 (3.0%)	480 (3.6%)	480 (3.6%)	0.058	0.000
Chronic kidney disease	600 (4.0%)	1,690 (8.4%)	590 (4.4%)	590 (4.4%)	0.184	0.000
Heart failure	2,380 (15.9%)	3,570 (17.8%)	2,090 (15.9%)	2,120 (16.1%)	0.051	0.006
Coronary artery disease	2,710 (18.1%)	4,590 (22.9%)	2,490 (18.9%)	2,520 (19.2%)	0.118	0.007
Peripheral arterial disease	1,040 (6.9%)	1,630 (8.1%)	950 (7.2%)	980 (7.5%)	0.044	0.011
Hypertension	9,510 (63.5%)	12,270 (61.1%)	8,210 (62.3%)	8,240 (62.5%)	0.049	0.004
Diabetes	2,520 (16.8%)	3,490 (17.4%)	2,210 (16.8%)	2,210 (16.8%)	0.016	0.000
Chronic obstructive pulmonary disease	1,980 (13.2%)	2,570 (12.8%)	1,710 (13.0%)	1,710 (13.0%)	0.011	0.000
Liver disease	160 (1.0%)	240 (1.2%)	140 (1.1%)	150 (1.1%)	0.013	0.001
Alcoholism	480 (3.2%)	590 (2.9%)	420 (3.2%)	400 (3.1%)	0.016	0.005
Dementia	440 (3.0%)	220 (1.1%)	210 (1.6%)	210 (1.6%)	0.132	0.003
Cancer 6 months before and including index date	590 (3.9%)	930 (4.6%)	550 (4.1%)	580 (4.4%)	0.034	0.012
Platelet inhibitors (excluding heparin)	4,860 (32.5%)	6,760 (33.7%)	4,240 (32.2%)	4,310 (32.7%)	0.026	0.011
Low -dose aspirin	3,420 (22.8%)	5,110 (25.5%)	3,070 (23.3%)	3,150 (23.9%)	0.062	0.014
ADP receptor blockers	1,680 (11.2%)	2,260 (11.2%)	1,420 (10.7%)	1,410 (10.7%)	0.000	0.000
Renin -angiotensin system inhibitors	6,290 (42.0%)	8,420 (42.0%)	5,550 (42.1%)	5,530 (41.9%)	0.000	0.004

Angiotensin - converting enzyme inhibitors	3,100 (20.7%)	4,510 (22.5%)	2,800 (21.3%)	2,760 (21.0%)	0.044	0.007
Angiotensin II antagonists, plain	1,920 (12.8%)	2,220 (11.0%)	1,610 (12.2%)	1,600 (12.1%)	0.055	0.002
Angiotensin II antagonists, combinations	970 (6.5%)	1,210 (6.0%)	860 (6.5%)	880 (6.7%)	0.019	0.006
Beta-blockers	9,400 (62.7%)	12,420 (61.9%)	8,320 (63.1%)	8,260 (62.7%)	0.017	0.009
Proton pump inhibitors	3,440 (22.9%)	4,510 (22.5%)	2,940 (22.3%)	2,970 (22.6%)	0.011	0.005
Non-steroidal anti-inflammatory drugs	1,400 (9.4%)	1,980 (9.9%)	1,280 (9.7%)	1,310 (9.9%)	0.017	0.007
Statins	5,040 (33.7%)	6,990 (34.8%)	4,470 (33.9%)	4,510 (34.2%)	0.024	0.007
Antidiabetic agents	1,880 (12.6%)	2,650 (13.2%)	1,680 (12.8%)	1,680 (12.8%)	0.019	0.000
Loop diuretics	3,980 (26.5%)	5,800 (28.9%)	3,480 (26.4%)	3,460 (26.2%)	0.052	0.004
Non-loop diuretics	180 (1.2%)	350 (1.7%)	170 (1.3%)	150 (1.2%)	0.046	0.008
Alpha adrenergic blockers	2,660 (17.8%)	3,670 (18.3%)	2,350 (17.8%)	2,340 (17.7%)	0.013	0.002
Amiodarone	560 (3.7%)	970 (4.9%)	520 (3.9%)	520 (4.0%)	0.055	0.002
Dronedarone	10 (0.1%)	30 (0.1%)	10 (0.1%)	10 (0.1%)	0.019	0.008
Antihypertensive, combination drugs	1,600 (10.7%)	2,110 (10.5%)	1,440 (10.9%)	1,460 (11.1%)	0.006	0.004
Calcium channel blockers	3,430 (22.9%)	4,790 (23.9%)	3,020 (22.9%)	3,060 (23.2%)	0.023	0.008
Selective serotonin reuptake inhibitors	1,070 (7.1%)	1,150 (5.7%)	840 (6.4%)	830 (6.3%)	0.056	0.004
Drugs used in alcohol dependence	30 (0.2%)	50 (0.2%)	30 (0.2%)	20 (0.2%)	0.011	0.005
CHA2DS2-VASc, mean(SD)	3.4 (1.69)	3.1 (1.67)	3.3 (1.65)	3.3 (1.66)	0.191	0.008
CHA2DS2-VASc:0-1	1,980 (13.2%)	3,580 (17.8%)	1,970 (14.9%)	1,940 (14.7%)	0.128	0.005
CHA2DS2-VASc:2-3	5,860 (39.1%)	8,410 (41.9%)	5,490 (41.7%)	5,470 (41.5%)	0.057	0.002
CHA2DS2-VASc:>=4	7,140 (47.6%)	8,080 (40.2%)	5,720 (43.4%)	5,760 (43.7%)	0.150	0.006
CHADS2, mean(SD)	1.9 (1.28)	1.6 (1.21)	1.7 (1.23)	1.8 (1.24)	0.186	0.003
CHADS2:0	2,000 (13.4%)	3,470 (17.3%)	1,970 (14.9%)	2,020 (15.3%)	0.109	0.010
CHADS2:1	4,280 (28.6%)	6,320 (31.5%)	4,050 (30.7%)	3,980 (30.2%)	0.064	0.011
CHADS2:>=2	8,700 (58.1%)	10,280 (51.2%)	7,160 (54.3%)	7,170 (54.5%)	0.138	0.002
HAS-BLED, mean(SD)	2.2 (1.13)	2.1 (1.17)	2.2 (1.12)	2.2 (1.12)	0.089	0.007
HAS-BLED:<3	9,070 (60.5%)	12,660 (63.1%)	8,290 (62.9%)	8,270 (62.7%)	0.053	0.003
HAS-BLED:>=3	5,920 (39.5%)	7,410 (36.9%)	4,890 (37.1%)	4,910 (37.3%)	0.053	0.003
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.7 - 0.7)	0.7 (0.0 - 1.1)	0.091	0.001
log_beddays, median(IQR)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.9)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.8)	0.147	0.005
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.108	0.007
income, median(IQR), k€	120.8 (86.8 - 186.9)	122.8 (88.9 - 187.6)	122.7 (88.3 - 189.5)	122.5 (88.3 - 188.4)	0.003	0.009
education:Secondary compulsory	5,810 (38.8%)	8,430 (42.0%)	5,210 (39.6%)	5,260 (39.9%)	0.065	0.008
education:Vocational / High school	5,910 (39.5%)	8,140 (40.6%)	5,340 (40.5%)	5,310 (40.3%)	0.022	0.005
education:Higher education	2,630 (17.5%)	2,980 (14.8%)	2,240 (17.0%)	2,220 (16.9%)	0.073	0.004
education:Unknown	630 (4.2%)	520 (2.6%)	380 (2.9%)	390 (2.9%)	0.088	0.002
employment:Employed or self -employed	2,330 (15.6%)	3,720 (18.5%)	2,210 (16.8%)	2,200 (16.7%)	0.079	0.001
employment:Unemployed	600 (4.0%)	1,190 (5.9%)	580 (4.4%)	570 (4.3%)	0.089	0.004
employment:Retired	11,940 (79.7%)	15,010 (74.8%)	10,280 (78.1%)	10,290 (78.1%)	0.116	0.002
employment:Unknown	110 (0.7%)	150 (0.7%)	100 (0.8%)	110 (0.8%)	0.001	0.004

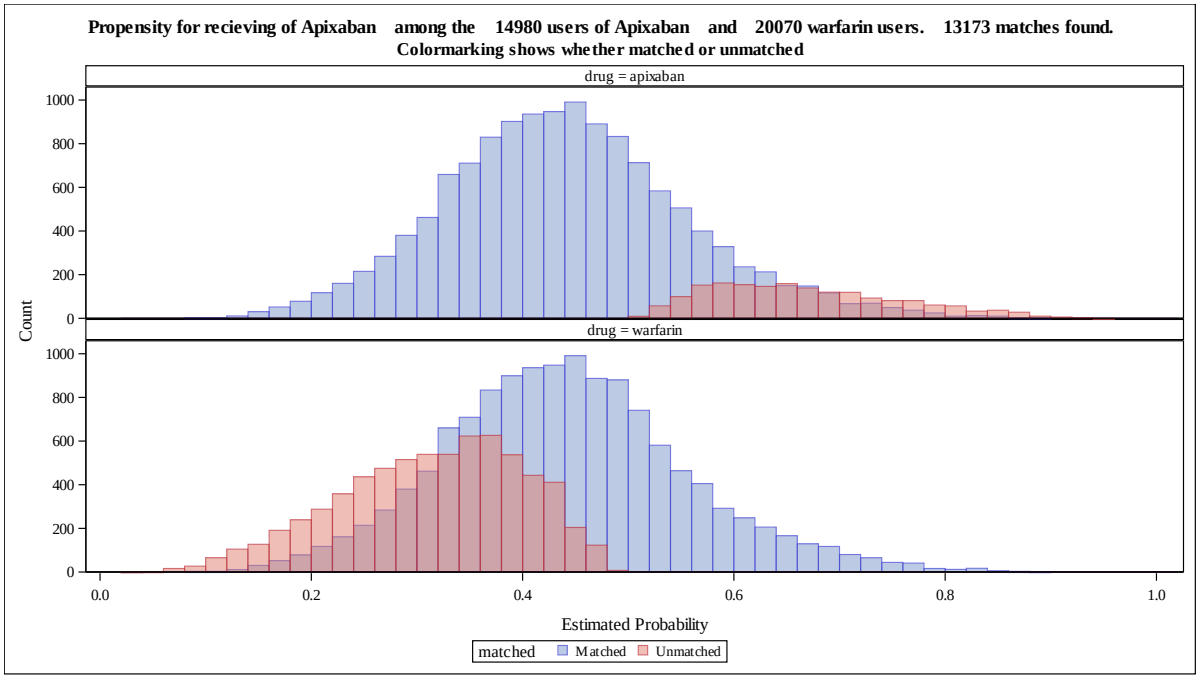
Propensity for recieving of Apixaban among the 14980 users of Apixaban and 20070 warfarin users. 13173 matches found.
Colormarking shows whether matched or unmatched
drug = apixaban
drug = warfarin
Count
0
200
400
600
800
1000
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.33 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin and standardised mean differences before and after matching, Norway

Characteristic	Apixaban (rounded) before matching N=17780	Warfarin (rounded) before matching N=11949	Apixaban (rounded) after matching N=10598	Warfarin (rounded) after matching N=10598	Standardised mean difference before matching (max= 0.37)	Standardised mean difference after matching (max= 0.05)
Time from AF diag:< 1 month	12,690 (71.3%)	6,410 (53.6%)	6,190 (58.4%)	6,190 (58.4%)	0.372	0.001
Time from AF diag:1 - 6 month	1,480 (8.3%)	1,340 (11.2%)	1,160 (10.9%)	1,140 (10.7%)	0.098	0.005
Time from AF diag:6 - 60 months	3,620 (20.3%)	4,200 (35.2%)	3,250 (30.7%)	3,270 (30.9%)	0.335	0.004
Sex:Female	7,900 (44.4%)	4,740 (39.7%)	4,340 (41.0%)	4,330 (40.8%)	0.097	0.002
Sex:Male	9,880 (55.6%)	7,210 (60.3%)	6,260 (59.0%)	6,270 (59.2%)	0.097	0.002
Age, median(IQR)	74.7 (67.5 - 83.0)	75.3 (66.7 - 83.2)	75.1 (66.8 - 83.2)	75.2 (66.8 - 83.1)	0.045	0.004
Age -group:< 55 years	940 (5.3%)	830 (7.0%)	690 (6.5%)	660 (6.2%)	0.071	0.012
Age -group:55-<65 years	2,260 (12.7%)	1,690 (14.2%)	1,440 (13.6%)	1,510 (14.3%)	0.043	0.019
Age -group:65-<75 years	5,840 (32.8%)	3,360 (28.1%)	3,130 (29.5%)	3,080 (29.1%)	0.103	0.010
Age -group:75-<85 years	5,410 (30.4%)	3,860 (32.3%)	3,350 (31.6%)	3,380 (31.9%)	0.040	0.006
Age -group:>= 85 years	3,340 (18.8%)	2,210 (18.5%)	1,990 (18.8%)	1,970 (18.6%)	0.007	0.006
CCI-group:0	6,280 (35.3%)	3,340 (27.9%)	3,260 (30.8%)	3,130 (29.5%)	0.159	0.027
CCI-group:1-2	6,090 (34.2%)	3,810 (31.9%)	3,470 (32.8%)	3,530 (33.3%)	0.050	0.013
CCI-group:>=3	5,420 (30.5%)	4,800 (40.2%)	3,870 (36.5%)	3,940 (37.1%)	0.204	0.013
Prior bleeding (any)	2,310 (13.0%)	1,780 (14.9%)	1,500 (14.2%)	1,490 (14.1%)	0.054	0.003
Prior gastrointestinal bleeding	200 (1.1%)	190 (1.6%)	150 (1.4%)	150 (1.4%)	0.043	0.005
Prior intracranial bleeding	220 (1.2%)	160 (1.3%)	140 (1.3%)	140 (1.3%)	0.008	0.002
Prior stroke (any)	2,130 (12.0%)	1,440 (12.0%)	1,280 (12.0%)	1,290 (12.1%)	0.000	0.003
Prior ischaemic stroke	2,080 (11.7%)	1,380 (11.5%)	1,230 (11.6%)	1,240 (11.7%)	0.005	0.001
Prior haemorrhagic stroke	140 (0.8%)	110 (0.9%)	90 (0.9%)	90 (0.9%)	0.014	0.003
Prior systemic embolism	90 (0.5%)	140 (1.2%)	80 (0.8%)	80 (0.8%)	0.075	0.003
Prior transient ischaemic attack	720 (4.0%)	460 (3.9%)	400 (3.8%)	420 (3.9%)	0.008	0.006
Chronic kidney disease	1,330 (7.5%)	1,560 (13.1%)	1,140 (10.8%)	1,160 (10.9%)	0.184	0.005
Heart failure	3,280 (18.4%)	3,110 (26.0%)	2,470 (23.3%)	2,510 (23.6%)	0.183	0.007
Coronary artery disease	4,620 (26.0%)	4,410 (36.9%)	3,510 (33.2%)	3,530 (33.3%)	0.237	0.003
Peripheral arterial disease	1,730 (9.7%)	1,370 (11.5%)	1,120 (10.6%)	1,130 (10.7%)	0.056	0.004
Hypertension	10,530 (59.2%)	7,270 (60.8%)	6,350 (59.9%)	6,360 (60.0%)	0.032	0.003
Diabetes	2,630 (14.8%)	2,100 (17.6%)	1,730 (16.4%)	1,760 (16.6%)	0.077	0.006
Chronic obstructive pulmonary disease	2,630 (14.8%)	1,850 (15.5%)	1,640 (15.5%)	1,620 (15.3%)	0.020	0.005
Liver disease	150 (0.9%)	150 (1.3%)	110 (1.1%)	120 (1.2%)	0.042	0.011
Alcoholism	340 (1.9%)	170 (1.4%)	160 (1.5%)	160 (1.5%)	0.039	0.002
Dementia	360 (2.0%)	230 (1.9%)	200 (1.9%)	200 (1.9%)	0.008	0.001
Cancer 6 months before and including index date	1,040 (5.8%)	810 (6.8%)	690 (6.5%)	690 (6.5%)	0.038	0.001

Platelet inhibitors (excluding heparin)	7,470 (42.0%)	5,400 (45.2%)	4,720 (44.6%)	4,680 (44.2%)	0.063	0.007
Low -dose aspirin	7,080 (39.8%)	5,060 (42.4%)	4,440 (41.9%)	4,400 (41.5%)	0.052	0.007
ADP receptor blockers	900 (5.0%)	1,130 (9.5%)	800 (7.5%)	820 (7.7%)	0.172	0.008
Renin - angiotensin system inhibitors	7,970 (44.8%)	5,500 (46.0%)	4,810 (45.4%)	4,810 (45.4%)	0.025	0.001
Angiotensin - converting enzyme inhibitors	2,930 (16.5%)	2,500 (20.9%)	2,030 (19.2%)	2,060 (19.4%)	0.114	0.006
Angiotensin II antagonists, plain	2,610 (14.7%)	1,640 (13.7%)	1,460 (13.8%)	1,470 (13.9%)	0.028	0.002
Angiotensin II antagonists, combinations	2,540 (14.3%)	1,450 (12.2%)	1,380 (13.0%)	1,350 (12.8%)	0.063	0.009
Beta-blockers	12,340 (69.4%)	8,410 (70.4%)	7,430 (70.1%)	7,430 (70.1%)	0.021	0.001
Proton pump inhibitors	3,810 (21.4%)	2,690 (22.5%)	2,340 (22.0%)	2,320 (21.9%)	0.027	0.004
H2-receptor antagonists	230 (1.3%)	170 (1.4%)	140 (1.3%)	140 (1.3%)	0.009	0.002
Non-steroidal anti-inflammatory drugs	1,610 (9.1%)	910 (7.6%)	850 (8.0%)	850 (8.0%)	0.053	0.001
Statins	6,800 (38.2%)	5,020 (42.0%)	4,250 (40.1%)	4,290 (40.4%)	0.077	0.006
Antidiabetic agents	1,750 (9.9%)	1,400 (11.7%)	1,150 (10.9%)	1,170 (11.1%)	0.060	0.006
Loop diuretics	3,580 (20.1%)	3,390 (28.4%)	2,690 (25.4%)	2,680 (25.3%)	0.194	0.003
Non-loop diuretics	280 (1.6%)	230 (1.9%)	190 (1.8%)	190 (1.8%)	0.025	0.001
Alpha adrenergic blockers	1,150 (6.5%)	960 (8.0%)	790 (7.4%)	800 (7.5%)	0.060	0.003
Amiodarone	690 (3.9%)	700 (5.9%)	550 (5.2%)	560 (5.3%)	0.093	0.003
Dronedarone	260 (1.5%)	130 (1.1%)	120 (1.1%)	130 (1.2%)	0.033	0.005
Antihypertensive, combination drugs	2,950 (16.6%)	1,740 (14.6%)	1,640 (15.5%)	1,610 (15.2%)	0.057	0.009
Calcium channel blockers	3,840 (21.6%)	2,640 (22.1%)	2,340 (22.1%)	2,310 (21.8%)	0.013	0.008
Selective serotonin reuptake inhibitors	800 (4.5%)	530 (4.5%)	480 (4.5%)	460 (4.4%)	0.001	0.007
Drugs used in alcohol dependence	30 (0.1%)	20 (0.1%)	20 (0.1%)	10 (0.1%)	0.006	0.005
CHA2DS2-VASc, mean(SD)	3.1 (1.71)	3.3 (1.86)	3.2 (1.78)	3.2 (1.83)	0.102	0.006
CHA2DS2-VASc:0 -1	3,290 (18.5%)	2,240 (18.7%)	1,940 (18.3%)	2,020 (19.0%)	0.006	0.019
CHA2DS2-VASc:2 -3	7,760 (43.6%)	4,370 (36.6%)	4,320 (40.7%)	4,040 (38.1%)	0.144	0.053
CHA2DS2-VASc:>=4	6,730 (37.9%)	5,340 (44.7%)	4,340 (41.0%)	4,540 (42.8%)	0.139	0.037
CHADS2, mean(SD)	1.5 (1.29)	1.7 (1.35)	1.6 (1.32)	1.6 (1.33)	0.121	0.007
CHADS2:0	4,150 (23.3%)	2,530 (21.1%)	2,290 (21.6%)	2,320 (21.9%)	0.053	0.006
CHADS2:1	5,860 (33.0%)	3,480 (29.1%)	3,320 (31.3%)	3,200 (30.2%)	0.083	0.024
CHADS2:>=2	7,770 (43.7%)	5,940 (49.7%)	5,000 (47.1%)	5,080 (48.0%)	0.121	0.017
HAS-BLED, mean(SD)	2.0 (1.19)	2.1 (1.26)	2.1 (1.24)	2.1 (1.23)	0.093	0.002
HAS-BLED:<3	11,940 (67.2%)	7,410 (62.0%)	6,780 (64.0%)	6,770 (63.9%)	0.107	0.003
HAS-BLED:>=3	5,840 (32.8%)	4,540 (38.0%)	3,820 (36.0%)	3,830 (36.1%)	0.107	0.003
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.166	0.009
log_beddays, median(IQR)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	0.007	0.001
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.149	0.004

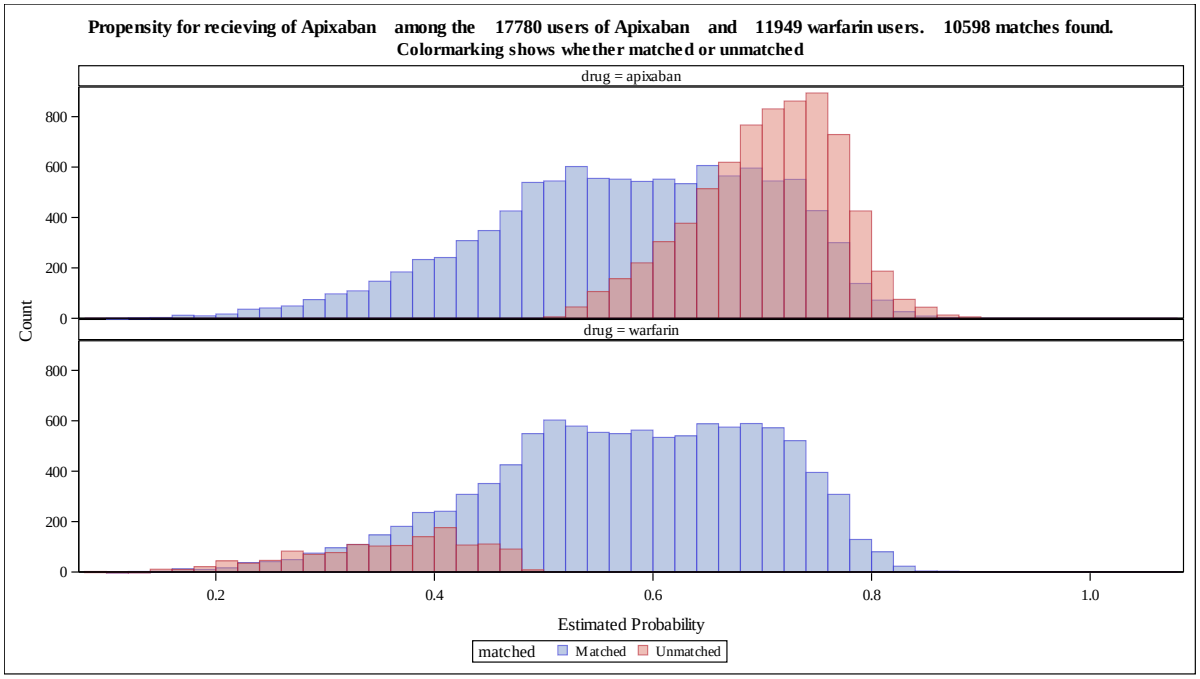
Propensity for recieving of Apixaban among the 17780 users of Apixaban and 11949 warfarin users. 10598 matches found.
Colormarking shows whether matched or unmatched
drug = apixaban
drug = warfarin
Count
0
200
400
600
800
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.34 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin and standardised mean differences before and after matching, Sweden

Characteristic	Apixaban (rounded) before matching N=38825	Warfarin (rounded) before matching N=47152	Apixaban (rounded) after matching N=31810	Warfarin (rounded) after matching N=31810	Standardised mean difference before matching (max= 0.42)	Standardised mean difference after matching (max= 0.03)
Time from AF diag:< 1 month	26,060 (67.1%)	28,530 (60.5%)	20,710 (65.1%)	20,730 (65.2%)	0.138	0.001
Time from AF diag:1 - 6 month	3,040 (7.8%)	4,220 (9.0%)	2,550 (8.0%)	2,520 (7.9%)	0.041	0.003
Time from AF diag:6 - 60 months	9,720 (25.0%)	14,400 (30.5%)	8,550 (26.9%)	8,550 (26.9%)	0.123	0.000
Sex:Female	17,900 (46.1%)	20,290 (43.0%)	14,200 (44.6%)	14,160 (44.5%)	0.062	0.002
Sex:Male	20,930 (53.9%)	26,860 (57.0%)	17,610 (55.4%)	17,650 (55.5%)	0.062	0.002
Age, median(IQR)	75.7 (68.5 - 83.6)	75.6 (68.4 - 82.6)	75.4 (68.2 - 83.0)	75.3 (68.2 - 82.9)	0.051	0.006
Age -group:< 55 years	1,730 (4.5%)	2,130 (4.5%)	1,500 (4.7%)	1,450 (4.6%)	0.002	0.007
Age -group:55-<65 years	4,450 (11.4%)	5,540 (11.8%)	3,740 (11.7%)	3,860 (12.1%)	0.010	0.012
Age -group:65-<75 years	12,300 (31.7%)	14,880 (31.6%)	10,240 (32.2%)	10,210 (32.1%)	0.003	0.002
Age -group:75-<85 years	12,310 (31.7%)	16,570 (35.1%)	10,420 (32.8%)	10,330 (32.5%)	0.073	0.006
Age -group:>= 85 years	8,040 (20.7%)	8,030 (17.0%)	5,910 (18.6%)	5,960 (18.7%)	0.094	0.004
CCI-group:0	16,110 (41.5%)	17,670 (37.5%)	13,130 (41.3%)	13,270 (41.7%)	0.082	0.009
CCI-group:1-2	13,120 (33.8%)	15,790 (33.5%)	10,750 (33.8%)	10,570 (33.2%)	0.007	0.012
CCI-group:>=3	9,600 (24.7%)	13,700 (29.0%)	7,930 (24.9%)	7,980 (25.1%)	0.098	0.003
Prior bleeding (any)	4,180 (10.8%)	5,150 (10.9%)	3,360 (10.5%)	3,300 (10.4%)	0.005	0.006
Prior gastrointestinal bleeding	280 (0.7%)	360 (0.8%)	230 (0.7%)	230 (0.7%)	0.005	0.002
Prior intracranial bleeding	480 (1.2%)	410 (0.9%)	330 (1.0%)	310 (1.0%)	0.035	0.006
Prior stroke (any)	5,370 (13.8%)	6,200 (13.1%)	4,200 (13.2%)	4,180 (13.1%)	0.020	0.002
Prior ischaemic stroke	5,170 (13.3%)	6,080 (12.9%)	4,080 (12.8%)	4,070 (12.8%)	0.012	0.001
Prior haemorrhagic stroke	430 (1.1%)	330 (0.7%)	290 (0.9%)	270 (0.8%)	0.042	0.010
Prior systemic embolism	240 (0.6%)	510 (1.1%)	230 (0.7%)	220 (0.7%)	0.050	0.005
Prior transient ischaemic attack	1,770 (4.5%)	2,050 (4.3%)	1,430 (4.5%)	1,370 (4.3%)	0.010	0.010
Chronic kidney disease	1,580 (4.1%)	3,280 (7.0%)	1,440 (4.5%)	1,470 (4.6%)	0.127	0.003
Heart failure	7,990 (20.6%)	11,330 (24.0%)	6,650 (20.9%)	6,650 (20.9%)	0.083	0.000
Coronary artery disease	8,250 (21.3%)	12,460 (26.4%)	7,040 (22.1%)	7,060 (22.2%)	0.121	0.002
Peripheral arterial disease	2,070 (5.3%)	3,030 (6.4%)	1,770 (5.6%)	1,810 (5.7%)	0.047	0.005
Hypertension	27,740 (71.5%)	34,570 (73.3%)	22,790 (71.6%)	22,810 (71.7%)	0.042	0.002
Diabetes	6,640 (17.1%)	9,090 (19.3%)	5,580 (17.5%)	5,600 (17.6%)	0.056	0.002
Chronic obstructive pulmonary disease	4,550 (11.7%)	5,700 (12.1%)	3,670 (11.5%)	3,640 (11.4%)	0.011	0.003
Liver disease	300 (0.8%)	430 (0.9%)	250 (0.8%)	260 (0.8%)	0.015	0.004
Alcoholism	950 (2.4%)	1,030 (2.2%)	740 (2.3%)	750 (2.4%)	0.018	0.002
Dementia	1,020 (2.6%)	770 (1.6%)	700 (2.2%)	640 (2.0%)	0.069	0.012
Cancer 6 months before and including index date	220 (0.6%)	400 (0.9%)	200 (0.6%)	210 (0.7%)	0.033	0.004

Platelet inhibitors (excluding heparin)	14,520 (37.4%)	18,680 (39.6%)	12,050 (37.9%)	12,120 (38.1%)	0.046	0.004
Low -dose aspirin	13,090 (33.7%)	17,010 (36.1%)	10,920 (34.3%)	11,000 (34.6%)	0.050	0.005
ADP receptor blockers	2,280 (5.9%)	3,710 (7.9%)	1,970 (6.2%)	1,920 (6.0%)	0.079	0.007
Renin - angiotensin system inhibitors	19,010 (49.0%)	24,140 (51.2%)	15,750 (49.5%)	15,780 (49.6%)	0.045	0.002
Angiotensin - converting enzyme inhibitors	9,870 (25.4%)	13,490 (28.6%)	8,360 (26.3%)	8,430 (26.5%)	0.072	0.005
Angiotensin II antagonists, plain	6,690 (17.2%)	8,000 (17.0%)	5,420 (17.0%)	5,380 (16.9%)	0.007	0.003
Angiotensin II antagonists, combinations	2,310 (5.9%)	2,540 (5.4%)	1,840 (5.8%)	1,850 (5.8%)	0.023	0.001
Beta-blockers	29,780 (76.7%)	36,150 (76.7%)	24,270 (76.3%)	24,290 (76.3%)	0.001	0.001
Proton pump inhibitors	8,390 (21.6%)	10,150 (21.5%)	6,760 (21.2%)	6,750 (21.2%)	0.002	0.001
H2-receptor antagonists	150 (0.4%)	210 (0.4%)	130 (0.4%)	130 (0.4%)	0.009	0.001
Non-steroidal anti-inflammatory drugs	2,610 (6.7%)	2,970 (6.3%)	2,130 (6.7%)	2,090 (6.6%)	0.017	0.005
Statins	12,710 (32.7%)	16,730 (35.5%)	10,530 (33.1%)	10,580 (33.3%)	0.058	0.003
Antidiabetic agents	4,590 (11.8%)	6,350 (13.5%)	3,870 (12.2%)	3,880 (12.2%)	0.050	0.001
Loop diuretics	8,940 (23.0%)	12,990 (27.5%)	7,590 (23.8%)	7,510 (23.6%)	0.104	0.006
Non-loop diuretics	440 (1.1%)	650 (1.4%)	370 (1.2%)	370 (1.2%)	0.022	0.001
Alpha adrenergic blockers	8,720 (22.5%)	11,180 (23.7%)	7,260 (22.8%)	7,300 (23.0%)	0.030	0.004
Amiodarone	440 (1.1%)	890 (1.9%)	410 (1.3%)	440 (1.4%)	0.060	0.007
Dronedarone	410 (1.0%)	440 (0.9%)	320 (1.0%)	310 (1.0%)	0.011	0.002
Antihypertensive, combination drugs	3,380 (8.7%)	3,850 (8.2%)	2,730 (8.6%)	2,740 (8.6%)	0.019	0.001
Calcium channel blockers	9,730 (25.1%)	12,240 (26.0%)	8,030 (25.2%)	8,040 (25.3%)	0.021	0.001
Selective serotonin reuptake inhibitors	2,760 (7.1%)	3,110 (6.6%)	2,140 (6.7%)	2,160 (6.8%)	0.020	0.002
Drugs used in alcohol dependence	60 (0.1%)	60 (0.1%)	50 (0.1%)	40 (0.1%)	0.008	0.005
CHA2DS2-VASc, mean(SD)	3.5 (1.75)	3.6 (1.75)	3.5 (1.75)	3.4 (1.74)	0.045	0.006
CHA2DS2-VASc:0 -1	5,150 (13.3%)	5,700 (12.1%)	4,310 (13.5%)	4,270 (13.4%)	0.035	0.003
CHA2DS2-VASc:2 -3	14,820 (38.2%)	17,540 (37.2%)	12,250 (38.5%)	12,290 (38.6%)	0.020	0.003
CHA2DS2-VASc:>=4	18,860 (48.6%)	23,910 (50.7%)	15,260 (48.0%)	15,260 (48.0%)	0.042	0.000
CHADS2, mean(SD)	2.8 (1.48)	2.9 (1.47)	2.8 (1.48)	2.8 (1.47)	0.040	0.007
CHADS2:0	1,850 (4.8%)	2,300 (4.9%)	1,560 (4.9%)	1,760 (5.5%)	0.005	0.028
CHADS2:1	5,690 (14.7%)	6,040 (12.8%)	4,730 (14.9%)	4,440 (13.9%)	0.054	0.026
CHADS2:>=2	31,280 (80.6%)	38,810 (82.3%)	25,530 (80.2%)	25,620 (80.5%)	0.045	0.007
HAS-BLED, mean(SD)	1.9 (0.90)	1.9 (0.92)	1.9 (0.90)	1.9 (0.91)	0.047	0.008
HAS-BLED:<3	30,360 (78.2%)	36,080 (76.5%)	24,930 (78.4%)	25,020 (78.7%)	0.040	0.007
HAS-BLED:>=3	8,460 (21.8%)	11,080 (23.5%)	6,880 (21.6%)	6,790 (21.3%)	0.040	0.007
log_n_hosp, median(IQR)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.057	0.011

log_beddays, median(IQR)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.088	0.006
log_n_outpatient, median(IQR)	0.7 (0.0 - 1.1)	0.0 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.419	0.007
income, median(IQR), k€	52.2 (42.3 - 78.7)	49.8 (40.5 - 72.3)	51.7 (41.7 - 77.1)	52.1 (42.0 - 77.5)	0.066	0.003
education:Secondary compulsory	14,640 (37.7%)	18,850 (40.0%)	12,110 (38.1%)	12,070 (37.9%)	0.046	0.003
education:Vocational / High school	14,790 (38.1%)	18,480 (39.2%)	12,320 (38.7%)	12,310 (38.7%)	0.023	0.001
education:Higher education	8,970 (23.1%)	9,340 (19.8%)	7,040 (22.1%)	7,100 (22.3%)	0.081	0.004
education:Unknown	430 (1.1%)	490 (1.0%)	340 (1.1%)	340 (1.1%)	0.005	0.002

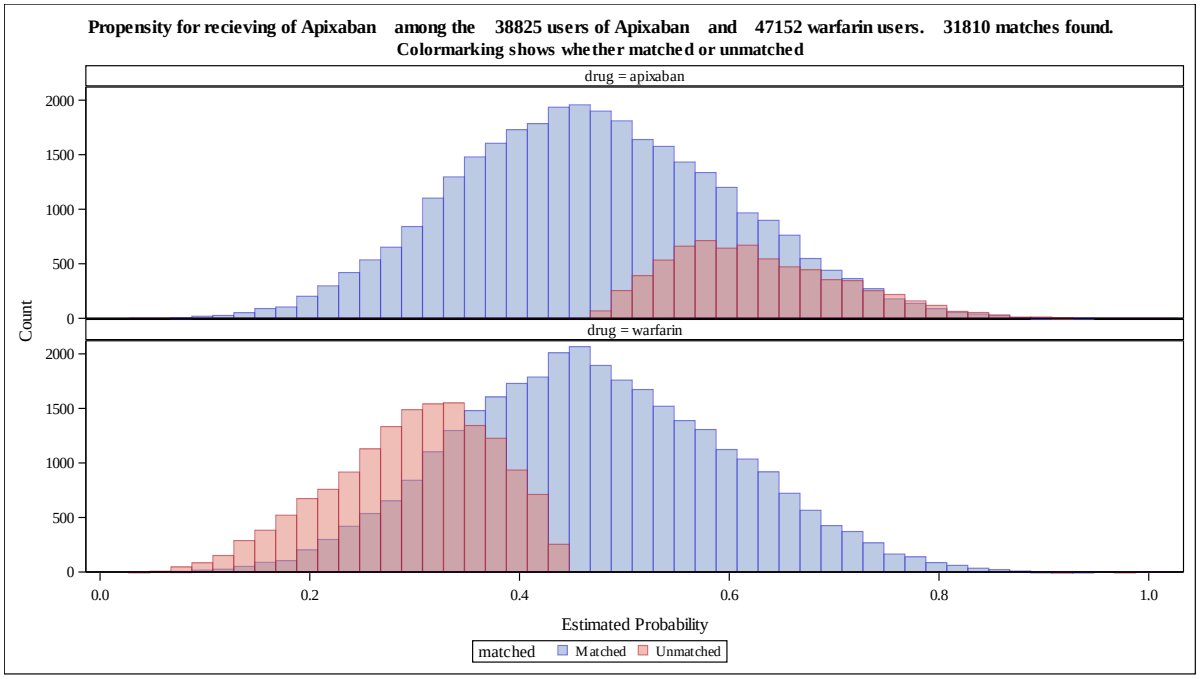
Propensity for recieving of Apixaban among the 38825 users of Apixaban and 47152 warfarin users. 31810 matches found.
Colormarking shows whether matched or unmatched
drug = apixaban
drug = warfarin
Count
2000
1500
1000
500
0
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.35 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin in Denmark, Norway, or Sweden and standardised mean differences before and after matching

Characteristic	Dabigatran (rounded) before matching N=31209	Warfarin (rounded) before matching N=79171	Dabigatran (rounded) after matching N=28428	Warfarin (rounded) after matching N=28428	Standardised mean difference before matching (max= 0.47)	Standardised mean difference after matching (max= 0.03)
index_year:2013	12,570 (40.3%)	35,000 (44.2%)	11,450 (40.3%)	11,510 (40.5%)	0.080	0.004
index_year:2014	10,470 (33.5%)	23,330 (29.5%)	9,360 (32.9%)	9,320 (32.8%)	0.088	0.003
index_year:2015	4,220 (13.5%)	13,390 (16.9%)	4,150 (14.6%)	4,130 (14.5%)	0.095	0.002
index_year:2016	3,960 (12.7%)	7,460 (9.4%)	3,470 (12.2%)	3,470 (12.2%)	0.104	0.001
Time from AF diag:< 1 month	20,160 (64.6%)	47,550 (60.1%)	17,980 (63.3%)	17,900 (63.0%)	0.094	0.006
Time from AF diag:1 - 6 month	2,640 (8.5%)	7,970 (10.1%)	2,530 (8.9%)	2,530 (8.9%)	0.055	0.000
Time from AF diag:6 - 60 months	8,410 (26.9%)	23,650 (29.9%)	7,910 (27.8%)	8,000 (28.1%)	0.065	0.007
Sex:Female	12,260 (39.3%)	32,980 (41.7%)	11,300 (39.7%)	11,360 (40.0%)	0.048	0.004
Sex:Male	18,950 (60.7%)	46,190 (58.3%)	17,130 (60.3%)	17,070 (60.0%)	0.048	0.004
Age, median(IQR)	71.0 (64.6 - 78.7)	75.0 (67.5 - 82.2)	71.7 (65.0 - 79.3)	71.7 (64.9 - 79.3)	0.277	0.002
Age -group:< 55 years	2,430 (7.8%)	4,480 (5.7%)	2,220 (7.8%)	2,230 (7.9%)	0.085	0.002
Age -group:55-<65 years	5,740 (18.4%)	10,100 (12.8%)	4,920 (17.3%)	4,970 (17.5%)	0.156	0.004
Age -group:65-<75 years	11,790 (37.8%)	25,060 (31.6%)	10,370 (36.5%)	10,290 (36.2%)	0.129	0.006
Age -group:75-<85 years	8,080 (25.9%)	26,700 (33.7%)	7,810 (27.5%)	7,800 (27.4%)	0.172	0.001
Age -group:>= 85 years	3,170 (10.2%)	12,830 (16.2%)	3,110 (10.9%)	3,140 (11.0%)	0.180	0.003
CCI-group:0	15,330 (49.1%)	29,610 (37.4%)	13,490 (47.4%)	13,290 (46.8%)	0.239	0.014
CCI-group:1-2	10,290 (33.0%)	25,600 (32.3%)	9,540 (33.6%)	9,390 (33.0%)	0.013	0.011
CCI-group:>=3	5,590 (17.9%)	23,960 (30.3%)	5,400 (19.0%)	5,750 (20.2%)	0.292	0.031
Prior bleeding (any)	2,810 (9.0%)	8,870 (11.2%)	2,630 (9.2%)	2,660 (9.3%)	0.073	0.004
Prior gastrointestinal bleeding	240 (0.8%)	820 (1.0%)	240 (0.8%)	220 (0.8%)	0.027	0.008
Prior intracranial bleeding	280 (0.9%)	710 (0.9%)	250 (0.9%)	270 (1.0%)	0.001	0.007
Prior stroke (any)	3,380 (10.8%)	9,610 (12.1%)	3,110 (10.9%)	3,150 (11.1%)	0.041	0.004
Prior ischaemic stroke	3,300 (10.6%)	9,400 (11.9%)	3,040 (10.7%)	3,070 (10.8%)	0.042	0.004
Prior haemorrhagic stroke	200 (0.6%)	520 (0.7%)	190 (0.7%)	190 (0.7%)	0.001	0.003
Prior systemic embolism	130 (0.4%)	760 (1.0%)	130 (0.5%)	150 (0.5%)	0.064	0.008
Prior transient ischaemic attack	1,160 (3.7%)	3,120 (3.9%)	1,040 (3.7%)	1,060 (3.7%)	0.012	0.004
Chronic kidney disease	560 (1.8%)	6,530 (8.2%)	560 (2.0%)	610 (2.1%)	0.300	0.014
Heart failure	4,330 (13.9%)	18,010 (22.7%)	4,240 (14.9%)	4,280 (15.1%)	0.231	0.004
Coronary artery disease	5,510 (17.7%)	21,450 (27.1%)	5,360 (18.9%)	5,360 (18.9%)	0.228	0.000
Peripheral arterial disease	1,630 (5.2%)	6,030 (7.6%)	1,580 (5.6%)	1,620 (5.7%)	0.098	0.005
Hypertension	18,970 (60.8%)	54,110 (68.3%)	17,480 (61.5%)	17,390 (61.2%)	0.158	0.006
Diabetes	4,290 (13.7%)	14,680 (18.5%)	4,070 (14.3%)	4,070 (14.3%)	0.130	0.000
Chronic obstructive pulmonary disease	3,260 (10.5%)	10,120 (12.8%)	3,080 (10.8%)	3,140 (11.0%)	0.072	0.006
Liver disease	260 (0.8%)	820 (1.0%)	250 (0.9%)	260 (0.9%)	0.020	0.007
Alcoholism	860 (2.7%)	1,790 (2.3%)	760 (2.7%)	770 (2.7%)	0.031	0.002
Dementia	420 (1.3%)	1,220 (1.5%)	370 (1.3%)	370 (1.3%)	0.017	0.001
Cancer 6 months before and including index date	880 (2.8%)	2,140 (2.7%)	840 (2.9%)	880 (3.1%)	0.007	0.009

Platelet inhibitors (excluding heparin)	10,350 (33.2%)	30,840 (39.0%)	9,620 (33.9%)	9,720 (34.2%)	0.120	0.007
Low -dose aspirin	9,180 (29.4%)	27,180 (34.3%)	8,480 (29.8%)	8,550 (30.1%)	0.106	0.005
ADP receptor blockers	1,650 (5.3%)	7,100 (9.0%)	1,610 (5.7%)	1,660 (5.8%)	0.144	0.007
Renin - angiotensin system inhibitors	13,040 (41.8%)	38,070 (48.1%)	12,070 (42.5%)	12,000 (42.2%)	0.127	0.005
Angiotensin - converting enzyme inhibitors	5,970 (19.1%)	20,500 (25.9%)	5,700 (20.0%)	5,700 (20.0%)	0.163	0.000
Angiotensin II antagonists, plain	3,960 (12.7%)	11,850 (15.0%)	3,640 (12.8%)	3,600 (12.7%)	0.066	0.004
Angiotensin II antagonists, combinations	2,720 (8.7%)	5,210 (6.6%)	2,360 (8.3%)	2,350 (8.2%)	0.081	0.002
Beta-blockers	21,750 (69.7%)	56,980 (72.0%)	19,730 (69.4%)	19,680 (69.2%)	0.050	0.004
Proton pump inhibitors	5,180 (16.6%)	17,350 (21.9%)	4,950 (17.4%)	5,010 (17.6%)	0.135	0.006
Non-steroidal anti-inflammatory drugs	3,000 (9.6%)	5,860 (7.4%)	2,660 (9.3%)	2,680 (9.4%)	0.079	0.003
Statins	9,850 (31.6%)	28,740 (36.3%)	9,140 (32.2%)	9,110 (32.0%)	0.100	0.002
Antidiabetic agents	3,070 (9.8%)	10,410 (13.1%)	2,920 (10.3%)	2,940 (10.3%)	0.104	0.002
Loop diuretics	5,370 (17.2%)	22,170 (28.0%)	5,310 (18.7%)	5,390 (19.0%)	0.260	0.008
Non-loop diuretics	370 (1.2%)	1,230 (1.6%)	340 (1.2%)	310 (1.1%)	0.030	0.009
Alpha adrenergic blockers	4,610 (14.8%)	15,810 (20.0%)	4,400 (15.5%)	4,430 (15.6%)	0.137	0.003
Amiodarone	640 (2.0%)	2,560 (3.2%)	640 (2.2%)	650 (2.3%)	0.074	0.003
Dronedarone	100 (0.3%)	600 (0.8%)	100 (0.3%)	110 (0.4%)	0.062	0.006
Antihypertensive, combination drugs	3,810 (12.2%)	7,700 (9.7%)	3,370 (11.9%)	3,360 (11.8%)	0.079	0.001
Calcium channel blockers	6,710 (21.5%)	19,680 (24.9%)	6,260 (22.0%)	6,320 (22.2%)	0.079	0.005
Selective serotonin reuptake inhibitors	1,550 (5.0%)	4,790 (6.1%)	1,440 (5.1%)	1,470 (5.2%)	0.048	0.006
Drugs used in alcohol dependence	80 (0.3%)	120 (0.2%)	70 (0.2%)	60 (0.2%)	0.024	0.002
CHA2DS2-VASc, mean(SD)	2.8 (1.70)	3.4 (1.76)	2.9 (1.70)	2.9 (1.71)	0.352	0.002
CHA2DS2-VASc:0 -1	7,480 (24.0%)	11,520 (14.6%)	6,330 (22.3%)	6,380 (22.4%)	0.241	0.004
CHA2DS2-VASc:2 -3	13,780 (44.2%)	30,330 (38.3%)	12,510 (44.0%)	12,260 (43.1%)	0.119	0.018
CHA2DS2-VASc:>=4	9,950 (31.9%)	37,330 (47.1%)	9,590 (33.7%)	9,800 (34.5%)	0.316	0.015
CHADS2, mean(SD)	1.7 (1.38)	2.4 (1.51)	1.8 (1.38)	1.8 (1.39)	0.467	0.003
CHADS2:0	6,300 (20.2%)	8,300 (10.5%)	5,140 (18.1%)	5,430 (19.1%)	0.272	0.027
CHADS2:1	9,440 (30.2%)	15,840 (20.0%)	8,470 (29.8%)	8,150 (28.7%)	0.237	0.025
CHADS2:>=2	15,470 (49.6%)	55,030 (69.5%)	14,830 (52.2%)	14,850 (52.2%)	0.415	0.001
HAS-BLED, mean(SD)	1.8 (1.07)	2.0 (1.05)	1.8 (1.07)	1.8 (1.08)	0.187	0.001
HAS-BLED:<3	23,530 (75.4%)	56,150 (70.9%)	21,260 (74.8%)	21,110 (74.3%)	0.101	0.012
HAS-BLED:>=3	7,680 (24.6%)	23,020 (29.1%)	7,170 (25.2%)	7,320 (25.7%)	0.101	0.012
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.193	0.003
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.016	0.008
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.114	0.001

Table 15.36 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin and standardised mean differences before and after matching, Denmark

Characteristic	Dabigatran (rounded) before matching N=12446	Warfarin (rounded) before matching N=20070	Dabigatran (rounded) after matching N=11465	Warfarin (rounded) after matching N=11465	Standardised mean difference before matching (max= 0.33)	Standardised mean difference after matching (max= 0.03)
index_year:2013	5,380 (43.2%)	6,810 (33.9%)	4,860 (42.4%)	4,860 (42.4%)	0.192	0.000
index_year:2014	4,380 (35.2%)	5,400 (26.9%)	3,920 (34.2%)	3,900 (34.0%)	0.179	0.003
index_year:2015	1,630 (13.1%)	4,580 (22.8%)	1,620 (14.2%)	1,640 (14.3%)	0.257	0.004
index_year:2016	1,060 (8.5%)	3,280 (16.4%)	1,060 (9.3%)	1,060 (9.3%)	0.238	0.000
Time from AF diag:< 1 month	8,470 (68.1%)	12,620 (62.9%)	7,620 (66.5%)	7,610 (66.4%)	0.110	0.002
Time from AF diag:1 - 6 month	1,130 (9.1%)	2,410 (12.0%)	1,120 (9.7%)	1,120 (9.7%)	0.095	0.000
Time from AF diag:6 - 60 months	2,840 (22.8%)	5,040 (25.1%)	2,730 (23.8%)	2,740 (23.9%)	0.054	0.002
Sex:Female	4,990 (40.1%)	7,950 (39.6%)	4,630 (40.4%)	4,660 (40.6%)	0.009	0.004
Sex:Male	7,460 (59.9%)	12,120 (60.4%)	6,830 (59.6%)	6,810 (59.4%)	0.009	0.004
Age, median(IQR)	71.2 (64.6 - 78.9)	73.3 (66.1 - 80.6)	71.8 (65.0 - 79.3)	71.8 (65.0 - 79.4)	0.117	0.003
Age -group:< 55 years	950 (7.6%)	1,520 (7.6%)	870 (7.6%)	850 (7.4%)	0.000	0.007
Age -group:55-<65 years	2,300 (18.5%)	2,870 (14.3%)	1,980 (17.2%)	2,000 (17.4%)	0.113	0.006
Age -group:65-<75 years	4,600 (37.0%)	6,820 (34.0%)	4,170 (36.4%)	4,180 (36.5%)	0.062	0.002
Age -group:75-<85 years	3,290 (26.4%)	6,280 (31.3%)	3,180 (27.7%)	3,130 (27.3%)	0.107	0.011
Age -group:>= 85 years	1,320 (10.6%)	2,580 (12.9%)	1,270 (11.0%)	1,310 (11.4%)	0.072	0.011
CCI-group:0	6,450 (51.8%)	8,600 (42.8%)	5,780 (50.4%)	5,700 (49.8%)	0.180	0.013
CCI-group:1-2	3,950 (31.7%)	6,000 (29.9%)	3,710 (32.4%)	3,640 (31.7%)	0.040	0.013
CCI-group:>=3	2,050 (16.5%)	5,470 (27.2%)	1,970 (17.2%)	2,120 (18.5%)	0.263	0.033
Prior bleeding (any)	1,000 (8.0%)	1,940 (9.7%)	930 (8.1%)	940 (8.2%)	0.058	0.003
Prior gastrointestinal bleeding	110 (0.9%)	270 (1.4%)	110 (1.0%)	100 (0.9%)	0.045	0.005
Prior intracranial bleeding	100 (0.8%)	140 (0.7%)	80 (0.7%)	90 (0.8%)	0.012	0.005
Prior stroke (any)	1,270 (10.2%)	1,980 (9.8%)	1,140 (9.9%)	1,180 (10.3%)	0.012	0.013
Prior ischaemic stroke	1,250 (10.0%)	1,940 (9.7%)	1,120 (9.8%)	1,160 (10.2%)	0.012	0.013
Prior haemorrhagic stroke	50 (0.4%)	90 (0.4%)	50 (0.4%)	50 (0.5%)	0.002	0.005
Prior systemic embolism	30 (0.3%)	110 (0.5%)	30 (0.3%)	30 (0.3%)	0.044	0.003
Prior transient ischaemic attack	430 (3.4%)	600 (3.0%)	370 (3.2%)	390 (3.4%)	0.023	0.008
Chronic kidney disease	170 (1.4%)	1,690 (8.4%)	170 (1.5%)	160 (1.4%)	0.331	0.006
Heart failure	1,600 (12.8%)	3,570 (17.8%)	1,570 (13.7%)	1,560 (13.6%)	0.138	0.003
Coronary artery disease	2,040 (16.4%)	4,590 (22.9%)	2,010 (17.5%)	2,050 (17.9%)	0.163	0.010
Peripheral arterial disease	620 (5.0%)	1,630 (8.1%)	620 (5.4%)	610 (5.3%)	0.126	0.001
Hypertension	7,440 (59.8%)	12,270 (61.1%)	6,890 (60.1%)	6,840 (59.7%)	0.027	0.009
Diabetes	1,690 (13.6%)	3,490 (17.4%)	1,620 (14.1%)	1,610 (14.0%)	0.105	0.003
Chronic obstructive pulmonary disease	1,250 (10.0%)	2,570 (12.8%)	1,200 (10.4%)	1,250 (10.9%)	0.087	0.013
Liver disease	100 (0.8%)	240 (1.2%)	100 (0.8%)	110 (1.0%)	0.039	0.013
Alcoholism	410 (3.3%)	590 (2.9%)	360 (3.1%)	360 (3.1%)	0.019	0.002
Dementia	200 (1.6%)	220 (1.1%)	160 (1.4%)	160 (1.4%)	0.046	0.001

Cancer 6 months before and including index date	390 (3.1%)	930 (4.6%)	380 (3.3%)	420 (3.6%)	0.078	0.018
Platelet inhibitors (excluding heparin)	3,610 (29.0%)	6,760 (33.7%)	3,450 (30.1%)	3,510 (30.6%)	0.101	0.010
Low -dose aspirin	2,810 (22.6%)	5,110 (25.5%)	2,680 (23.4%)	2,710 (23.6%)	0.067	0.006
ADP receptor blockers	990 (7.9%)	2,260 (11.2%)	960 (8.3%)	1,010 (8.8%)	0.113	0.017
Renin - angiotensin system inhibitors	5,020 (40.4%)	8,420 (42.0%)	4,670 (40.8%)	4,660 (40.7%)	0.033	0.002
Angiotensin - converting enzyme inhibitors	2,490 (20.0%)	4,510 (22.5%)	2,360 (20.5%)	2,350 (20.5%)	0.060	0.000
Angiotensin II antagonists, plain	1,330 (10.7%)	2,220 (11.0%)	1,240 (10.8%)	1,230 (10.7%)	0.012	0.003
Angiotensin II antagonists, combinations	880 (7.1%)	1,210 (6.0%)	780 (6.8%)	780 (6.8%)	0.042	0.001
Beta-blockers	8,150 (65.5%)	12,420 (61.9%)	7,400 (64.5%)	7,360 (64.2%)	0.074	0.006
Proton pump inhibitors	2,120 (17.0%)	4,510 (22.5%)	2,040 (17.8%)	2,080 (18.2%)	0.138	0.010
Non-steroidal anti-inflammatory drugs	1,340 (10.8%)	1,980 (9.9%)	1,230 (10.7%)	1,240 (10.8%)	0.030	0.003
Statins	3,910 (31.4%)	6,990 (34.8%)	3,670 (32.0%)	3,680 (32.1%)	0.073	0.003
Antidiabetic agents	1,310 (10.5%)	2,650 (13.2%)	1,250 (10.9%)	1,260 (11.0%)	0.084	0.001
Loop diuretics	2,500 (20.1%)	5,800 (28.9%)	2,460 (21.5%)	2,500 (21.8%)	0.206	0.008
Non-loop diuretics	160 (1.3%)	350 (1.7%)	160 (1.4%)	140 (1.2%)	0.034	0.016
Alpha adrenergic blockers	2,140 (17.2%)	3,670 (18.3%)	2,010 (17.5%)	2,000 (17.5%)	0.029	0.002
Amiodarone	390 (3.1%)	970 (4.9%)	390 (3.4%)	400 (3.5%)	0.087	0.004
Dronedarone	10 (0.1%)	30 (0.1%)	10 (0.1%)	10 (0.1%)	0.017	0.010
Antihypertensive, combination drugs	1,460 (11.7%)	2,110 (10.5%)	1,310 (11.4%)	1,320 (11.5%)	0.037	0.004
Calcium channel blockers	2,810 (22.6%)	4,790 (23.9%)	2,620 (22.8%)	2,630 (22.9%)	0.030	0.002
Selective serotonin reuptake inhibitors	690 (5.5%)	1,150 (5.7%)	630 (5.5%)	640 (5.6%)	0.010	0.005
Drugs used in alcohol dependence	40 (0.3%)	50 (0.2%)	30 (0.3%)	30 (0.3%)	0.019	0.002
CHA2DS2-VASc, mean(SD)	2.8 (1.64)	3.1 (1.67)	2.9 (1.63)	2.9 (1.64)	0.169	0.005
CHA2DS2-VASc:0 -1	2,750 (22.1%)	3,580 (17.8%)	2,400 (20.9%)	2,420 (21.1%)	0.107	0.005
CHA2DS2-VASc:2 -3	5,640 (45.3%)	8,410 (41.9%)	5,190 (45.2%)	5,090 (44.4%)	0.069	0.017
CHA2DS2-VASc:>=4	4,050 (32.6%)	8,080 (40.2%)	3,880 (33.9%)	3,950 (34.5%)	0.160	0.013
CHADS2, mean(SD)	1.5 (1.16)	1.6 (1.21)	1.5 (1.16)	1.5 (1.18)	0.138	0.002
CHADS2:0	2,510 (20.2%)	3,470 (17.3%)	2,200 (19.2%)	2,320 (20.2%)	0.074	0.026
CHADS2:1	4,480 (36.0%)	6,320 (31.5%)	4,090 (35.7%)	3,930 (34.3%)	0.095	0.028
CHADS2:>=2	5,460 (43.8%)	10,280 (51.2%)	5,180 (45.1%)	5,210 (45.5%)	0.148	0.006
HAS-BLED, mean(SD)	2.0 (1.10)	2.1 (1.17)	2.0 (1.09)	2.0 (1.11)	0.155	0.005
HAS-BLED:<3	8,680 (69.8%)	12,660 (63.1%)	7,920 (69.1%)	7,810 (68.1%)	0.142	0.020

HAS-BLED:>=3	3,760 (30.2%)	7,410 (36.9%)	3,550 (30.9%)	3,650 (31.9%)	0.142	0.020
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.123	0.006
log_beddays, median(IQR)	0.7 (0.0 - 1.6)	1.1 (0.0 - 1.9)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.263	0.006
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.007	0.006
income, median(IQR), k€	136.8 (94.7 - 226.6)	122.8 (88.9 - 187.6)	131.7 (93.0 - 211.8)	131.2 (92.5 - 212.8)	0.114	0.006
education:Secondary compulsory	4,400 (35.3%)	8,430 (42.0%)	4,250 (37.1%)	4,310 (37.6%)	0.137	0.011
education:Vocational / High school	5,250 (42.2%)	8,140 (40.6%)	4,820 (42.1%)	4,750 (41.4%)	0.033	0.013
education:Higher education	2,400 (19.3%)	2,980 (14.8%)	2,050 (17.9%)	2,050 (17.9%)	0.119	0.000
education:Unknown	390 (3.2%)	520 (2.6%)	340 (3.0%)	360 (3.1%)	0.034	0.010
employment:Employed or self - employed	3,070 (24.7%)	3,720 (18.5%)	2,570 (22.4%)	2,590 (22.5%)	0.150	0.003
employment:Unemployed	710 (5.7%)	1,190 (5.9%)	660 (5.8%)	670 (5.9%)	0.011	0.003
employment:Retired	8,580 (68.9%)	15,010 (74.8%)	8,140 (71.0%)	8,120 (70.9%)	0.131	0.003
employment:Unknown	90 (0.8%)	150 (0.7%)	90 (0.8%)	90 (0.7%)	0.002	0.006

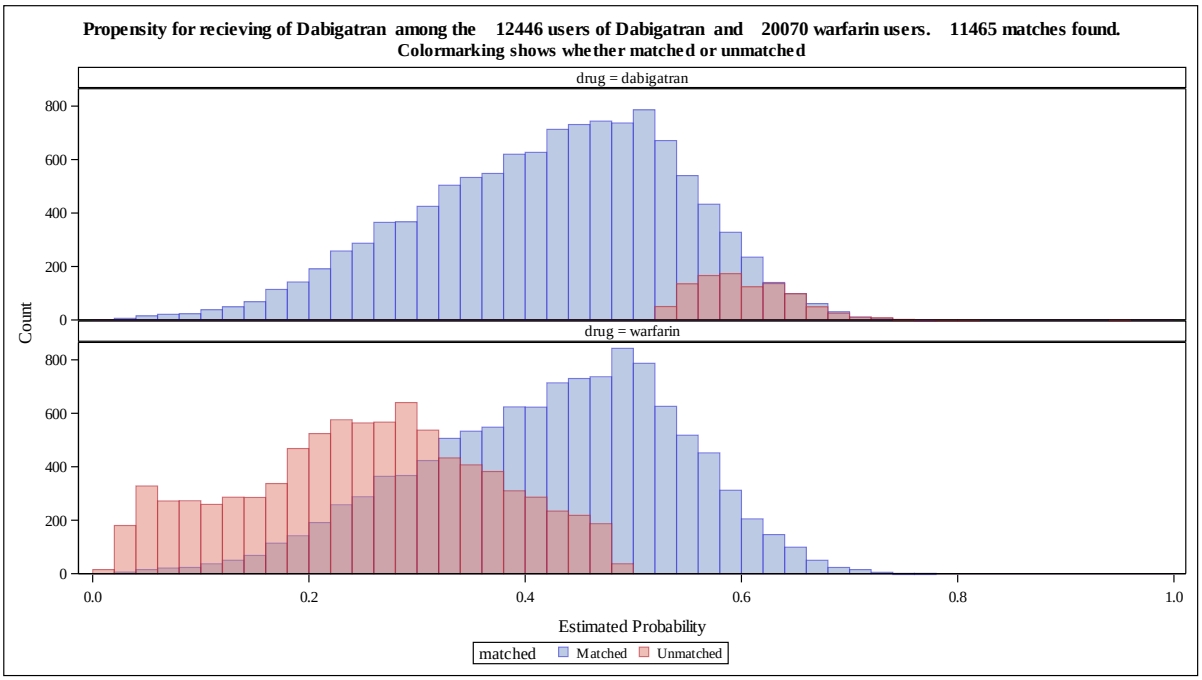

Table 15.37 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin and standardised mean differences before and after matching, Norway

Characteristic	Dabigatran (rounded) before matching N= 8684	Warfarin (rounded) before matching N=11949	Dabigatran (rounded) after matching N= 7205	Warfarin (rounded) after matching N= 7205	Standardised mean difference before matching (max= 0.43)	Standardised mean difference after matching (max= 0.05)
index_year:2013	4,160 (48.0%)	5,810 (48.6%)	3,570 (49.5%)	3,590 (49.8%)	0.013	0.005
index_year:2014	2,850 (32.8%)	3,450 (28.8%)	2,200 (30.6%)	2,230 (31.0%)	0.087	0.008
index_year:2015	930 (10.7%)	1,760 (14.8%)	860 (12.0%)	850 (11.7%)	0.123	0.006
index_year:2016	740 (8.5%)	930 (7.8%)	570 (7.9%)	540 (7.5%)	0.026	0.015
Time from AF diag:< 1 month	5,370 (61.9%)	6,410 (53.6%)	4,240 (58.8%)	4,220 (58.5%)	0.167	0.006
Time from AF diag:1 - 6 month	720 (8.2%)	1,340 (11.2%)	650 (9.1%)	660 (9.2%)	0.100	0.003
Time from AF diag:6 - 60 months	2,600 (29.9%)	4,200 (35.2%)	2,320 (32.1%)	2,330 (32.3%)	0.113	0.004
Sex:Female	3,310 (38.1%)	4,740 (39.7%)	2,790 (38.8%)	2,820 (39.1%)	0.032	0.007
Sex:Male	5,370 (61.9%)	7,210 (60.3%)	4,410 (61.2%)	4,390 (60.9%)	0.032	0.007
Age, median(IQR)	70.7 (64.6 - 78.8)	75.3 (66.7 - 83.2)	72.2 (64.8 - 80.3)	72.2 (64.9 - 80.2)	0.266	0.004
Age -group:< 55 years	720 (8.3%)	830 (7.0%)	630 (8.7%)	590 (8.2%)	0.050	0.021
Age -group:55-<65 years	1,600 (18.4%)	1,690 (14.2%)	1,210 (16.8%)	1,230 (17.1%)	0.115	0.009
Age -group:65-<75 years	3,300 (38.0%)	3,360 (28.1%)	2,440 (33.9%)	2,450 (33.9%)	0.212	0.001
Age -group:75-<85 years	2,170 (25.0%)	3,860 (32.3%)	2,040 (28.3%)	2,050 (28.5%)	0.161	0.004
Age -group:>= 85 years	900 (10.3%)	2,210 (18.5%)	890 (12.4%)	890 (12.4%)	0.235	0.000
CCI-group:0	3,870 (44.6%)	3,340 (27.9%)	2,880 (40.0%)	2,810 (39.0%)	0.352	0.021
CCI-group:1-2	3,010 (34.6%)	3,810 (31.9%)	2,610 (36.2%)	2,540 (35.2%)	0.058	0.021
CCI-group:>=3	1,800 (20.8%)	4,800 (40.2%)	1,710 (23.8%)	1,860 (25.8%)	0.431	0.047
Prior bleeding (any)	900 (10.4%)	1,780 (14.9%)	820 (11.4%)	860 (11.9%)	0.135	0.016
Prior gastrointestinal bleeding	80 (0.9%)	190 (1.6%)	70 (1.0%)	70 (1.0%)	0.062	0.007
Prior intracranial bleeding	80 (0.9%)	160 (1.3%)	70 (1.0%)	70 (1.0%)	0.044	0.003
Prior stroke (any)	810 (9.4%)	1,440 (12.0%)	740 (10.3%)	750 (10.4%)	0.086	0.003
Prior ischaemic stroke	790 (9.1%)	1,380 (11.5%)	720 (10.0%)	730 (10.1%)	0.079	0.002
Prior haemorrhagic stroke	50 (0.6%)	110 (0.9%)	50 (0.6%)	50 (0.6%)	0.035	0.002
Prior systemic embolism	50 (0.5%)	140 (1.2%)	50 (0.6%)	50 (0.7%)	0.070	0.002
Prior transient ischaemic attack	300 (3.5%)	460 (3.9%)	260 (3.6%)	270 (3.7%)	0.022	0.002
Chronic kidney disease	250 (2.9%)	1,560 (13.1%)	250 (3.5%)	290 (4.0%)	0.381	0.028
Heart failure	1,220 (14.1%)	3,110 (26.0%)	1,180 (16.3%)	1,220 (16.9%)	0.302	0.015
Coronary artery disease	1,850 (21.3%)	4,410 (36.9%)	1,750 (24.3%)	1,720 (23.9%)	0.349	0.010
Peripheral arterial disease	560 (6.5%)	1,370 (11.5%)	530 (7.4%)	530 (7.4%)	0.175	0.001
Hypertension	4,900 (56.5%)	7,270 (60.8%)	4,120 (57.1%)	4,110 (57.1%)	0.088	0.001
Diabetes	1,090 (12.5%)	2,100 (17.6%)	980 (13.5%)	960 (13.3%)	0.142	0.007
Chronic obstructive pulmonary disease	1,060 (12.2%)	1,850 (15.5%)	940 (13.0%)	960 (13.4%)	0.096	0.009
Liver disease	80 (0.9%)	150 (1.3%)	70 (0.9%)	70 (1.0%)	0.038	0.006
Alcoholism	160 (1.9%)	170 (1.4%)	120 (1.7%)	120 (1.7%)	0.035	0.003
Dementia	100 (1.2%)	230 (1.9%)	100 (1.4%)	110 (1.5%)	0.056	0.010

Cancer 6 months before and including index date	430 (4.9%)	810 (6.8%)	400 (5.5%)	400 (5.6%)	0.077	0.004
Platelet inhibitors (excluding heparin)	3,330 (38.4%)	5,400 (45.2%)	2,820 (39.2%)	2,860 (39.7%)	0.138	0.010
Low -dose aspirin	3,240 (37.3%)	5,060 (42.4%)	2,730 (37.9%)	2,750 (38.2%)	0.104	0.007
ADP receptor blockers	230 (2.6%)	1,130 (9.5%)	230 (3.2%)	240 (3.3%)	0.290	0.006
Renin - angiotensin system inhibitors	3,550 (40.8%)	5,500 (46.0%)	3,020 (41.9%)	2,970 (41.2%)	0.106	0.013
Angiotensin - converting enzyme inhibitors	1,220 (14.1%)	2,500 (20.9%)	1,110 (15.5%)	1,110 (15.4%)	0.181	0.003
Angiotensin II antagonists, plain	1,130 (13.0%)	1,640 (13.7%)	940 (13.0%)	920 (12.7%)	0.021	0.007
Angiotensin II antagonists, combinations	1,210 (14.0%)	1,450 (12.2%)	980 (13.6%)	950 (13.2%)	0.054	0.009
Beta-blockers	5,950 (68.5%)	8,410 (70.4%)	4,920 (68.3%)	4,920 (68.3%)	0.040	0.001
Proton pump inhibitors	1,300 (14.9%)	2,690 (22.5%)	1,170 (16.2%)	1,180 (16.4%)	0.196	0.006
H2-receptor antagonists	110 (1.2%)	170 (1.4%)	90 (1.3%)	100 (1.3%)	0.015	0.006
Non-steroidal anti-inflammatory drugs	890 (10.2%)	910 (7.6%)	670 (9.4%)	670 (9.3%)	0.091	0.003
Statins	2,930 (33.8%)	5,020 (42.0%)	2,550 (35.4%)	2,540 (35.3%)	0.170	0.001
Antidiabetic agents	730 (8.4%)	1,400 (11.7%)	660 (9.1%)	660 (9.1%)	0.112	0.001
Loop diuretics	1,230 (14.2%)	3,390 (28.4%)	1,210 (16.7%)	1,220 (16.9%)	0.353	0.004
Non-loop diuretics	130 (1.4%)	230 (1.9%)	100 (1.4%)	110 (1.5%)	0.038	0.003
Alpha adrenergic blockers	480 (5.5%)	960 (8.0%)	430 (6.0%)	430 (6.0%)	0.100	0.002
Amiodarone	170 (2.0%)	700 (5.9%)	170 (2.4%)	180 (2.5%)	0.203	0.008
Dronedarone	30 (0.4%)	130 (1.1%)	30 (0.5%)	30 (0.5%)	0.083	0.000
Antihypertensive, combination drugs	1,410 (16.2%)	1,740 (14.6%)	1,150 (16.0%)	1,120 (15.5%)	0.046	0.012
Calcium channel blockers	1,600 (18.4%)	2,640 (22.1%)	1,390 (19.3%)	1,400 (19.4%)	0.093	0.002
Selective serotonin reuptake inhibitors	330 (3.8%)	530 (4.5%)	290 (4.0%)	290 (4.1%)	0.034	0.004
Drugs used in alcohol dependence	20 (0.2%)	20 (0.1%)	20 (0.2%)	10 (0.2%)	0.025	0.006
CHA2DS2-VASc, mean(SD)	2.6 (1.68)	3.3 (1.86)	2.7 (1.72)	2.7 (1.75)	0.387	0.001
CHA2DS2-VASc:0 -1	2,470 (28.5%)	2,240 (18.7%)	1,800 (25.0%)	1,870 (25.9%)	0.232	0.022
CHA2DS2-VASc:2 -3	3,870 (44.5%)	4,370 (36.6%)	3,180 (44.2%)	3,010 (41.7%)	0.162	0.050
CHA2DS2-VASc:>=4	2,340 (27.0%)	5,340 (44.7%)	2,220 (30.9%)	2,330 (32.4%)	0.376	0.033
CHADS2, mean(SD)	1.2 (1.21)	1.7 (1.35)	1.4 (1.23)	1.4 (1.25)	0.351	0.005
CHADS2:0	2,810 (32.4%)	2,530 (21.1%)	2,020 (28.0%)	2,130 (29.5%)	0.256	0.033
CHADS2:1	2,920 (33.6%)	3,480 (29.1%)	2,430 (33.8%)	2,330 (32.4%)	0.096	0.030
CHADS2:>=2	2,960 (34.0%)	5,940 (49.7%)	2,750 (38.2%)	2,750 (38.1%)	0.322	0.002
HAS-BLED, mean(SD)	1.8 (1.15)	2.1 (1.26)	1.8 (1.16)	1.8 (1.18)	0.302	0.006
HAS-BLED:<3	6,470 (74.5%)	7,410 (62.0%)	5,240 (72.7%)	5,160 (71.6%)	0.270	0.024

HAS-BLED:>=3	2,210 (25.5%)	4,540 (38.0%)	1,970 (27.3%)	2,050 (28.4%)	0.270	0.024
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.394	0.004
log_beddays, median(IQR)	1.1 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	0.121	0.001
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.062	0.011

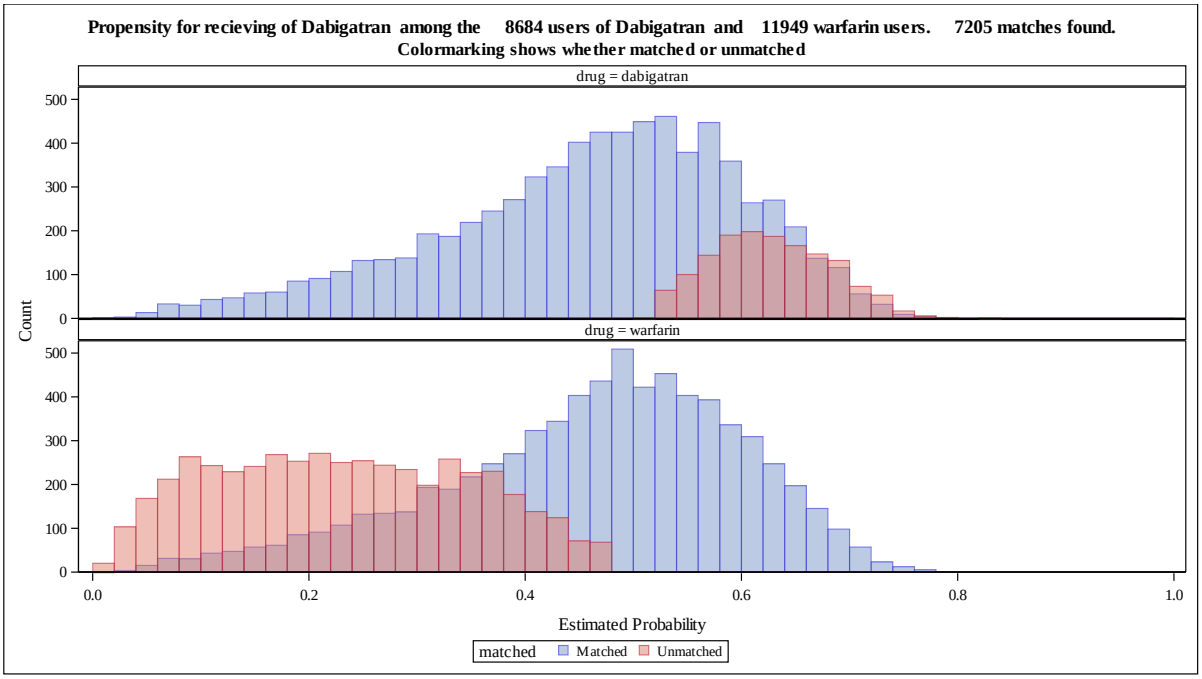
Propensity for recieving of Dabigatran among the 8684 users of Dabigatran and 11949 warfarin users. 7205 matches found.
Colormarking shows whether matched or unmatched
drug = dabigatran
drug = warfarin
Count
0
100
200
300
400
500
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.38 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin and standardised mean differences before and after matching, Sweden

Characteristic	Dabigatran (rounded) before matching N=10079	Warfarin (rounded) before matching N=47152	Dabigatran (rounded) after matching N= 9758	Warfarin (rounded) after matching N= 9758	Standardised mean difference before matching (max= 0.43)	Standardised mean difference after matching (max= 0.03)
index_year:2013	3,020 (30.0%)	22,380 (47.5%)	3,020 (31.0%)	3,060 (31.4%)	0.365	0.009
index_year:2014	3,240 (32.1%)	14,490 (30.7%)	3,240 (33.2%)	3,180 (32.6%)	0.031	0.012
index_year:2015	1,670 (16.5%)	7,040 (14.9%)	1,670 (17.1%)	1,640 (16.8%)	0.044	0.006
index_year:2016	2,150 (21.4%)	3,240 (6.9%)	1,830 (18.8%)	1,870 (19.1%)	0.425	0.009
Time from AF diag:< 1 month	6,310 (62.6%)	28,530 (60.5%)	6,130 (62.8%)	6,070 (62.2%)	0.044	0.012
Time from AF diag:1 - 6 month	800 (7.9%)	4,220 (9.0%)	760 (7.8%)	750 (7.7%)	0.038	0.003
Time from AF diag:6 - 60 months	2,970 (29.5%)	14,400 (30.5%)	2,870 (29.4%)	2,930 (30.1%)	0.023	0.014
Sex:Female	3,960 (39.3%)	20,290 (43.0%)	3,870 (39.7%)	3,890 (39.8%)	0.076	0.003
Sex:Male	6,120 (60.7%)	26,860 (57.0%)	5,890 (60.3%)	5,870 (60.2%)	0.076	0.003
Age, median(IQR)	71.1 (64.7 - 78.4)	75.6 (68.4 - 82.6)	71.4 (65.0 - 78.6)	71.3 (64.7 - 78.5)	0.359	0.014
Age -group:< 55 years	770 (7.6%)	2,130 (4.5%)	720 (7.3%)	800 (8.2%)	0.131	0.031
Age -group:55-<65 years	1,840 (18.3%)	5,540 (11.8%)	1,740 (17.8%)	1,740 (17.8%)	0.183	0.001
Age -group:65-<75 years	3,890 (38.6%)	14,880 (31.6%)	3,750 (38.5%)	3,660 (37.5%)	0.149	0.020
Age -group:75-<85 years	2,620 (26.0%)	16,570 (35.1%)	2,590 (26.6%)	2,620 (26.9%)	0.200	0.007
Age -group:>= 85 years	960 (9.5%)	8,030 (17.0%)	960 (9.8%)	940 (9.7%)	0.224	0.005
CCI-group:0	5,020 (49.8%)	17,670 (37.5%)	4,830 (49.5%)	4,780 (49.0%)	0.250	0.010
CCI-group:1-2	3,330 (33.0%)	15,790 (33.5%)	3,220 (33.0%)	3,210 (32.9%)	0.010	0.002
CCI-group:>=3	1,740 (17.2%)	13,700 (29.0%)	1,710 (17.6%)	1,770 (18.1%)	0.283	0.015
Prior bleeding (any)	910 (9.0%)	5,150 (10.9%)	880 (9.0%)	860 (8.8%)	0.063	0.005
Prior gastrointestinal bleeding	50 (0.5%)	360 (0.8%)	50 (0.5%)	50 (0.5%)	0.028	0.012
Prior intracranial bleeding	110 (1.1%)	410 (0.9%)	100 (1.0%)	110 (1.2%)	0.021	0.013
Prior stroke (any)	1,290 (12.8%)	6,200 (13.1%)	1,230 (12.6%)	1,210 (12.4%)	0.009	0.005
Prior ischaemic stroke	1,250 (12.4%)	6,080 (12.9%)	1,190 (12.2%)	1,180 (12.1%)	0.014	0.005
Prior haemorrhagic stroke	100 (1.0%)	330 (0.7%)	90 (0.9%)	100 (1.0%)	0.029	0.004
Prior systemic embolism	60 (0.5%)	510 (1.1%)	50 (0.6%)	70 (0.7%)	0.060	0.016
Prior transient ischaemic attack	430 (4.3%)	2,050 (4.3%)	410 (4.2%)	410 (4.2%)	0.004	0.001
Chronic kidney disease	130 (1.3%)	3,280 (7.0%)	130 (1.4%)	160 (1.6%)	0.286	0.022
Heart failure	1,520 (15.0%)	11,330 (24.0%)	1,500 (15.4%)	1,510 (15.5%)	0.228	0.003
Coronary artery disease	1,620 (16.1%)	12,460 (26.4%)	1,610 (16.5%)	1,590 (16.3%)	0.255	0.003
Peripheral arterial disease	440 (4.4%)	3,030 (6.4%)	430 (4.4%)	470 (4.8%)	0.090	0.018
Hypertension	6,630 (65.7%)	34,570 (73.3%)	6,470 (66.3%)	6,440 (66.0%)	0.166	0.007
Diabetes	1,510 (15.0%)	9,090 (19.3%)	1,480 (15.2%)	1,510 (15.5%)	0.113	0.008
Chronic obstructive pulmonary disease	960 (9.5%)	5,700 (12.1%)	950 (9.7%)	930 (9.5%)	0.083	0.005
Liver disease	80 (0.8%)	430 (0.9%)	80 (0.9%)	80 (0.9%)	0.007	0.001
Alcoholism	290 (2.9%)	1,030 (2.2%)	280 (2.8%)	290 (2.9%)	0.044	0.007
Dementia	110 (1.1%)	770 (1.6%)	110 (1.1%)	100 (1.0%)	0.048	0.011

Cancer 6 months before and including index date	60 (0.6%)	400 (0.9%)	60 (0.6%)	60 (0.6%)	0.029	0.001
Platelet inhibitors (excluding heparin)	3,410 (33.8%)	18,680 (39.6%)	3,350 (34.3%)	3,360 (34.4%)	0.120	0.002
Low -dose aspirin	3,130 (31.0%)	17,010 (36.1%)	3,070 (31.5%)	3,090 (31.7%)	0.106	0.004
ADP receptor blockers	430 (4.3%)	3,710 (7.9%)	430 (4.4%)	410 (4.2%)	0.151	0.008
Renin - angiotensin system inhibitors	4,480 (44.4%)	24,140 (51.2%)	4,380 (44.9%)	4,370 (44.7%)	0.137	0.003
Angiotensin - converting enzyme inhibitors	2,260 (22.4%)	13,490 (28.6%)	2,230 (22.8%)	2,240 (22.9%)	0.144	0.002
Angiotensin II antagonists, plain	1,510 (14.9%)	8,000 (17.0%)	1,470 (15.0%)	1,450 (14.9%)	0.055	0.004
Angiotensin II antagonists, combinations	630 (6.2%)	2,540 (5.4%)	600 (6.2%)	610 (6.2%)	0.035	0.001
Beta-blockers	7,650 (75.9%)	36,150 (76.7%)	7,420 (76.0%)	7,390 (75.8%)	0.017	0.006
Proton pump inhibitors	1,770 (17.5%)	10,150 (21.5%)	1,740 (17.8%)	1,740 (17.8%)	0.101	0.000
H2-receptor antagonists	20 (0.2%)	210 (0.4%)	20 (0.2%)	20 (0.2%)	0.040	0.007
Non-steroidal anti-inflammatory drugs	770 (7.6%)	2,970 (6.3%)	750 (7.7%)	780 (7.9%)	0.052	0.009
Statins	3,010 (29.9%)	16,730 (35.5%)	2,930 (30.0%)	2,880 (29.6%)	0.120	0.010
Antidiabetic agents	1,030 (10.3%)	6,350 (13.5%)	1,010 (10.4%)	1,020 (10.5%)	0.100	0.002
Loop diuretics	1,640 (16.3%)	12,990 (27.5%)	1,640 (16.8%)	1,680 (17.2%)	0.274	0.010
Non-loop diuretics	90 (0.9%)	650 (1.4%)	80 (0.9%)	70 (0.7%)	0.051	0.012
Alpha adrenergic blockers	2,000 (19.8%)	11,180 (23.7%)	1,960 (20.1%)	2,000 (20.5%)	0.095	0.009
Amiodarone	80 (0.8%)	890 (1.9%)	80 (0.8%)	70 (0.7%)	0.099	0.007
Dronedarone	50 (0.5%)	440 (0.9%)	50 (0.5%)	70 (0.7%)	0.049	0.017
Antihypertensive, combination drugs	940 (9.3%)	3,850 (8.2%)	910 (9.3%)	920 (9.4%)	0.042	0.002
Calcium channel blockers	2,300 (22.8%)	12,240 (26.0%)	2,250 (23.0%)	2,290 (23.5%)	0.073	0.010
Selective serotonin reuptake inhibitors	530 (5.3%)	3,110 (6.6%)	520 (5.3%)	540 (5.6%)	0.056	0.009
Drugs used in alcohol dependence	20 (0.2%)	60 (0.1%)	20 (0.2%)	20 (0.2%)	0.018	0.005
CHA2DS2-VASc, mean(SD)	2.9 (1.76)	3.6 (1.75)	3.0 (1.76)	3.0 (1.75)	0.356	0.001
CHA2DS2-VASc:0 -1	2,260 (22.4%)	5,700 (12.1%)	2,130 (21.8%)	2,090 (21.4%)	0.275	0.011
CHA2DS2-VASc:2 -3	4,270 (42.4%)	17,540 (37.2%)	4,140 (42.4%)	4,160 (42.6%)	0.106	0.004
CHA2DS2-VASc:>=4	3,550 (35.2%)	23,910 (50.7%)	3,490 (35.7%)	3,510 (36.0%)	0.317	0.005
CHADS2, mean(SD)	2.4 (1.50)	2.9 (1.47)	2.4 (1.49)	2.4 (1.50)	0.328	0.008
CHADS2:0	980 (9.7%)	2,300 (4.9%)	920 (9.4%)	990 (10.1%)	0.187	0.025
CHADS2:1	2,040 (20.2%)	6,040 (12.8%)	1,940 (19.9%)	1,880 (19.3%)	0.201	0.016
CHADS2:>=2	7,060 (70.0%)	38,810 (82.3%)	6,900 (70.7%)	6,890 (70.6%)	0.291	0.002
HAS-BLED, mean(SD)	1.7 (0.93)	1.9 (0.92)	1.7 (0.93)	1.7 (0.94)	0.275	0.016
HAS-BLED:<3	8,380 (83.1%)	36,080 (76.5%)	8,100 (83.0%)	8,140 (83.4%)	0.165	0.011
HAS-BLED:>=3	1,700 (16.9%)	11,080 (23.5%)	1,660 (17.0%)	1,620 (16.6%)	0.165	0.011
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.232	0.000
log_beddays, median(IQR)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.053	0.016

log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.091	0.008
income, median(IQR), k€	60.6 (44.0 - 95.1)	49.8 (40.5 - 72.3)	59.3 (43.8 - 92.7)	58.9 (43.6 - 90.7)	0.188	0.006
education:Secondary compulsory	2,960 (29.4%)	18,850 (40.0%)	2,930 (30.0%)	2,900 (29.7%)	0.224	0.007
education:Vocational / High school	3,990 (39.6%)	18,480 (39.2%)	3,880 (39.8%)	3,920 (40.2%)	0.009	0.008
education:Higher education	3,010 (29.9%)	9,340 (19.8%)	2,840 (29.1%)	2,840 (29.1%)	0.235	0.001
education:Unknown	110 (1.1%)	490 (1.0%)	110 (1.1%)	100 (1.0%)	0.004	0.011

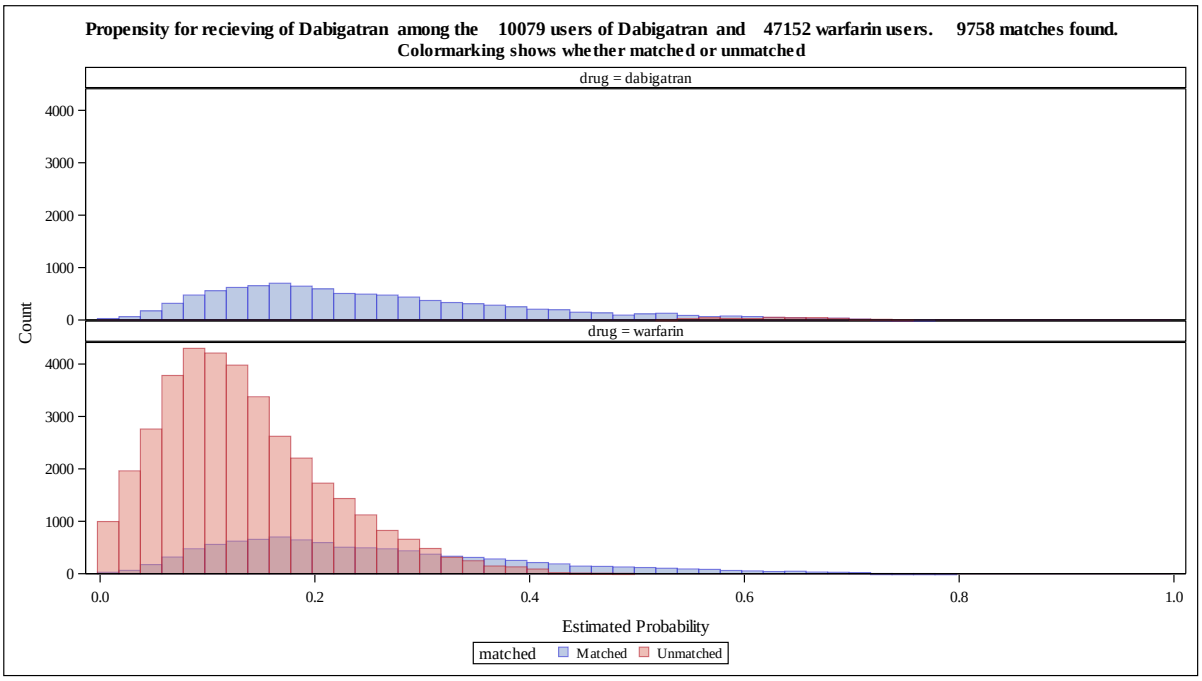

Table 15.39 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin in Denmark, Norway, and Sweden and standardised mean differences before and after matching

Characteristic	Rivaroxaban (rounded) before matching N=37580	Warfarin (rounded) before matching N=79171	Rivaroxaban (rounded) after matching N=30599	Warfarin (rounded) after matching N=30599	Standardised mean difference before matching (max= 0.58)	Standardised mean difference after matching (max= 0.04)
index_year:2013	6,950 (18.5%)	35,000 (44.2%)	6,910 (22.6%)	6,870 (22.5%)	0.577	0.003
index_year:2014	8,280 (22.0%)	23,330 (29.5%)	8,000 (26.1%)	7,790 (25.5%)	0.170	0.016
index_year:2015	11,100 (29.5%)	13,390 (16.9%)	9,140 (29.9%)	9,390 (30.7%)	0.302	0.017
index_year:2016	11,250 (29.9%)	7,460 (9.4%)	6,550 (21.4%)	6,550 (21.4%)	0.534	0.000
Time from AF diag:< 1 month	23,240 (61.8%)	47,550 (60.1%)	18,600 (60.8%)	18,480 (60.4%)	0.036	0.008
Time from AF diag:1 - 6 month	3,730 (9.9%)	7,970 (10.1%)	3,150 (10.3%)	3,220 (10.5%)	0.005	0.007
Time from AF diag:6 - 60 months	10,610 (28.2%)	23,650 (29.9%)	8,850 (28.9%)	8,910 (29.1%)	0.036	0.004
Sex:Female	16,680 (44.4%)	32,980 (41.7%)	13,420 (43.9%)	13,420 (43.8%)	0.055	0.000
Sex:Male	20,900 (55.6%)	46,190 (58.3%)	17,180 (56.1%)	17,180 (56.2%)	0.055	0.000
Age, median(IQR)	74.2 (67.3 - 82.0)	75.0 (67.5 - 82.2)	74.6 (67.4 - 82.3)	74.7 (67.4 - 82.4)	0.003	0.004
Age -group:< 55 years	1,770 (4.7%)	4,480 (5.7%)	1,550 (5.1%)	1,520 (5.0%)	0.043	0.004
Age -group:55-<65 years	4,960 (13.2%)	10,100 (12.8%)	4,010 (13.1%)	4,060 (13.3%)	0.013	0.005
Age -group:65-<75 years	13,030 (34.7%)	25,060 (31.6%)	10,140 (33.1%)	10,030 (32.8%)	0.064	0.007
Age -group:75-<85 years	11,460 (30.5%)	26,700 (33.7%)	9,620 (31.4%)	9,650 (31.5%)	0.069	0.002
Age -group:>= 85 years	6,360 (16.9%)	12,830 (16.2%)	5,290 (17.3%)	5,340 (17.4%)	0.019	0.004
CCI-group:0	16,040 (42.7%)	29,610 (37.4%)	12,670 (41.4%)	12,530 (40.9%)	0.108	0.009
CCI-group:1-2	12,760 (33.9%)	25,600 (32.3%)	10,360 (33.8%)	10,020 (32.7%)	0.034	0.023
CCI-group:>=3	8,780 (23.4%)	23,960 (30.3%)	7,570 (24.7%)	8,050 (26.3%)	0.156	0.036
Prior bleeding (any)	3,860 (10.3%)	8,870 (11.2%)	3,250 (10.6%)	3,320 (10.9%)	0.030	0.008
Prior gastrointestinal bleeding	330 (0.9%)	820 (1.0%)	280 (0.9%)	290 (1.0%)	0.017	0.005
Prior intracranial bleeding	420 (1.1%)	710 (0.9%)	330 (1.1%)	330 (1.1%)	0.021	0.001
Prior stroke (any)	4,860 (12.9%)	9,610 (12.1%)	3,910 (12.8%)	3,980 (13.0%)	0.024	0.007
Prior ischaemic stroke	4,720 (12.6%)	9,400 (11.9%)	3,800 (12.4%)	3,870 (12.7%)	0.021	0.007
Prior haemorrhagic stroke	300 (0.8%)	520 (0.7%)	230 (0.8%)	230 (0.7%)	0.015	0.001
Prior systemic embolism	220 (0.6%)	760 (1.0%)	200 (0.7%)	230 (0.7%)	0.042	0.010
Prior transient ischaemic attack	1,470 (3.9%)	3,120 (3.9%)	1,210 (4.0%)	1,200 (3.9%)	0.002	0.003
Chronic kidney disease	1,320 (3.5%)	6,530 (8.2%)	1,280 (4.2%)	1,420 (4.6%)	0.202	0.022
Heart failure	6,160 (16.4%)	18,010 (22.7%)	5,480 (17.9%)	5,540 (18.1%)	0.161	0.006
Coronary artery disease	7,530 (20.0%)	21,450 (27.1%)	6,670 (21.8%)	6,820 (22.3%)	0.167	0.012
Peripheral arterial disease	2,460 (6.5%)	6,030 (7.6%)	2,080 (6.8%)	2,160 (7.1%)	0.042	0.011
Hypertension	24,330 (64.8%)	54,110 (68.3%)	20,050 (65.5%)	20,130 (65.8%)	0.076	0.005
Diabetes	5,990 (15.9%)	14,680 (18.5%)	5,050 (16.5%)	5,150 (16.8%)	0.069	0.009
Chronic obstructive pulmonary disease	4,620 (12.3%)	10,120 (12.8%)	3,820 (12.5%)	3,890 (12.7%)	0.014	0.007
Liver disease	330 (0.9%)	820 (1.0%)	280 (0.9%)	310 (1.0%)	0.017	0.010
Alcoholism	1,030 (2.7%)	1,790 (2.3%)	790 (2.6%)	810 (2.7%)	0.031	0.004
Dementia	900 (2.4%)	1,220 (1.5%)	670 (2.2%)	650 (2.1%)	0.061	0.005

Cancer 6 months before and including index date	1,240 (3.3%)	2,140 (2.7%)	1,010 (3.3%)	1,030 (3.4%)	0.036	0.002
Platelet inhibitors (excluding heparin)	14,110 (37.6%)	30,840 (39.0%)	11,610 (37.9%)	11,720 (38.3%)	0.029	0.008
Low -dose aspirin	12,330 (32.8%)	27,180 (34.3%)	10,090 (33.0%)	10,180 (33.3%)	0.032	0.006
ADP receptor blockers	2,370 (6.3%)	7,100 (9.0%)	2,120 (6.9%)	2,200 (7.2%)	0.100	0.010
Renin - angiotensin system inhibitors	16,480 (43.9%)	38,070 (48.1%)	13,640 (44.6%)	13,700 (44.8%)	0.085	0.003
Angiotensin - converting enzyme inhibitors	7,310 (19.5%)	20,500 (25.9%)	6,460 (21.1%)	6,440 (21.0%)	0.154	0.002
Angiotensin II antagonists, plain	5,320 (14.2%)	11,850 (15.0%)	4,340 (14.2%)	4,370 (14.3%)	0.023	0.002
Angiotensin II antagonists, combinations	3,420 (9.1%)	5,210 (6.6%)	2,480 (8.1%)	2,550 (8.3%)	0.094	0.008
Beta-blockers	25,190 (67.0%)	56,980 (72.0%)	20,820 (68.0%)	20,740 (67.8%)	0.107	0.005
Proton pump inhibitors	7,500 (20.0%)	17,350 (21.9%)	6,320 (20.7%)	6,350 (20.7%)	0.048	0.002
Non-steroidal anti-inflammatory drugs	3,110 (8.3%)	5,860 (7.4%)	2,470 (8.1%)	2,470 (8.1%)	0.032	0.000
Statins	12,530 (33.4%)	28,740 (36.3%)	10,410 (34.0%)	10,450 (34.2%)	0.062	0.003
Antidiabetic agents	4,280 (11.4%)	10,410 (13.1%)	3,600 (11.8%)	3,700 (12.1%)	0.053	0.010
Loop diuretics	7,840 (20.8%)	22,170 (28.0%)	6,960 (22.8%)	7,070 (23.1%)	0.167	0.008
Non-loop diuretics	450 (1.2%)	1,230 (1.6%)	380 (1.3%)	410 (1.3%)	0.031	0.009
Alpha adrenergic blockers	6,160 (16.4%)	15,810 (20.0%)	5,360 (17.5%)	5,410 (17.7%)	0.093	0.005
Amiodarone	730 (1.9%)	2,560 (3.2%)	690 (2.2%)	700 (2.3%)	0.082	0.003
Dronedarone	160 (0.4%)	600 (0.8%)	140 (0.5%)	150 (0.5%)	0.044	0.001
Antihypertensive, combination drugs	4,680 (12.5%)	7,700 (9.7%)	3,540 (11.6%)	3,600 (11.8%)	0.087	0.007
Calcium channel blockers	8,600 (22.9%)	19,680 (24.9%)	7,150 (23.4%)	7,220 (23.6%)	0.046	0.005
Selective serotonin reuptake inhibitors	2,310 (6.1%)	4,790 (6.1%)	1,890 (6.2%)	1,870 (6.1%)	0.004	0.002
Drugs used in alcohol dependence	70 (0.2%)	120 (0.2%)	60 (0.2%)	60 (0.2%)	0.010	0.000
CHA2DS2-VASc, mean(SD)	3.2 (1.71)	3.4 (1.76)	3.3 (1.72)	3.3 (1.75)	0.118	0.011
CHA2DS2-VASc:0 -1	6,150 (16.4%)	11,520 (14.6%)	4,750 (15.5%)	4,920 (16.1%)	0.050	0.015
CHA2DS2-VASc:2 -3	16,020 (42.6%)	30,330 (38.3%)	12,800 (41.8%)	12,200 (39.9%)	0.088	0.040
CHA2DS2-VASc:>=4	15,410 (41.0%)	37,330 (47.1%)	13,050 (42.7%)	13,480 (44.1%)	0.124	0.028
CHADS2, mean(SD)	2.0 (1.45)	2.4 (1.51)	2.1 (1.45)	2.1 (1.48)	0.237	0.006
CHADS2:0	5,430 (14.4%)	8,300 (10.5%)	3,860 (12.6%)	4,280 (14.0%)	0.120	0.041
CHADS2:1	9,770 (26.0%)	15,840 (20.0%)	7,700 (25.2%)	7,130 (23.3%)	0.143	0.043
CHADS2:>=2	22,380 (59.6%)	55,030 (69.5%)	19,050 (62.3%)	19,180 (62.7%)	0.209	0.009
HAS-BLED, mean(SD)	2.0 (1.04)	2.0 (1.05)	2.0 (1.04)	2.0 (1.07)	0.030	0.007
HAS-BLED:<3	27,060 (72.0%)	56,150 (70.9%)	21,890 (71.5%)	21,520 (70.3%)	0.024	0.027
HAS-BLED:>=3	10,530 (28.0%)	23,020 (29.1%)	8,710 (28.5%)	9,080 (29.7%)	0.024	0.027

log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.140	0.012
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.012	0.012
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.014	0.006

Table 15.40 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin and standardised mean differences before and after matching, Denmark

Characteristic	Rivaroxaban (rounded) before matching N=12682	Warfarin (rounded) before matching N=20070	Rivaroxaban (rounded) after matching N=10537	Warfarin (rounded) after matching N=10537	Standardised mean difference before matching (max= 0.52)	Standardised mean difference after matching (max= 0.06)
index_year:2013	2,350 (18.5%)	6,810 (33.9%)	2,320 (22.1%)	2,270 (21.5%)	0.356	0.013
index_year:2014	1,880 (14.8%)	5,400 (26.9%)	1,860 (17.7%)	1,840 (17.5%)	0.300	0.005
index_year:2015	3,510 (27.7%)	4,580 (22.8%)	3,200 (30.4%)	3,380 (32.1%)	0.111	0.037
index_year:2016	4,950 (39.0%)	3,280 (16.4%)	3,150 (29.9%)	3,040 (28.9%)	0.523	0.022
Time from AF diag:< 1 month	8,370 (66.0%)	12,620 (62.9%)	6,830 (64.8%)	6,720 (63.8%)	0.065	0.020
Time from AF diag:1 - 6 month	1,470 (11.6%)	2,410 (12.0%)	1,260 (12.0%)	1,270 (12.0%)	0.013	0.001
Time from AF diag:6 - 60 months	2,850 (22.4%)	5,040 (25.1%)	2,450 (23.3%)	2,550 (24.2%)	0.063	0.022
Sex:Female	5,710 (45.0%)	7,950 (39.6%)	4,570 (43.3%)	4,580 (43.5%)	0.109	0.003
Sex:Male	6,970 (55.0%)	12,120 (60.4%)	5,970 (56.7%)	5,960 (56.5%)	0.109	0.003
Age, median(IQR)	74.1 (67.2 - 82.1)	73.3 (66.1 - 80.6)	73.9 (66.9 - 81.6)	74.0 (67.0 - 81.8)	0.143	0.008
Age -group:< 55 years	630 (5.0%)	1,520 (7.6%)	590 (5.6%)	590 (5.6%)	0.107	0.002
Age -group:55-<65 years	1,700 (13.4%)	2,870 (14.3%)	1,460 (13.9%)	1,420 (13.4%)	0.027	0.013
Age -group:65-<75 years	4,370 (34.4%)	6,820 (34.0%)	3,620 (34.3%)	3,590 (34.1%)	0.009	0.006
Age -group:75-<85 years	3,770 (29.7%)	6,280 (31.3%)	3,180 (30.2%)	3,210 (30.4%)	0.034	0.006
Age -group:>= 85 years	2,220 (17.5%)	2,580 (12.9%)	1,690 (16.0%)	1,730 (16.4%)	0.130	0.011
CCI-group:0	5,750 (45.3%)	8,600 (42.8%)	4,770 (45.3%)	4,810 (45.7%)	0.050	0.008
CCI-group:1-2	4,280 (33.8%)	6,000 (29.9%)	3,530 (33.5%)	3,260 (30.9%)	0.083	0.055
CCI-group:>=3	2,650 (20.9%)	5,470 (27.2%)	2,240 (21.3%)	2,470 (23.4%)	0.148	0.052
Prior bleeding (any)	1,100 (8.7%)	1,940 (9.7%)	930 (8.9%)	940 (8.9%)	0.035	0.001
Prior gastrointestinal bleeding	130 (1.0%)	270 (1.4%)	110 (1.1%)	120 (1.1%)	0.032	0.003
Prior intracranial bleeding	130 (1.0%)	140 (0.7%)	90 (0.8%)	90 (0.8%)	0.031	0.002
Prior stroke (any)	1,740 (13.7%)	1,980 (9.8%)	1,310 (12.4%)	1,330 (12.6%)	0.121	0.005
Prior ischaemic stroke	1,710 (13.5%)	1,940 (9.7%)	1,290 (12.2%)	1,310 (12.4%)	0.118	0.006
Prior haemorrhagic stroke	80 (0.6%)	90 (0.4%)	50 (0.5%)	50 (0.5%)	0.026	0.003
Prior systemic embolism	50 (0.4%)	110 (0.5%)	40 (0.4%)	50 (0.5%)	0.027	0.013
Prior transient ischaemic attack	420 (3.3%)	600 (3.0%)	350 (3.3%)	360 (3.4%)	0.018	0.008
Chronic kidney disease	360 (2.8%)	1,690 (8.4%)	350 (3.4%)	380 (3.6%)	0.245	0.016
Heart failure	1,850 (14.6%)	3,570 (17.8%)	1,590 (15.1%)	1,610 (15.2%)	0.087	0.005
Coronary artery disease	2,140 (16.8%)	4,590 (22.9%)	1,910 (18.1%)	1,940 (18.4%)	0.151	0.007
Peripheral arterial disease	780 (6.1%)	1,630 (8.1%)	690 (6.6%)	730 (7.0%)	0.078	0.015
Hypertension	7,820 (61.7%)	12,270 (61.1%)	6,470 (61.4%)	6,470 (61.4%)	0.012	0.000
Diabetes	1,970 (15.5%)	3,490 (17.4%)	1,660 (15.7%)	1,690 (16.0%)	0.051	0.009

Chronic obstructive pulmonary disease	1,540 (12.1%)	2,570 (12.8%)	1,290 (12.3%)	1,340 (12.7%)	0.020	0.013
Liver disease	110 (0.9%)	240 (1.2%)	100 (1.0%)	110 (1.1%)	0.031	0.010
Alcoholism	410 (3.2%)	590 (2.9%)	330 (3.1%)	340 (3.2%)	0.017	0.006
Dementia	310 (2.5%)	220 (1.1%)	190 (1.8%)	190 (1.8%)	0.103	0.002
Cancer 6 months before and including index date	510 (4.0%)	930 (4.6%)	440 (4.2%)	450 (4.3%)	0.030	0.005
Platelet inhibitors (excluding heparin)	3,960 (31.2%)	6,760 (33.7%)	3,350 (31.8%)	3,410 (32.3%)	0.053	0.013
Low -dose aspirin	2,910 (23.0%)	5,110 (25.5%)	2,480 (23.5%)	2,540 (24.1%)	0.058	0.013
ADP receptor blockers	1,200 (9.5%)	2,260 (11.2%)	1,020 (9.7%)	1,030 (9.7%)	0.059	0.003
Renin - angiotensin system inhibitors	5,170 (40.7%)	8,420 (42.0%)	4,330 (41.1%)	4,320 (41.0%)	0.025	0.003
Angiotensin - converting enzyme inhibitors	2,550 (20.1%)	4,510 (22.5%)	2,200 (20.8%)	2,210 (20.9%)	0.058	0.002
Angiotensin II antagonists, plain	1,400 (11.1%)	2,220 (11.0%)	1,160 (11.0%)	1,130 (10.8%)	0.001	0.007
Angiotensin II antagonists, combinations	910 (7.2%)	1,210 (6.0%)	710 (6.7%)	740 (7.0%)	0.047	0.009
Beta-blockers	7,880 (62.2%)	12,420 (61.9%)	6,510 (61.7%)	6,470 (61.4%)	0.005	0.007
Proton pump inhibitors	2,620 (20.7%)	4,510 (22.5%)	2,240 (21.2%)	2,220 (21.1%)	0.044	0.003
Non-steroidal anti-inflammatory drugs	1,270 (10.0%)	1,980 (9.9%)	1,070 (10.2%)	1,090 (10.4%)	0.006	0.007
Statins	4,170 (32.9%)	6,990 (34.8%)	3,520 (33.4%)	3,500 (33.2%)	0.042	0.003
Antidiabetic agents	1,500 (11.9%)	2,650 (13.2%)	1,270 (12.0%)	1,300 (12.3%)	0.041	0.009
Loop diuretics	3,020 (23.8%)	5,800 (28.9%)	2,620 (24.8%)	2,620 (24.8%)	0.115	0.000
Non-loop diuretics	150 (1.2%)	350 (1.7%)	140 (1.3%)	160 (1.5%)	0.042	0.015
Alpha adrenergic blockers	2,280 (17.9%)	3,670 (18.3%)	1,940 (18.4%)	1,930 (18.3%)	0.009	0.002
Amiodarone	370 (2.9%)	970 (4.9%)	340 (3.3%)	350 (3.3%)	0.101	0.005
Dronedarone	20 (0.1%)	30 (0.1%)	20 (0.1%)	10 (0.1%)	0.003	0.005
Antihypertensive, combination drugs	1,470 (11.6%)	2,110 (10.5%)	1,190 (11.3%)	1,190 (11.3%)	0.035	0.000
Calcium channel blockers	2,940 (23.2%)	4,790 (23.9%)	2,470 (23.5%)	2,480 (23.5%)	0.017	0.001
Selective serotonin reuptake inhibitors	830 (6.5%)	1,150 (5.7%)	660 (6.3%)	670 (6.3%)	0.032	0.002
Drugs used in alcohol dependence	30 (0.2%)	50 (0.2%)	30 (0.2%)	30 (0.3%)	0.000	0.004
CHA2DS2-VASc, mean(SD)	3.2 (1.65)	3.1 (1.67)	3.1 (1.66)	3.2 (1.69)	0.051	0.015
CHA2DS2-VASc:0 -1	2,000 (15.8%)	3,580 (17.8%)	1,740 (16.5%)	1,770 (16.8%)	0.055	0.008
CHA2DS2-VASc:2 -3	5,480 (43.2%)	8,410 (41.9%)	4,590 (43.5%)	4,380 (41.5%)	0.026	0.040
CHA2DS2-VASc:>=4	5,200 (41.0%)	8,080 (40.2%)	4,220 (40.0%)	4,390 (41.7%)	0.016	0.034

CHADS2, mean(SD)	1.7 (1.24)	1.6 (1.21)	1.7 (1.23)	1.7 (1.25)	0.051	0.010
CHADS2:0	2,020 (16.0%)	3,470 (17.3%)	1,710 (16.3%)	1,840 (17.5%)	0.035	0.032
CHADS2:1	4,040 (31.9%)	6,320 (31.5%)	3,430 (32.5%)	3,150 (29.9%)	0.008	0.056
CHADS2:>=2	6,620 (52.2%)	10,280 (51.2%)	5,400 (51.2%)	5,550 (52.6%)	0.019	0.028
HAS-BLED, mean(SD)	2.1 (1.09)	2.1 (1.17)	2.1 (1.10)	2.1 (1.13)	0.009	0.012
HAS-BLED:<3	8,240 (65.0%)	12,660 (63.1%)	6,850 (65.0%)	6,730 (63.9%)	0.039	0.024
HAS-BLED:>=3	4,450 (35.0%)	7,410 (36.9%)	3,690 (35.0%)	3,810 (36.1%)	0.039	0.024
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.037	0.003
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.9)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.8)	0.190	0.016
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.064	0.008
income, median(IQR), k€	124.6 (88.5 - 195.1)	122.8 (88.9 - 187.6)	123.5 (88.5 - 193.1)	123.7 (88.5 - 192.5)	0.039	0.009
education:Secondary compulsory	5,000 (39.4%)	8,430 (42.0%)	4,230 (40.2%)	4,240 (40.2%)	0.052	0.002
education:Vocational / High school	4,980 (39.3%)	8,140 (40.6%)	4,220 (40.1%)	4,210 (40.0%)	0.026	0.002
education:Higher education	2,260 (17.8%)	2,980 (14.8%)	1,740 (16.5%)	1,750 (16.6%)	0.080	0.003
education:Unknown	440 (3.5%)	520 (2.6%)	340 (3.2%)	330 (3.1%)	0.053	0.004
employment:Employed or self-employed	2,240 (17.7%)	3,720 (18.5%)	1,900 (18.0%)	1,870 (17.8%)	0.022	0.006
employment:Unemployed	590 (4.7%)	1,190 (5.9%)	530 (5.0%)	520 (5.0%)	0.058	0.001
employment:Retired	9,770 (77.0%)	15,010 (74.8%)	8,040 (76.3%)	8,070 (76.6%)	0.051	0.006
employment:Unknown	80 (0.7%)	150 (0.7%)	70 (0.7%)	70 (0.7%)	0.009	0.002

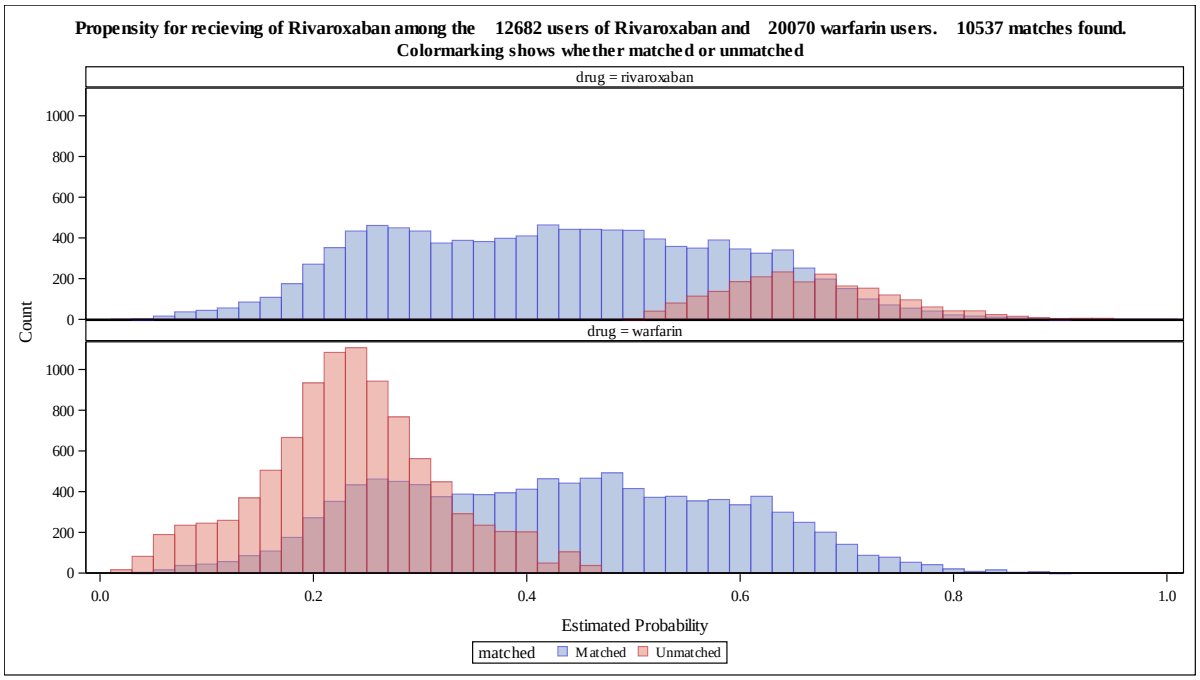

Table 15.41 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin and standardised mean differences before and after matching, Norway

Characteristic	Rivaroxaban (rounded) before matching N=10565	Warfarin (rounded) before matching N=11949	Rivaroxaban (rounded) after matching N= 7268	Warfarin (rounded) after matching N= 7268	Standardised mean difference before matching (max= 0.49)	Standardised mean difference after matching (max= 0.06)
index_year:2013	2,710 (25.6%)	5,810 (48.6%)	2,690 (37.0%)	2,670 (36.7%)	0.490	0.006
index_year:2014	2,590 (24.5%)	3,450 (28.8%)	2,330 (32.1%)	2,250 (31.0%)	0.097	0.023
index_year:2015	2,850 (27.0%)	1,760 (14.8%)	1,470 (20.2%)	1,500 (20.7%)	0.304	0.013
index_year:2016	2,420 (22.9%)	930 (7.8%)	780 (10.8%)	850 (11.7%)	0.428	0.027
Time from AF diag:< 1 month	6,440 (60.9%)	6,410 (53.6%)	4,110 (56.5%)	4,130 (56.8%)	0.148	0.005
Time from AF diag:1 - 6 month	960 (9.0%)	1,340 (11.2%)	750 (10.3%)	760 (10.5%)	0.072	0.005
Time from AF diag:6 - 60 months	3,170 (30.0%)	4,200 (35.2%)	2,410 (33.1%)	2,380 (32.7%)	0.110	0.008
Sex:Female	4,510 (42.7%)	4,740 (39.7%)	3,130 (43.1%)	3,080 (42.4%)	0.062	0.015
Sex:Male	6,050 (57.3%)	7,210 (60.3%)	4,130 (56.9%)	4,190 (57.6%)	0.062	0.015
Age, median(IQR)	73.4 (66.7 - 81.5)	75.3 (66.7 - 83.2)	74.8 (66.9 - 82.8)	74.6 (66.8 - 82.6)	0.047	0.016
Age -group:< 55 years	550 (5.2%)	830 (7.0%)	420 (5.7%)	420 (5.8%)	0.072	0.004
Age -group:55-<65 years	1,520 (14.4%)	1,690 (14.2%)	1,020 (14.1%)	1,050 (14.4%)	0.008	0.011
Age -group:65-<75 years	3,760 (35.6%)	3,360 (28.1%)	2,240 (30.8%)	2,270 (31.3%)	0.161	0.011
Age -group:75-<85 years	3,090 (29.2%)	3,860 (32.3%)	2,250 (30.9%)	2,240 (30.8%)	0.067	0.001
Age -group:>= 85 years	1,650 (15.6%)	2,210 (18.5%)	1,350 (18.5%)	1,280 (17.6%)	0.078	0.024
CCI-group:0	4,040 (38.3%)	3,340 (27.9%)	2,430 (33.4%)	2,410 (33.1%)	0.221	0.008
CCI-group:1-2	3,750 (35.5%)	3,810 (31.9%)	2,590 (35.7%)	2,500 (34.4%)	0.075	0.027
CCI-group:>=3	2,780 (26.3%)	4,800 (40.2%)	2,240 (30.9%)	2,360 (32.5%)	0.298	0.035
Prior bleeding (any)	1,260 (11.9%)	1,780 (14.9%)	950 (13.1%)	1,000 (13.7%)	0.088	0.018
Prior gastrointestinal bleeding	120 (1.2%)	190 (1.6%)	90 (1.3%)	100 (1.3%)	0.038	0.004
Prior intracranial bleeding	110 (1.0%)	160 (1.3%)	90 (1.2%)	90 (1.3%)	0.027	0.005
Prior stroke (any)	1,260 (11.9%)	1,440 (12.0%)	940 (12.9%)	950 (13.1%)	0.002	0.006
Prior ischaemic stroke	1,230 (11.6%)	1,380 (11.5%)	910 (12.5%)	920 (12.7%)	0.001	0.005
Prior haemorrhagic stroke	70 (0.6%)	110 (0.9%)	50 (0.7%)	60 (0.8%)	0.029	0.011
Prior systemic embolism	60 (0.5%)	140 (1.2%)	50 (0.7%)	60 (0.8%)	0.070	0.008
Prior transient ischaemic attack	430 (4.1%)	460 (3.9%)	330 (4.5%)	310 (4.3%)	0.012	0.013
Chronic kidney disease	580 (5.5%)	1,560 (13.1%)	550 (7.5%)	630 (8.7%)	0.263	0.043
Heart failure	1,600 (15.2%)	3,110 (26.0%)	1,360 (18.7%)	1,380 (19.0%)	0.271	0.006
Coronary artery disease	2,510 (23.8%)	4,410 (36.9%)	2,040 (28.1%)	2,080 (28.6%)	0.288	0.012
Peripheral arterial disease	970 (9.2%)	1,370 (11.5%)	720 (9.9%)	730 (10.1%)	0.076	0.004
Hypertension	6,260 (59.2%)	7,270 (60.8%)	4,380 (60.2%)	4,400 (60.5%)	0.032	0.006
Diabetes	1,490 (14.1%)	2,100 (17.6%)	1,110 (15.2%)	1,120 (15.4%)	0.097	0.005
Chronic obstructive pulmonary disease	1,430 (13.5%)	1,850 (15.5%)	1,030 (14.2%)	1,040 (14.3%)	0.057	0.002
Liver disease	110 (1.0%)	150 (1.3%)	80 (1.0%)	90 (1.2%)	0.026	0.012
Alcoholism	250 (2.3%)	170 (1.4%)	140 (1.9%)	140 (1.9%)	0.067	0.002
Dementia	180 (1.7%)	230 (1.9%)	150 (2.0%)	140 (1.9%)	0.012	0.007

Cancer 6 months before and including index date	640 (6.0%)	810 (6.8%)	480 (6.6%)	480 (6.5%)	0.029	0.002
Platelet inhibitors (excluding heparin)	4,450 (42.1%)	5,400 (45.2%)	3,160 (43.5%)	3,120 (42.9%)	0.061	0.012
Low -dose aspirin	4,270 (40.4%)	5,060 (42.4%)	3,000 (41.3%)	2,950 (40.6%)	0.039	0.016
ADP receptor blockers	330 (3.1%)	1,130 (9.5%)	320 (4.4%)	360 (4.9%)	0.264	0.025
Renin - angiotensin system inhibitors	4,430 (42.0%)	5,500 (46.0%)	3,090 (42.6%)	3,130 (43.0%)	0.082	0.009
Angiotensin - converting enzyme inhibitors	1,390 (13.2%)	2,500 (20.9%)	1,130 (15.6%)	1,130 (15.6%)	0.207	0.000
Angiotensin II antagonists, plain	1,460 (13.8%)	1,640 (13.7%)	990 (13.6%)	1,010 (13.8%)	0.003	0.008
Angiotensin II antagonists, combinations	1,600 (15.1%)	1,450 (12.2%)	990 (13.6%)	990 (13.7%)	0.087	0.002
Beta-blockers	6,730 (63.7%)	8,410 (70.4%)	4,780 (65.8%)	4,810 (66.1%)	0.143	0.007
Proton pump inhibitors	1,990 (18.8%)	2,690 (22.5%)	1,450 (20.0%)	1,480 (20.3%)	0.092	0.009
H2-receptor antagonists	150 (1.4%)	170 (1.4%)	100 (1.4%)	100 (1.3%)	0.005	0.005
Non-steroidal anti-inflammatory drugs	960 (9.1%)	910 (7.6%)	630 (8.6%)	590 (8.1%)	0.053	0.018
Statins	3,800 (36.0%)	5,020 (42.0%)	2,730 (37.6%)	2,760 (38.0%)	0.123	0.008
Antidiabetic agents	1,000 (9.5%)	1,400 (11.7%)	740 (10.2%)	750 (10.3%)	0.074	0.005
Loop diuretics	1,760 (16.6%)	3,390 (28.4%)	1,490 (20.5%)	1,510 (20.8%)	0.285	0.007
Non-loop diuretics	150 (1.4%)	230 (1.9%)	110 (1.6%)	110 (1.5%)	0.039	0.004
Alpha adrenergic blockers	610 (5.8%)	960 (8.0%)	470 (6.4%)	480 (6.6%)	0.089	0.009
Amiodarone	230 (2.1%)	700 (5.9%)	210 (2.9%)	220 (3.1%)	0.191	0.008
Dronedarone	70 (0.7%)	130 (1.1%)	60 (0.9%)	60 (0.8%)	0.046	0.003
Antihypertensive, combination drugs	1,850 (17.5%)	1,740 (14.6%)	1,170 (16.1%)	1,190 (16.3%)	0.080	0.006
Calcium channel blockers	2,190 (20.8%)	2,640 (22.1%)	1,560 (21.5%)	1,540 (21.2%)	0.033	0.007
Selective serotonin reuptake inhibitors	490 (4.6%)	530 (4.5%)	350 (4.8%)	330 (4.6%)	0.007	0.011
Drugs used in alcohol dependence	20 (0.2%)	20 (0.1%)	10 (0.2%)	10 (0.2%)	0.016	0.007
CHA2DS2-VASc, mean(SD)	2.9 (1.70)	3.3 (1.86)	3.1 (1.74)	3.1 (1.82)	0.185	0.009
CHA2DS2-VASc:0 -1	2,220 (21.0%)	2,240 (18.7%)	1,340 (18.5%)	1,500 (20.6%)	0.056	0.053
CHA2DS2-VASc:2 -3	4,690 (44.4%)	4,370 (36.6%)	3,040 (41.8%)	2,840 (39.0%)	0.159	0.058
CHA2DS2-VASc:>=4	3,660 (34.6%)	5,340 (44.7%)	2,890 (39.7%)	2,940 (40.4%)	0.206	0.015
CHADS2, mean(SD)	1.4 (1.26)	1.7 (1.35)	1.6 (1.29)	1.6 (1.33)	0.192	0.012
CHADS2:0	2,770 (26.2%)	2,530 (21.1%)	1,590 (21.9%)	1,770 (24.4%)	0.119	0.058
CHADS2:1	3,470 (32.8%)	3,480 (29.1%)	2,320 (31.9%)	2,210 (30.4%)	0.080	0.031
CHADS2:>=2	4,330 (41.0%)	5,940 (49.7%)	3,360 (46.3%)	3,290 (45.2%)	0.176	0.021
HAS-BLED, mean(SD)	2.0 (1.15)	2.1 (1.26)	2.1 (1.18)	2.1 (1.23)	0.132	0.004
HAS-BLED:<3	7,350 (69.6%)	7,410 (62.0%)	4,850 (66.8%)	4,690 (64.6%)	0.160	0.046

HAS-BLED:>=3	3,210 (30.4%)	4,540 (38.0%)	2,420 (33.2%)	2,580 (35.4%)	0.160	0.046
log_n_hosp, median(IQR)	0.7 (0.0 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.341	0.015
log_beddays, median(IQR)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	0.057	0.008
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.066	0.015

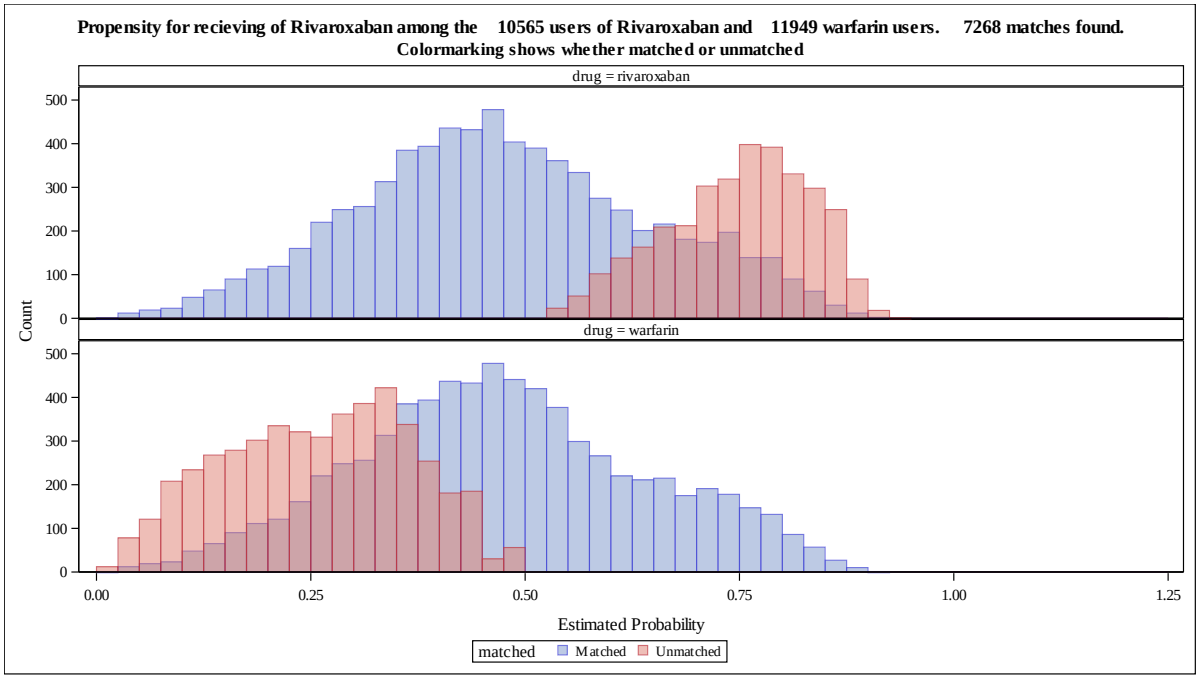
Propensity for recieving of Rivaroxaban among the 10565 users of Rivaroxaban and 11949 warfarin users. 7268 matches found.
Colormarking shows whether matched or unmatched
drug = rivaroxaban
drug = warfarin
Count
0
100
200
300
400
500
0.00
0.25
0.50
0.75
1.00
1.25
Estimated Probability
matched
Matched
Unmatched

Table 15.42 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin and standardised mean differences before and after matching, Sweden

Characteristic	Rivaroxaban (rounded) before matching N=14333	Warfarin (rounded) before matching N=47152	Rivaroxaban (rounded) after matching N=12794	Warfarin (rounded) after matching N=12794	Standardised mean difference before matching (max= 0.80)	Standardised mean difference after matching (max= 0.04)
index_year:2013	1,900 (13.2%)	22,380 (47.5%)	1,890 (14.8%)	1,940 (15.2%)	0.803	0.010
index_year:2014	3,810 (26.6%)	14,490 (30.7%)	3,810 (29.8%)	3,700 (28.9%)	0.092	0.019
index_year:2015	4,740 (33.1%)	7,040 (14.9%)	4,480 (35.0%)	4,500 (35.2%)	0.434	0.004
index_year:2016	3,890 (27.1%)	3,240 (6.9%)	2,620 (20.5%)	2,660 (20.8%)	0.560	0.008
Time from AF diag:< 1 month	8,440 (58.9%)	28,530 (60.5%)	7,660 (59.9%)	7,630 (59.6%)	0.033	0.005
Time from AF diag:1 - 6 month	1,310 (9.1%)	4,220 (9.0%)	1,140 (8.9%)	1,190 (9.3%)	0.005	0.013
Time from AF diag:6 - 60 months	4,590 (32.0%)	14,400 (30.5%)	3,990 (31.2%)	3,980 (31.1%)	0.032	0.002
Sex:Female	6,450 (45.0%)	20,290 (43.0%)	5,720 (44.7%)	5,760 (45.0%)	0.040	0.005
Sex:Male	7,880 (55.0%)	26,860 (57.0%)	7,070 (55.3%)	7,040 (55.0%)	0.040	0.005
Age, median(IQR)	74.9 (67.8 - 82.5)	75.6 (68.4 - 82.6)	75.1 (68.0 - 82.6)	75.3 (68.2 - 82.7)	0.015	0.012
Age -group:< 55 years	590 (4.1%)	2,130 (4.5%)	540 (4.3%)	510 (3.9%)	0.021	0.015
Age -group:55-<65 years	1,740 (12.1%)	5,540 (11.8%)	1,520 (11.9%)	1,590 (12.5%)	0.012	0.018
Age -group:65-<75 years	4,910 (34.2%)	14,880 (31.6%)	4,280 (33.5%)	4,170 (32.6%)	0.057	0.019
Age -group:75-<85 years	4,610 (32.2%)	16,570 (35.1%)	4,190 (32.8%)	4,200 (32.8%)	0.063	0.001
Age -group:>= 85 years	2,490 (17.3%)	8,030 (17.0%)	2,260 (17.6%)	2,320 (18.2%)	0.008	0.014
CCI-group:0	6,250 (43.6%)	17,670 (37.5%)	5,470 (42.8%)	5,310 (41.5%)	0.126	0.025
CCI-group:1-2	4,730 (33.0%)	15,790 (33.5%)	4,240 (33.1%)	4,260 (33.3%)	0.010	0.004
CCI-group:>=3	3,350 (23.4%)	13,700 (29.0%)	3,090 (24.1%)	3,220 (25.2%)	0.129	0.024
Prior bleeding (any)	1,510 (10.5%)	5,150 (10.9%)	1,360 (10.6%)	1,390 (10.8%)	0.012	0.007
Prior gastrointestinal bleeding	80 (0.5%)	360 (0.8%)	70 (0.5%)	80 (0.6%)	0.028	0.009
Prior intracranial bleeding	180 (1.3%)	410 (0.9%)	160 (1.2%)	150 (1.2%)	0.039	0.004
Prior stroke (any)	1,860 (12.9%)	6,200 (13.1%)	1,660 (13.0%)	1,700 (13.3%)	0.006	0.009
Prior ischaemic stroke	1,790 (12.5%)	6,080 (12.9%)	1,610 (12.6%)	1,650 (12.9%)	0.013	0.009
Prior haemorrhagic stroke	150 (1.1%)	330 (0.7%)	130 (1.0%)	120 (0.9%)	0.039	0.006
Prior systemic embolism	120 (0.9%)	510 (1.1%)	120 (0.9%)	130 (1.0%)	0.024	0.009
Prior transient ischaemic attack	610 (4.3%)	2,050 (4.3%)	540 (4.2%)	530 (4.1%)	0.004	0.005
Chronic kidney disease	390 (2.7%)	3,280 (7.0%)	380 (3.0%)	410 (3.2%)	0.200	0.010
Heart failure	2,710 (18.9%)	11,330 (24.0%)	2,530 (19.8%)	2,560 (20.0%)	0.125	0.006
Coronary artery disease	2,890 (20.1%)	12,460 (26.4%)	2,720 (21.2%)	2,810 (21.9%)	0.149	0.017
Peripheral arterial disease	720 (5.0%)	3,030 (6.4%)	660 (5.2%)	700 (5.5%)	0.062	0.013
Hypertension	10,250 (71.5%)	34,570 (73.3%)	9,200 (71.9%)	9,260 (72.4%)	0.040	0.010
Diabetes	2,540 (17.7%)	9,090 (19.3%)	2,290 (17.9%)	2,340 (18.3%)	0.040	0.012
Chronic obstructive pulmonary disease	1,660 (11.6%)	5,700 (12.1%)	1,500 (11.7%)	1,520 (11.9%)	0.016	0.005
Liver disease	110 (0.8%)	430 (0.9%)	100 (0.8%)	110 (0.9%)	0.016	0.008
Alcoholism	370 (2.6%)	1,030 (2.2%)	320 (2.5%)	330 (2.6%)	0.026	0.005
Dementia	400 (2.8%)	770 (1.6%)	340 (2.6%)	320 (2.5%)	0.080	0.006

Cancer 6 months before and including index date	100 (0.7%)	400 (0.9%)	90 (0.7%)	100 (0.8%)	0.021	0.005
Platelet inhibitors (excluding heparin)	5,700 (39.8%)	18,680 (39.6%)	5,110 (39.9%)	5,200 (40.6%)	0.004	0.015
Low -dose aspirin	5,140 (35.9%)	17,010 (36.1%)	4,610 (36.0%)	4,690 (36.7%)	0.004	0.014
ADP receptor blockers	840 (5.9%)	3,710 (7.9%)	790 (6.1%)	820 (6.4%)	0.078	0.010
Renin - angiotensin system inhibitors	6,880 (48.0%)	24,140 (51.2%)	6,220 (48.6%)	6,250 (48.9%)	0.064	0.005
Angiotensin - converting enzyme inhibitors	3,370 (23.5%)	13,490 (28.6%)	3,130 (24.5%)	3,100 (24.2%)	0.116	0.006
Angiotensin II antagonists, plain	2,460 (17.1%)	8,000 (17.0%)	2,200 (17.2%)	2,230 (17.4%)	0.004	0.006
Angiotensin II antagonists, combinations	910 (6.3%)	2,540 (5.4%)	780 (6.1%)	820 (6.4%)	0.041	0.012
Beta-blockers	10,580 (73.8%)	36,150 (76.7%)	9,530 (74.5%)	9,470 (74.0%)	0.066	0.011
Proton pump inhibitors	2,900 (20.2%)	10,150 (21.5%)	2,640 (20.6%)	2,650 (20.7%)	0.033	0.002
H2-receptor antagonists	60 (0.4%)	210 (0.4%)	50 (0.4%)	60 (0.5%)	0.004	0.005
Non-steroidal anti-inflammatory drugs	880 (6.1%)	2,970 (6.3%)	770 (6.0%)	790 (6.1%)	0.008	0.005
Statins	4,560 (31.8%)	16,730 (35.5%)	4,170 (32.6%)	4,190 (32.7%)	0.077	0.004
Antidiabetic agents	1,780 (12.4%)	6,350 (13.5%)	1,590 (12.4%)	1,650 (12.9%)	0.032	0.015
Loop diuretics	3,060 (21.4%)	12,990 (27.5%)	2,860 (22.3%)	2,940 (23.0%)	0.144	0.015
Non-loop diuretics	140 (1.0%)	650 (1.4%)	130 (1.0%)	150 (1.1%)	0.036	0.012
Alpha adrenergic blockers	3,270 (22.8%)	11,180 (23.7%)	2,950 (23.1%)	3,000 (23.4%)	0.021	0.008
Amiodarone	130 (0.9%)	890 (1.9%)	130 (1.0%)	120 (1.0%)	0.081	0.005
Dronedarone	70 (0.5%)	440 (0.9%)	70 (0.5%)	70 (0.6%)	0.053	0.006
Antihypertensive, combination drugs	1,360 (9.5%)	3,850 (8.2%)	1,180 (9.2%)	1,230 (9.6%)	0.047	0.014
Calcium channel blockers	3,470 (24.2%)	12,240 (26.0%)	3,120 (24.4%)	3,200 (25.0%)	0.041	0.015
Selective serotonin reuptake inhibitors	1,000 (7.0%)	3,110 (6.6%)	880 (6.9%)	870 (6.8%)	0.015	0.002
Drugs used in alcohol dependence	20 (0.2%)	60 (0.1%)	20 (0.2%)	20 (0.2%)	0.009	0.000
CHA2DS2-VASc, mean(SD)	3.4 (1.73)	3.6 (1.75)	3.4 (1.73)	3.5 (1.74)	0.095	0.020
CHA2DS2-VASc:0 -1	1,940 (13.5%)	5,700 (12.1%)	1,670 (13.1%)	1,650 (12.9%)	0.042	0.005
CHA2DS2-VASc:2 -3	5,860 (40.9%)	17,540 (37.2%)	5,170 (40.4%)	4,990 (39.0%)	0.075	0.029
CHA2DS2-VASc:>=4	6,540 (45.6%)	23,910 (50.7%)	5,950 (46.5%)	6,150 (48.1%)	0.102	0.032
CHADS2, mean(SD)	2.7 (1.46)	2.9 (1.47)	2.8 (1.46)	2.8 (1.47)	0.082	0.014
CHADS2:0	640 (4.4%)	2,300 (4.9%)	550 (4.3%)	670 (5.3%)	0.021	0.044
CHADS2:1	2,260 (15.8%)	6,040 (12.8%)	1,960 (15.3%)	1,770 (13.9%)	0.085	0.041
CHADS2:>=2	11,430 (79.8%)	38,810 (82.3%)	10,290 (80.4%)	10,350 (80.9%)	0.065	0.012
HAS-BLED, mean(SD)	1.9 (0.87)	1.9 (0.92)	1.9 (0.87)	1.9 (0.89)	0.079	0.009

HAS-BLED:<3	11,460 (80.0%)	36,080 (76.5%)	10,190 (79.6%)	10,100 (78.9%)	0.084	0.018
HAS-BLED:>=3	2,870 (20.0%)	11,080 (23.5%)	2,600 (20.4%)	2,700 (21.1%)	0.084	0.018
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.186	0.017
log_beddays, median(IQR)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.062	0.011
log_n_outpatient, median(IQR)	0.7 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.252	0.008
income, median(IQR), k€	52.1 (41.9 - 78.9)	49.8 (40.5 - 72.3)	51.6 (41.8 - 77.0)	51.4 (41.5 - 77.2)	0.056	0.001
education:Secondary compulsory	5,350 (37.3%)	18,850 (40.0%)	4,840 (37.8%)	4,850 (37.9%)	0.055	0.002
education:Vocational / High school	5,470 (38.2%)	18,480 (39.2%)	4,950 (38.7%)	4,950 (38.7%)	0.021	0.000
education:Higher education	3,340 (23.3%)	9,340 (19.8%)	2,850 (22.3%)	2,840 (22.2%)	0.085	0.002
education:Unknown	180 (1.2%)	490 (1.0%)	160 (1.2%)	160 (1.3%)	0.018	0.003

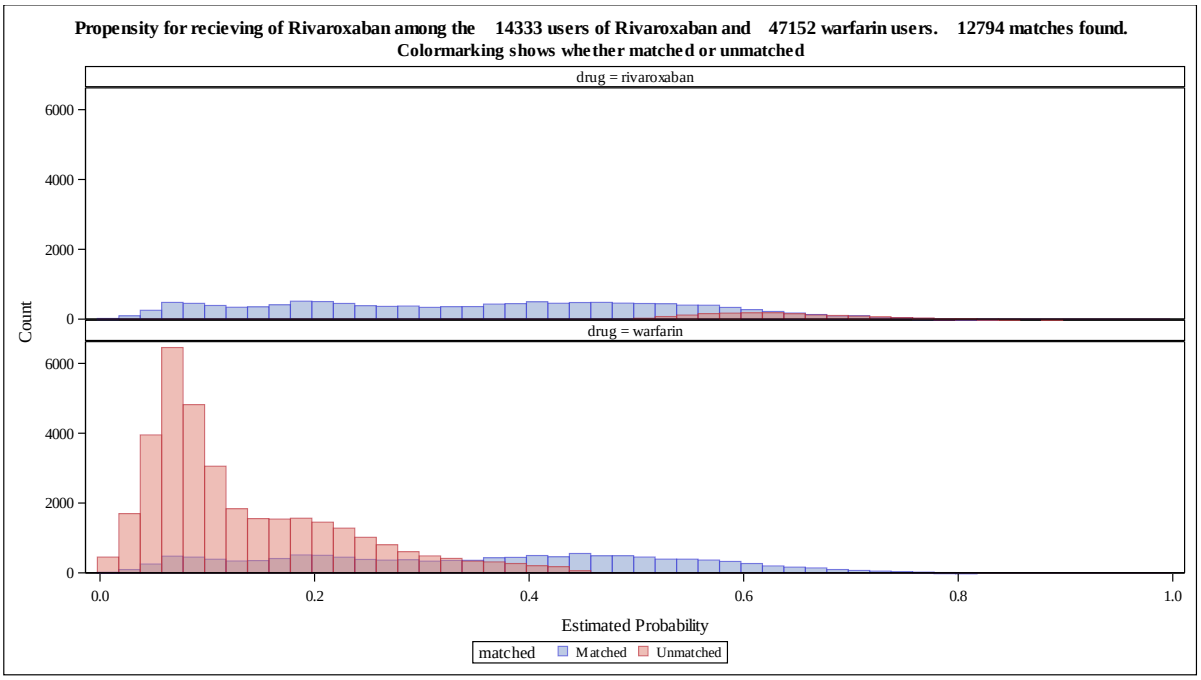

Table 15.43 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin in Denmark, Norway, or Sweden and standardised mean differences before and after matching – STANDARD DOSE

Characteristic	Apixaban (rounded) before matching N=50310	Warfarin (rounded) before matching N=79171	Apixaban (rounded) after matching N=42672	Warfarin (rounded) after matching N=42672	Standardised mean difference before matching (max= 0.29)	Standardised mean difference after matching (max= 0.03)
Time from AF diag:< 1 month	35,640 (70.8%)	47,550 (60.1%)	28,930 (67.8%)	28,860 (67.6%)	0.228	0.003
Time from AF diag:1 - 6 month	3,980 (7.9%)	7,970 (10.1%)	3,660 (8.6%)	3,670 (8.6%)	0.075	0.001
Time from AF diag:6 - 60 months	10,690 (21.2%)	23,650 (29.9%)	10,090 (23.6%)	10,140 (23.8%)	0.199	0.003
Sex:Female	20,060 (39.9%)	32,980 (41.7%)	16,980 (39.8%)	16,790 (39.3%)	0.036	0.009
Sex:Male	30,250 (60.1%)	46,190 (58.3%)	25,700 (60.2%)	25,880 (60.7%)	0.036	0.009
Age, median(IQR)	71.8 (65.8 - 77.8)	75.0 (67.5 - 82.2)	72.2 (65.9 - 78.5)	72.1 (66.0 - 78.4)	0.266	0.006
Age -group:< 55 years	3,220 (6.4%)	4,480 (5.7%)	2,740 (6.4%)	2,640 (6.2%)	0.031	0.010
Age -group:55-<65 years	7,990 (15.9%)	10,100 (12.8%)	6,620 (15.5%)	6,730 (15.8%)	0.089	0.007
Age -group:65-<75 years	20,970 (41.7%)	25,060 (31.6%)	16,810 (39.4%)	16,980 (39.8%)	0.209	0.008
Age -group:75-<85 years	14,600 (29.0%)	26,700 (33.7%)	13,010 (30.5%)	12,920 (30.3%)	0.102	0.004
Age -group:>= 85 years	3,550 (7.0%)	12,830 (16.2%)	3,490 (8.2%)	3,390 (7.9%)	0.289	0.009
CCI-group:0	22,970 (45.7%)	29,610 (37.4%)	18,970 (44.5%)	19,220 (45.0%)	0.168	0.012
CCI-group:1-2	17,280 (34.4%)	25,600 (32.3%)	14,710 (34.5%)	14,180 (33.2%)	0.043	0.026
CCI-group:>=3	10,060 (20.0%)	23,960 (30.3%)	9,000 (21.1%)	9,280 (21.7%)	0.239	0.016
Prior bleeding (any)	4,670 (9.3%)	8,870 (11.2%)	4,080 (9.6%)	4,070 (9.5%)	0.063	0.000
Prior gastrointestinal bleeding	340 (0.7%)	820 (1.0%)	320 (0.7%)	330 (0.8%)	0.040	0.004
Prior intracranial bleeding	450 (0.9%)	710 (0.9%)	380 (0.9%)	370 (0.9%)	0.000	0.002
Prior stroke (any)	5,800 (11.5%)	9,610 (12.1%)	4,930 (11.6%)	4,910 (11.5%)	0.019	0.002
Prior ischaemic stroke	5,630 (11.2%)	9,400 (11.9%)	4,790 (11.2%)	4,770 (11.2%)	0.021	0.002
Prior haemorrhagic stroke	340 (0.7%)	520 (0.7%)	300 (0.7%)	300 (0.7%)	0.002	0.001
Prior systemic embolism	220 (0.4%)	760 (1.0%)	210 (0.5%)	200 (0.5%)	0.063	0.003
Prior transient ischaemic attack	1,840 (3.7%)	3,120 (3.9%)	1,580 (3.7%)	1,540 (3.6%)	0.015	0.006
Chronic kidney disease	1,170 (2.3%)	6,530 (8.2%)	1,150 (2.7%)	1,150 (2.7%)	0.267	0.000
Heart failure	7,480 (14.9%)	18,010 (22.7%)	6,870 (16.1%)	6,870 (16.1%)	0.203	0.000
Coronary artery disease	9,310 (18.5%)	21,450 (27.1%)	8,480 (19.9%)	8,490 (19.9%)	0.206	0.000
Peripheral arterial disease	2,990 (5.9%)	6,030 (7.6%)	2,540 (6.0%)	2,580 (6.0%)	0.067	0.004
Hypertension	32,380 (64.4%)	54,110 (68.3%)	27,810 (65.2%)	27,900 (65.4%)	0.084	0.004
Diabetes	8,010 (15.9%)	14,680 (18.5%)	7,020 (16.4%)	7,050 (16.5%)	0.069	0.002
Chronic obstructive pulmonary disease	5,730 (11.4%)	10,120 (12.8%)	4,950 (11.6%)	4,880 (11.4%)	0.043	0.005
Liver disease	410 (0.8%)	820 (1.0%)	370 (0.9%)	380 (0.9%)	0.022	0.002
Alcoholism	1,380 (2.7%)	1,790 (2.3%)	1,130 (2.6%)	1,110 (2.6%)	0.031	0.002
Dementia	630 (1.3%)	1,220 (1.5%)	550 (1.3%)	560 (1.3%)	0.024	0.002

Cancer 6 months before and including index date	1,200 (2.4%)	2,140 (2.7%)	1,010 (2.4%)	970 (2.3%)	0.020	0.005
Platelet inhibitors (excluding heparin)	16,790 (33.4%)	30,840 (39.0%)	14,630 (34.3%)	14,850 (34.8%)	0.117	0.011
Low -dose aspirin	14,950 (29.7%)	27,180 (34.3%)	12,960 (30.4%)	13,160 (30.8%)	0.099	0.010
ADP receptor blockers	2,630 (5.2%)	7,100 (9.0%)	2,510 (5.9%)	2,540 (6.0%)	0.146	0.003
Renin - angiotensin system inhibitors	23,250 (46.2%)	38,070 (48.1%)	19,790 (46.4%)	19,790 (46.4%)	0.037	0.000
Angiotensin - converting enzyme inhibitors	10,680 (21.2%)	20,500 (25.9%)	9,640 (22.6%)	9,680 (22.7%)	0.110	0.002
Angiotensin II antagonists, plain	7,790 (15.5%)	11,850 (15.0%)	6,440 (15.1%)	6,410 (15.0%)	0.014	0.002
Angiotensin II antagonists, combinations	4,410 (8.8%)	5,210 (6.6%)	3,360 (7.9%)	3,330 (7.8%)	0.082	0.002
Beta-blockers	36,420 (72.4%)	56,980 (72.0%)	30,860 (72.3%)	30,860 (72.3%)	0.009	0.000
Proton pump inhibitors	9,670 (19.2%)	17,350 (21.9%)	8,300 (19.4%)	8,250 (19.3%)	0.066	0.003
Non-steroidal anti-inflammatory drugs	4,370 (8.7%)	5,860 (7.4%)	3,560 (8.3%)	3,580 (8.4%)	0.047	0.001
Statins	17,400 (34.6%)	28,740 (36.3%)	14,770 (34.6%)	14,820 (34.7%)	0.036	0.002
Antidiabetic agents	5,840 (11.6%)	10,410 (13.1%)	5,090 (11.9%)	5,120 (12.0%)	0.047	0.002
Loop diuretics	8,470 (16.8%)	22,170 (28.0%)	7,970 (18.7%)	7,910 (18.5%)	0.270	0.004
Non-loop diuretics	630 (1.3%)	1,230 (1.6%)	550 (1.3%)	530 (1.2%)	0.026	0.005
Alpha adrenergic blockers	8,390 (16.7%)	15,810 (20.0%)	7,620 (17.9%)	7,610 (17.8%)	0.085	0.001
Amiodarone	1,120 (2.2%)	2,560 (3.2%)	1,050 (2.5%)	1,030 (2.4%)	0.062	0.004
Dronedarone	620 (1.2%)	600 (0.8%)	430 (1.0%)	440 (1.0%)	0.048	0.002
Antihypertensive, combination drugs	5,990 (11.9%)	7,700 (9.7%)	4,730 (11.1%)	4,730 (11.1%)	0.070	0.000
Calcium channel blockers	11,570 (23.0%)	19,680 (24.9%)	9,950 (23.3%)	10,050 (23.5%)	0.044	0.005
Selective serotonin reuptake inhibitors	2,690 (5.3%)	4,790 (6.1%)	2,360 (5.5%)	2,290 (5.4%)	0.031	0.007
Drugs used in alcohol dependence	100 (0.2%)	120 (0.2%)	70 (0.2%)	80 (0.2%)	0.010	0.003
CHA2DS2-VASc, mean(SD)	2.9 (1.64)	3.4 (1.76)	3.0 (1.65)	3.0 (1.68)	0.276	0.006
CHA2DS2-VASc:0 -1	10,050 (20.0%)	11,520 (14.6%)	7,990 (18.7%)	8,170 (19.1%)	0.144	0.011
CHA2DS2-VASc:2 -3	23,000 (45.7%)	30,330 (38.3%)	19,140 (44.9%)	18,890 (44.3%)	0.151	0.012
CHA2DS2-VASc:>=4	17,260 (34.3%)	37,330 (47.1%)	15,540 (36.4%)	15,610 (36.6%)	0.263	0.004
CHADS2, mean(SD)	2.0 (1.42)	2.4 (1.51)	2.1 (1.42)	2.1 (1.43)	0.272	0.007
CHADS2:0	7,580 (15.1%)	8,300 (10.5%)	5,510 (12.9%)	5,880 (13.8%)	0.138	0.025
CHADS2:1	13,200 (26.2%)	15,840 (20.0%)	10,820 (25.3%)	10,380 (24.3%)	0.148	0.024
CHADS2:>=2	29,530 (58.7%)	55,030 (69.5%)	26,350 (61.7%)	26,420 (61.9%)	0.227	0.003
HAS-BLED, mean(SD)	1.8 (1.00)	2.0 (1.05)	1.8 (1.00)	1.8 (1.01)	0.188	0.001
HAS-BLED:<3	39,110 (77.7%)	56,150 (70.9%)	32,920 (77.2%)	32,770 (76.8%)	0.156	0.009

HAS-BLED:>=3	11,200 (22.3%)	23,020 (29.1%)	9,750 (22.8%)	9,900 (23.2%)	0.156	0.009
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.157	0.011
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.7 (0.0 - 1.6)	0.034	0.002
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.196	0.013

Table 15.44 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin in Denmark, Norway, or Sweden and standardised mean differences before and after matching – REDUCED DOSE

Characteristic	Apixaban (rounded) before matching N=21275	Warfarin (rounded) before matching N=79171	Apixaban (rounded) after matching N=18794	Warfarin (rounded) after matching N=18794	Standardised mean difference before matching (max= 1.07)	Standardised mean difference after matching (max= 0.03)
Time from AF diag:< 1 month	13,600 (63.9%)	47,550 (60.1%)	11,900 (63.3%)	11,830 (62.9%)	0.079	0.008
Time from AF diag:1 - 6 month	2,200 (10.3%)	7,970 (10.1%)	1,980 (10.6%)	2,020 (10.8%)	0.009	0.007
Time from AF diag:6 - 60 months	5,480 (25.8%)	23,650 (29.9%)	4,910 (26.1%)	4,940 (26.3%)	0.092	0.004
Sex:Female	12,850 (60.4%)	32,980 (41.7%)	10,900 (58.0%)	10,790 (57.4%)	0.382	0.012
Sex:Male	8,420 (39.6%)	46,190 (58.3%)	7,900 (42.0%)	8,010 (42.6%)	0.382	0.012
Age, median(IQR)	85.4 (80.5 - 89.7)	75.0 (67.5 - 82.2)	84.5 (79.9 - 88.7)	84.5 (80.0 - 88.5)	1.066	0.001
Age -group:< 55 years	110 (0.5%)	4,480 (5.7%)	110 (0.6%)	100 (0.5%)	0.302	0.006
Age -group:55-<65 years	430 (2.0%)	10,100 (12.8%)	430 (2.3%)	410 (2.2%)	0.419	0.006
Age -group:65-<75 years	1,920 (9.0%)	25,060 (31.6%)	1,920 (10.2%)	1,880 (10.0%)	0.586	0.007
Age -group:75-<85 years	7,730 (36.3%)	26,700 (33.7%)	7,530 (40.1%)	7,640 (40.7%)	0.055	0.012
Age -group:>= 85 years	11,090 (52.1%)	12,830 (16.2%)	8,810 (46.9%)	8,770 (46.6%)	0.818	0.005
CCI-group:0	5,440 (25.6%)	29,610 (37.4%)	5,000 (26.6%)	5,120 (27.2%)	0.256	0.014
CCI-group:1-2	7,260 (34.1%)	25,600 (32.3%)	6,440 (34.3%)	6,180 (32.9%)	0.038	0.030
CCI-group:>=3	8,570 (40.3%)	23,960 (30.3%)	7,350 (39.1%)	7,500 (39.9%)	0.211	0.016
Prior bleeding (any)	3,350 (15.7%)	8,870 (11.2%)	2,850 (15.2%)	2,860 (15.2%)	0.133	0.001
Prior gastrointestinal bleeding	330 (1.6%)	820 (1.0%)	280 (1.5%)	300 (1.6%)	0.047	0.009
Prior intracranial bleeding	450 (2.1%)	710 (0.9%)	340 (1.8%)	330 (1.7%)	0.100	0.005
Prior stroke (any)	4,250 (20.0%)	9,610 (12.1%)	3,480 (18.5%)	3,450 (18.3%)	0.214	0.005
Prior ischaemic stroke	4,110 (19.3%)	9,400 (11.9%)	3,380 (18.0%)	3,350 (17.8%)	0.206	0.004
Prior haemorrhagic stroke	350 (1.7%)	520 (0.7%)	260 (1.4%)	260 (1.4%)	0.094	0.000
Prior systemic embolism	180 (0.8%)	760 (1.0%)	170 (0.9%)	180 (1.0%)	0.014	0.007
Prior transient ischaemic attack	1,250 (5.9%)	3,120 (3.9%)	1,050 (5.6%)	1,020 (5.4%)	0.090	0.007
Chronic kidney disease	2,340 (11.0%)	6,530 (8.2%)	2,070 (11.0%)	2,200 (11.7%)	0.093	0.022
Heart failure	6,170 (29.0%)	18,010 (22.7%)	5,350 (28.5%)	5,350 (28.5%)	0.144	0.000
Coronary artery disease	6,270 (29.5%)	21,450 (27.1%)	5,640 (30.0%)	5,750 (30.6%)	0.053	0.013
Peripheral arterial disease	1,860 (8.7%)	6,030 (7.6%)	1,670 (8.9%)	1,690 (9.0%)	0.040	0.004
Hypertension	15,400 (72.4%)	54,110 (68.3%)	13,590 (72.3%)	13,670 (72.7%)	0.089	0.010
Diabetes	3,780 (17.7%)	14,680 (18.5%)	3,390 (18.0%)	3,470 (18.5%)	0.021	0.011
Chronic obstructive pulmonary disease	3,430 (16.1%)	10,120 (12.8%)	3,010 (16.0%)	3,070 (16.3%)	0.095	0.009
Liver disease	190 (0.9%)	820 (1.0%)	170 (0.9%)	170 (0.9%)	0.012	0.001
Alcoholism	390 (1.8%)	1,790 (2.3%)	350 (1.9%)	350 (1.8%)	0.029	0.001
Dementia	1,190 (5.6%)	1,220 (1.5%)	800 (4.3%)	770 (4.1%)	0.220	0.007
Cancer 6 months before and including index date	650 (3.0%)	2,140 (2.7%)	580 (3.1%)	610 (3.3%)	0.020	0.009

Platelet inhibitors (excluding heparin)	10,070 (47.3%)	30,840 (39.0%)	8,760 (46.6%)	8,900 (47.3%)	0.170	0.014
Low -dose aspirin	8,640 (40.6%)	27,180 (34.3%)	7,580 (40.3%)	7,690 (40.9%)	0.130	0.012
ADP receptor blockers	2,230 (10.5%)	7,100 (9.0%)	1,940 (10.3%)	2,010 (10.7%)	0.051	0.012
Renin - angiotensin system inhibitors	10,020 (47.1%)	38,070 (48.1%)	8,940 (47.6%)	8,920 (47.5%)	0.020	0.002
Angiotensin - converting enzyme inhibitors	5,210 (24.5%)	20,500 (25.9%)	4,660 (24.8%)	4,660 (24.8%)	0.032	0.001
Angiotensin II antagonists, plain	3,430 (16.1%)	11,850 (15.0%)	3,030 (16.1%)	2,980 (15.9%)	0.031	0.007
Angiotensin II antagonists, combinations	1,410 (6.6%)	5,210 (6.6%)	1,270 (6.8%)	1,290 (6.9%)	0.001	0.003
Beta-blockers	15,110 (71.0%)	56,980 (72.0%)	13,380 (71.2%)	13,380 (71.2%)	0.021	0.000
Proton pump inhibitors	5,960 (28.0%)	17,350 (21.9%)	5,080 (27.0%)	5,240 (27.9%)	0.142	0.019
Non-steroidal anti-inflammatory drugs	1,250 (5.9%)	5,860 (7.4%)	1,140 (6.0%)	1,130 (6.0%)	0.061	0.000
Statins	7,150 (33.6%)	28,740 (36.3%)	6,540 (34.8%)	6,610 (35.2%)	0.057	0.008
Antidiabetic agents	2,390 (11.2%)	10,410 (13.1%)	2,190 (11.6%)	2,240 (11.9%)	0.058	0.009
Loop diuretics	8,030 (37.7%)	22,170 (28.0%)	6,980 (37.2%)	7,040 (37.5%)	0.208	0.006
Non-loop diuretics	270 (1.3%)	1,230 (1.6%)	250 (1.3%)	270 (1.4%)	0.024	0.008
Alpha adrenergic blockers	4,150 (19.5%)	15,810 (20.0%)	3,730 (19.9%)	3,770 (20.0%)	0.011	0.005
Amiodarone	570 (2.7%)	2,560 (3.2%)	520 (2.8%)	530 (2.8%)	0.033	0.003
Dronedarone	60 (0.3%)	600 (0.8%)	50 (0.3%)	40 (0.2%)	0.068	0.016
Antihypertensive, combination drugs	1,940 (9.1%)	7,700 (9.7%)	1,760 (9.4%)	1,780 (9.5%)	0.020	0.003
Calcium channel blockers	5,430 (25.5%)	19,680 (24.9%)	4,800 (25.5%)	4,870 (25.9%)	0.015	0.008
Selective serotonin reuptake inhibitors	1,930 (9.1%)	4,790 (6.1%)	1,580 (8.4%)	1,550 (8.2%)	0.114	0.007
Drugs used in alcohol dependence	10 (0.1%)	120 (0.2%)	10 (0.1%)	10 (0.1%)	0.026	0.006
CHA2DS2-VASc, mean(SD)	4.4 (1.50)	3.4 (1.76)	4.3 (1.49)	4.3 (1.54)	0.619	0.006
CHA2DS2-VASc:0 -1	370 (1.7%)	11,520 (14.6%)	370 (2.0%)	450 (2.4%)	0.482	0.030
CHA2DS2-VASc:2 -3	5,430 (25.5%)	30,330 (38.3%)	5,040 (26.8%)	4,890 (26.0%)	0.276	0.018
CHA2DS2-VASc:>=4	15,470 (72.7%)	37,330 (47.1%)	13,380 (71.2%)	13,450 (71.6%)	0.541	0.008
CHADS2, mean(SD)	3.0 (1.44)	2.4 (1.51)	3.0 (1.43)	3.0 (1.44)	0.447	0.006
CHADS2:0	420 (2.0%)	8,300 (10.5%)	420 (2.3%)	440 (2.3%)	0.357	0.005
CHADS2:1	2,630 (12.4%)	15,840 (20.0%)	2,360 (12.6%)	2,290 (12.2%)	0.208	0.011
CHADS2:>=2	18,220 (85.6%)	55,030 (69.5%)	16,010 (85.2%)	16,060 (85.5%)	0.394	0.008
HAS-BLED, mean(SD)	2.4 (0.99)	2.0 (1.05)	2.4 (0.98)	2.4 (0.99)	0.388	0.012
HAS-BLED:<3	12,260 (57.6%)	56,150 (70.9%)	11,060 (58.8%)	10,960 (58.3%)	0.280	0.010
HAS-BLED:>=3	9,020 (42.4%)	23,020 (29.1%)	7,740 (41.2%)	7,830 (41.7%)	0.280	0.010
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.288	0.002

log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.045	0.016
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.302	0.007

Table 15.45 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin and standardised mean differences before and after matching, Denmark – STANDARD DOSE

Characteristic	Apixaban (rounded) before matching N= 9709	Warfarin (rounded) before matching N=20070	Apixaban (rounded) after matching N= 9373	Warfarin (rounded) after matching N= 9373	Standardised mean difference before matching (max= 0.30)	Standardised mean difference after matching (max= 0.06)
Time from AF diag:< 1 month	6,950 (71.6%)	12,620 (62.9%)	6,660 (71.0%)	6,650 (70.9%)	0.187	0.003
Time from AF diag:1 - 6 month	1,100 (11.3%)	2,410 (12.0%)	1,070 (11.4%)	1,050 (11.2%)	0.022	0.006
Time from AF diag:6 - 60 months	1,660 (17.1%)	5,040 (25.1%)	1,650 (17.6%)	1,680 (17.9%)	0.198	0.009
Sex:Female	3,860 (39.7%)	7,950 (39.6%)	3,710 (39.6%)	3,700 (39.5%)	0.002	0.001
Sex:Male	5,850 (60.3%)	12,120 (60.4%)	5,660 (60.4%)	5,670 (60.5%)	0.002	0.001
Age, median(IQR)	71.4 (65.5 - 77.1)	73.3 (66.1 - 80.6)	71.4 (65.5 - 77.3)	71.5 (65.7 - 77.2)	0.155	0.018
Age -group:< 55 years	630 (6.5%)	1,520 (7.6%)	620 (6.7%)	570 (6.0%)	0.043	0.025
Age -group:55-<65 years	1,600 (16.4%)	2,870 (14.3%)	1,550 (16.5%)	1,530 (16.3%)	0.059	0.006
Age -group:65-<75 years	4,230 (43.6%)	6,820 (34.0%)	4,000 (42.7%)	4,070 (43.4%)	0.198	0.014
Age -group:75-<85 years	2,640 (27.2%)	6,280 (31.3%)	2,590 (27.6%)	2,590 (27.7%)	0.089	0.001
Age -group:>= 85 years	610 (6.3%)	2,580 (12.9%)	610 (6.5%)	620 (6.6%)	0.226	0.005
CCI-group:0	4,490 (46.3%)	8,600 (42.8%)	4,400 (46.9%)	4,490 (47.9%)	0.069	0.020
CCI-group:1-2	3,420 (35.3%)	6,000 (29.9%)	3,260 (34.8%)	3,000 (32.0%)	0.114	0.058
CCI-group:>=3	1,790 (18.5%)	5,470 (27.2%)	1,720 (18.3%)	1,880 (20.1%)	0.210	0.044
Prior bleeding (any)	810 (8.3%)	1,940 (9.7%)	790 (8.4%)	780 (8.4%)	0.048	0.001
Prior gastrointestinal bleeding	80 (0.8%)	270 (1.4%)	80 (0.9%)	90 (0.9%)	0.051	0.007
Prior intracranial bleeding	90 (0.9%)	140 (0.7%)	90 (0.9%)	80 (0.9%)	0.025	0.002
Prior stroke (any)	1,430 (14.7%)	1,980 (9.8%)	1,240 (13.3%)	1,230 (13.1%)	0.149	0.005
Prior ischaemic stroke	1,400 (14.5%)	1,940 (9.7%)	1,220 (13.0%)	1,200 (12.8%)	0.147	0.005
Prior haemorrhagic stroke	60 (0.6%)	90 (0.4%)	60 (0.6%)	60 (0.6%)	0.031	0.001
Prior systemic embolism	40 (0.4%)	110 (0.5%)	40 (0.4%)	40 (0.4%)	0.024	0.005
Prior transient ischaemic attack	380 (3.9%)	600 (3.0%)	340 (3.6%)	320 (3.4%)	0.048	0.008
Chronic kidney disease	180 (1.8%)	1,690 (8.4%)	180 (1.9%)	160 (1.7%)	0.303	0.013
Heart failure	1,280 (13.2%)	3,570 (17.8%)	1,260 (13.4%)	1,300 (13.8%)	0.127	0.012
Coronary artery disease	1,540 (15.8%)	4,590 (22.9%)	1,510 (16.1%)	1,530 (16.3%)	0.179	0.006
Peripheral arterial disease	560 (5.7%)	1,630 (8.1%)	540 (5.8%)	560 (5.9%)	0.094	0.007
Hypertension	5,900 (60.7%)	12,270 (61.1%)	5,650 (60.3%)	5,710 (60.9%)	0.008	0.013
Diabetes	1,590 (16.4%)	3,490 (17.4%)	1,530 (16.3%)	1,540 (16.4%)	0.026	0.003
Chronic obstructive pulmonary disease	1,070 (11.0%)	2,570 (12.8%)	1,040 (11.1%)	1,070 (11.4%)	0.055	0.009
Liver disease	100 (1.0%)	240 (1.2%)	90 (1.0%)	100 (1.0%)	0.019	0.002
Alcoholism	340 (3.5%)	590 (2.9%)	310 (3.4%)	320 (3.4%)	0.033	0.004
Dementia	130 (1.3%)	220 (1.1%)	110 (1.2%)	120 (1.3%)	0.019	0.007
Cancer 6 months before and including index date	340 (3.5%)	930 (4.6%)	340 (3.6%)	320 (3.4%)	0.057	0.010

Platelet inhibitors (excluding heparin)	2,750 (28.3%)	6,760 (33.7%)	2,680 (28.6%)	2,740 (29.2%)	0.117	0.014
Low -dose aspirin	1,960 (20.2%)	5,110 (25.5%)	1,930 (20.6%)	2,000 (21.3%)	0.127	0.018
ADP receptor blockers	880 (9.1%)	2,260 (11.2%)	860 (9.1%)	850 (9.1%)	0.071	0.001
Renin - angiotensin system inhibitors	4,130 (42.5%)	8,420 (42.0%)	3,960 (42.3%)	3,950 (42.2%)	0.011	0.002
Angiotensin - converting enzyme inhibitors	1,980 (20.4%)	4,510 (22.5%)	1,930 (20.6%)	1,940 (20.7%)	0.050	0.003
Angiotensin II antagonists, plain	1,240 (12.8%)	2,220 (11.0%)	1,160 (12.4%)	1,120 (12.0%)	0.053	0.012
Angiotensin II antagonists, combinations	680 (7.0%)	1,210 (6.0%)	650 (7.0%)	640 (6.8%)	0.038	0.006
Beta-blockers	6,210 (64.0%)	12,420 (61.9%)	5,980 (63.8%)	5,990 (63.9%)	0.043	0.002
Proton pump inhibitors	1,850 (19.1%)	4,510 (22.5%)	1,790 (19.1%)	1,790 (19.1%)	0.084	0.001
Non-steroidal anti-inflammatory drugs	990 (10.2%)	1,980 (9.9%)	960 (10.2%)	990 (10.6%)	0.012	0.013
Statins	3,360 (34.6%)	6,990 (34.8%)	3,200 (34.1%)	3,230 (34.5%)	0.004	0.007
Antidiabetic agents	1,270 (13.1%)	2,650 (13.2%)	1,210 (12.9%)	1,220 (13.0%)	0.004	0.003
Loop diuretics	1,890 (19.5%)	5,800 (28.9%)	1,870 (20.0%)	1,880 (20.1%)	0.220	0.003
Non-loop diuretics	120 (1.2%)	350 (1.7%)	120 (1.2%)	120 (1.2%)	0.043	0.001
Alpha adrenergic blockers	1,590 (16.4%)	3,670 (18.3%)	1,550 (16.5%)	1,500 (16.0%)	0.050	0.014
Amiodarone	320 (3.3%)	970 (4.9%)	320 (3.4%)	310 (3.3%)	0.081	0.004
Dronedarone	10 (0.1%)	30 (0.1%)	10 (0.1%)	10 (0.1%)	0.013	0.008
Antihypertensive, combination drugs	1,120 (11.5%)	2,110 (10.5%)	1,070 (11.4%)	1,080 (11.5%)	0.031	0.002
Calcium channel blockers	2,160 (22.2%)	4,790 (23.9%)	2,090 (22.3%)	2,120 (22.6%)	0.040	0.007
Selective serotonin reuptake inhibitors	550 (5.7%)	1,150 (5.7%)	520 (5.5%)	490 (5.2%)	0.003	0.011
Drugs used in alcohol dependence	30 (0.3%)	50 (0.2%)	20 (0.2%)	30 (0.3%)	0.007	0.006
CHA2DS2-VASc, mean(SD)	3.0 (1.62)	3.1 (1.67)	2.9 (1.62)	2.9 (1.65)	0.091	0.008
CHA2DS2-VASc:0 -1	1,880 (19.4%)	3,580 (17.8%)	1,850 (19.8%)	1,850 (19.7%)	0.040	0.002
CHA2DS2-VASc:2 -3	4,420 (45.5%)	8,410 (41.9%)	4,310 (45.9%)	4,300 (45.9%)	0.073	0.001
CHA2DS2-VASc:>=4	3,410 (35.1%)	8,080 (40.2%)	3,210 (34.3%)	3,230 (34.4%)	0.107	0.003
CHADS2, mean(SD)	1.6 (1.23)	1.6 (1.21)	1.6 (1.21)	1.6 (1.23)	0.050	0.001
CHADS2:0	1,860 (19.2%)	3,470 (17.3%)	1,830 (19.6%)	1,870 (19.9%)	0.050	0.008
CHADS2:1	3,320 (34.1%)	6,320 (31.5%)	3,240 (34.5%)	3,200 (34.2%)	0.057	0.007
CHADS2:>=2	4,530 (46.7%)	10,280 (51.2%)	4,300 (45.9%)	4,300 (45.9%)	0.092	0.000
HAS-BLED, mean(SD)	2.0 (1.11)	2.1 (1.17)	2.0 (1.11)	2.0 (1.12)	0.078	0.015
HAS-BLED:<3	6,490 (66.8%)	12,660 (63.1%)	6,320 (67.5%)	6,250 (66.7%)	0.078	0.016
HAS-BLED:>=3	3,220 (33.2%)	7,410 (36.9%)	3,050 (32.5%)	3,120 (33.3%)	0.078	0.016
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.036	0.008
log_beddays, median(IQR)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.9)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.8)	0.143	0.005
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.074	0.015
income, median(IQR), k€	140.6 (100.7 - 221.9)	122.8 (88.9 - 187.6)	139.1 (100.0 - 218.3)	138.1 (99.5 - 218.2)	0.142	0.004

education:Secondary compulsory	3,240 (33.4%)	8,430 (42.0%)	3,200 (34.1%)	3,200 (34.1%)	0.178	0.000
education:Vocational / High school	4,300 (44.3%)	8,140 (40.6%)	4,140 (44.2%)	4,180 (44.6%)	0.076	0.009
education:Higher education	1,960 (20.2%)	2,980 (14.8%)	1,830 (19.5%)	1,780 (19.0%)	0.140	0.014
education:Unknown	200 (2.1%)	520 (2.6%)	200 (2.1%)	210 (2.3%)	0.033	0.007
employment:Employed or self - employed	2,180 (22.4%)	3,720 (18.5%)	2,090 (22.3%)	2,040 (21.8%)	0.097	0.012
employment:Unemployed	530 (5.5%)	1,190 (5.9%)	520 (5.5%)	490 (5.3%)	0.020	0.012
employment:Retired	6,890 (71.0%)	15,010 (74.8%)	6,670 (71.1%)	6,750 (72.0%)	0.086	0.018
employment:Unknown	110 (1.1%)	150 (0.7%)	100 (1.0%)	90 (1.0%)	0.037	0.005

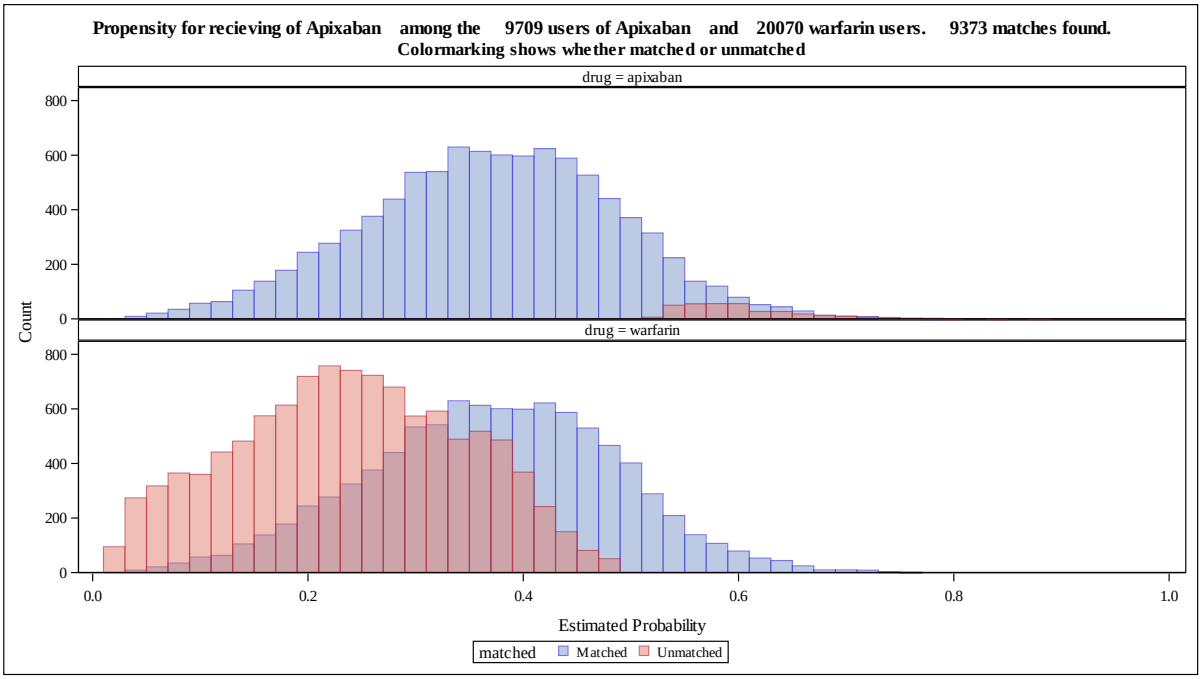

Table 15.46 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin and standardised mean differences before and after matching, Denmark – REDUCED DOSE

Characteristic	Apixaban (rounded) before matching N= 5271	Warfarin (rounded) before matching N=20070	Apixaban (rounded) after matching N= 4596	Warfarin (rounded) after matching N= 4596	Standardised mean difference before matching (max= 1.18)	Standardised mean difference after matching (max= 0.07)
Time from AF diag:< 1 month	3,540 (67.1%)	12,620 (62.9%)	3,100 (67.5%)	3,120 (67.8%)	0.089	0.006
Time from AF diag:1 - 6 month	570 (10.7%)	2,410 (12.0%)	510 (11.1%)	510 (11.1%)	0.041	0.000
Time from AF diag:6 - 60 months	1,170 (22.2%)	5,040 (25.1%)	980 (21.3%)	970 (21.1%)	0.070	0.006
Sex:Female	3,250 (61.7%)	7,950 (39.6%)	2,690 (58.4%)	2,700 (58.7%)	0.453	0.005
Sex:Male	2,020 (38.3%)	12,120 (60.4%)	1,910 (41.6%)	1,900 (41.3%)	0.453	0.005
Age, median(IQR)	85.0 (80.2 - 89.6)	73.3 (66.1 - 80.6)	84.0 (79.4 - 88.2)	84.0 (79.5 - 88.1)	1.181	0.006
Age -group:< 55 years	30 (0.5%)	1,520 (7.6%)	30 (0.5%)	30 (0.7%)	0.368	0.014
Age -group:55-<65 years	120 (2.2%)	2,870 (14.3%)	120 (2.5%)	90 (2.0%)	0.451	0.034
Age -group:65-<75 years	520 (9.8%)	6,820 (34.0%)	520 (11.3%)	520 (11.4%)	0.610	0.003
Age -group:75-<85 years	1,970 (37.3%)	6,280 (31.3%)	1,920 (41.8%)	1,930 (41.9%)	0.128	0.003
Age -group:>= 85 years	2,640 (50.2%)	2,580 (12.9%)	2,020 (43.8%)	2,020 (44.0%)	0.877	0.004
CCI-group:0	1,540 (29.2%)	8,600 (42.8%)	1,410 (30.7%)	1,490 (32.5%)	0.288	0.037
CCI-group:1-2	1,910 (36.3%)	6,000 (29.9%)	1,680 (36.5%)	1,520 (33.2%)	0.136	0.070
CCI-group:>=3	1,820 (34.5%)	5,470 (27.2%)	1,510 (32.8%)	1,580 (34.4%)	0.159	0.034
Prior bleeding (any)	720 (13.7%)	1,940 (9.7%)	600 (13.1%)	600 (13.1%)	0.124	0.001
Prior gastrointestinal bleeding	120 (2.2%)	270 (1.4%)	100 (2.1%)	110 (2.3%)	0.065	0.015
Prior intracranial bleeding	110 (2.1%)	140 (0.7%)	80 (1.7%)	80 (1.6%)	0.118	0.003
Prior stroke (any)	1,110 (21.1%)	1,980 (9.8%)	830 (18.1%)	820 (17.7%)	0.315	0.009
Prior ischaemic stroke	1,090 (20.7%)	1,940 (9.7%)	820 (17.8%)	800 (17.4%)	0.310	0.009
Prior haemorrhagic stroke	70 (1.3%)	90 (0.4%)	50 (1.1%)	50 (1.0%)	0.096	0.009
Prior systemic embolism	30 (0.5%)	110 (0.5%)	30 (0.6%)	30 (0.7%)	0.000	0.011
Prior transient ischaemic attack	230 (4.4%)	600 (3.0%)	200 (4.3%)	170 (3.8%)	0.076	0.025
Chronic kidney disease	420 (8.0%)	1,690 (8.4%)	400 (8.6%)	410 (8.9%)	0.015	0.010
Heart failure	1,090 (20.8%)	3,570 (17.8%)	950 (20.6%)	970 (21.0%)	0.076	0.010
Coronary artery disease	1,180 (22.3%)	4,590 (22.9%)	1,070 (23.2%)	1,070 (23.3%)	0.013	0.004
Peripheral arterial disease	480 (9.2%)	1,630 (8.1%)	440 (9.6%)	460 (10.0%)	0.038	0.015
Hypertension	3,610 (68.5%)	12,270 (61.1%)	3,130 (68.0%)	3,120 (68.0%)	0.155	0.001
Diabetes	920 (17.5%)	3,490 (17.4%)	810 (17.7%)	820 (17.8%)	0.003	0.002
Chronic obstructive pulmonary disease	910 (17.2%)	2,570 (12.8%)	790 (17.2%)	810 (17.6%)	0.123	0.011
Liver disease	60 (1.2%)	240 (1.2%)	50 (1.2%)	50 (1.1%)	0.002	0.004
Alcoholism	140 (2.6%)	590 (2.9%)	120 (2.7%)	110 (2.5%)	0.018	0.015
Dementia	320 (6.0%)	220 (1.1%)	170 (3.7%)	160 (3.6%)	0.268	0.009
Cancer 6 months before and including index date	250 (4.7%)	930 (4.6%)	230 (5.0%)	240 (5.2%)	0.005	0.010
Platelet inhibitors (excluding heparin)	2,120 (40.2%)	6,760 (33.7%)	1,830 (39.9%)	1,840 (40.0%)	0.134	0.003
Low -dose aspirin	1,460 (27.7%)	5,110 (25.5%)	1,300 (28.3%)	1,300 (28.3%)	0.051	0.000

ADP receptor blockers	800 (15.2%)	2,260 (11.2%)	660 (14.3%)	680 (14.9%)	0.117	0.015
Renin - angiotensin system inhibitors	2,160 (40.9%)	8,420 (42.0%)	1,920 (41.9%)	1,910 (41.6%)	0.021	0.006
Angiotensin - converting enzyme inhibitors	1,110 (21.1%)	4,510 (22.5%)	990 (21.5%)	1,000 (21.8%)	0.034	0.006
Angiotensin II antagonists, plain	680 (12.9%)	2,220 (11.0%)	590 (12.9%)	570 (12.4%)	0.057	0.016
Angiotensin II antagonists, combinations	300 (5.6%)	1,210 (6.0%)	280 (6.0%)	290 (6.3%)	0.019	0.012
Beta-blockers	3,180 (60.4%)	12,420 (61.9%)	2,790 (60.7%)	2,810 (61.0%)	0.031	0.006
Proton pump inhibitors	1,590 (30.1%)	4,510 (22.5%)	1,330 (28.9%)	1,370 (29.9%)	0.174	0.022
Non-steroidal anti-inflammatory drugs	410 (7.8%)	1,980 (9.9%)	380 (8.2%)	380 (8.2%)	0.074	0.002
Statins	1,680 (31.9%)	6,990 (34.8%)	1,530 (33.3%)	1,540 (33.6%)	0.062	0.006
Antidiabetic agents	620 (11.7%)	2,650 (13.2%)	560 (12.2%)	560 (12.1%)	0.047	0.001
Loop diuretics	2,080 (39.5%)	5,800 (28.9%)	1,800 (39.1%)	1,790 (39.0%)	0.225	0.003
Non-loop diuretics	60 (1.1%)	350 (1.7%)	60 (1.2%)	50 (1.2%)	0.052	0.004
Alpha adrenergic blockers	1,070 (20.3%)	3,670 (18.3%)	950 (20.6%)	940 (20.5%)	0.052	0.004
Amiodarone	240 (4.6%)	970 (4.9%)	220 (4.7%)	230 (4.9%)	0.011	0.010
Dronedarone	<5	30 (0.1%)	<5	<5	0.030	0.012
Antihypertensive, combination drugs	490 (9.2%)	2,110 (10.5%)	450 (9.8%)	460 (10.0%)	0.044	0.007
Calcium channel blockers	1,280 (24.2%)	4,790 (23.9%)	1,120 (24.3%)	1,130 (24.5%)	0.008	0.004
Selective serotonin reuptake inhibitors	520 (9.8%)	1,150 (5.7%)	410 (8.9%)	400 (8.8%)	0.152	0.005
Drugs used in alcohol dependence	<5	50 (0.2%)	<5	<5	0.055	0.000
CHA2DS2-VASc, mean(SD)	4.3 (1.45)	3.1 (1.67)	4.2 (1.43)	4.2 (1.47)	0.759	0.004
CHA2DS2-VASc:0 -1	100 (1.9%)	3,580 (17.8%)	100 (2.2%)	120 (2.5%)	0.555	0.024
CHA2DS2-VASc:2 -3	1,440 (27.3%)	8,410 (41.9%)	1,350 (29.5%)	1,320 (28.7%)	0.311	0.016
CHA2DS2-VASc:>=4	3,730 (70.8%)	8,080 (40.2%)	3,140 (68.4%)	3,160 (68.7%)	0.646	0.008
CHADS2, mean(SD)	2.4 (1.20)	1.6 (1.21)	2.3 (1.17)	2.3 (1.19)	0.640	0.002
CHADS2:0	140 (2.6%)	3,470 (17.3%)	140 (3.0%)	160 (3.4%)	0.505	0.023
CHADS2:1	960 (18.3%)	6,320 (31.5%)	880 (19.1%)	870 (19.0%)	0.309	0.004
CHADS2:>=2	4,170 (79.1%)	10,280 (51.2%)	3,580 (77.9%)	3,570 (77.6%)	0.612	0.006
HAS-BLED, mean(SD)	2.6 (1.07)	2.1 (1.17)	2.5 (1.07)	2.5 (1.08)	0.406	0.001
HAS-BLED:<3	2,580 (48.9%)	12,660 (63.1%)	2,320 (50.4%)	2,310 (50.3%)	0.288	0.002
HAS-BLED:>=3	2,690 (51.1%)	7,410 (36.9%)	2,280 (49.6%)	2,290 (49.7%)	0.288	0.002
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.327	0.019
log_beddays, median(IQR)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.9)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.8)	0.154	0.002
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.166	0.034
income, median(IQR), k€	97.3 (77.9 - 127.7)	122.8 (88.9 - 187.6)	98.9 (78.3 - 131.0)	97.7 (77.5 - 128.7)	0.301	0.006
education:Secondary compulsory	2,570 (48.8%)	8,430 (42.0%)	2,310 (50.3%)	2,340 (50.9%)	0.136	0.011
education:Vocational / High school	1,610 (30.5%)	8,140 (40.6%)	1,450 (31.6%)	1,460 (31.8%)	0.210	0.004
education:Higher education	670 (12.7%)	2,980 (14.8%)	580 (12.6%)	560 (12.2%)	0.063	0.013
education:Unknown	420 (8.0%)	520 (2.6%)	250 (5.4%)	230 (5.1%)	0.244	0.014

employment:Employed or self - employed	150 (2.9%)	3,720 (18.5%)	150 (3.3%)	170 (3.7%)	0.521	0.021
employment:Unemployed	70 (1.3%)	1,190 (5.9%)	70 (1.5%)	60 (1.2%)	0.250	0.021
employment:Retired	5,040 (95.7%)	15,010 (74.8%)	4,370 (95.1%)	4,360 (95.0%)	0.615	0.007
employment:Unknown	10 (0.1%)	150 (0.7%)	10 (0.1%)	10 (0.1%)	0.096	0.000

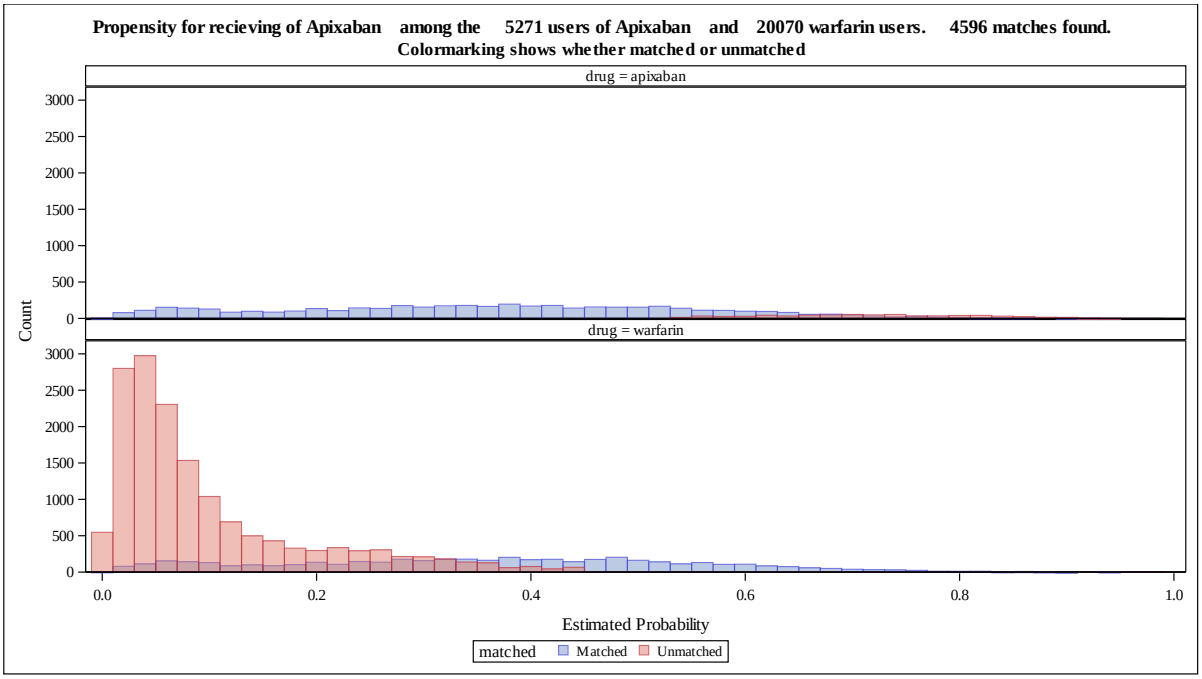
Propensity for recieving of Apixaban among the 5271 users of Apixaban and 20070 warfarin users. 4596 matches found.
Colormarking shows whether matched or unmatched
drug = apixaban
drug = warfarin
Count
3000
2500
2000
1500
1000
500
0
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.47 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin and standardised mean differences before and after matching, Norway – STANDARD DOSE

Characteristic	Apixaban (rounded) before matching N=12963	Warfarin (rounded) before matching N=11949	Apixaban (rounded) after matching N= 8456	Warfarin (rounded) after matching N= 8456	Standardised mean difference before matching (max= 0.41)	Standardised mean difference after matching (max= 0.06)
Time from AF diag:< 1 month	9,440 (72.8%)	6,410 (53.6%)	5,290 (62.5%)	5,280 (62.5%)	0.405	0.001
Time from AF diag:1 - 6 month	910 (7.0%)	1,340 (11.2%)	770 (9.1%)	770 (9.1%)	0.147	0.002
Time from AF diag:6 - 60 months	2,620 (20.2%)	4,200 (35.2%)	2,400 (28.4%)	2,400 (28.4%)	0.339	0.000
Sex:Female	5,110 (39.4%)	4,740 (39.7%)	3,260 (38.5%)	3,260 (38.5%)	0.006	0.000
Sex:Male	7,860 (60.6%)	7,210 (60.3%)	5,200 (61.5%)	5,200 (61.5%)	0.006	0.000
Age, median(IQR)	71.6 (65.5 - 78.0)	75.3 (66.7 - 83.2)	72.7 (65.5 - 80.3)	72.9 (65.6 - 80.2)	0.249	0.004
Age -group:< 55 years	900 (6.9%)	830 (7.0%)	650 (7.6%)	600 (7.1%)	0.002	0.022
Age -group:55-<65 years	2,110 (16.3%)	1,690 (14.2%)	1,340 (15.8%)	1,390 (16.4%)	0.059	0.016
Age -group:65-<75 years	5,310 (40.9%)	3,360 (28.1%)	2,870 (34.0%)	2,890 (34.2%)	0.273	0.005
Age -group:75-<85 years	3,660 (28.2%)	3,860 (32.3%)	2,650 (31.4%)	2,640 (31.3%)	0.088	0.002
Age -group:>= 85 years	990 (7.7%)	2,210 (18.5%)	950 (11.3%)	940 (11.1%)	0.326	0.005
CCI-group:0	5,160 (39.8%)	3,340 (27.9%)	2,900 (34.3%)	2,860 (33.8%)	0.254	0.010
CCI-group:1-2	4,570 (35.2%)	3,810 (31.9%)	3,000 (35.4%)	2,910 (34.4%)	0.071	0.021
CCI-group:>=3	3,230 (24.9%)	4,800 (40.2%)	2,560 (30.2%)	2,680 (31.7%)	0.330	0.032
Prior bleeding (any)	1,380 (10.7%)	1,780 (14.9%)	1,040 (12.3%)	1,040 (12.2%)	0.127	0.002
Prior gastrointestinal bleeding	100 (0.8%)	190 (1.6%)	90 (1.1%)	80 (1.0%)	0.073	0.009
Prior intracranial bleeding	120 (0.9%)	160 (1.3%)	90 (1.1%)	90 (1.1%)	0.039	0.001
Prior stroke (any)	1,370 (10.5%)	1,440 (12.0%)	950 (11.2%)	950 (11.3%)	0.047	0.003
Prior ischaemic stroke	1,330 (10.3%)	1,380 (11.5%)	920 (10.8%)	920 (10.9%)	0.041	0.003
Prior haemorrhagic stroke	70 (0.5%)	110 (0.9%)	60 (0.7%)	60 (0.7%)	0.042	0.004
Prior systemic embolism	50 (0.4%)	140 (1.2%)	50 (0.5%)	40 (0.5%)	0.091	0.007
Prior transient ischaemic attack	470 (3.6%)	460 (3.9%)	330 (3.8%)	310 (3.6%)	0.015	0.011
Chronic kidney disease	520 (4.0%)	1,560 (13.1%)	510 (6.0%)	560 (6.6%)	0.327	0.025
Heart failure	1,980 (15.2%)	3,110 (26.0%)	1,640 (19.3%)	1,680 (19.9%)	0.269	0.013
Coronary artery disease	2,980 (23.0%)	4,410 (36.9%)	2,420 (28.7%)	2,460 (29.1%)	0.307	0.010
Peripheral arterial disease	1,150 (8.9%)	1,370 (11.5%)	810 (9.6%)	840 (9.9%)	0.086	0.010
Hypertension	7,430 (57.3%)	7,270 (60.8%)	4,910 (58.0%)	4,940 (58.4%)	0.072	0.007
Diabetes	1,870 (14.4%)	2,100 (17.6%)	1,320 (15.6%)	1,330 (15.7%)	0.088	0.002
Chronic obstructive pulmonary disease	1,780 (13.7%)	1,850 (15.5%)	1,270 (15.0%)	1,210 (14.4%)	0.050	0.017

Liver disease	110 (0.8%)	150 (1.3%)	90 (1.0%)	80 (0.9%)	0.045	0.010
Alcoholism	260 (2.0%)	170 (1.4%)	140 (1.7%)	140 (1.6%)	0.046	0.003
Dementia	160 (1.2%)	230 (1.9%)	130 (1.5%)	130 (1.5%)	0.054	0.002
Cancer 6 months before and including index date	710 (5.5%)	810 (6.8%)	520 (6.1%)	500 (5.9%)	0.054	0.008
Platelet inhibitors (excluding heparin)	5,020 (38.7%)	5,400 (45.2%)	3,580 (42.4%)	3,600 (42.5%)	0.130	0.004
Low -dose aspirin	4,770 (36.8%)	5,060 (42.4%)	3,380 (40.0%)	3,390 (40.1%)	0.113	0.002
ADP receptor blockers	480 (3.7%)	1,130 (9.5%)	460 (5.4%)	480 (5.6%)	0.234	0.009
Renin - angiotensin system inhibitors	5,790 (44.6%)	5,500 (46.0%)	3,740 (44.2%)	3,790 (44.9%)	0.028	0.014
Angiotensin - converting enzyme inhibitors	1,960 (15.1%)	2,500 (20.9%)	1,470 (17.4%)	1,500 (17.8%)	0.151	0.010
Angiotensin II antagonists, plain	1,920 (14.8%)	1,640 (13.7%)	1,150 (13.6%)	1,180 (14.0%)	0.032	0.009
Angiotensin II antagonists, combinations	1,960 (15.1%)	1,450 (12.2%)	1,150 (13.6%)	1,160 (13.7%)	0.086	0.004
Beta-blockers	8,920 (68.8%)	8,410 (70.4%)	5,860 (69.3%)	5,870 (69.4%)	0.035	0.003
Proton pump inhibitors	2,460 (19.0%)	2,690 (22.5%)	1,670 (19.8%)	1,700 (20.1%)	0.088	0.007
H2-receptor antagonists	150 (1.2%)	170 (1.4%)	100 (1.2%)	110 (1.2%)	0.018	0.002
Non-steroidal anti-inflammatory drugs	1,280 (9.9%)	910 (7.6%)	740 (8.8%)	730 (8.6%)	0.081	0.007
Statins	4,960 (38.3%)	5,020 (42.0%)	3,340 (39.5%)	3,380 (40.0%)	0.076	0.009
Antidiabetic agents	1,280 (9.9%)	1,400 (11.7%)	890 (10.5%)	900 (10.7%)	0.060	0.005
Loop diuretics	1,970 (15.2%)	3,390 (28.4%)	1,690 (20.0%)	1,710 (20.2%)	0.323	0.007
Non-loop diuretics	200 (1.6%)	230 (1.9%)	150 (1.7%)	140 (1.6%)	0.029	0.006
Alpha adrenergic blockers	770 (5.9%)	960 (8.0%)	570 (6.8%)	600 (7.1%)	0.083	0.015
Amiodarone	480 (3.7%)	700 (5.9%)	420 (4.9%)	410 (4.8%)	0.102	0.007
Dronedarone	240 (1.9%)	130 (1.1%)	110 (1.3%)	120 (1.4%)	0.064	0.007
Antihypertensive, combination drugs	2,260 (17.5%)	1,740 (14.6%)	1,350 (16.0%)	1,360 (16.1%)	0.079	0.004
Calcium channel blockers	2,700 (20.9%)	2,640 (22.1%)	1,770 (21.0%)	1,780 (21.1%)	0.031	0.002
Selective serotonin reuptake inhibitors	490 (3.8%)	530 (4.5%)	340 (4.1%)	340 (4.0%)	0.035	0.004
Drugs used in alcohol dependence	20 (0.2%)	20 (0.1%)	10 (0.1%)	10 (0.2%)	0.010	0.006
CHA2DS2-VASc, mean(SD)	2.7 (1.63)	3.3 (1.86)	2.9 (1.70)	2.9 (1.77)	0.309	0.010
CHA2DS2-VASc:0 -1	3,120 (24.1%)	2,240 (18.7%)	1,800 (21.3%)	1,910 (22.5%)	0.131	0.031
CHA2DS2-VASc:2 -3	6,020 (46.5%)	4,370 (36.6%)	3,740 (44.3%)	3,470 (41.1%)	0.201	0.065
CHA2DS2-VASc:>=4	3,820 (29.4%)	5,340 (44.7%)	2,920 (34.5%)	3,080 (36.4%)	0.320	0.040
CHADS2, mean(SD)	1.3 (1.22)	1.7 (1.35)	1.5 (1.26)	1.5 (1.28)	0.301	0.003

CHADS2:0	3,900 (30.1%)	2,530 (21.1%)	2,130 (25.1%)	2,210 (26.1%)	0.207	0.022
CHADS2:1	4,370 (33.7%)	3,480 (29.1%)	2,820 (33.4%)	2,700 (31.9%)	0.099	0.032
CHADS2:>=2	4,690 (36.1%)	5,940 (49.7%)	3,510 (41.5%)	3,560 (42.0%)	0.277	0.011
HAS-BLED, mean(SD)	1.8 (1.14)	2.1 (1.26)	1.9 (1.18)	1.9 (1.20)	0.245	0.006
HAS-BLED:<3	9,430 (72.7%)	7,410 (62.0%)	5,880 (69.5%)	5,760 (68.1%)	0.230	0.029
HAS-BLED:>=3	3,540 (27.3%)	4,540 (38.0%)	2,580 (30.5%)	2,690 (31.9%)	0.230	0.029
log_n_hosp, median(IQR)	0.7 (0.0 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.279	0.002
log_beddays, median(IQR)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	0.003	0.001
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.155	0.005

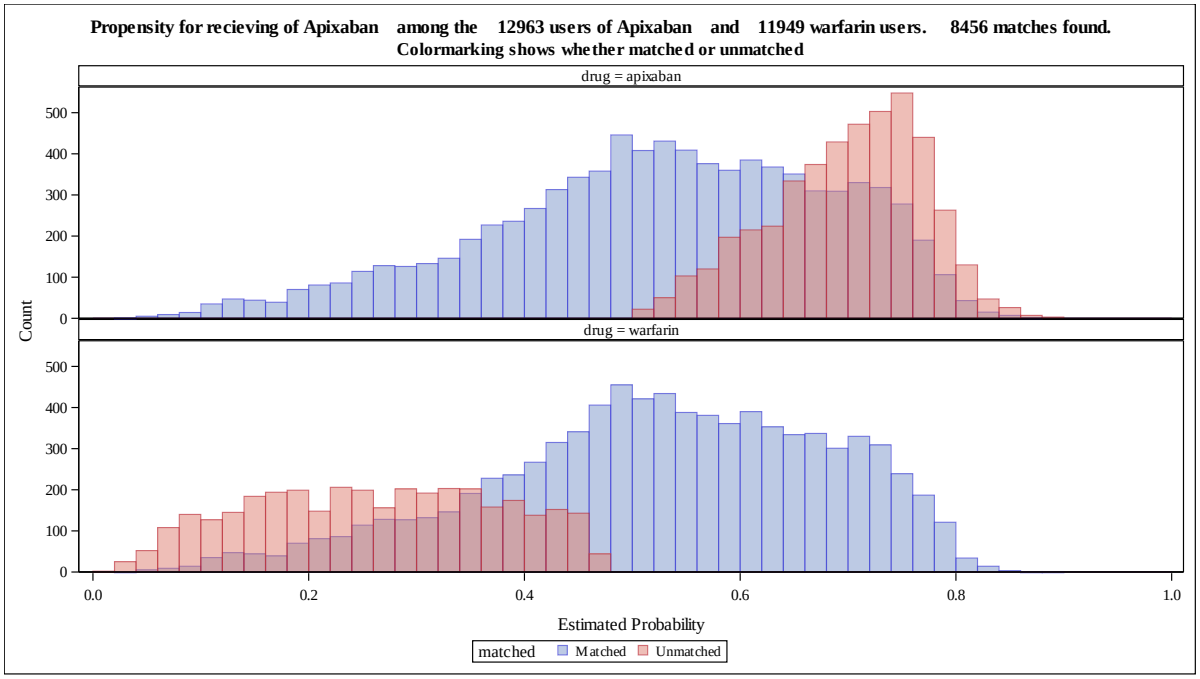
Propensity for recieving of Apixaban among the 12963 users of Apixaban and 11949 warfarin users. 8456 matches found.
Colormarking shows whether matched or unmatched
drug = apixaban
drug = warfarin
Count
0
100
200
300
400
500
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.48 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin and standardised mean differences before and after matching, Norway – REDUCED DOSE

Characteristic	Apixaban (rounded) before matching N= 4817	Warfarin (rounded) before matching N=11949	Apixaban (rounded) after matching N= 4215	Warfarin (rounded) after matching N= 4215	Standardised mean difference before matching (max= 0.90)	Standardised mean difference after matching (max= 0.08)
Time from AF diag:< 1 month	3,250 (67.5%)	6,410 (53.6%)	2,740 (65.0%)	2,730 (64.7%)	0.286	0.006
Time from AF diag:1 - 6 month	570 (11.9%)	1,340 (11.2%)	530 (12.5%)	520 (12.4%)	0.021	0.002
Time from AF diag:6 - 60 months	1,000 (20.7%)	4,200 (35.2%)	950 (22.6%)	970 (23.0%)	0.327	0.009
Sex:Female	2,800 (58.0%)	4,740 (39.7%)	2,320 (55.1%)	2,300 (54.5%)	0.374	0.012
Sex:Male	2,020 (42.0%)	7,210 (60.3%)	1,890 (44.9%)	1,920 (45.5%)	0.374	0.012
Age, median(IQR)	84.8 (79.6 - 89.3)	75.3 (66.7 - 83.2)	83.9 (78.6 - 88.2)	83.8 (78.4 - 88.1)	0.899	0.006
Age -group:< 55 years	40 (0.8%)	830 (7.0%)	40 (0.9%)	40 (0.9%)	0.321	0.002
Age -group:55-<65 years	150 (3.1%)	1,690 (14.2%)	150 (3.6%)	150 (3.5%)	0.401	0.005
Age -group:65-<75 years	530 (11.0%)	3,360 (28.1%)	530 (12.5%)	500 (11.8%)	0.442	0.020
Age -group:75-<85 years	1,750 (36.3%)	3,860 (32.3%)	1,690 (40.0%)	1,750 (41.6%)	0.086	0.031
Age -group:>= 85 years	2,350 (48.8%)	2,210 (18.5%)	1,810 (43.0%)	1,780 (42.2%)	0.675	0.015
CCI-group:0	1,110 (23.1%)	3,340 (27.9%)	970 (23.0%)	910 (21.6%)	0.110	0.032
CCI-group:1-2	1,520 (31.6%)	3,810 (31.9%)	1,330 (31.6%)	1,360 (32.3%)	0.008	0.014
CCI-group:>=3	2,180 (45.3%)	4,800 (40.2%)	1,920 (45.4%)	1,940 (46.1%)	0.104	0.014
Prior bleeding (any)	930 (19.3%)	1,780 (14.9%)	780 (18.5%)	780 (18.5%)	0.117	0.001
Prior gastrointestinal bleeding	90 (1.9%)	190 (1.6%)	80 (1.9%)	90 (2.1%)	0.024	0.014
Prior intracranial bleeding	100 (2.1%)	160 (1.3%)	80 (1.9%)	80 (1.8%)	0.060	0.005
Prior stroke (any)	770 (15.9%)	1,440 (12.0%)	650 (15.3%)	650 (15.4%)	0.113	0.004
Prior ischaemic stroke	750 (15.5%)	1,380 (11.5%)	630 (14.9%)	630 (14.9%)	0.117	0.000
Prior haemorrhagic stroke	70 (1.4%)	110 (0.9%)	50 (1.1%)	50 (1.2%)	0.047	0.016
Prior systemic embolism	40 (0.8%)	140 (1.2%)	40 (0.9%)	50 (1.1%)	0.039	0.024
Prior transient ischaemic attack	250 (5.2%)	460 (3.9%)	210 (4.9%)	230 (5.4%)	0.063	0.020
Chronic kidney disease	810 (16.8%)	1,560 (13.1%)	710 (16.7%)	750 (17.7%)	0.105	0.026
Heart failure	1,300 (27.1%)	3,110 (26.0%)	1,160 (27.4%)	1,170 (27.7%)	0.024	0.006
Coronary artery disease	1,640 (33.9%)	4,410 (36.9%)	1,490 (35.4%)	1,520 (35.9%)	0.062	0.010
Peripheral arterial disease	580 (12.1%)	1,370 (11.5%)	520 (12.3%)	540 (12.8%)	0.018	0.016
Hypertension	3,110 (64.5%)	7,270 (60.8%)	2,710 (64.4%)	2,740 (65.0%)	0.076	0.013
Diabetes	760 (15.8%)	2,100 (17.6%)	690 (16.5%)	710 (16.9%)	0.048	0.012
Chronic obstructive pulmonary disease	850 (17.6%)	1,850 (15.5%)	750 (17.8%)	770 (18.3%)	0.058	0.011
Liver disease	50 (1.0%)	150 (1.3%)	40 (0.9%)	40 (0.9%)	0.032	0.005
Alcoholism	80 (1.7%)	170 (1.4%)	60 (1.5%)	70 (1.7%)	0.021	0.013
Dementia	200 (4.1%)	230 (1.9%)	150 (3.4%)	160 (3.7%)	0.130	0.015
Cancer 6 months before and including index date	330 (6.9%)	810 (6.8%)	290 (6.9%)	310 (7.4%)	0.004	0.019

Platelet inhibitors (excluding heparin)	2,450 (50.9%)	5,400 (45.2%)	2,110 (50.2%)	2,120 (50.3%)	0.115	0.004
Low -dose aspirin	2,310 (47.9%)	5,060 (42.4%)	1,980 (47.1%)	1,990 (47.2%)	0.111	0.002
ADP receptor blockers	410 (8.6%)	1,130 (9.5%)	390 (9.2%)	400 (9.4%)	0.031	0.009
Renin - angiotensin system inhibitors	2,180 (45.3%)	5,500 (46.0%)	1,930 (45.9%)	1,910 (45.3%)	0.016	0.012
Angiotensin - converting enzyme inhibitors	970 (20.1%)	2,500 (20.9%)	870 (20.5%)	860 (20.5%)	0.021	0.001
Angiotensin II antagonists, plain	690 (14.4%)	1,640 (13.7%)	600 (14.3%)	580 (13.8%)	0.020	0.016
Angiotensin II antagonists, combinations	580 (12.0%)	1,450 (12.2%)	510 (12.2%)	510 (12.0%)	0.004	0.004
Beta-blockers	3,430 (71.2%)	8,410 (70.4%)	3,030 (71.8%)	3,000 (71.1%)	0.018	0.015
Proton pump inhibitors	1,350 (27.9%)	2,690 (22.5%)	1,130 (26.8%)	1,200 (28.4%)	0.124	0.036
H2-receptor antagonists	80 (1.6%)	170 (1.4%)	60 (1.5%)	70 (1.6%)	0.015	0.010
Non-steroidal anti-inflammatory drugs	330 (6.9%)	910 (7.6%)	290 (6.9%)	300 (7.1%)	0.026	0.009
Statins	1,840 (38.2%)	5,020 (42.0%)	1,680 (40.0%)	1,680 (39.7%)	0.078	0.004
Antidiabetic agents	470 (9.8%)	1,400 (11.7%)	440 (10.3%)	440 (10.3%)	0.061	0.001
Loop diuretics	1,600 (33.3%)	3,390 (28.4%)	1,420 (33.8%)	1,440 (34.2%)	0.106	0.009
Non-loop diuretics	80 (1.7%)	230 (1.9%)	70 (1.8%)	80 (1.9%)	0.015	0.007
Alpha adrenergic blockers	380 (8.0%)	960 (8.0%)	340 (8.1%)	360 (8.6%)	0.002	0.017
Amiodarone	210 (4.3%)	700 (5.9%)	190 (4.5%)	180 (4.2%)	0.070	0.014
Dronedarone	20 (0.4%)	130 (1.1%)	20 (0.4%)	20 (0.4%)	0.082	0.004
Antihypertensive, combination drugs	690 (14.3%)	1,740 (14.6%)	610 (14.4%)	600 (14.3%)	0.006	0.005
Calcium channel blockers	1,130 (23.5%)	2,640 (22.1%)	980 (23.1%)	990 (23.5%)	0.033	0.009
Selective serotonin reuptake inhibitors	310 (6.4%)	530 (4.5%)	250 (5.9%)	240 (5.6%)	0.085	0.012
Drugs used in alcohol dependence	10 (0.1%)	20 (0.1%)	10 (0.1%)	10 (0.1%)	0.006	0.000
CHA2DS2-VASc, mean(SD)	4.0 (1.54)	3.3 (1.86)	4.0 (1.55)	4.1 (1.58)	0.459	0.037
CHA2DS2-VASc:0 -1	170 (3.4%)	2,240 (18.7%)	170 (3.9%)	180 (4.2%)	0.503	0.013
CHA2DS2-VASc:2 -3	1,740 (36.0%)	4,370 (36.6%)	1,540 (36.5%)	1,390 (32.9%)	0.012	0.076
CHA2DS2-VASc:>=4	2,920 (60.6%)	5,340 (44.7%)	2,510 (59.6%)	2,650 (63.0%)	0.322	0.069
CHADS2, mean(SD)	2.1 (1.26)	1.7 (1.35)	2.1 (1.26)	2.2 (1.26)	0.346	0.042
CHADS2:0	250 (5.1%)	2,530 (21.1%)	250 (5.9%)	240 (5.7%)	0.487	0.008
CHADS2:1	1,490 (30.8%)	3,480 (29.1%)	1,300 (30.8%)	1,180 (27.9%)	0.037	0.065
CHADS2:>=2	3,080 (64.0%)	5,940 (49.7%)	2,670 (63.3%)	2,800 (66.4%)	0.291	0.066
HAS-BLED, mean(SD)	2.5 (1.16)	2.1 (1.26)	2.5 (1.16)	2.5 (1.16)	0.308	0.033
HAS-BLED:<3	2,510 (52.2%)	7,410 (62.0%)	2,240 (53.0%)	2,170 (51.4%)	0.200	0.032
HAS-BLED:>=3	2,300 (47.8%)	4,540 (38.0%)	1,980 (47.0%)	2,050 (48.6%)	0.200	0.032
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.145	0.020
log_beddays, median(IQR)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	0.031	0.008
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.132	0.005

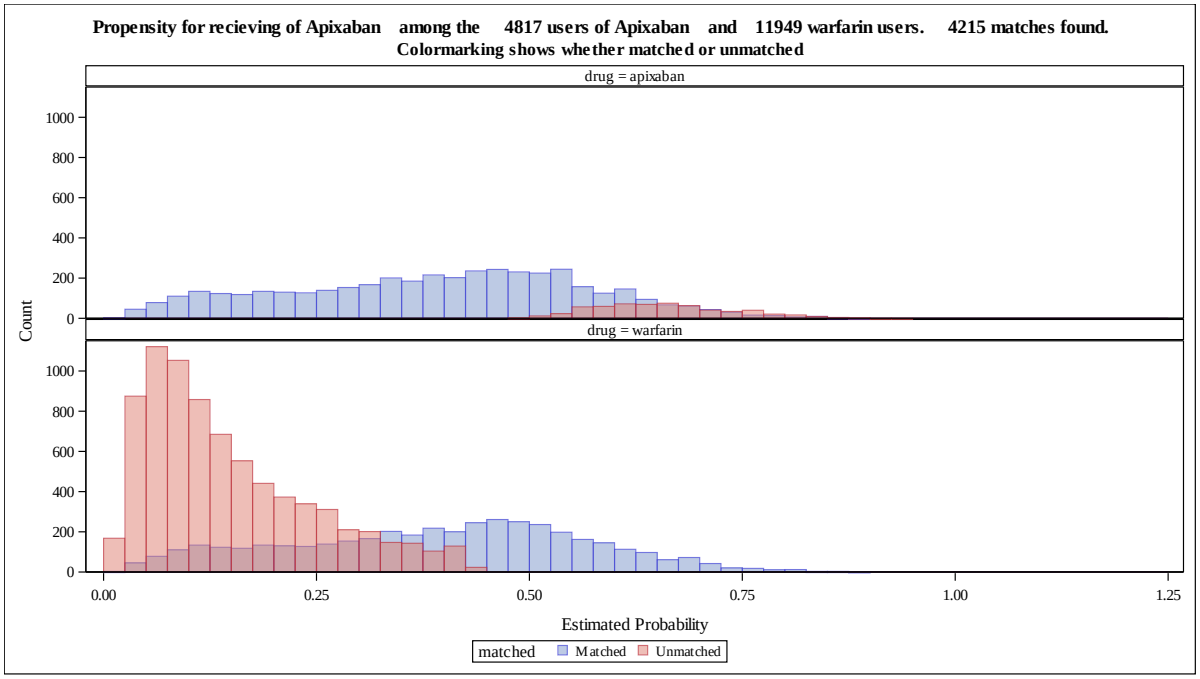
Propensity for recieving of Apixaban among the 4817 users of Apixaban and 11949 warfarin users. 4215 matches found.
Colormarking shows whether matched or unmatched
drug = apixaban
drug = warfarin
Count
0
200
400
600
800
1000
0.00
0.25
0.50
0.75
1.00
1.25
Estimated Probability
matched
Matched
Unmatched

Table 15.49 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin and standardised mean differences before and after matching, Sweden – STANDARD DOSE

Characteristic	Apixaban (rounded) before matching N=27638	Warfarin (rounded) before matching N=47152	Apixaban (rounded) after matching N=24843	Warfarin (rounded) after matching N=24843	Standardised mean difference before matching (max= 0.35)	Standardised mean difference after matching (max= 0.04)
Time from AF diag:< 1 month	19,250 (69.7%)	28,530 (60.5%)	16,980 (68.4%)	16,940 (68.2%)	0.193	0.004
Time from AF diag:1 - 6 month	1,980 (7.2%)	4,220 (9.0%)	1,830 (7.4%)	1,850 (7.5%)	0.066	0.004
Time from AF diag:6 - 60 months	6,410 (23.2%)	14,400 (30.5%)	6,030 (24.3%)	6,050 (24.4%)	0.167	0.002
Sex:Female	11,100 (40.1%)	20,290 (43.0%)	10,010 (40.3%)	9,830 (39.6%)	0.059	0.015
Sex:Male	16,540 (59.9%)	26,860 (57.0%)	14,830 (59.7%)	15,010 (60.4%)	0.059	0.015
Age, median(IQR)	72.0 (65.9 - 77.9)	75.6 (68.4 - 82.6)	72.4 (66.1 - 78.4)	72.2 (66.2 - 78.2)	0.322	0.019
Age -group:< 55 years	1,690 (6.1%)	2,130 (4.5%)	1,470 (5.9%)	1,480 (6.0%)	0.072	0.001
Age -group:55-<65 years	4,280 (15.5%)	5,540 (11.8%)	3,730 (15.0%)	3,820 (15.4%)	0.109	0.010
Age -group:65-<75 years	11,430 (41.4%)	14,880 (31.6%)	9,940 (40.0%)	10,030 (40.4%)	0.205	0.007
Age -group:75-<85 years	8,290 (30.0%)	16,570 (35.1%)	7,760 (31.3%)	7,690 (30.9%)	0.110	0.007
Age -group:>= 85 years	1,940 (7.0%)	8,030 (17.0%)	1,930 (7.8%)	1,830 (7.4%)	0.311	0.015
CCI-group:0	13,310 (48.2%)	17,670 (37.5%)	11,670 (47.0%)	11,860 (47.8%)	0.217	0.016
CCI-group:1-2	9,290 (33.6%)	15,790 (33.5%)	8,450 (34.0%)	8,260 (33.3%)	0.003	0.016
CCI-group:>=3	5,040 (18.2%)	13,700 (29.0%)	4,720 (19.0%)	4,720 (19.0%)	0.257	0.001
Prior bleeding (any)	2,480 (9.0%)	5,150 (10.9%)	2,250 (9.1%)	2,260 (9.1%)	0.065	0.000
Prior gastrointestinal bleeding	150 (0.5%)	360 (0.8%)	140 (0.6%)	160 (0.6%)	0.026	0.008
Prior intracranial bleeding	240 (0.9%)	410 (0.9%)	200 (0.8%)	200 (0.8%)	0.000	0.001
Prior stroke (any)	3,000 (10.9%)	6,200 (13.1%)	2,740 (11.0%)	2,720 (11.0%)	0.070	0.003
Prior ischaemic stroke	2,900 (10.5%)	6,080 (12.9%)	2,660 (10.7%)	2,640 (10.6%)	0.075	0.002
Prior haemorrhagic stroke	210 (0.8%)	330 (0.7%)	180 (0.7%)	180 (0.7%)	0.007	0.000
Prior systemic embolism	130 (0.5%)	510 (1.1%)	130 (0.5%)	120 (0.5%)	0.068	0.004
Prior transient ischaemic attack	1,000 (3.6%)	2,050 (4.3%)	920 (3.7%)	910 (3.7%)	0.037	0.003
Chronic kidney disease	470 (1.7%)	3,280 (7.0%)	470 (1.9%)	430 (1.7%)	0.260	0.011
Heart failure	4,220 (15.3%)	11,330 (24.0%)	3,980 (16.0%)	3,900 (15.7%)	0.222	0.009
Coronary artery disease	4,790 (17.3%)	12,460 (26.4%)	4,550 (18.3%)	4,490 (18.1%)	0.221	0.006
Peripheral arterial disease	1,280 (4.6%)	3,030 (6.4%)	1,190 (4.8%)	1,190 (4.8%)	0.079	0.001
Hypertension	19,060 (69.0%)	34,570 (73.3%)	17,250 (69.4%)	17,250 (69.4%)	0.096	0.000
Diabetes	4,550 (16.5%)	9,090 (19.3%)	4,170 (16.8%)	4,180 (16.8%)	0.073	0.001
Chronic obstructive pulmonary disease	2,880 (10.4%)	5,700 (12.1%)	2,650 (10.7%)	2,600 (10.5%)	0.053	0.006
Liver disease	210 (0.8%)	430 (0.9%)	190 (0.8%)	210 (0.8%)	0.015	0.006
Alcoholism	780 (2.8%)	1,030 (2.2%)	670 (2.7%)	660 (2.6%)	0.040	0.004
Dementia	350 (1.3%)	770 (1.6%)	320 (1.3%)	310 (1.3%)	0.031	0.000
Cancer 6 months before and including index date	160 (0.6%)	400 (0.9%)	150 (0.6%)	150 (0.6%)	0.035	0.000
Platelet inhibitors (excluding heparin)	9,020 (32.6%)	18,680 (39.6%)	8,370 (33.7%)	8,510 (34.3%)	0.146	0.012
Low -dose aspirin	8,220 (29.7%)	17,010 (36.1%)	7,650 (30.8%)	7,770 (31.3%)	0.135	0.011
ADP receptor blockers	1,270 (4.6%)	3,710 (7.9%)	1,190 (4.8%)	1,210 (4.9%)	0.136	0.004
Renin -angiotensin system inhibitors	13,340 (48.2%)	24,140 (51.2%)	12,100 (48.7%)	12,040 (48.5%)	0.059	0.005
Angiotensin -converting enzyme inhibitors	6,730 (24.4%)	13,490 (28.6%)	6,240 (25.1%)	6,240 (25.1%)	0.096	0.000
Angiotensin II antagonists, plain	4,640 (16.8%)	8,000 (17.0%)	4,120 (16.6%)	4,100 (16.5%)	0.005	0.002
Angiotensin II antagonists, combinations	1,770 (6.4%)	2,540 (5.4%)	1,560 (6.3%)	1,530 (6.2%)	0.043	0.004

Beta-blockers	21,290 (77.0%)	36,150 (76.7%)	19,030 (76.6%)	19,010 (76.5%)	0.009	0.002
Proton pump inhibitors	5,360 (19.4%)	10,150 (21.5%)	4,830 (19.5%)	4,760 (19.2%)	0.052	0.008
H2-receptor antagonists	100 (0.4%)	210 (0.4%)	90 (0.4%)	100 (0.4%)	0.015	0.006
Non-steroidal anti-inflammatory drugs	2,100 (7.6%)	2,970 (6.3%)	1,870 (7.5%)	1,860 (7.5%)	0.051	0.001
Statins	9,080 (32.8%)	16,730 (35.5%)	8,230 (33.1%)	8,210 (33.0%)	0.056	0.002
Antidiabetic agents	3,290 (11.9%)	6,350 (13.5%)	2,990 (12.0%)	3,000 (12.1%)	0.048	0.001
Loop diuretics	4,600 (16.6%)	12,990 (27.5%)	4,410 (17.7%)	4,310 (17.4%)	0.265	0.010
Non-loop diuretics	310 (1.1%)	650 (1.4%)	290 (1.2%)	270 (1.1%)	0.023	0.007
Alpha adrenergic blockers	6,030 (21.8%)	11,180 (23.7%)	5,500 (22.1%)	5,500 (22.1%)	0.046	0.000
Amiodarone	330 (1.2%)	890 (1.9%)	320 (1.3%)	310 (1.2%)	0.057	0.003
Dronedarone	370 (1.3%)	440 (0.9%)	310 (1.2%)	310 (1.3%)	0.038	0.002
Antihypertensive, combination drugs	2,610 (9.4%)	3,850 (8.2%)	2,310 (9.3%)	2,290 (9.2%)	0.045	0.002
Calcium channel blockers	6,710 (24.3%)	12,240 (26.0%)	6,080 (24.5%)	6,150 (24.7%)	0.039	0.006
Selective serotonin reuptake inhibitors	1,650 (6.0%)	3,110 (6.6%)	1,500 (6.0%)	1,460 (5.9%)	0.026	0.006
Drugs used in alcohol dependence	50 (0.2%)	60 (0.1%)	40 (0.2%)	40 (0.2%)	0.016	0.000
CHA2DS2-VASc, mean(SD)	3.0 (1.64)	3.6 (1.75)	3.1 (1.65)	3.0 (1.66)	0.319	0.018
CHA2DS2-VASc:0-1	5,040 (18.2%)	5,700 (12.1%)	4,340 (17.5%)	4,420 (17.8%)	0.172	0.008
CHA2DS2-VASc:2-3	12,560 (45.4%)	17,540 (37.2%)	11,090 (44.6%)	11,120 (44.7%)	0.168	0.002
CHA2DS2-VASc:>=4	10,040 (36.3%)	23,910 (50.7%)	9,410 (37.9%)	9,310 (37.5%)	0.293	0.008
CHADS2, mean(SD)	2.4 (1.40)	2.9 (1.47)	2.5 (1.41)	2.5 (1.41)	0.297	0.013
CHADS2:0	1,820 (6.6%)	2,300 (4.9%)	1,550 (6.2%)	1,810 (7.3%)	0.073	0.041
CHADS2:1	5,510 (19.9%)	6,040 (12.8%)	4,760 (19.1%)	4,480 (18.0%)	0.193	0.029
CHADS2:>=2	20,320 (73.5%)	38,810 (82.3%)	18,540 (74.6%)	18,560 (74.7%)	0.213	0.002
HAS-BLED, mean(SD)	1.7 (0.87)	1.9 (0.92)	1.7 (0.87)	1.7 (0.88)	0.224	0.008
HAS-BLED:<3	23,200 (83.9%)	36,080 (76.5%)	20,720 (83.4%)	20,750 (83.5%)	0.187	0.003
HAS-BLED:>=3	4,440 (16.1%)	11,080 (23.5%)	4,120 (16.6%)	4,090 (16.5%)	0.187	0.003
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.200	0.015
log_beddays, median(IQR)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.089	0.007
log_n_outpatient, median(IQR)	0.7 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.353	0.025
income, median(IQR), k€	57.4 (44.1 - 87.9)	49.8 (40.5 - 72.3)	55.9 (43.5 - 85.0)	55.9 (43.5 - 84.2)	0.129	0.006
education:Secondary compulsory	8,870 (32.1%)	18,850 (40.0%)	8,260 (33.3%)	8,170 (32.9%)	0.164	0.008
education:Vocational / High school	11,280 (40.8%)	18,480 (39.2%)	10,170 (40.9%)	10,290 (41.4%)	0.033	0.010
education:Higher education	7,260 (26.3%)	9,340 (19.8%)	6,200 (25.0%)	6,160 (24.8%)	0.154	0.003
education:Unknown	230 (0.8%)	490 (1.0%)	210 (0.8%)	230 (0.9%)	0.022	0.006

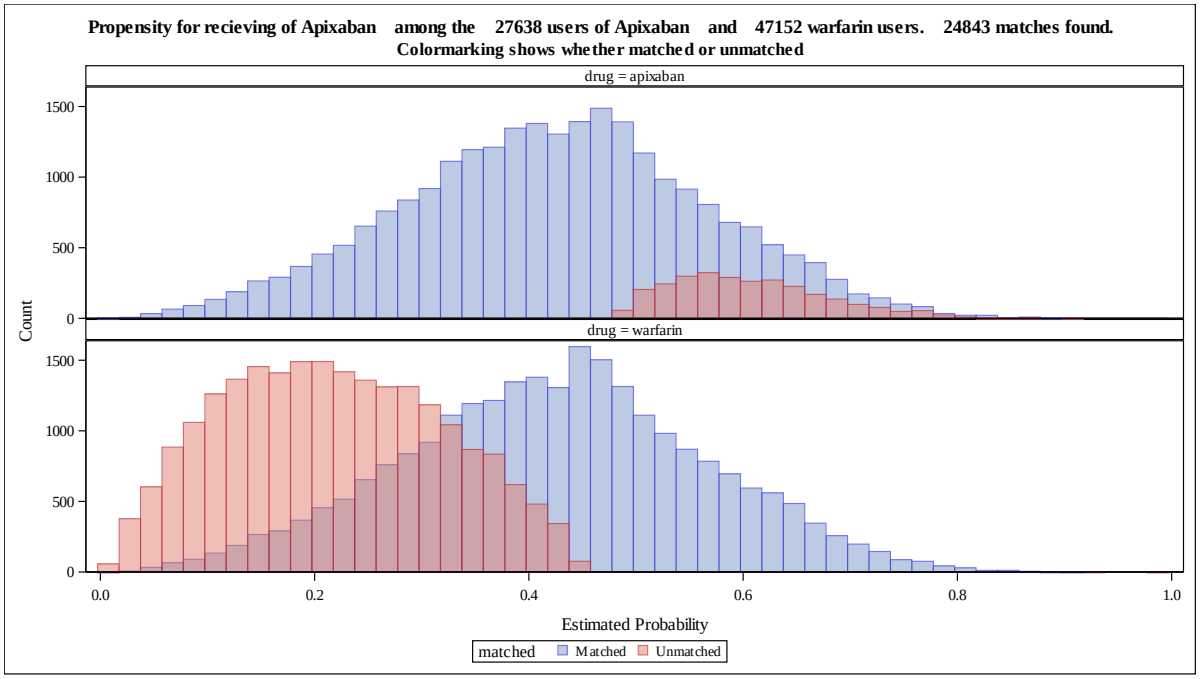
Propensity for recieving of Apixaban among the 27638 users of Apixaban and 47152 warfarin users. 24843 matches found.
Colormarking shows whether matched or unmatched
drug = apixaban
drug = warfarin
Count
1500
1000
500
0
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.50 Baseline characteristics of patients with non-valvular atrial fibrillation initiating apixaban or warfarin and standardised mean differences before and after matching, Sweden – REDUCED DOSE

Characteristic	Apixaban (rounded) before matching N=11187	Warfarin (rounded) before matching N=47152	Apixaban (rounded) after matching N= 9983	Warfarin (rounded) after matching N= 9983	Standardised mean difference before matching (max= 1.10)	Standardised mean difference after matching (max= 0.05)
Time from AF diag:< 1 month	6,810 (60.9%)	28,530 (60.5%)	6,060 (60.7%)	5,990 (60.0%)	0.007	0.015
Time from AF diag:1 - 6 month	1,060 (9.5%)	4,220 (9.0%)	950 (9.5%)	990 (9.9%)	0.019	0.014
Time from AF diag:6 - 60 months	3,320 (29.7%)	14,400 (30.5%)	2,970 (29.8%)	3,010 (30.1%)	0.020	0.007
Sex:Female	6,800 (60.8%)	20,290 (43.0%)	5,890 (59.0%)	5,790 (58.0%)	0.362	0.019
Sex:Male	4,380 (39.2%)	26,860 (57.0%)	4,100 (41.0%)	4,190 (42.0%)	0.362	0.019
Age, median(IQR)	85.8 (81.2 - 89.9)	75.6 (68.4 - 82.6)	85.0 (80.5 - 89.0)	85.0 (80.7 - 88.9)	1.097	0.004
Age -group:< 55 years	40 (0.4%)	2,130 (4.5%)	40 (0.4%)	30 (0.3%)	0.271	0.020
Age -group:55-<65 years	160 (1.5%)	5,540 (11.8%)	160 (1.6%)	170 (1.7%)	0.423	0.008
Age -group:65-<75 years	870 (7.8%)	14,880 (31.6%)	870 (8.7%)	850 (8.6%)	0.627	0.006
Age -group:75-<85 years	4,020 (35.9%)	16,570 (35.1%)	3,920 (39.3%)	3,960 (39.7%)	0.016	0.008
Age -group:>= 85 years	6,100 (54.5%)	8,030 (17.0%)	4,980 (49.9%)	4,960 (49.7%)	0.849	0.004
CCI-group:0	2,790 (25.0%)	17,670 (37.5%)	2,620 (26.3%)	2,710 (27.2%)	0.272	0.020
CCI-group:1-2	3,830 (34.2%)	15,790 (33.5%)	3,430 (34.4%)	3,290 (33.0%)	0.016	0.029
CCI-group:>=3	4,570 (40.8%)	13,700 (29.0%)	3,930 (39.4%)	3,980 (39.8%)	0.249	0.010
Prior bleeding (any)	1,700 (15.2%)	5,150 (10.9%)	1,470 (14.7%)	1,480 (14.8%)	0.127	0.003
Prior gastrointestinal bleeding	120 (1.1%)	360 (0.8%)	100 (1.0%)	100 (1.0%)	0.037	0.002
Prior intracranial bleeding	240 (2.1%)	410 (0.9%)	180 (1.8%)	180 (1.8%)	0.103	0.005
Prior stroke (any)	2,370 (21.2%)	6,200 (13.1%)	2,000 (20.1%)	1,980 (19.8%)	0.214	0.006
Prior ischaemic stroke	2,270 (20.3%)	6,080 (12.9%)	1,930 (19.4%)	1,920 (19.2%)	0.200	0.003
Prior haemorrhagic stroke	220 (1.9%)	330 (0.7%)	170 (1.7%)	170 (1.7%)	0.109	0.002
Prior systemic embolism	110 (1.0%)	510 (1.1%)	110 (1.1%)	110 (1.1%)	0.010	0.002
Prior transient ischaemic attack	770 (6.9%)	2,050 (4.3%)	650 (6.5%)	620 (6.2%)	0.109	0.011
Chronic kidney disease	1,110 (9.9%)	3,280 (7.0%)	970 (9.7%)	1,040 (10.4%)	0.107	0.025
Heart failure	3,780 (33.7%)	11,330 (24.0%)	3,240 (32.5%)	3,210 (32.2%)	0.216	0.006
Coronary artery disease	3,460 (31.0%)	12,460 (26.4%)	3,080 (30.8%)	3,160 (31.7%)	0.100	0.018
Peripheral arterial disease	790 (7.1%)	3,030 (6.4%)	710 (7.2%)	690 (7.0%)	0.025	0.008
Hypertension	8,680 (77.6%)	34,570 (73.3%)	7,750 (77.6%)	7,800 (78.2%)	0.100	0.014
Diabetes	2,090 (18.7%)	9,090 (19.3%)	1,890 (18.9%)	1,940 (19.5%)	0.014	0.015
Chronic obstructive pulmonary disease	1,670 (14.9%)	5,700 (12.1%)	1,460 (14.6%)	1,490 (14.9%)	0.083	0.007
Liver disease	90 (0.8%)	430 (0.9%)	80 (0.8%)	80 (0.8%)	0.014	0.002
Alcoholism	170 (1.5%)	1,030 (2.2%)	160 (1.6%)	160 (1.6%)	0.046	0.001
Dementia	670 (6.0%)	770 (1.6%)	490 (4.9%)	450 (4.5%)	0.230	0.015
Cancer 6 months before and including index date	70 (0.6%)	400 (0.9%)	70 (0.7%)	70 (0.7%)	0.030	0.001
Platelet inhibitors (excluding heparin)	5,500 (49.2%)	18,680 (39.6%)	4,820 (48.2%)	4,930 (49.4%)	0.193	0.024
Low -dose aspirin	4,870 (43.5%)	17,010 (36.1%)	4,290 (43.0%)	4,400 (44.1%)	0.153	0.022
ADP receptor blockers	1,010 (9.1%)	3,710 (7.9%)	890 (8.9%)	930 (9.3%)	0.043	0.013
Renin -angiotensin system inhibitors	5,680 (50.8%)	24,140 (51.2%)	5,080 (50.9%)	5,100 (51.1%)	0.009	0.003
Angiotensin - converting enzyme inhibitors	3,130 (28.0%)	13,490 (28.6%)	2,800 (28.1%)	2,800 (28.0%)	0.013	0.001
Angiotensin II antagonists, plain	2,060 (18.4%)	8,000 (17.0%)	1,830 (18.4%)	1,830 (18.4%)	0.037	0.000
Angiotensin II antagonists, combinations	530 (4.8%)	2,540 (5.4%)	490 (4.9%)	490 (4.9%)	0.029	0.004
Beta-blockers	8,490 (75.9%)	36,150 (76.7%)	7,560 (75.7%)	7,580 (75.9%)	0.017	0.004
Proton pump inhibitors	3,030 (27.1%)	10,150 (21.5%)	2,620 (26.3%)	2,670 (26.7%)	0.130	0.011
H2-receptor antagonists	50 (0.5%)	210 (0.4%)	50 (0.5%)	50 (0.5%)	0.004	0.003

Non-steroidal anti-inflammatory drugs	510 (4.5%)	2,970 (6.3%)	470 (4.7%)	450 (4.5%)	0.078	0.007
Statins	3,630 (32.4%)	16,730 (35.5%)	3,320 (33.3%)	3,390 (34.0%)	0.065	0.015
Antidiabetic agents	1,300 (11.6%)	6,350 (13.5%)	1,190 (11.9%)	1,250 (12.5%)	0.056	0.018
Loop diuretics	4,340 (38.8%)	12,990 (27.5%)	3,760 (37.7%)	3,810 (38.1%)	0.241	0.009
Non-loop diuretics	130 (1.2%)	650 (1.4%)	120 (1.2%)	140 (1.4%)	0.020	0.014
Alpha adrenergic blockers	2,700 (24.1%)	11,180 (23.7%)	2,440 (24.5%)	2,460 (24.7%)	0.009	0.005
Amiodarone	120 (1.1%)	890 (1.9%)	120 (1.2%)	130 (1.3%)	0.068	0.009
Dronedarone	40 (0.3%)	440 (0.9%)	40 (0.4%)	20 (0.2%)	0.077	0.024
Antihypertensive, combination drugs	770 (6.8%)	3,850 (8.2%)	700 (7.0%)	720 (7.2%)	0.050	0.006
Calcium channel blockers	3,020 (27.0%)	12,240 (26.0%)	2,700 (27.1%)	2,750 (27.5%)	0.023	0.010
Selective serotonin reuptake inhibitors	1,100 (9.9%)	3,110 (6.6%)	920 (9.3%)	910 (9.1%)	0.119	0.006
Drugs used in alcohol dependence	10 (0.1%)	60 (0.1%)	10 (0.1%)	<5	0.019	0.013
CHA2DS2-VASc, mean(SD)	4.6 (1.47)	3.6 (1.75)	4.6 (1.47)	4.5 (1.52)	0.659	0.006
CHA2DS2-VASc:0-1	110 (0.9%)	5,700 (12.1%)	110 (1.1%)	160 (1.6%)	0.463	0.047
CHA2DS2-VASc:2-3	2,260 (20.2%)	17,540 (37.2%)	2,150 (21.5%)	2,190 (21.9%)	0.383	0.010
CHA2DS2-VASc:>=4	8,820 (78.9%)	23,910 (50.7%)	7,730 (77.4%)	7,640 (76.5%)	0.617	0.022
CHADS2, mean(SD)	3.7 (1.26)	2.9 (1.47)	3.7 (1.25)	3.7 (1.28)	0.621	0.004
CHADS2:0	40 (0.3%)	2,300 (4.9%)	40 (0.4%)	40 (0.4%)	0.289	0.006
CHADS2:1	190 (1.7%)	6,040 (12.8%)	190 (1.9%)	250 (2.5%)	0.441	0.042
CHADS2:>=2	10,970 (98.0%)	38,810 (82.3%)	9,760 (97.8%)	9,700 (97.1%)	0.547	0.041
HAS-BLED, mean(SD)	2.3 (0.84)	1.9 (0.92)	2.3 (0.83)	2.3 (0.85)	0.396	0.006
HAS-BLED:<3	7,170 (64.1%)	36,080 (76.5%)	6,510 (65.2%)	6,480 (64.9%)	0.275	0.005
HAS-BLED:>=3	4,020 (35.9%)	11,080 (23.5%)	3,480 (34.8%)	3,500 (35.1%)	0.275	0.005
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.291	0.011
log_beddays, median(IQR)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.086	0.028
log_n_outpatient, median(IQR)	0.7 (0.0 - 1.1)	0.0 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.581	0.007
income, median(IQR), k€	45.9 (39.3 - 56.5)	49.8 (40.5 - 72.3)	45.9 (39.1 - 56.8)	46.1 (39.3 - 56.8)	0.127	0.010
education:Secondary compulsory	5,770 (51.6%)	18,850 (40.0%)	5,080 (50.9%)	5,040 (50.5%)	0.235	0.008
education:Vocational / High school	3,510 (31.3%)	18,480 (39.2%)	3,180 (31.9%)	3,190 (31.9%)	0.165	0.000
education:Higher education	1,720 (15.3%)	9,340 (19.8%)	1,550 (15.5%)	1,590 (15.9%)	0.118	0.011
education:Unknown	200 (1.7%)	490 (1.0%)	170 (1.7%)	170 (1.7%)	0.060	0.000

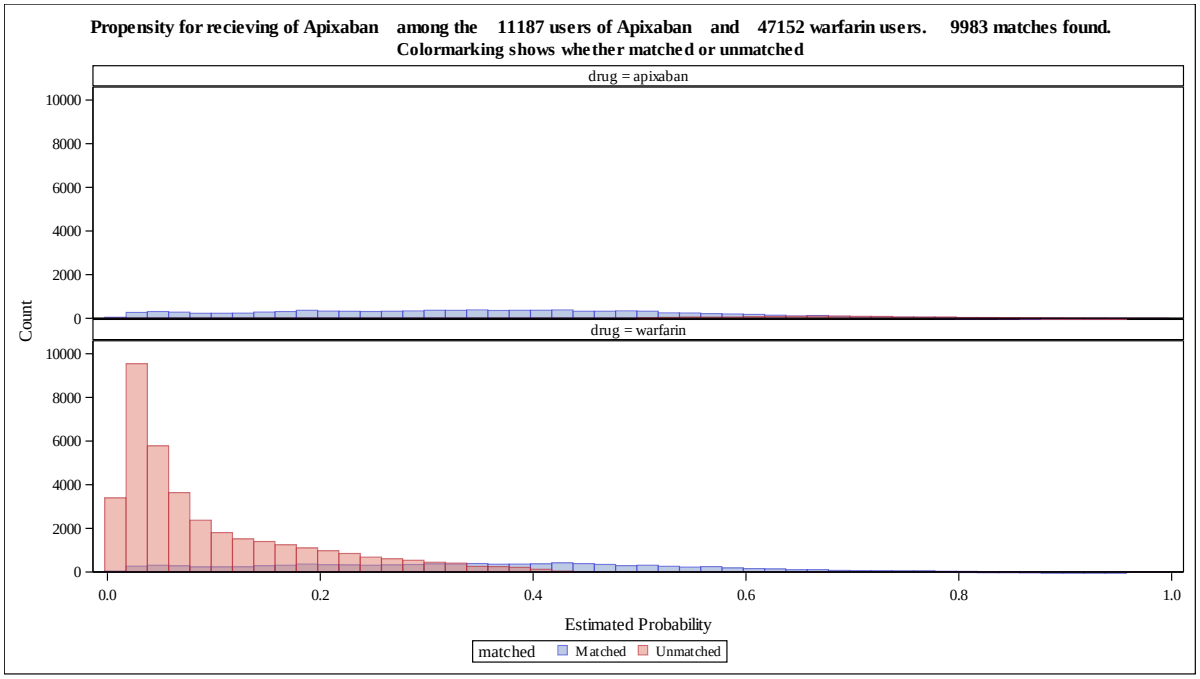
Propensity for recieving of Apixaban among the 11187 users of Apixaban and 47152 warfarin users. 9983 matches found.
Colormarking shows whether matched or unmatched
drug = apixaban
drug = warfarin
Count
10000
8000
6000
4000
2000
0
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.51 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin in Denmark, Norway, or Sweden and standardised mean differences before and after matching – STANDARD DOSE

Characteristic	Dabigatran (rounded) before matching N=20478	Warfarin (rounded) before matching N=79171	Dabigatran (rounded) after matching N=18701	Warfarin (rounded) after matching N=18701	Standardised mean difference before matching (max= 0.78)	Standardised mean difference after matching (max= 0.04)
index_year:2013	7,920 (38.7%)	35,000 (44.2%)	7,340 (39.3%)	7,390 (39.5%)	0.112	0.005
index_year:2014	7,130 (34.8%)	23,330 (29.5%)	6,350 (34.0%)	6,310 (33.8%)	0.114	0.004
index_year:2015	2,820 (13.8%)	13,390 (16.9%)	2,750 (14.7%)	2,730 (14.6%)	0.087	0.003
index_year:2016	2,610 (12.7%)	7,460 (9.4%)	2,260 (12.1%)	2,270 (12.2%)	0.106	0.002
Time from AF diag:< 1 month	13,600 (66.4%)	47,550 (60.1%)	12,120 (64.8%)	11,980 (64.1%)	0.132	0.015
Time from AF diag:1 - 6 month	1,540 (7.5%)	7,970 (10.1%)	1,490 (8.0%)	1,530 (8.2%)	0.090	0.007
Time from AF diag:6 - 60 months	5,340 (26.1%)	23,650 (29.9%)	5,090 (27.2%)	5,190 (27.8%)	0.085	0.012
Sex:Female	6,560 (32.1%)	32,980 (41.7%)	6,110 (32.7%)	6,050 (32.4%)	0.200	0.007
Sex:Male	13,910 (67.9%)	46,190 (58.3%)	12,590 (67.3%)	12,650 (67.6%)	0.200	0.007
Age, median(IQR)	67.6 (61.5 - 72.4)	75.0 (67.5 - 82.2)	67.9 (61.7 - 72.7)	67.9 (61.7 - 72.8)	0.775	0.001
Age -group:< 55 years	2,330 (11.4%)	4,480 (5.7%)	2,110 (11.3%)	2,130 (11.4%)	0.206	0.003
Age -group:55-<65 years	5,240 (25.6%)	10,100 (12.8%)	4,610 (24.7%)	4,640 (24.8%)	0.330	0.003
Age -group:65-<75 years	10,030 (49.0%)	25,060 (31.6%)	9,120 (48.8%)	9,040 (48.3%)	0.359	0.009
Age -group:75-<85 years	2,760 (13.5%)	26,700 (33.7%)	2,740 (14.7%)	2,780 (14.9%)	0.490	0.006
Age -group:>= 85 years	120 (0.6%)	12,830 (16.2%)	120 (0.6%)	120 (0.6%)	0.588	0.000
CCI-group:0	11,480 (56.1%)	29,610 (37.4%)	10,150 (54.3%)	10,100 (54.0%)	0.381	0.005
CCI-group:1-2	6,410 (31.3%)	25,600 (32.3%)	6,030 (32.2%)	5,840 (31.2%)	0.022	0.022
CCI-group:>=3	2,590 (12.6%)	23,960 (30.3%)	2,530 (13.5%)	2,770 (14.8%)	0.440	0.037
Prior bleeding (any)	1,430 (7.0%)	8,870 (11.2%)	1,360 (7.3%)	1,380 (7.4%)	0.147	0.005
Prior gastrointestinal bleeding	100 (0.5%)	820 (1.0%)	100 (0.5%)	80 (0.4%)	0.066	0.013
Prior intracranial bleeding	120 (0.6%)	710 (0.9%)	110 (0.6%)	120 (0.6%)	0.038	0.006
Prior stroke (any)	1,650 (8.1%)	9,610 (12.1%)	1,550 (8.3%)	1,540 (8.2%)	0.135	0.001
Prior ischaemic stroke	1,620 (7.9%)	9,400 (11.9%)	1,520 (8.1%)	1,510 (8.1%)	0.133	0.001
Prior haemorrhagic stroke	70 (0.4%)	520 (0.7%)	70 (0.4%)	80 (0.4%)	0.042	0.003
Prior systemic embolism	50 (0.2%)	760 (1.0%)	50 (0.2%)	40 (0.2%)	0.096	0.003
Prior transient ischaemic attack	570 (2.8%)	3,120 (3.9%)	530 (2.8%)	500 (2.7%)	0.066	0.009
Chronic kidney disease	180 (0.9%)	6,530 (8.2%)	180 (1.0%)	180 (0.9%)	0.358	0.003
Heart failure	2,300 (11.2%)	18,010 (22.7%)	2,240 (12.0%)	2,280 (12.2%)	0.311	0.006
Coronary artery disease	2,870 (14.0%)	21,450 (27.1%)	2,810 (15.0%)	2,850 (15.2%)	0.327	0.005
Peripheral arterial disease	840 (4.1%)	6,030 (7.6%)	810 (4.3%)	840 (4.5%)	0.151	0.009
Hypertension	11,580 (56.6%)	54,110 (68.3%)	10,730 (57.4%)	10,670 (57.1%)	0.245	0.007
Diabetes	2,630 (12.8%)	14,680 (18.5%)	2,520 (13.5%)	2,550 (13.7%)	0.157	0.006
Chronic obstructive pulmonary disease	1,750 (8.5%)	10,120 (12.8%)	1,670 (8.9%)	1,660 (8.9%)	0.138	0.001
Liver disease	170 (0.8%)	820 (1.0%)	170 (0.9%)	170 (0.9%)	0.020	0.001
Alcoholism	630 (3.1%)	1,790 (2.3%)	580 (3.1%)	610 (3.2%)	0.050	0.008
Dementia	80 (0.4%)	1,220 (1.5%)	80 (0.4%)	70 (0.4%)	0.118	0.009
Cancer 6 months before and including index date	480 (2.3%)	2,140 (2.7%)	460 (2.4%)	430 (2.3%)	0.024	0.008
Platelet inhibitors (excluding heparin)	5,740 (28.0%)	30,840 (39.0%)	5,400 (28.9%)	5,500 (29.4%)	0.234	0.012
Low -dose aspirin	5,180 (25.3%)	27,180 (34.3%)	4,860 (26.0%)	4,930 (26.4%)	0.198	0.009
ADP receptor blockers	720 (3.5%)	7,100 (9.0%)	720 (3.8%)	740 (4.0%)	0.226	0.006
Renin -angiotensin system inhibitors	8,250 (40.3%)	38,070 (48.1%)	7,650 (40.9%)	7,640 (40.8%)	0.158	0.001
Angiotensin - converting enzyme inhibitors	3,690 (18.0%)	20,500 (25.9%)	3,550 (19.0%)	3,570 (19.1%)	0.191	0.003
Angiotensin II antagonists, plain	2,430 (11.9%)	11,850 (15.0%)	2,240 (12.0%)	2,170 (11.6%)	0.091	0.011
Angiotensin II antagonists, combinations	1,810 (8.8%)	5,210 (6.6%)	1,560 (8.4%)	1,560 (8.3%)	0.084	0.000
Beta-blockers	14,670 (71.6%)	56,980 (72.0%)	13,310 (71.2%)	13,170 (70.4%)	0.008	0.016

Proton pump inhibitors	2,770 (13.5%)	17,350 (21.9%)	2,660 (14.2%)	2,660 (14.2%)	0.221	0.001
Non-steroidal anti-inflammatory drugs	2,090 (10.2%)	5,860 (7.4%)	1,840 (9.8%)	1,880 (10.0%)	0.099	0.006
Statins	6,110 (29.8%)	28,740 (36.3%)	5,710 (30.5%)	5,750 (30.7%)	0.138	0.005
Antidiabetic agents	1,910 (9.3%)	10,410 (13.1%)	1,840 (9.9%)	1,870 (10.0%)	0.122	0.004
Loop diuretics	2,490 (12.2%)	22,170 (28.0%)	2,460 (13.1%)	2,460 (13.1%)	0.404	0.001
Non-loop diuretics	230 (1.1%)	1,230 (1.6%)	210 (1.1%)	200 (1.1%)	0.039	0.005
Alpha adrenergic blockers	2,690 (13.2%)	15,810 (20.0%)	2,600 (13.9%)	2,620 (14.0%)	0.184	0.003
Amiodarone	350 (1.7%)	2,560 (3.2%)	350 (1.9%)	350 (1.9%)	0.098	0.001
Dronedarone	70 (0.4%)	600 (0.8%)	70 (0.4%)	80 (0.4%)	0.054	0.003
Antihypertensive, combination drugs	2,540 (12.4%)	7,700 (9.7%)	2,240 (12.0%)	2,250 (12.0%)	0.086	0.002
Calcium channel blockers	3,960 (19.3%)	19,680 (24.9%)	3,760 (20.1%)	3,760 (20.1%)	0.133	0.001
Selective serotonin reuptake inhibitors	810 (3.9%)	4,790 (6.1%)	770 (4.1%)	760 (4.1%)	0.097	0.002
Drugs used in alcohol dependence	60 (0.3%)	120 (0.2%)	50 (0.3%)	50 (0.3%)	0.033	0.001
CHA2DS2-VASc, mean(SD)	2.2 (1.48)	3.4 (1.76)	2.3 (1.48)	2.3 (1.52)	0.732	0.004
CHA2DS2-VASc:0 - 1	7,010 (34.2%)	11,520 (14.6%)	6,020 (32.2%)	6,200 (33.1%)	0.471	0.020
CHA2DS2-VASc:2 - 3	9,810 (47.9%)	30,330 (38.3%)	9,120 (48.8%)	8,820 (47.2%)	0.195	0.032
CHA2DS2-VASc:>=4	3,660 (17.8%)	37,330 (47.1%)	3,560 (19.0%)	3,680 (19.7%)	0.659	0.016
CHADS2, mean(SD)	1.3 (1.21)	2.4 (1.51)	1.4 (1.22)	1.4 (1.24)	0.769	0.009
CHADS2:0	5,800 (28.3%)	8,300 (10.5%)	4,850 (25.9%)	5,090 (27.2%)	0.463	0.029
CHADS2:1	7,070 (34.5%)	15,840 (20.0%)	6,510 (34.8%)	6,300 (33.7%)	0.331	0.024
CHADS2:>=2	7,610 (37.1%)	55,030 (69.5%)	7,340 (39.3%)	7,320 (39.1%)	0.686	0.003
HAS-BLED, mean(SD)	1.6 (1.03)	2.0 (1.05)	1.6 (1.03)	1.6 (1.05)	0.428	0.008
HAS-BLED:<3	16,950 (82.8%)	56,150 (70.9%)	15,340 (82.0%)	15,250 (81.5%)	0.284	0.013
HAS-BLED:>=3	3,530 (17.2%)	23,020 (29.1%)	3,360 (18.0%)	3,450 (18.5%)	0.284	0.013
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.308	0.003
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.054	0.010
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.126	0.001

Table 15.52 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin in Denmark, Norway, or Sweden and standardised mean differences before and after matching – REDUCED DOSE

Characteristic	Dabigatran (rounded) before matching N=10731	Warfarin (rounded) before matching N=79171	Dabigatran (rounded) after matching N=10669	Warfarin (rounded) after matching N=10669	Standardised mean difference before matching (max= 0.62)	Standardised mean difference after matching (max= 0.07)
index_year:2013	4,640 (43.3%)	35,000 (44.2%)	4,600 (43.1%)	4,660 (43.7%)	0.019	0.011
index_year:2014	3,340 (31.2%)	23,330 (29.5%)	3,330 (31.2%)	3,260 (30.5%)	0.037	0.015
index_year:2015	1,400 (13.0%)	13,390 (16.9%)	1,400 (13.1%)	1,420 (13.3%)	0.109	0.006
index_year:2016	1,350 (12.6%)	7,460 (9.4%)	1,340 (12.5%)	1,340 (12.5%)	0.101	0.001
Time from AF diag:< 1 month	6,560 (61.1%)	47,550 (60.1%)	6,530 (61.2%)	6,480 (60.7%)	0.022	0.010
Time from AF diag:1 - 6 month	1,100 (10.3%)	7,970 (10.1%)	1,100 (10.3%)	1,140 (10.6%)	0.007	0.012
Time from AF diag:6 - 60 months	3,070 (28.6%)	23,650 (29.9%)	3,050 (28.5%)	3,060 (28.7%)	0.028	0.003
Sex:Female	5,700 (53.1%)	32,980 (41.7%)	5,650 (52.9%)	5,710 (53.5%)	0.230	0.012
Sex:Male	5,030 (46.9%)	46,190 (58.3%)	5,020 (47.1%)	4,960 (46.5%)	0.230	0.012
Age, median(IQR)	81.3 (75.9 - 85.7)	75.0 (67.5 - 82.2)	81.3 (75.9 - 85.7)	81.4 (76.2 - 85.9)	0.617	0.007
Age -group:< 55 years	110 (1.0%)	4,480 (5.7%)	110 (1.0%)	120 (1.1%)	0.263	0.014
Age -group:55-<65 years	500 (4.6%)	10,100 (12.8%)	500 (4.7%)	510 (4.8%)	0.291	0.004
Age -group:65-<75 years	1,760 (16.4%)	25,060 (31.6%)	1,760 (16.5%)	1,700 (15.9%)	0.362	0.016
Age -group:75-<85 years	5,310 (49.5%)	26,700 (33.7%)	5,280 (49.5%)	5,200 (48.7%)	0.324	0.016
Age -group:>= 85 years	3,050 (28.4%)	12,830 (16.2%)	3,020 (28.3%)	3,150 (29.5%)	0.297	0.026
CCI-group:0	3,850 (35.9%)	29,610 (37.4%)	3,840 (36.0%)	3,820 (35.8%)	0.031	0.004
CCI-group:1-2	3,880 (36.1%)	25,600 (32.3%)	3,860 (36.1%)	3,740 (35.0%)	0.080	0.023
CCI-group:>=3	3,000 (28.0%)	23,960 (30.3%)	2,980 (27.9%)	3,120 (29.2%)	0.050	0.029
Prior bleeding (any)	1,380 (12.9%)	8,870 (11.2%)	1,370 (12.8%)	1,430 (13.4%)	0.051	0.017
Prior gastrointestinal bleeding	150 (1.4%)	820 (1.0%)	150 (1.4%)	170 (1.5%)	0.031	0.016
Prior intracranial bleeding	170 (1.6%)	710 (0.9%)	160 (1.5%)	160 (1.5%)	0.060	0.004
Prior stroke (any)	1,730 (16.1%)	9,610 (12.1%)	1,710 (16.0%)	1,730 (16.2%)	0.114	0.006
Prior ischaemic stroke	1,680 (15.6%)	9,400 (11.9%)	1,660 (15.5%)	1,680 (15.7%)	0.109	0.006
Prior haemorrhagic stroke	130 (1.2%)	520 (0.7%)	130 (1.2%)	130 (1.2%)	0.057	0.001
Prior systemic embolism	90 (0.8%)	760 (1.0%)	90 (0.8%)	80 (0.8%)	0.016	0.006
Prior transient ischaemic attack	590 (5.5%)	3,120 (3.9%)	580 (5.4%)	570 (5.3%)	0.074	0.005
Chronic kidney disease	370 (3.5%)	6,530 (8.2%)	370 (3.5%)	390 (3.7%)	0.204	0.009
Heart failure	2,040 (19.0%)	18,010 (22.7%)	2,030 (19.0%)	2,070 (19.4%)	0.093	0.009
Coronary artery disease	2,640 (24.6%)	21,450 (27.1%)	2,630 (24.7%)	2,680 (25.1%)	0.058	0.010
Peripheral arterial disease	790 (7.4%)	6,030 (7.6%)	790 (7.4%)	790 (7.4%)	0.009	0.000
Hypertension	7,390 (68.9%)	54,110 (68.3%)	7,340 (68.8%)	7,340 (68.8%)	0.011	0.001
Diabetes	1,660 (15.5%)	14,680 (18.5%)	1,650 (15.5%)	1,670 (15.7%)	0.082	0.005
Chronic obstructive pulmonary disease	1,520 (14.2%)	10,120 (12.8%)	1,510 (14.1%)	1,560 (14.6%)	0.040	0.012
Liver disease	90 (0.8%)	820 (1.0%)	90 (0.8%)	90 (0.9%)	0.021	0.004
Alcoholism	230 (2.1%)	1,790 (2.3%)	220 (2.1%)	220 (2.1%)	0.008	0.001
Dementia	340 (3.1%)	1,220 (1.5%)	320 (3.0%)	310 (2.9%)	0.106	0.002
Cancer 6 months before and including index date	400 (3.7%)	2,140 (2.7%)	400 (3.8%)	420 (3.9%)	0.059	0.009
Platelet inhibitors (excluding heparin)	4,620 (43.0%)	30,840 (39.0%)	4,580 (42.9%)	4,570 (42.8%)	0.083	0.002
Low -dose aspirin	3,990 (37.2%)	27,180 (34.3%)	3,960 (37.1%)	3,950 (37.0%)	0.060	0.003
ADP receptor blockers	920 (8.6%)	7,100 (9.0%)	910 (8.6%)	920 (8.7%)	0.013	0.004
Renin -angiotensin system inhibitors	4,800 (44.7%)	38,070 (48.1%)	4,770 (44.7%)	4,730 (44.3%)	0.068	0.007
Angiotensin - converting enzyme inhibitors	2,280 (21.3%)	20,500 (25.9%)	2,270 (21.3%)	2,180 (20.4%)	0.109	0.022
Angiotensin II antagonists, plain	1,530 (14.3%)	11,850 (15.0%)	1,520 (14.2%)	1,580 (14.8%)	0.020	0.016
Angiotensin II antagonists, combinations	920 (8.5%)	5,210 (6.6%)	910 (8.5%)	910 (8.5%)	0.074	0.001
Beta-blockers	7,090 (66.0%)	56,980 (72.0%)	7,060 (66.1%)	7,020 (65.8%)	0.129	0.008

Proton pump inhibitors	2,410 (22.5%)	17,350 (21.9%)	2,400 (22.5%)	2,470 (23.2%)	0.013	0.015
Non-steroidal anti-inflammatory drugs	900 (8.4%)	5,860 (7.4%)	890 (8.3%)	880 (8.3%)	0.038	0.003
Statins	3,740 (34.9%)	28,740 (36.3%)	3,730 (35.0%)	3,760 (35.2%)	0.030	0.005
Antidiabetic agents	1,160 (10.8%)	10,410 (13.1%)	1,160 (10.8%)	1,140 (10.7%)	0.072	0.003
Loop diuretics	2,880 (26.9%)	22,170 (28.0%)	2,880 (27.0%)	2,900 (27.2%)	0.026	0.005
Non-loop diuretics	150 (1.4%)	1,230 (1.6%)	150 (1.4%)	140 (1.3%)	0.014	0.002
Alpha adrenergic blockers	1,920 (17.9%)	15,810 (20.0%)	1,910 (17.9%)	1,900 (17.8%)	0.054	0.003
Amiodarone	290 (2.7%)	2,560 (3.2%)	290 (2.7%)	280 (2.7%)	0.033	0.003
Dronedarone	20 (0.2%)	600 (0.8%)	20 (0.2%)	20 (0.2%)	0.078	0.002
Antihypertensive, combination drugs	1,270 (11.8%)	7,700 (9.7%)	1,260 (11.8%)	1,250 (11.7%)	0.067	0.001
Calcium channel blockers	2,750 (25.6%)	19,680 (24.9%)	2,730 (25.6%)	2,730 (25.6%)	0.018	0.000
Selective serotonin reuptake inhibitors	740 (6.9%)	4,790 (6.1%)	730 (6.8%)	720 (6.8%)	0.034	0.002
Drugs used in alcohol dependence	20 (0.2%)	120 (0.2%)	20 (0.2%)	20 (0.2%)	0.006	0.002
CHA2DS2-VASc, mean(SD)	3.9 (1.53)	3.4 (1.76)	3.9 (1.53)	3.9 (1.60)	0.303	0.012
CHA2DS2-VASc:0 -1	470 (4.4%)	11,520 (14.6%)	470 (4.4%)	630 (5.9%)	0.352	0.068
CHA2DS2-VASc:2 -3	3,970 (37.0%)	30,330 (38.3%)	3,960 (37.1%)	3,650 (34.2%)	0.027	0.061
CHA2DS2-VASc:>=4	6,290 (58.6%)	37,330 (47.1%)	6,240 (58.5%)	6,390 (59.9%)	0.231	0.029
CHADS2, mean(SD)	2.4 (1.38)	2.4 (1.51)	2.4 (1.38)	2.4 (1.41)	0.034	0.007
CHADS2:0	510 (4.7%)	8,300 (10.5%)	510 (4.7%)	650 (6.1%)	0.219	0.061
CHADS2:1	2,360 (22.0%)	15,840 (20.0%)	2,350 (22.0%)	2,160 (20.3%)	0.049	0.044
CHADS2:>=2	7,860 (73.3%)	55,030 (69.5%)	7,810 (73.2%)	7,850 (73.6%)	0.083	0.009
HAS-BLED, mean(SD)	2.3 (0.98)	2.0 (1.05)	2.3 (0.97)	2.3 (1.01)	0.270	0.000
HAS-BLED:<3	6,580 (61.3%)	56,150 (70.9%)	6,560 (61.5%)	6,460 (60.5%)	0.204	0.020
HAS-BLED:>=3	4,150 (38.7%)	23,020 (29.1%)	4,110 (38.5%)	4,210 (39.5%)	0.204	0.020
log_n_hosp, median(IQR)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.017	0.017
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.056	0.016
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.091	0.004

Table 15.53 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin and standardised mean differences before and after matching, Denmark – STANDARD DOSE

Characteristic	Dabigatran (rounded) before matching N= 7853	Warfarin (rounded) before matching N=20070	Dabigatran (rounded) after matching N= 7338	Warfarin (rounded) after matching N= 7338	Standardised mean difference before matching (max= 0.66)	Standardised mean difference after matching (max= 0.04)
index_year:2013	3,330 (42.4%)	6,810 (33.9%)	3,080 (41.9%)	3,060 (41.6%)	0.175	0.006
index_year:2014	2,810 (35.8%)	5,400 (26.9%)	2,550 (34.8%)	2,590 (35.3%)	0.193	0.011
index_year:2015	1,030 (13.1%)	4,580 (22.8%)	1,030 (14.0%)	1,020 (13.9%)	0.256	0.003
index_year:2016	680 (8.7%)	3,280 (16.4%)	680 (9.3%)	680 (9.2%)	0.232	0.004
Time from AF diag:< 1 month	5,440 (69.2%)	12,620 (62.9%)	4,960 (67.6%)	4,890 (66.7%)	0.134	0.019
Time from AF diag:1 - 6 month	680 (8.7%)	2,410 (12.0%)	680 (9.2%)	710 (9.6%)	0.110	0.014
Time from AF diag:6 - 60 months	1,740 (22.1%)	5,040 (25.1%)	1,710 (23.2%)	1,740 (23.7%)	0.071	0.011
Sex:Female	2,510 (32.0%)	7,950 (39.6%)	2,390 (32.5%)	2,380 (32.5%)	0.159	0.001
Sex:Male	5,340 (68.0%)	12,120 (60.4%)	4,950 (67.5%)	4,960 (67.5%)	0.159	0.001
Age, median(IQR)	67.3 (61.2 - 71.9)	73.3 (66.1 - 80.6)	67.6 (61.5 - 72.2)	67.8 (61.6 - 72.4)	0.656	0.014
Age -group:< 55 years	900 (11.4%)	1,520 (7.6%)	840 (11.4%)	820 (11.2%)	0.132	0.006
Age -group:55-<65 years	2,100 (26.7%)	2,870 (14.3%)	1,870 (25.5%)	1,840 (25.0%)	0.311	0.012
Age -group:65-<75 years	3,900 (49.6%)	6,820 (34.0%)	3,670 (50.0%)	3,700 (50.4%)	0.321	0.007
Age -group:75-<85 years	950 (12.1%)	6,280 (31.3%)	950 (12.9%)	970 (13.2%)	0.479	0.010
Age -group:>= 85 years	10 (0.2%)	2,580 (12.9%)	10 (0.2%)	10 (0.2%)	0.533	0.003
CCI-group:0	4,620 (58.8%)	8,600 (42.8%)	4,210 (57.3%)	4,180 (56.9%)	0.324	0.009
CCI-group:1-2	2,340 (29.7%)	6,000 (29.9%)	2,240 (30.6%)	2,180 (29.7%)	0.004	0.020
CCI-group:>=3	900 (11.4%)	5,470 (27.2%)	890 (12.1%)	980 (13.4%)	0.409	0.040
Prior bleeding (any)	490 (6.3%)	1,940 (9.7%)	470 (6.4%)	480 (6.5%)	0.127	0.004
Prior gastrointestinal bleeding	40 (0.5%)	270 (1.4%)	40 (0.5%)	40 (0.5%)	0.090	0.004
Prior intracranial bleeding	30 (0.4%)	140 (0.7%)	30 (0.4%)	40 (0.5%)	0.036	0.006
Prior stroke (any)	620 (7.8%)	1,980 (9.8%)	580 (7.9%)	580 (8.0%)	0.071	0.004
Prior ischaemic stroke	610 (7.7%)	1,940 (9.7%)	570 (7.8%)	580 (7.9%)	0.069	0.004
Prior haemorrhagic stroke	20 (0.3%)	90 (0.4%)	20 (0.3%)	20 (0.3%)	0.029	0.008
Prior systemic embolism	10 (0.2%)	110 (0.5%)	10 (0.2%)	10 (0.2%)	0.062	0.000
Prior transient ischaemic attack	210 (2.7%)	600 (3.0%)	190 (2.6%)	190 (2.6%)	0.020	0.001
Chronic kidney disease	50 (0.7%)	1,690 (8.4%)	50 (0.7%)	50 (0.7%)	0.377	0.008
Heart failure	850 (10.8%)	3,570 (17.8%)	830 (11.3%)	860 (11.7%)	0.202	0.014
Coronary artery disease	1,060 (13.5%)	4,590 (22.9%)	1,040 (14.2%)	1,050 (14.3%)	0.244	0.004
Peripheral arterial disease	320 (4.1%)	1,630 (8.1%)	320 (4.3%)	320 (4.4%)	0.169	0.005
Hypertension	4,360 (55.5%)	12,270 (61.1%)	4,090 (55.7%)	4,080 (55.5%)	0.113	0.004
Diabetes	1,010 (12.8%)	3,490 (17.4%)	980 (13.3%)	990 (13.5%)	0.128	0.006
Chronic obstructive pulmonary disease	590 (7.5%)	2,570 (12.8%)	580 (7.9%)	570 (7.7%)	0.177	0.007
Liver disease	70 (0.9%)	240 (1.2%)	70 (0.9%)	60 (0.8%)	0.029	0.010
Alcoholism	290 (3.7%)	590 (2.9%)	270 (3.7%)	280 (3.9%)	0.040	0.011
Dementia	40 (0.5%)	220 (1.1%)	40 (0.6%)	30 (0.4%)	0.062	0.015
Cancer 6 months before and including index date	200 (2.6%)	930 (4.6%)	200 (2.8%)	190 (2.6%)	0.108	0.012
Platelet inhibitors (excluding heparin)	1,860 (23.7%)	6,760 (33.7%)	1,800 (24.5%)	1,840 (25.1%)	0.223	0.014
Low -dose aspirin	1,490 (19.0%)	5,110 (25.5%)	1,440 (19.6%)	1,460 (19.8%)	0.156	0.006
ADP receptor blockers	420 (5.4%)	2,260 (11.2%)	420 (5.7%)	430 (5.9%)	0.213	0.006
Renin -angiotensin system inhibitors	3,080 (39.3%)	8,420 (42.0%)	2,890 (39.4%)	2,930 (39.9%)	0.055	0.009
Angiotensin -converting enzyme inhibitors	1,530 (19.5%)	4,510 (22.5%)	1,460 (19.9%)	1,460 (19.9%)	0.074	0.001
Angiotensin II antagonists, plain	770 (9.8%)	2,220 (11.0%)	720 (9.8%)	710 (9.7%)	0.041	0.004
Angiotensin II antagonists, combinations	550 (7.0%)	1,210 (6.0%)	490 (6.7%)	510 (6.9%)	0.037	0.007

Beta-blockers	5,310 (67.6%)	12,420 (61.9%)	4,890 (66.6%)	4,820 (65.6%)	0.120	0.021
Proton pump inhibitors	1,060 (13.5%)	4,510 (22.5%)	1,040 (14.2%)	1,010 (13.8%)	0.234	0.011
Non-steroidal anti-inflammatory drugs	890 (11.3%)	1,980 (9.9%)	800 (11.0%)	820 (11.2%)	0.046	0.007
Statins	2,340 (29.8%)	6,990 (34.8%)	2,230 (30.4%)	2,240 (30.5%)	0.107	0.002
Antidiabetic agents	810 (10.3%)	2,650 (13.2%)	790 (10.8%)	800 (10.9%)	0.090	0.006
Loop diuretics	1,150 (14.7%)	5,800 (28.9%)	1,140 (15.5%)	1,150 (15.7%)	0.349	0.005
Non-loop diuretics	90 (1.2%)	350 (1.7%)	90 (1.2%)	80 (1.1%)	0.047	0.009
Alpha adrenergic blockers	1,140 (14.5%)	3,670 (18.3%)	1,100 (14.9%)	1,110 (15.1%)	0.101	0.003
Amiodarone	200 (2.6%)	970 (4.9%)	200 (2.8%)	210 (2.8%)	0.119	0.004
Dronedarone	10 (0.1%)	30 (0.1%)	10 (0.1%)	<5	0.020	0.006
Antihypertensive, combination drugs	930 (11.8%)	2,110 (10.5%)	850 (11.5%)	870 (11.9%)	0.042	0.012
Calcium channel blockers	1,600 (20.4%)	4,790 (23.9%)	1,520 (20.7%)	1,520 (20.7%)	0.084	0.002
Selective serotonin reuptake inhibitors	340 (4.3%)	1,150 (5.7%)	330 (4.4%)	310 (4.2%)	0.067	0.012
Drugs used in alcohol dependence	30 (0.4%)	50 (0.2%)	30 (0.4%)	30 (0.4%)	0.029	0.000
CHA2DS2-VASc, mean(SD)	2.2 (1.41)	3.1 (1.67)	2.3 (1.42)	2.3 (1.46)	0.573	0.010
CHA2DS2-VASc:0-1	2,580 (32.8%)	3,580 (17.8%)	2,310 (31.5%)	2,350 (32.0%)	0.350	0.012
CHA2DS2-VASc:2-3	3,940 (50.1%)	8,410 (41.9%)	3,720 (50.7%)	3,600 (49.1%)	0.165	0.032
CHA2DS2-VASc:>=4	1,340 (17.1%)	8,080 (40.2%)	1,310 (17.9%)	1,390 (18.9%)	0.530	0.027
CHADS2, mean(SD)	1.1 (1.01)	1.6 (1.21)	1.1 (1.01)	1.1 (1.03)	0.484	0.006
CHADS2:0	2,320 (29.5%)	3,470 (17.3%)	2,110 (28.7%)	2,140 (29.1%)	0.292	0.009
CHADS2:1	3,330 (42.4%)	6,320 (31.5%)	3,100 (42.3%)	3,050 (41.6%)	0.228	0.014
CHADS2:>=2	2,200 (28.0%)	10,280 (51.2%)	2,130 (29.0%)	2,150 (29.3%)	0.488	0.006
HAS-BLED, mean(SD)	1.7 (1.08)	2.1 (1.17)	1.7 (1.08)	1.7 (1.09)	0.383	0.010
HAS-BLED:<3	6,110 (77.8%)	12,660 (63.1%)	5,660 (77.2%)	5,560 (75.7%)	0.327	0.034
HAS-BLED:>=3	1,740 (22.2%)	7,410 (36.9%)	1,680 (22.8%)	1,780 (24.3%)	0.327	0.034
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.226	0.003
log_beddays, median(IQR)	0.7 (0.0 - 1.6)	1.1 (0.0 - 1.9)	0.7 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.305	0.015
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.012	0.007
income, median(IQR), k€	168.7 (113.9 - 268.2)	122.8 (88.9 - 187.6)	162.3 (111.7 - 258.8)	161.2 (111.2 - 255.0)	0.252	0.009
education:Secondary compulsory	2,250 (28.7%)	8,430 (42.0%)	2,190 (29.9%)	2,180 (29.7%)	0.282	0.004
education:Vocational / High school	3,660 (46.7%)	8,140 (40.6%)	3,420 (46.6%)	3,460 (47.2%)	0.123	0.012
education:Higher education	1,780 (22.6%)	2,980 (14.8%)	1,570 (21.4%)	1,540 (21.0%)	0.200	0.010
education:Unknown	160 (2.1%)	520 (2.6%)	150 (2.1%)	150 (2.1%)	0.034	0.002
employment:Employed or self - employed	2,800 (35.7%)	3,720 (18.5%)	2,470 (33.6%)	2,400 (32.6%)	0.394	0.020
employment:Unemployed	620 (7.8%)	1,190 (5.9%)	590 (8.1%)	600 (8.1%)	0.074	0.002
employment:Retired	4,350 (55.4%)	15,010 (74.8%)	4,210 (57.3%)	4,270 (58.1%)	0.415	0.017
employment:Unknown	80 (1.0%)	150 (0.7%)	80 (1.0%)	80 (1.1%)	0.031	0.007

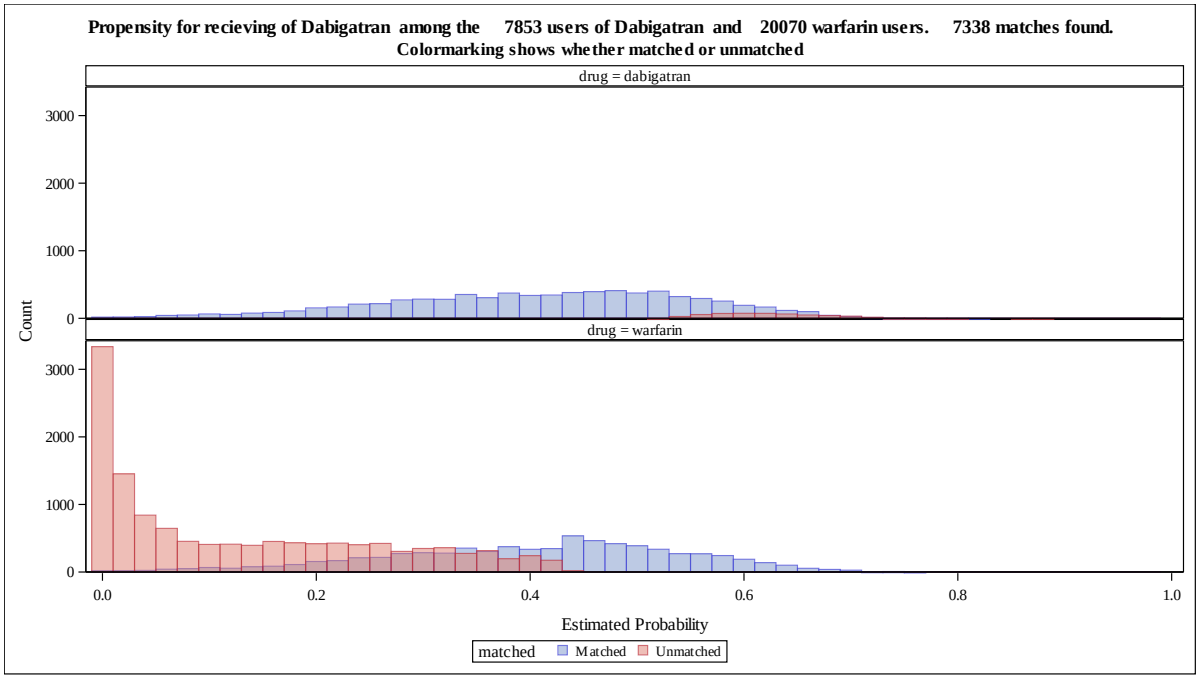
Propensity for recieving of Dabigatran among the 7853 users of Dabigatran and 20070 warfarin users. 7338 matches found.
Colormarking shows whether matched or unmatched
drug = dabigatran
drug = warfarin
Count
3000
2000
1000
0
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.54 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin and standardised mean differences before and after matching, Denmark – REDUCED DOSE

Characteristic	Dabigatran (rounded) before matching N= 4593	Warfarin (rounded) before matching N=20070	Dabigatran (rounded) after matching N= 4556	Warfarin (rounded) after matching N= 4556	Standardised mean difference before matching (max= 0.78)	Standardised mean difference after matching (max= 0.08)
index_year:2013	2,050 (44.7%)	6,810 (33.9%)	2,020 (44.4%)	2,020 (44.3%)	0.221	0.001
index_year:2014	1,560 (34.1%)	5,400 (26.9%)	1,560 (34.2%)	1,520 (33.3%)	0.156	0.019
index_year:2015	600 (13.0%)	4,580 (22.8%)	600 (13.1%)	630 (13.7%)	0.258	0.017
index_year:2016	380 (8.3%)	3,280 (16.4%)	380 (8.3%)	400 (8.7%)	0.248	0.013
Time from AF diag:< 1 month	3,040 (66.2%)	12,620 (62.9%)	3,020 (66.3%)	3,020 (66.4%)	0.069	0.001
Time from AF diag:1 - 6 month	450 (9.9%)	2,410 (12.0%)	450 (9.9%)	450 (9.9%)	0.069	0.001
Time from AF diag:6 - 60 months	1,100 (24.0%)	5,040 (25.1%)	1,080 (23.8%)	1,080 (23.7%)	0.027	0.001
Sex:Female	2,480 (53.9%)	7,950 (39.6%)	2,450 (53.7%)	2,500 (54.8%)	0.289	0.021
Sex:Male	2,120 (46.1%)	12,120 (60.4%)	2,110 (46.3%)	2,060 (45.2%)	0.289	0.021
Age, median(IQR)	81.3 (76.2 - 85.7)	73.3 (66.1 - 80.6)	81.3 (76.2 - 85.7)	81.4 (76.5 - 85.9)	0.780	0.012
Age -group:< 55 years	50 (1.0%)	1,520 (7.6%)	50 (1.0%)	50 (1.2%)	0.329	0.017
Age -group:55-<65 years	200 (4.4%)	2,870 (14.3%)	200 (4.4%)	200 (4.4%)	0.346	0.001
Age -group:65-<75 years	700 (15.3%)	6,820 (34.0%)	700 (15.5%)	670 (14.8%)	0.443	0.019
Age -group:75-<85 years	2,340 (50.9%)	6,280 (31.3%)	2,320 (51.0%)	2,260 (49.7%)	0.408	0.026
Age -group:>= 85 years	1,300 (28.3%)	2,580 (12.9%)	1,280 (28.1%)	1,370 (30.0%)	0.390	0.041
CCI-group:0	1,830 (39.8%)	8,600 (42.8%)	1,820 (40.0%)	1,830 (40.1%)	0.063	0.002
CCI-group:1-2	1,620 (35.2%)	6,000 (29.9%)	1,610 (35.3%)	1,580 (34.6%)	0.112	0.013
CCI-group:>=3	1,150 (25.1%)	5,470 (27.2%)	1,130 (24.8%)	1,150 (25.3%)	0.049	0.013
Prior bleeding (any)	510 (11.0%)	1,940 (9.7%)	500 (11.0%)	520 (11.5%)	0.045	0.017
Prior gastrointestinal bleeding	70 (1.5%)	270 (1.4%)	70 (1.5%)	70 (1.6%)	0.016	0.007
Prior intracranial bleeding	70 (1.4%)	140 (0.7%)	60 (1.3%)	60 (1.3%)	0.071	0.004
Prior stroke (any)	660 (14.3%)	1,980 (9.8%)	650 (14.2%)	630 (13.8%)	0.137	0.009
Prior ischaemic stroke	640 (14.0%)	1,940 (9.7%)	630 (13.8%)	620 (13.5%)	0.134	0.009
Prior haemorrhagic stroke	30 (0.7%)	90 (0.4%)	30 (0.7%)	30 (0.7%)	0.042	0.003
Prior systemic embolism	20 (0.4%)	110 (0.5%)	20 (0.4%)	10 (0.3%)	0.017	0.026
Prior transient ischaemic attack	220 (4.7%)	600 (3.0%)	210 (4.6%)	210 (4.5%)	0.088	0.002
Chronic kidney disease	120 (2.5%)	1,690 (8.4%)	120 (2.6%)	120 (2.7%)	0.260	0.008
Heart failure	750 (16.4%)	3,570 (17.8%)	750 (16.4%)	750 (16.5%)	0.038	0.004
Coronary artery disease	980 (21.4%)	4,590 (22.9%)	980 (21.4%)	1,040 (22.8%)	0.036	0.034
Peripheral arterial disease	300 (6.6%)	1,630 (8.1%)	300 (6.6%)	300 (6.7%)	0.059	0.002
Hypertension	3,080 (67.1%)	12,270 (61.1%)	3,050 (67.0%)	3,070 (67.4%)	0.125	0.009
Diabetes	680 (14.9%)	3,490 (17.4%)	670 (14.8%)	700 (15.3%)	0.068	0.013
Chronic obstructive pulmonary disease	660 (14.4%)	2,570 (12.8%)	650 (14.4%)	660 (14.5%)	0.047	0.003
Liver disease	30 (0.6%)	240 (1.2%)	30 (0.6%)	30 (0.6%)	0.058	0.006
Alcoholism	120 (2.6%)	590 (2.9%)	110 (2.5%)	110 (2.4%)	0.021	0.004
Dementia	160 (3.5%)	220 (1.1%)	140 (3.1%)	130 (2.7%)	0.161	0.022
Cancer 6 months before and including index date	180 (4.0%)	930 (4.6%)	180 (4.0%)	190 (4.3%)	0.030	0.011
Platelet inhibitors (excluding heparin)	1,750 (38.1%)	6,760 (33.7%)	1,730 (38.1%)	1,740 (38.2%)	0.093	0.003
Low -dose aspirin	1,320 (28.7%)	5,110 (25.5%)	1,310 (28.7%)	1,320 (28.9%)	0.073	0.004
ADP receptor blockers	560 (12.2%)	2,260 (11.2%)	560 (12.2%)	570 (12.5%)	0.031	0.009
Renin -angiotensin system inhibitors	1,940 (42.2%)	8,420 (42.0%)	1,920 (42.2%)	1,900 (41.6%)	0.005	0.012
Angiotensin -converting enzyme inhibitors	970 (21.0%)	4,510 (22.5%)	960 (21.0%)	930 (20.4%)	0.036	0.015
Angiotensin II antagonists, plain	560 (12.2%)	2,220 (11.0%)	550 (12.2%)	570 (12.6%)	0.037	0.013
Angiotensin II antagonists, combinations	330 (7.3%)	1,210 (6.0%)	330 (7.2%)	330 (7.2%)	0.049	0.003
Beta-blockers	2,840 (61.8%)	12,420 (61.9%)	2,820 (61.9%)	2,830 (62.1%)	0.001	0.003

Proton pump inhibitors	1,050 (22.9%)	4,510 (22.5%)	1,050 (23.0%)	1,060 (23.3%)	0.012	0.007
Non-steroidal anti-inflammatory drugs	460 (9.9%)	1,980 (9.9%)	450 (9.9%)	450 (9.8%)	0.001	0.004
Statins	1,560 (34.1%)	6,990 (34.8%)	1,560 (34.2%)	1,570 (34.4%)	0.016	0.006
Antidiabetic agents	500 (10.8%)	2,650 (13.2%)	490 (10.8%)	500 (11.0%)	0.075	0.006
Loop diuretics	1,350 (29.3%)	5,800 (28.9%)	1,340 (29.4%)	1,360 (29.8%)	0.009	0.008
Non-loop diuretics	70 (1.6%)	350 (1.7%)	70 (1.5%)	80 (1.7%)	0.012	0.012
Alpha adrenergic blockers	990 (21.6%)	3,670 (18.3%)	990 (21.7%)	980 (21.4%)	0.084	0.006
Amiodarone	190 (4.1%)	970 (4.9%)	190 (4.1%)	190 (4.1%)	0.037	0.000
Dronedarone	<5	30 (0.1%)	<5	10 (0.1%)	0.012	0.007
Antihypertensive, combination drugs	530 (11.4%)	2,110 (10.5%)	520 (11.4%)	510 (11.1%)	0.029	0.010
Calcium channel blockers	1,210 (26.4%)	4,790 (23.9%)	1,200 (26.4%)	1,230 (27.0%)	0.058	0.014
Selective serotonin reuptake inhibitors	350 (7.6%)	1,150 (5.7%)	340 (7.5%)	330 (7.3%)	0.076	0.010
Drugs used in alcohol dependence	10 (0.2%)	50 (0.2%)	10 (0.2%)	10 (0.2%)	0.001	0.005
CHA2DS2-VASc, mean(SD)	3.9 (1.45)	3.1 (1.67)	3.9 (1.45)	3.9 (1.51)	0.487	0.021
CHA2DS2-VASc:0 - 1	170 (3.7%)	3,580 (17.8%)	170 (3.8%)	230 (5.0%)	0.467	0.062
CHA2DS2-VASc:2 - 3	1,710 (37.2%)	8,410 (41.9%)	1,710 (37.4%)	1,570 (34.5%)	0.096	0.061
CHA2DS2-VASc:>=4	2,710 (59.0%)	8,080 (40.2%)	2,680 (58.8%)	2,750 (60.4%)	0.383	0.034
CHADS2, mean(SD)	2.1 (1.14)	1.6 (1.21)	2.1 (1.13)	2.1 (1.18)	0.407	0.009
CHADS2:0	190 (4.2%)	3,470 (17.3%)	190 (4.2%)	270 (6.0%)	0.434	0.081
CHADS2:1	1,150 (25.0%)	6,320 (31.5%)	1,150 (25.1%)	1,040 (22.7%)	0.145	0.057
CHADS2:>=2	3,260 (70.9%)	10,280 (51.2%)	3,220 (70.7%)	3,250 (71.3%)	0.411	0.014
HAS-BLED, mean(SD)	2.4 (0.99)	2.1 (1.17)	2.4 (0.99)	2.4 (1.03)	0.240	0.007
HAS-BLED:<3	2,570 (56.0%)	12,660 (63.1%)	2,560 (56.1%)	2,530 (55.5%)	0.145	0.014
HAS-BLED:>=3	2,020 (44.0%)	7,410 (36.9%)	2,000 (43.9%)	2,030 (44.5%)	0.145	0.014
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.046	0.023
log_beddays, median(IQR)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.9)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.8)	0.193	0.023
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.040	0.012
income, median(IQR), k€	104.2 (78.7 - 144.1)	122.8 (88.9 - 187.6)	104.3 (78.8 - 144.5)	104.1 (78.1 - 144.9)	0.240	0.006
education:Secondary compulsory	2,150 (46.8%)	8,430 (42.0%)	2,140 (47.0%)	2,180 (47.7%)	0.096	0.015
education:Vocational / High school	1,590 (34.6%)	8,140 (40.6%)	1,580 (34.6%)	1,550 (34.0%)	0.124	0.012
education:Higher education	630 (13.7%)	2,980 (14.8%)	620 (13.6%)	620 (13.6%)	0.033	0.001
education:Unknown	230 (5.0%)	520 (2.6%)	220 (4.8%)	210 (4.7%)	0.126	0.007
employment:Employed or self -employed	270 (5.8%)	3,720 (18.5%)	270 (5.8%)	250 (5.5%)	0.398	0.014
employment:Unemployed	90 (2.0%)	1,190 (5.9%)	90 (2.0%)	110 (2.3%)	0.202	0.020
employment:Retired	4,220 (91.9%)	15,010 (74.8%)	4,190 (91.9%)	4,190 (91.9%)	0.472	0.001
employment:Unknown	10 (0.3%)	150 (0.7%)	10 (0.3%)	10 (0.3%)	0.064	0.004

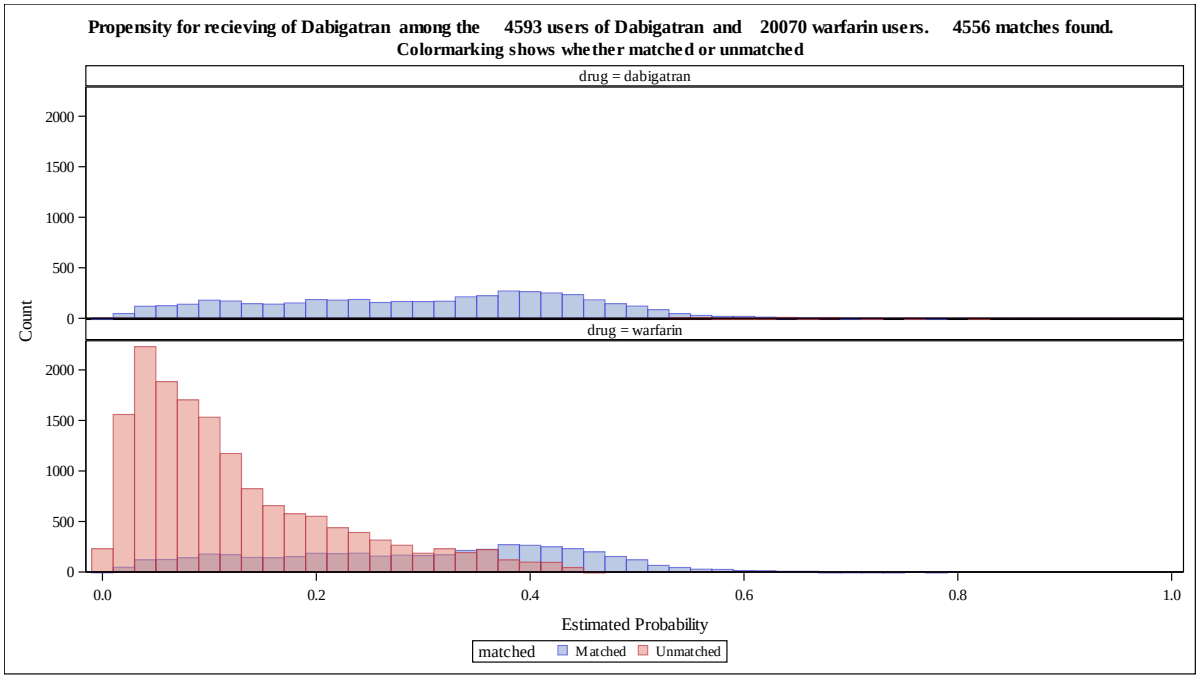
Propensity for recieving of Dabigatran among the 4593 users of Dabigatran and 20070 warfarin users. 4556 matches found.
Colormarking shows whether matched or unmatched
drug = dabigatran
drug = warfarin
Count
2000
1500
1000
500
0
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.55 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin and standardised mean differences before and after matching, Norway – STANDARD DOSE

Characteristic	Dabigatran (rounded) before matching N= 5630	Warfarin (rounded) before matching N=11949	Dabigatran (rounded) after matching N= 4590	Warfarin (rounded) after matching N= 4590	Standardised mean difference before matching (max= 0.77)	Standardised mean difference after matching (max= 0.09)
index_year:2013	2,570 (45.7%)	5,810 (48.6%)	2,240 (48.9%)	2,260 (49.2%)	0.058	0.006
index_year:2014	1,960 (34.8%)	3,450 (28.8%)	1,450 (31.5%)	1,430 (31.0%)	0.128	0.010
index_year:2015	620 (11.0%)	1,760 (14.8%)	540 (11.8%)	550 (11.9%)	0.114	0.003
index_year:2016	480 (8.6%)	930 (7.8%)	360 (7.8%)	360 (7.9%)	0.028	0.003
Time from AF diag:< 1 month	3,610 (64.1%)	6,410 (53.6%)	2,750 (60.0%)	2,670 (58.2%)	0.213	0.035
Time from AF diag:1 - 6 month	380 (6.7%)	1,340 (11.2%)	340 (7.4%)	350 (7.6%)	0.160	0.007
Time from AF diag:6 - 60 months	1,650 (29.3%)	4,200 (35.2%)	1,500 (32.6%)	1,570 (34.2%)	0.127	0.033
Sex:Female	1,690 (30.1%)	4,740 (39.7%)	1,420 (31.0%)	1,390 (30.4%)	0.202	0.013
Sex:Male	3,940 (69.9%)	7,210 (60.3%)	3,170 (69.0%)	3,200 (69.6%)	0.202	0.013
Age, median(IQR)	67.4 (61.1 - 71.9)	75.3 (66.7 - 83.2)	67.7 (61.2 - 72.8)	67.7 (61.1 - 72.9)	0.746	0.004
Age -group:< 55 years	680 (12.1%)	830 (7.0%)	570 (12.4%)	560 (12.3%)	0.177	0.003
Age -group:55-<65 years	1,460 (25.9%)	1,690 (14.2%)	1,130 (24.6%)	1,170 (25.6%)	0.296	0.022
Age -group:65-<75 years	2,760 (49.1%)	3,360 (28.1%)	2,190 (47.6%)	2,120 (46.3%)	0.442	0.027
Age -group:75-<85 years	680 (12.1%)	3,860 (32.3%)	660 (14.5%)	690 (14.9%)	0.501	0.014
Age -group:>= 85 years	40 (0.8%)	2,210 (18.5%)	40 (1.0%)	50 (1.0%)	0.630	0.002
CCI-group:0	2,880 (51.1%)	3,340 (27.9%)	2,110 (45.9%)	2,140 (46.5%)	0.487	0.011
CCI-group:1-2	1,920 (34.0%)	3,810 (31.9%)	1,690 (36.8%)	1,590 (34.6%)	0.045	0.045
CCI-group:>=3	840 (14.9%)	4,800 (40.2%)	790 (17.3%)	870 (18.9%)	0.590	0.041
Prior bleeding (any)	450 (8.0%)	1,780 (14.9%)	410 (8.9%)	420 (9.1%)	0.219	0.006
Prior gastrointestinal bleeding	30 (0.6%)	190 (1.6%)	30 (0.7%)	20 (0.5%)	0.100	0.032
Prior intracranial bleeding	30 (0.5%)	160 (1.3%)	30 (0.6%)	40 (0.8%)	0.086	0.021
Prior stroke (any)	410 (7.2%)	1,440 (12.0%)	360 (7.8%)	360 (7.8%)	0.163	0.002
Prior ischaemic stroke	400 (7.1%)	1,380 (11.5%)	350 (7.7%)	350 (7.6%)	0.154	0.004
Prior haemorrhagic stroke	20 (0.3%)	110 (0.9%)	20 (0.4%)	20 (0.4%)	0.076	0.007
Prior systemic embolism	20 (0.3%)	140 (1.2%)	20 (0.3%)	20 (0.4%)	0.105	0.004
Prior transient ischaemic attack	130 (2.3%)	460 (3.9%)	120 (2.6%)	110 (2.3%)	0.089	0.021
Chronic kidney disease	80 (1.4%)	1,560 (13.1%)	80 (1.7%)	70 (1.6%)	0.464	0.009
Heart failure	620 (10.9%)	3,110 (26.0%)	590 (12.8%)	580 (12.7%)	0.396	0.003
Coronary artery disease	960 (17.1%)	4,410 (36.9%)	920 (20.1%)	920 (20.0%)	0.457	0.004
Peripheral arterial disease	300 (5.3%)	1,370 (11.5%)	270 (5.9%)	290 (6.3%)	0.226	0.017
Hypertension	2,910 (51.7%)	7,270 (60.8%)	2,440 (53.2%)	2,410 (52.5%)	0.184	0.014
Diabetes	650 (11.5%)	2,100 (17.6%)	580 (12.7%)	590 (12.9%)	0.172	0.006
Chronic obstructive pulmonary disease	600 (10.7%)	1,850 (15.5%)	540 (11.7%)	540 (11.8%)	0.143	0.002
Liver disease	50 (0.9%)	150 (1.3%)	50 (1.0%)	50 (1.0%)	0.037	0.000
Alcoholism	120 (2.1%)	170 (1.4%)	100 (2.1%)	100 (2.1%)	0.055	0.003
Dementia	10 (0.2%)	230 (1.9%)	10 (0.3%)	10 (0.2%)	0.163	0.013
Cancer 6 months before and including index date	230 (4.1%)	810 (6.8%)	220 (4.7%)	210 (4.6%)	0.115	0.003
Platelet inhibitors (excluding heparin)	1,850 (32.8%)	5,400 (45.2%)	1,620 (35.3%)	1,640 (35.7%)	0.254	0.008
Low -dose aspirin	1,800 (32.0%)	5,060 (42.4%)	1,570 (34.3%)	1,590 (34.7%)	0.216	0.009
ADP receptor blockers	100 (1.8%)	1,130 (9.5%)	100 (2.2%)	100 (2.1%)	0.340	0.006
Renin -angiotensin system inhibitors	2,180 (38.7%)	5,500 (46.0%)	1,830 (39.8%)	1,800 (39.3%)	0.149	0.012
Angiotensin -converting enzyme inhibitors	690 (12.3%)	2,500 (20.9%)	640 (13.8%)	630 (13.7%)	0.234	0.004
Angiotensin II antagonists, plain	690 (12.3%)	1,640 (13.7%)	570 (12.4%)	540 (11.9%)	0.042	0.016

Angiotensin II antagonists, combinations	800 (14.2%)	1,450 (12.2%)	630 (13.6%)	620 (13.5%)	0.060	0.004
Beta-blockers	3,900 (69.2%)	8,410 (70.4%)	3,130 (68.1%)	3,090 (67.2%)	0.026	0.019
Proton pump inhibitors	680 (12.0%)	2,690 (22.5%)	610 (13.3%)	620 (13.4%)	0.280	0.004
H2-receptor antagonists	60 (1.1%)	170 (1.4%)	50 (1.1%)	50 (1.2%)	0.029	0.006
Non-steroidal anti-inflammatory drugs	620 (11.0%)	910 (7.6%)	470 (10.1%)	470 (10.3%)	0.119	0.004
Statins	1,800 (32.0%)	5,020 (42.0%)	1,560 (34.0%)	1,530 (33.3%)	0.208	0.015
Antidiabetic agents	420 (7.5%)	1,400 (11.7%)	390 (8.5%)	400 (8.7%)	0.144	0.006
Loop diuretics	530 (9.3%)	3,390 (28.4%)	510 (11.2%)	490 (10.8%)	0.502	0.013
Non-loop diuretics	70 (1.3%)	230 (1.9%)	60 (1.4%)	60 (1.2%)	0.048	0.013
Alpha adrenergic blockers	240 (4.3%)	960 (8.0%)	220 (4.8%)	220 (4.9%)	0.156	0.004
Amiodarone	100 (1.8%)	700 (5.9%)	100 (2.2%)	90 (2.0%)	0.215	0.009
Dronedarone	30 (0.5%)	130 (1.1%)	30 (0.6%)	30 (0.7%)	0.073	0.011
Antihypertensive, combination drugs	910 (16.2%)	1,740 (14.6%)	720 (15.8%)	720 (15.8%)	0.046	0.001
Calcium channel blockers	850 (15.1%)	2,640 (22.1%)	770 (16.8%)	780 (16.9%)	0.181	0.003
Selective serotonin reuptake inhibitors	170 (3.0%)	530 (4.5%)	140 (3.1%)	160 (3.5%)	0.077	0.022
Drugs used in alcohol dependence	20 (0.3%)	20 (0.1%)	10 (0.2%)	10 (0.2%)	0.035	0.005
CHA2DS2-VASc, mean(SD)	2.0 (1.43)	3.3 (1.86)	2.1 (1.46)	2.1 (1.56)	0.775	0.026
CHA2DS2-VASc:0-1	2,300 (40.8%)	2,240 (18.7%)	1,690 (36.7%)	1,830 (39.8%)	0.498	0.063
CHA2DS2-VASc:2-3	2,550 (45.3%)	4,370 (36.6%)	2,160 (47.1%)	1,950 (42.4%)	0.178	0.094
CHA2DS2-VASc:>=4	780 (13.9%)	5,340 (44.7%)	740 (16.2%)	820 (17.8%)	0.720	0.043
CHADS2, mean(SD)	0.9 (1.01)	1.7 (1.35)	1.0 (1.04)	0.9 (1.09)	0.683	0.029
CHADS2:0	2,540 (45.1%)	2,530 (21.1%)	1,850 (40.4%)	2,030 (44.2%)	0.527	0.079
CHADS2:1	1,860 (33.1%)	3,480 (29.1%)	1,600 (34.9%)	1,450 (31.6%)	0.085	0.070
CHADS2:>=2	1,230 (21.8%)	5,940 (49.7%)	1,130 (24.7%)	1,110 (24.1%)	0.609	0.013
HAS-BLED, mean(SD)	1.5 (1.09)	2.1 (1.26)	1.6 (1.11)	1.5 (1.14)	0.543	0.031
HAS-BLED:<3	4,620 (82.0%)	7,410 (62.0%)	3,660 (79.7%)	3,650 (79.6%)	0.456	0.003
HAS-BLED:>=3	1,010 (18.0%)	4,540 (38.0%)	930 (20.3%)	940 (20.4%)	0.456	0.003
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.7 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.508	0.005
log_beddays, median(IQR)	1.1 (0.7 - 1.6)	1.4 (0.7 - 1.8)	1.1 (0.7 - 1.8)	1.4 (0.7 - 1.8)	0.131	0.007
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.089	0.005

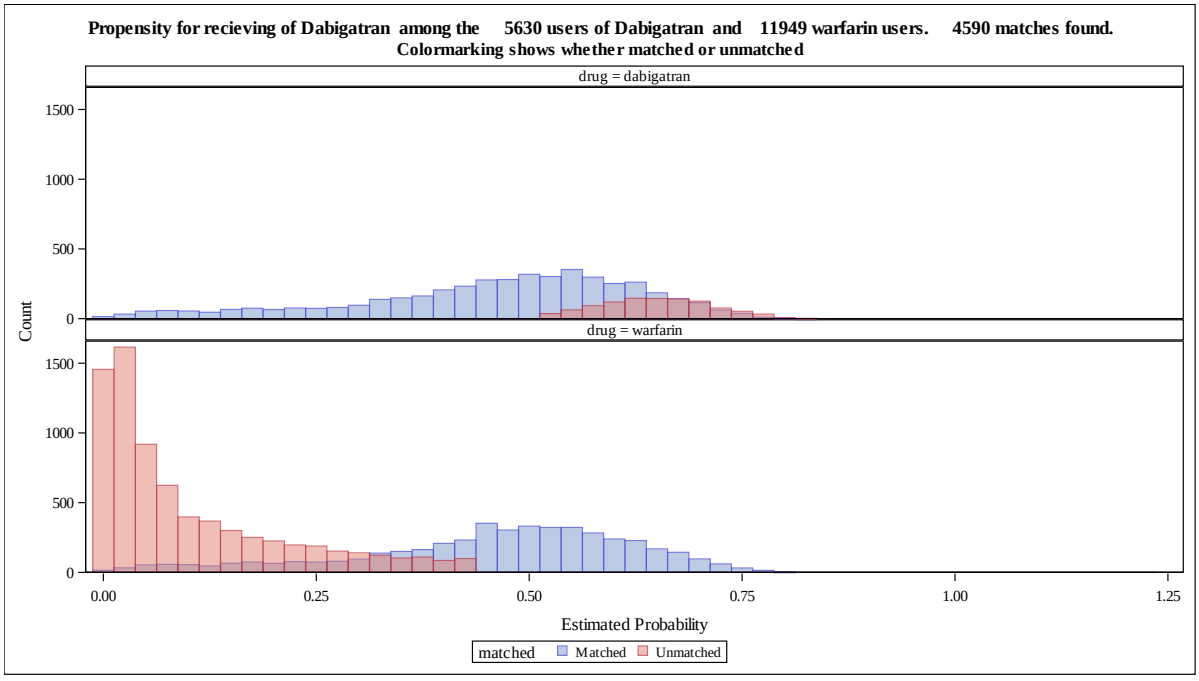

Table 15.56 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin and standardised mean differences before and after matching, Norway – REDUCED DOSE

Characteristic	Dabigatran (rounded) before matching N= 3054	Warfarin (rounded) before matching N=11949	Dabigatran (rounded) after matching N= 3035	Warfarin (rounded) after matching N= 3035	Standardised mean difference before matching (max= 0.57)	Standardised mean difference after matching (max= 0.10)
index_year:2013	1,590 (52.2%)	5,810 (48.6%)	1,580 (52.1%)	1,580 (52.0%)	0.072	0.003
index_year:2014	890 (29.2%)	3,450 (28.8%)	890 (29.4%)	890 (29.4%)	0.009	0.000
index_year:2015	310 (10.2%)	1,760 (14.8%)	310 (10.2%)	320 (10.7%)	0.139	0.014
index_year:2016	260 (8.4%)	930 (7.8%)	250 (8.3%)	240 (8.0%)	0.022	0.011
Time from AF diag:< 1 month	1,760 (57.8%)	6,410 (53.6%)	1,750 (57.7%)	1,720 (56.7%)	0.083	0.020
Time from AF diag:1 - 6 month	340 (11.2%)	1,340 (11.2%)	340 (11.1%)	350 (11.5%)	0.001	0.014
Time from AF diag:6 - 60 months	950 (31.1%)	4,200 (35.2%)	950 (31.2%)	960 (31.7%)	0.087	0.012
Sex:Female	1,620 (52.9%)	4,740 (39.7%)	1,600 (52.7%)	1,610 (53.1%)	0.269	0.009
Sex:Male	1,440 (47.1%)	7,210 (60.3%)	1,440 (47.3%)	1,420 (46.9%)	0.269	0.009
Age, median(IQR)	81.1 (75.6 - 85.7)	75.3 (66.7 - 83.2)	81.1 (75.5 - 85.7)	81.3 (75.8 - 85.8)	0.572	0.003
Age -group:< 55 years	40 (1.2%)	830 (7.0%)	40 (1.2%)	40 (1.3%)	0.296	0.012
Age -group:55-<65 years	140 (4.6%)	1,690 (14.2%)	140 (4.6%)	170 (5.5%)	0.333	0.041
Age -group:65-<75 years	540 (17.5%)	3,360 (28.1%)	540 (17.6%)	490 (16.0%)	0.254	0.043
Age -group:75-<85 years	1,490 (48.8%)	3,860 (32.3%)	1,480 (48.7%)	1,460 (48.2%)	0.341	0.009
Age -group:>= 85 years	850 (27.9%)	2,210 (18.5%)	850 (27.9%)	880 (29.0%)	0.224	0.023
CCI-group:0	1,000 (32.6%)	3,340 (27.9%)	990 (32.5%)	950 (31.1%)	0.103	0.030
CCI-group:1-2	1,090 (35.8%)	3,810 (31.9%)	1,090 (35.8%)	1,100 (36.1%)	0.082	0.006
CCI-group:>=3	960 (31.6%)	4,800 (40.2%)	960 (31.7%)	1,000 (32.8%)	0.180	0.023
Prior bleeding (any)	460 (14.9%)	1,780 (14.9%)	450 (14.9%)	480 (15.8%)	0.001	0.026
Prior gastrointestinal bleeding	50 (1.5%)	190 (1.6%)	50 (1.5%)	60 (1.8%)	0.005	0.026
Prior intracranial bleeding	50 (1.5%)	160 (1.3%)	50 (1.5%)	50 (1.7%)	0.017	0.013
Prior stroke (any)	410 (13.3%)	1,440 (12.0%)	410 (13.3%)	430 (14.3%)	0.040	0.028
Prior ischaemic stroke	390 (12.9%)	1,380 (11.5%)	390 (12.9%)	420 (13.9%)	0.041	0.030
Prior haemorrhagic stroke	30 (1.1%)	110 (0.9%)	30 (1.1%)	40 (1.2%)	0.023	0.006
Prior systemic embolism	30 (1.0%)	140 (1.2%)	30 (1.0%)	30 (0.9%)	0.018	0.007
Prior transient ischaemic attack	170 (5.6%)	460 (3.9%)	160 (5.4%)	170 (5.5%)	0.080	0.007
Chronic kidney disease	180 (5.7%)	1,560 (13.1%)	180 (5.8%)	180 (6.0%)	0.253	0.010
Heart failure	610 (19.8%)	3,110 (26.0%)	610 (19.9%)	600 (19.6%)	0.148	0.008
Coronary artery disease	880 (28.9%)	4,410 (36.9%)	880 (29.1%)	870 (28.7%)	0.171	0.009
Peripheral arterial disease	270 (8.8%)	1,370 (11.5%)	270 (8.8%)	250 (8.3%)	0.090	0.020
Hypertension	1,990 (65.2%)	7,270 (60.8%)	1,980 (65.1%)	2,000 (65.8%)	0.091	0.014
Diabetes	440 (14.3%)	2,100 (17.6%)	440 (14.4%)	440 (14.4%)	0.089	0.001
Chronic obstructive pulmonary disease	460 (15.0%)	1,850 (15.5%)	460 (15.0%)	450 (14.9%)	0.014	0.004
Liver disease	30 (0.9%)	150 (1.3%)	30 (0.9%)	30 (1.1%)	0.039	0.023
Alcoholism	40 (1.3%)	170 (1.4%)	40 (1.4%)	40 (1.3%)	0.007	0.009
Dementia	90 (3.0%)	230 (1.9%)	90 (3.0%)	100 (3.3%)	0.071	0.021
Cancer 6 months before and including index date	200 (6.4%)	810 (6.8%)	200 (6.5%)	210 (6.8%)	0.014	0.012
Platelet inhibitors (excluding heparin)	1,480 (48.6%)	5,400 (45.2%)	1,470 (48.3%)	1,420 (46.9%)	0.068	0.028
Low -dose aspirin	1,430 (47.0%)	5,060 (42.4%)	1,420 (46.7%)	1,380 (45.5%)	0.092	0.023
ADP receptor blockers	130 (4.3%)	1,130 (9.5%)	130 (4.3%)	120 (4.1%)	0.208	0.012
Renin -angiotensin system inhibitors	1,370 (44.7%)	5,500 (46.0%)	1,350 (44.6%)	1,350 (44.6%)	0.027	0.000
Angiotensin -converting enzyme inhibitors	530 (17.4%)	2,500 (20.9%)	530 (17.4%)	500 (16.5%)	0.089	0.025
Angiotensin II antagonists, plain	440 (14.3%)	1,640 (13.7%)	430 (14.3%)	440 (14.4%)	0.017	0.004
Angiotensin II antagonists, combinations	420 (13.6%)	1,450 (12.2%)	410 (13.5%)	430 (14.0%)	0.042	0.015
Beta-blockers	2,060 (67.4%)	8,410 (70.4%)	2,050 (67.5%)	2,020 (66.5%)	0.065	0.020
Proton pump inhibitors	620 (20.3%)	2,690 (22.5%)	620 (20.3%)	640 (20.9%)	0.056	0.015
H2-receptor antagonists	50 (1.5%)	170 (1.4%)	50 (1.5%)	40 (1.2%)	0.008	0.023
Non-steroidal anti-inflammatory drugs	260 (8.6%)	910 (7.6%)	260 (8.4%)	250 (8.2%)	0.037	0.010
Statins	1,130 (37.0%)	5,020 (42.0%)	1,130 (37.2%)	1,120 (37.0%)	0.102	0.003
Antidiabetic agents	310 (10.0%)	1,400 (11.7%)	310 (10.0%)	310 (10.3%)	0.056	0.010
Loop diuretics	700 (23.1%)	3,390 (28.4%)	700 (23.2%)	680 (22.2%)	0.122	0.022
Non-loop diuretics	50 (1.7%)	230 (1.9%)	50 (1.6%)	40 (1.4%)	0.019	0.022

Alpha adrenergic blockers	240 (7.8%)	960 (8.0%)	240 (7.8%)	230 (7.7%)	0.009	0.004
Amiodarone	70 (2.3%)	700 (5.9%)	70 (2.3%)	70 (2.1%)	0.182	0.011
Dronedarone	10 (0.3%)	130 (1.1%)	10 (0.3%)	10 (0.2%)	0.102	0.007
Antihypertensive, combination drugs	500 (16.2%)	1,740 (14.6%)	490 (16.1%)	510 (16.7%)	0.047	0.016
Calcium channel blockers	750 (24.5%)	2,640 (22.1%)	740 (24.3%)	740 (24.3%)	0.056	0.001
Selective serotonin reuptake inhibitors	160 (5.2%)	530 (4.5%)	160 (5.1%)	170 (5.5%)	0.036	0.015
Drugs used in alcohol dependence	<5	20 (0.1%)	<5	<5	0.002	0.010
CHA2DS2-VASc, mean(SD)	3.7 (1.54)	3.3 (1.86)	3.7 (1.54)	3.7 (1.66)	0.247	0.013
CHA2DS2-VASc:0 -1	180 (5.7%)	2,240 (18.7%)	180 (5.8%)	250 (8.2%)	0.405	0.095
CHA2DS2-VASc:2 -3	1,320 (43.1%)	4,370 (36.6%)	1,310 (43.1%)	1,160 (38.3%)	0.133	0.097
CHA2DS2-VASc:>=4	1,560 (51.2%)	5,340 (44.7%)	1,550 (51.1%)	1,620 (53.5%)	0.130	0.048
CHADS2, mean(SD)	1.9 (1.24)	1.7 (1.35)	1.9 (1.24)	1.9 (1.27)	0.174	0.019
CHADS2:0	270 (8.8%)	2,530 (21.1%)	270 (8.9%)	320 (10.6%)	0.350	0.058
CHADS2:1	1,060 (34.6%)	3,480 (29.1%)	1,050 (34.5%)	950 (31.2%)	0.117	0.070
CHADS2:>=2	1,730 (56.6%)	5,940 (49.7%)	1,720 (56.6%)	1,770 (58.2%)	0.138	0.032
HAS-BLED, mean(SD)	2.3 (1.06)	2.1 (1.26)	2.3 (1.06)	2.3 (1.11)	0.126	0.001
HAS-BLED:<3	1,850 (60.7%)	7,410 (62.0%)	1,850 (60.8%)	1,790 (59.1%)	0.028	0.036
HAS-BLED:>=3	1,200 (39.3%)	4,540 (38.0%)	1,190 (39.2%)	1,240 (40.9%)	0.028	0.036
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.193	0.012
log_beddays, median(IQR)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	0.103	0.016
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.014	0.010

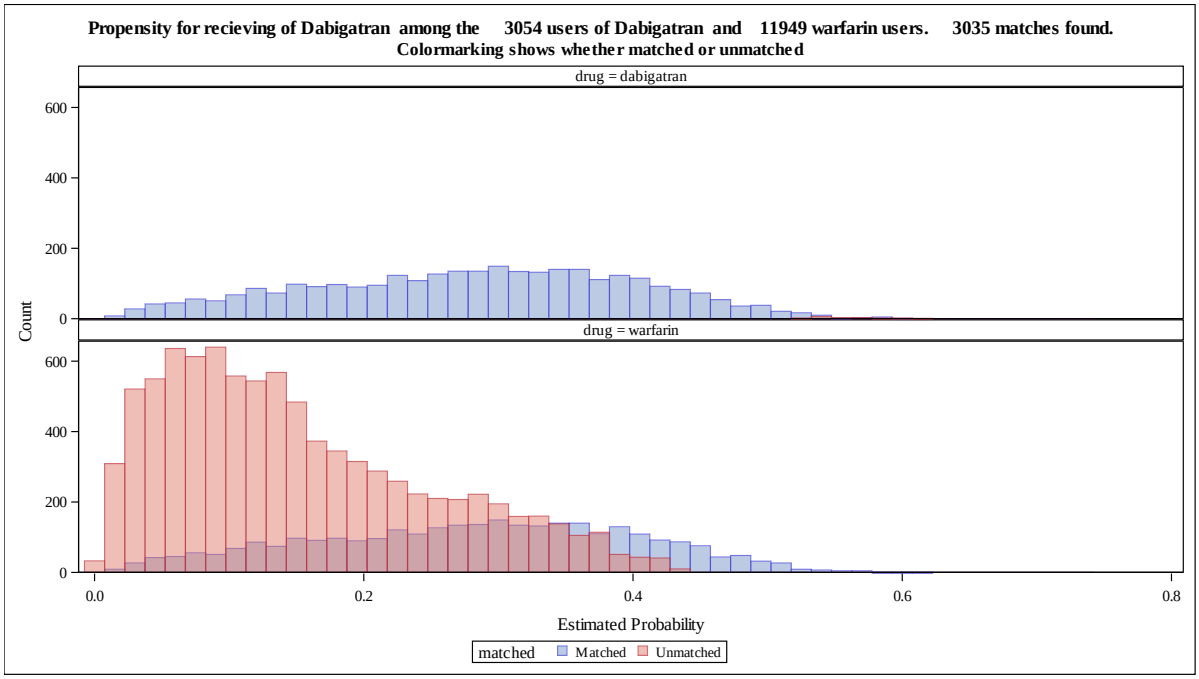

Table 15.57 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin and standardised mean differences before and after matching, Sweden – STANDARD DOSE

Characteristic	Dabigatran (rounded) before matching N= 6995	Warfarin (rounded) before matching N=47152	Dabigatran (rounded) after matching N= 6773	Warfarin (rounded) after matching N= 6773	Standardised mean difference before matching (max= 0.79)	Standardised mean difference after matching (max= 0.03)
index_year:2013	2,020 (28.9%)	22,380 (47.5%)	2,020 (29.8%)	2,080 (30.6%)	0.389	0.017
index_year:2014	2,350 (33.7%)	14,490 (30.7%)	2,350 (34.8%)	2,300 (33.9%)	0.063	0.017
index_year:2015	1,180 (16.8%)	7,040 (14.9%)	1,180 (17.4%)	1,160 (17.2%)	0.052	0.006
index_year:2016	1,440 (20.6%)	3,240 (6.9%)	1,220 (18.0%)	1,240 (18.3%)	0.407	0.006
Time from AF diag:< 1 month	4,560 (65.1%)	28,530 (60.5%)	4,410 (65.1%)	4,420 (65.2%)	0.096	0.003
Time from AF diag:1 - 6 month	490 (6.9%)	4,220 (9.0%)	480 (7.0%)	470 (7.0%)	0.074	0.002
Time from AF diag:6 - 60 months	1,950 (27.9%)	14,400 (30.5%)	1,890 (27.9%)	1,880 (27.8%)	0.058	0.002
Sex:Female	2,360 (33.7%)	20,290 (43.0%)	2,300 (34.0%)	2,280 (33.6%)	0.193	0.008
Sex:Male	4,640 (66.3%)	26,860 (57.0%)	4,470 (66.0%)	4,500 (66.4%)	0.193	0.008
Age, median(IQR)	68.3 (62.1 - 73.2)	75.6 (68.4 - 82.6)	68.4 (62.1 - 73.4)	68.3 (62.0 - 73.3)	0.794	0.009
Age -group:< 55 years	750 (10.7%)	2,130 (4.5%)	710 (10.5%)	740 (11.0%)	0.234	0.016
Age -group:55-<65 years	1,680 (24.1%)	5,540 (11.8%)	1,610 (23.8%)	1,630 (24.1%)	0.326	0.007
Age -group:65-<75 years	3,370 (48.2%)	14,880 (31.6%)	3,260 (48.2%)	3,220 (47.5%)	0.344	0.013
Age -group:75-<85 years	1,140 (16.2%)	16,570 (35.1%)	1,130 (16.7%)	1,120 (16.6%)	0.444	0.003
Age -group:>= 85 years	60 (0.9%)	8,030 (17.0%)	60 (0.9%)	60 (0.9%)	0.591	0.000
CCI-group:0	3,990 (57.0%)	17,670 (37.5%)	3,830 (56.5%)	3,780 (55.9%)	0.398	0.014
CCI-group:1-2	2,160 (30.9%)	15,790 (33.5%)	2,100 (31.0%)	2,070 (30.6%)	0.056	0.008
CCI-group:>=3	850 (12.2%)	13,700 (29.0%)	850 (12.5%)	920 (13.5%)	0.427	0.032
Prior bleeding (any)	490 (7.0%)	5,150 (10.9%)	480 (7.0%)	480 (7.1%)	0.136	0.004
Prior gastrointestinal bleeding	30 (0.4%)	360 (0.8%)	30 (0.4%)	20 (0.3%)	0.054	0.008
Prior intracranial bleeding	50 (0.8%)	410 (0.9%)	50 (0.8%)	50 (0.7%)	0.011	0.003
Prior stroke (any)	630 (9.0%)	6,200 (13.1%)	610 (9.0%)	600 (8.9%)	0.132	0.004
Prior ischaemic stroke	620 (8.8%)	6,080 (12.9%)	590 (8.8%)	590 (8.7%)	0.132	0.004
Prior haemorrhagic stroke	40 (0.5%)	330 (0.7%)	40 (0.5%)	30 (0.5%)	0.024	0.002
Prior systemic embolism	20 (0.2%)	510 (1.1%)	20 (0.3%)	10 (0.2%)	0.104	0.013
Prior transient ischaemic attack	220 (3.2%)	2,050 (4.3%)	210 (3.1%)	200 (3.0%)	0.060	0.009
Chronic kidney disease	50 (0.7%)	3,280 (7.0%)	50 (0.7%)	60 (0.8%)	0.329	0.008
Heart failure	840 (11.9%)	11,330 (24.0%)	830 (12.2%)	840 (12.4%)	0.319	0.004
Coronary artery disease	850 (12.1%)	12,460 (26.4%)	840 (12.5%)	880 (13.0%)	0.368	0.015
Peripheral arterial disease	220 (3.2%)	3,030 (6.4%)	220 (3.2%)	230 (3.3%)	0.154	0.005
Hypertension	4,310 (61.6%)	34,570 (73.3%)	4,200 (62.0%)	4,180 (61.8%)	0.252	0.005
Diabetes	970 (13.9%)	9,090 (19.3%)	960 (14.1%)	970 (14.3%)	0.144	0.006
Chronic obstructive pulmonary disease	560 (8.0%)	5,700 (12.1%)	550 (8.1%)	560 (8.2%)	0.137	0.002
Liver disease	50 (0.7%)	430 (0.9%)	50 (0.7%)	60 (0.9%)	0.019	0.015
Alcoholism	220 (3.1%)	1,030 (2.2%)	210 (3.2%)	230 (3.4%)	0.060	0.012
Dementia	20 (0.3%)	770 (1.6%)	20 (0.4%)	30 (0.4%)	0.131	0.002
Cancer 6 months before and including index date	40 (0.6%)	400 (0.9%)	40 (0.6%)	30 (0.5%)	0.035	0.012
Platelet inhibitors (excluding heparin)	2,030 (29.0%)	18,680 (39.6%)	1,980 (29.3%)	2,020 (29.8%)	0.225	0.013
Low -dose aspirin	1,890 (27.0%)	17,010 (36.1%)	1,850 (27.2%)	1,880 (27.8%)	0.196	0.012
ADP receptor blockers	200 (2.9%)	3,710 (7.9%)	200 (2.9%)	210 (3.1%)	0.223	0.012
Renin -angiotensin system inhibitors	2,980 (42.7%)	24,140 (51.2%)	2,920 (43.1%)	2,910 (42.9%)	0.172	0.004

Angiotensin -converting enzyme inhibitors	1,470 (21.0%)	13,490 (28.6%)	1,450 (21.5%)	1,480 (21.9%)	0.177	0.010
Angiotensin II antagonists, plain	970 (13.9%)	8,000 (17.0%)	950 (14.0%)	920 (13.5%)	0.085	0.015
Angiotensin II antagonists, combinations	460 (6.6%)	2,540 (5.4%)	440 (6.6%)	440 (6.4%)	0.049	0.005
Beta-blockers	5,460 (78.1%)	36,150 (76.7%)	5,290 (78.1%)	5,270 (77.8%)	0.034	0.008
Proton pump inhibitors	1,030 (14.7%)	10,150 (21.5%)	1,020 (15.0%)	1,030 (15.2%)	0.177	0.005
H2-receptor antagonists	20 (0.2%)	210 (0.4%)	20 (0.2%)	20 (0.2%)	0.038	0.003
Non-steroidal anti-inflammatory drugs	590 (8.4%)	2,970 (6.3%)	570 (8.4%)	590 (8.6%)	0.079	0.007
Statins	1,960 (28.1%)	16,730 (35.5%)	1,910 (28.3%)	1,980 (29.2%)	0.160	0.021
Antidiabetic agents	680 (9.6%)	6,350 (13.5%)	660 (9.8%)	670 (9.8%)	0.120	0.001
Loop diuretics	810 (11.6%)	12,990 (27.5%)	800 (11.9%)	810 (12.0%)	0.411	0.004
Non-loop diuretics	60 (0.9%)	650 (1.4%)	60 (0.8%)	60 (0.9%)	0.049	0.006
Alpha adrenergic blockers	1,310 (18.7%)	11,180 (23.7%)	1,280 (18.9%)	1,290 (19.0%)	0.122	0.003
Amiodarone	50 (0.7%)	890 (1.9%)	50 (0.7%)	50 (0.7%)	0.109	0.007
Dronedarone	40 (0.6%)	440 (0.9%)	40 (0.6%)	40 (0.6%)	0.040	0.002
Antihypertensive, combination drugs	700 (10.0%)	3,850 (8.2%)	670 (9.9%)	650 (9.6%)	0.063	0.009
Calcium channel blockers	1,510 (21.6%)	12,240 (26.0%)	1,470 (21.7%)	1,460 (21.6%)	0.103	0.002
Selective serotonin reuptake inhibitors	300 (4.3%)	3,110 (6.6%)	300 (4.4%)	290 (4.3%)	0.100	0.007
Drugs used in alcohol dependence	20 (0.2%)	60 (0.1%)	10 (0.2%)	10 (0.2%)	0.023	0.000
CHA2DS2-VASc, mean(SD)	2.4 (1.55)	3.6 (1.75)	2.4 (1.55)	2.4 (1.55)	0.706	0.004
CHA2DS2-VASc:0 -1	2,130 (30.5%)	5,700 (12.1%)	2,030 (29.9%)	2,020 (29.9%)	0.461	0.001
CHA2DS2-VASc:2 -3	3,330 (47.6%)	17,540 (37.2%)	3,240 (47.8%)	3,280 (48.4%)	0.211	0.011
CHA2DS2-VASc:>=4	1,540 (21.9%)	23,910 (50.7%)	1,510 (22.3%)	1,480 (21.8%)	0.627	0.012
CHADS2, mean(SD)	1.9 (1.32)	2.9 (1.47)	1.9 (1.32)	1.9 (1.33)	0.666	0.011
CHADS2:0	940 (13.4%)	2,300 (4.9%)	880 (13.0%)	920 (13.5%)	0.299	0.014
CHADS2:1	1,880 (26.9%)	6,040 (12.8%)	1,810 (26.7%)	1,800 (26.5%)	0.358	0.004
CHADS2:>=2	4,180 (59.7%)	38,810 (82.3%)	4,080 (60.3%)	4,060 (60.0%)	0.514	0.006
HAS-BLED, mean(SD)	1.5 (0.91)	1.9 (0.92)	1.5 (0.90)	1.5 (0.91)	0.498	0.013
HAS-BLED:<3	6,220 (89.0%)	36,080 (76.5%)	6,020 (88.9%)	6,040 (89.1%)	0.334	0.008
HAS-BLED:>=3	770 (11.0%)	11,080 (23.5%)	750 (11.1%)	740 (10.9%)	0.334	0.008
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.363	0.007
log_beddays, median(IQR)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.097	0.009
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.056	0.003
income, median(IQR), k€	70.7 (47.2 - 104.2)	49.8 (40.5 - 72.3)	69.1 (46.9 - 102.9)	69.4 (47.1 - 100.3)	0.261	0.001
education:Secondary compulsory	1,690 (24.1%)	18,850 (40.0%)	1,670 (24.6%)	1,670 (24.7%)	0.345	0.002
education:Vocational / High school	2,890 (41.3%)	18,480 (39.2%)	2,820 (41.7%)	2,810 (41.5%)	0.044	0.004
education:Higher education	2,360 (33.7%)	9,340 (19.8%)	2,230 (32.9%)	2,230 (32.9%)	0.318	0.000
education:Unknown	60 (0.8%)	490 (1.0%)	60 (0.8%)	60 (0.9%)	0.021	0.008

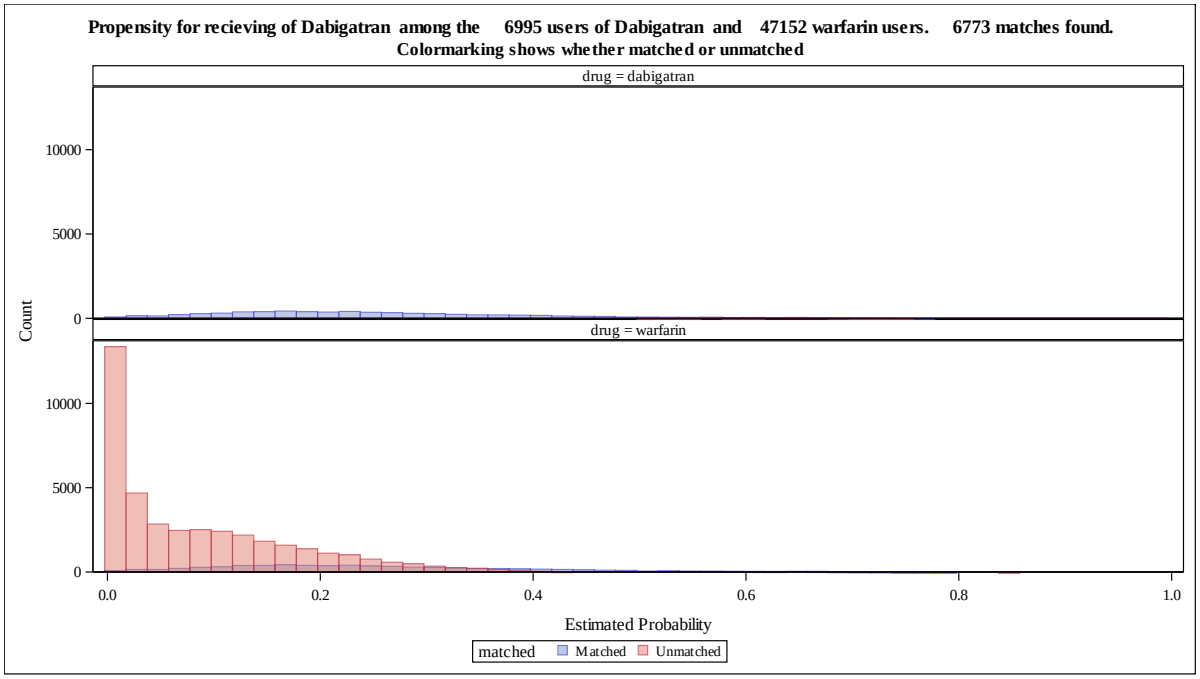
Propensity for recieving of Dabigatran among the 6995 users of Dabigatran and 47152 warfarin users. 6773 matches found.
Colormarking shows whether matched or unmatched
drug = dabigatran
drug = warfarin
Count
10000
5000
0
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.58 Baseline characteristics of patients with non-valvular atrial fibrillation initiating dabigatran or warfarin and standardised mean differences before and after matching, Sweden – REDUCED DOSE

Characteristic	Dabigatran (rounded) before matching N= 3084	Warfarin (rounded) before matching N=47152	Dabigatran (rounded) after matching N= 3078	Warfarin (rounded) after matching N= 3078	Standardised mean difference before matching (max= 0.56)	Standardised mean difference after matching (max= 0.07)
index_year:2013	1,000 (32.4%)	22,380 (47.5%)	1,000 (32.5%)	1,060 (34.5%)	0.312	0.044
index_year:2014	890 (28.7%)	14,490 (30.7%)	890 (28.8%)	850 (27.6%)	0.044	0.025
index_year:2015	490 (15.8%)	7,040 (14.9%)	490 (15.9%)	470 (15.2%)	0.025	0.017
index_year:2016	710 (23.1%)	3,240 (6.9%)	710 (22.9%)	700 (22.6%)	0.466	0.008
Time from AF diag:< 1 month	1,760 (56.9%)	28,530 (60.5%)	1,760 (57.1%)	1,730 (56.2%)	0.072	0.017
Time from AF diag:1 - 6 month	310 (10.0%)	4,220 (9.0%)	310 (10.0%)	340 (10.9%)	0.036	0.030
Time from AF diag:6 - 60 months	1,020 (33.0%)	14,400 (30.5%)	1,020 (33.0%)	1,010 (32.9%)	0.054	0.001
Sex:Female	1,600 (52.0%)	20,290 (43.0%)	1,600 (52.0%)	1,600 (52.0%)	0.181	0.001
Sex:Male	1,480 (48.0%)	26,860 (57.0%)	1,480 (48.0%)	1,480 (48.0%)	0.181	0.001
Age, median(IQR)	81.4 (75.8 - 85.8)	75.6 (68.4 - 82.6)	81.4 (75.8 - 85.8)	81.6 (75.9 - 85.7)	0.564	0.003
Age -group:< 55 years	20 (0.8%)	2,130 (4.5%)	20 (0.8%)	30 (0.9%)	0.234	0.011
Age -group:55-<65 years	160 (5.1%)	5,540 (11.8%)	160 (5.1%)	140 (4.6%)	0.242	0.024
Age -group:65-<75 years	520 (17.0%)	14,880 (31.6%)	520 (17.0%)	540 (17.6%)	0.345	0.015
Age -group:75-<85 years	1,480 (48.1%)	16,570 (35.1%)	1,480 (48.1%)	1,470 (47.7%)	0.265	0.008
Age -group:>= 85 years	900 (29.1%)	8,030 (17.0%)	890 (29.0%)	900 (29.3%)	0.288	0.006
CCI-group:0	1,030 (33.4%)	17,670 (37.5%)	1,030 (33.4%)	1,050 (34.0%)	0.086	0.011
CCI-group:1-2	1,170 (37.8%)	15,790 (33.5%)	1,160 (37.8%)	1,070 (34.6%)	0.091	0.066
CCI-group:>=3	890 (28.8%)	13,700 (29.0%)	890 (28.8%)	970 (31.4%)	0.006	0.057
Prior bleeding (any)	420 (13.5%)	5,150 (10.9%)	410 (13.4%)	420 (13.7%)	0.080	0.008
Prior gastrointestinal bleeding	30 (0.9%)	360 (0.8%)	30 (0.9%)	40 (1.1%)	0.020	0.019
Prior intracranial bleeding	50 (1.8%)	410 (0.9%)	50 (1.7%)	50 (1.5%)	0.078	0.021
Prior stroke (any)	660 (21.5%)	6,200 (13.1%)	660 (21.3%)	670 (21.7%)	0.222	0.008
Prior ischaemic stroke	640 (20.7%)	6,080 (12.9%)	630 (20.6%)	640 (20.8%)	0.210	0.004
Prior haemorrhagic stroke	60 (2.0%)	330 (0.7%)	60 (1.9%)	60 (1.9%)	0.111	0.005
Prior systemic embolism	40 (1.2%)	510 (1.1%)	40 (1.2%)	40 (1.3%)	0.013	0.009
Prior transient ischaemic attack	210 (6.7%)	2,050 (4.3%)	210 (6.7%)	190 (6.2%)	0.102	0.018
Chronic kidney disease	80 (2.7%)	3,280 (7.0%)	80 (2.7%)	90 (2.8%)	0.202	0.010
Heart failure	680 (22.0%)	11,330 (24.0%)	680 (22.1%)	720 (23.5%)	0.047	0.033
Coronary artery disease	770 (25.0%)	12,460 (26.4%)	770 (25.1%)	760 (24.8%)	0.032	0.006
Peripheral arterial disease	220 (7.2%)	3,030 (6.4%)	220 (7.1%)	240 (7.7%)	0.032	0.020
Hypertension	2,320 (75.1%)	34,570 (73.3%)	2,310 (75.1%)	2,270 (73.7%)	0.041	0.032
Diabetes	540 (17.5%)	9,090 (19.3%)	540 (17.5%)	540 (17.5%)	0.046	0.001
Chronic obstructive pulmonary disease	400 (13.0%)	5,700 (12.1%)	400 (13.0%)	450 (14.5%)	0.027	0.042
Liver disease	30 (1.1%)	430 (0.9%)	30 (1.1%)	30 (1.0%)	0.017	0.003
Alcoholism	70 (2.3%)	1,030 (2.2%)	70 (2.3%)	70 (2.4%)	0.007	0.009
Dementia	90 (2.8%)	770 (1.6%)	90 (2.8%)	90 (2.8%)	0.077	0.004
Cancer 6 months before and including index date	20 (0.7%)	400 (0.9%)	20 (0.7%)	20 (0.7%)	0.016	0.000
Platelet inhibitors (excluding heparin)	1,380 (44.9%)	18,680 (39.6%)	1,380 (44.8%)	1,410 (45.7%)	0.107	0.018
Low -dose aspirin	1,240 (40.2%)	17,010 (36.1%)	1,240 (40.3%)	1,250 (40.6%)	0.086	0.008
ADP receptor blockers	230 (7.5%)	3,710 (7.9%)	230 (7.4%)	230 (7.6%)	0.015	0.006

Renin -angiotensin system inhibitors	1,490 (48.3%)	24,140 (51.2%)	1,490 (48.4%)	1,480 (48.0%)	0.057	0.008
Angiotensin -converting enzyme inhibitors	790 (25.5%)	13,490 (28.6%)	790 (25.5%)	750 (24.3%)	0.070	0.029
Angiotensin II antagonists, plain	530 (17.3%)	8,000 (17.0%)	530 (17.3%)	570 (18.5%)	0.008	0.031
Angiotensin II antagonists, combinations	170 (5.4%)	2,540 (5.4%)	170 (5.5%)	160 (5.1%)	0.002	0.016
Beta-blockers	2,190 (71.0%)	36,150 (76.7%)	2,190 (71.1%)	2,170 (70.5%)	0.130	0.012
Proton pump inhibitors	740 (23.9%)	10,150 (21.5%)	740 (23.9%)	770 (25.1%)	0.058	0.028
H2-receptor antagonists	10 (0.2%)	210 (0.4%)	10 (0.2%)	<5	0.045	0.026
Non-steroidal anti-inflammatory drugs	190 (6.0%)	2,970 (6.3%)	180 (5.9%)	190 (6.1%)	0.013	0.007
Statins	1,050 (34.0%)	16,730 (35.5%)	1,050 (34.0%)	1,070 (34.6%)	0.032	0.013
Antidiabetic agents	360 (11.6%)	6,350 (13.5%)	360 (11.7%)	330 (10.8%)	0.055	0.029
Loop diuretics	830 (27.0%)	12,990 (27.5%)	830 (27.1%)	870 (28.1%)	0.011	0.024
Non-loop diuretics	30 (0.8%)	650 (1.4%)	30 (0.8%)	20 (0.8%)	0.055	0.004
Alpha adrenergic blockers	690 (22.2%)	11,180 (23.7%)	690 (22.3%)	690 (22.4%)	0.035	0.002
Amiodarone	30 (1.0%)	890 (1.9%)	30 (1.0%)	30 (1.0%)	0.076	0.000
Dronedarone	10 (0.4%)	440 (0.9%)	10 (0.4%)	10 (0.3%)	0.072	0.006
Antihypertensive, combination drugs	250 (7.9%)	3,850 (8.2%)	250 (8.0%)	240 (7.7%)	0.008	0.008
Calcium channel blockers	790 (25.7%)	12,240 (26.0%)	790 (25.7%)	770 (24.9%)	0.007	0.019
Selective serotonin reuptake inhibitors	230 (7.4%)	3,110 (6.6%)	230 (7.4%)	220 (7.3%)	0.031	0.005
Drugs used in alcohol dependence	<5	60 (0.1%)	<5	10 (0.2%)	0.003	0.009
CHA2DS2-VASc, mean(SD)	4.2 (1.59)	3.6 (1.75)	4.2 (1.59)	4.2 (1.66)	0.360	0.001
CHA2DS2-VASc:0 -1	130 (4.1%)	5,700 (12.1%)	130 (4.1%)	160 (5.0%)	0.298	0.047
CHA2DS2-VASc:2 -3	940 (30.6%)	17,540 (37.2%)	940 (30.7%)	910 (29.6%)	0.140	0.023
CHA2DS2-VASc:>=4	2,020 (65.3%)	23,910 (50.7%)	2,010 (65.3%)	2,010 (65.4%)	0.300	0.002
CHADS2, mean(SD)	3.4 (1.37)	2.9 (1.47)	3.4 (1.37)	3.4 (1.40)	0.369	0.004
CHADS2:0	50 (1.5%)	2,300 (4.9%)	50 (1.5%)	60 (1.9%)	0.196	0.035
CHADS2:1	160 (5.2%)	6,040 (12.8%)	160 (5.2%)	180 (5.8%)	0.270	0.029
CHADS2:>=2	2,880 (93.4%)	38,810 (82.3%)	2,870 (93.4%)	2,840 (92.3%)	0.344	0.043
HAS-BLED, mean(SD)	2.1 (0.83)	1.9 (0.92)	2.1 (0.83)	2.1 (0.85)	0.227	0.012
HAS-BLED:<3	2,150 (69.8%)	36,080 (76.5%)	2,150 (69.9%)	2,140 (69.4%)	0.151	0.013
HAS-BLED:>=3	930 (30.2%)	11,080 (23.5%)	930 (30.1%)	940 (30.6%)	0.151	0.013
log_n_hosp, median(IQR)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.043	0.015
log_beddays, median(IQR)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.046	0.032
log_n_outpatient, median(IQR)	0.7 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.168	0.004
income, median(IQR), k€	48.0 (40.0 - 66.2)	49.8 (40.5 - 72.3)	48.0 (40.1 - 66.2)	47.6 (39.6 - 66.0)	0.024	0.023
education:Secondary compulsory	1,280 (41.3%)	18,850 (40.0%)	1,270 (41.4%)	1,290 (41.9%)	0.028	0.011
education:Vocational / High school	1,100 (35.7%)	18,480 (39.2%)	1,100 (35.7%)	1,100 (35.8%)	0.071	0.001
education:Higher education	660 (21.3%)	9,340 (19.8%)	660 (21.3%)	630 (20.4%)	0.037	0.022
education:Unknown	50 (1.6%)	490 (1.0%)	50 (1.6%)	60 (1.9%)	0.050	0.025

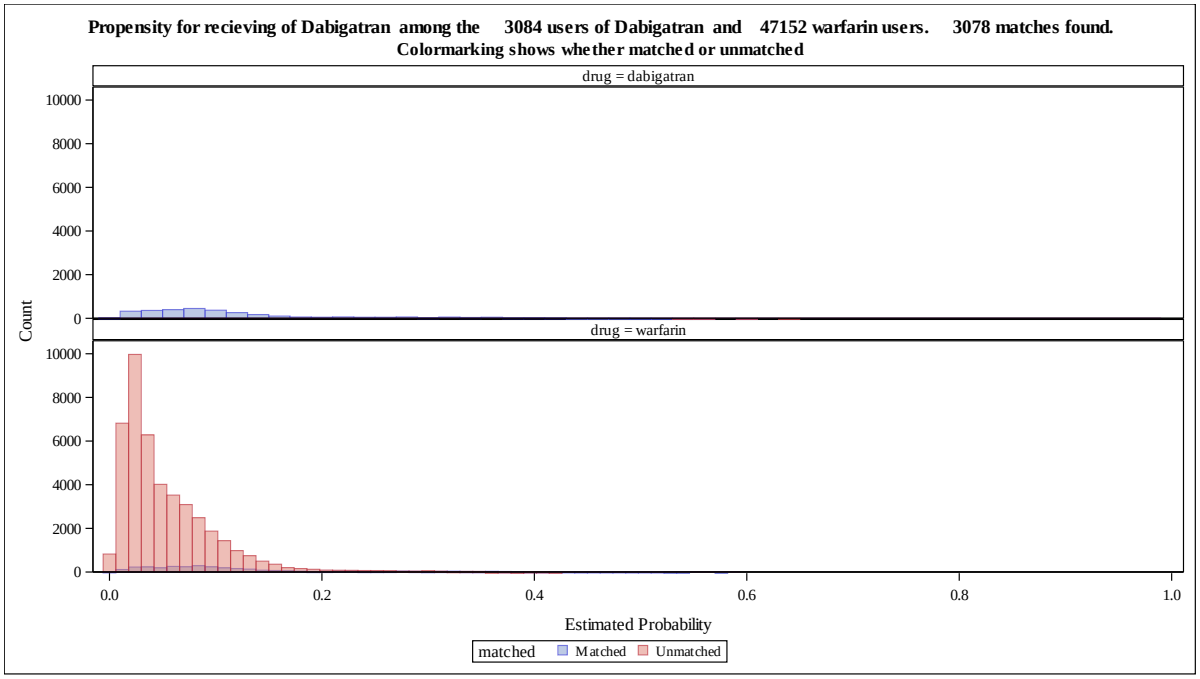
Propensity for recieving of Dabigatran among the 3084 users of Dabigatran and 47152 warfarin users. 3078 matches found.
Colormarking shows whether matched or unmatched
drug = dabigatran
drug = warfarin
Count
10000
8000
6000
4000
2000
0
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.59 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin in Denmark, Norway, or Sweden and standardised mean differences before and after matching – STANDARD DOSE

Characteristic	Rivaroxaban (rounded) before matching N=28366	Warfarin (rou nded) before matching N=79171	Rivaroxaban (rounded) after matching N=23703	Warfarin (rou nded) after matching N=23703	Standardised mean difference before matchi ng (max= 0.62)	Standardised mean difference after matching (max= 0.06)
index_year:2013	4,760 (16.8%)	35,000 (44.2%)	4,760 (20.1%)	4,680 (19.7%)	0.624	0.008
index_year:2014	5,960 (21.0%)	23,330 (29.5%)	5,800 (24.5%)	5,680 (24.0%)	0.196	0.012
index_year:2015	8,590 (30.3%)	13,390 (16.9%)	7,380 (31.1%)	7,520 (31.7%)	0.319	0.013
index_year:2016	9,070 (32.0%)	7,460 (9.4%)	5,770 (24.3%)	5,820 (24.6%)	0.579	0.006
Time from AF diag:< 1 month	17,990 (63.4%)	47,550 (60.1%)	14,760 (62.3%)	14,630 (61.7%)	0.069	0.011
Time from AF diag:1 - 6 month	2,720 (9.6%)	7,970 (10.1%)	2,370 (10.0%)	2,510 (10.6%)	0.016	0.019
Time from AF diag:6 - 60 months	7,650 (27.0%)	23,650 (29.9%)	6,570 (27.7%)	6,560 (27.7%)	0.064	0.001
Sex:Female	11,690 (41.2%)	32,980 (41.7%)	9,810 (41.4%)	9,830 (41.5%)	0.009	0.001
Sex:Male	16,680 (58.8%)	46,190 (58.3%)	13,890 (58.6%)	13,880 (58.5%)	0.009	0.001
Age, median(IQR)	71.8 (65.8 - 78.5)	75.0 (67.5 - 82.2)	72.5 (66.0 - 79.4)	72.7 (66.1 - 79.7)	0.225	0.021
Age -group:< 55 years	1,690 (6.0%)	4,480 (5.7%)	1,470 (6.2%)	1,400 (5.9%)	0.013	0.012
Age -group:55-<65 years	4,570 (16.1%)	10,100 (12.8%)	3,620 (15.3%)	3,670 (15.5%)	0.095	0.005
Age -group:65-<75 years	11,460 (40.4%)	25,060 (31.6%)	9,020 (38.1%)	8,850 (37.3%)	0.183	0.015
Age -group:75-<85 years	8,070 (28.4%)	26,700 (33.7%)	7,110 (30.0%)	7,170 (30.2%)	0.114	0.006
Age -group:>= 85 years	2,580 (9.1%)	12,830 (16.2%)	2,480 (10.5%)	2,620 (11.0%)	0.215	0.018
CCI-group:0	13,380 (47.2%)	29,610 (37.4%)	10,770 (45.4%)	10,750 (45.4%)	0.199	0.002
CCI-group:1-2	9,640 (34.0%)	25,600 (32.3%)	8,120 (34.3%)	7,710 (32.5%)	0.035	0.037
CCI-group:>=3	5,350 (18.9%)	23,960 (30.3%)	4,810 (20.3%)	5,240 (22.1%)	0.267	0.045
Prior bleeding (any)	2,560 (9.0%)	8,870 (11.2%)	2,230 (9.4%)	2,250 (9.5%)	0.072	0.003
Prior gastrointestinal bleeding	180 (0.6%)	820 (1.0%)	170 (0.7%)	170 (0.7%)	0.043	0.002
Prior intracranial bleeding	270 (0.9%)	710 (0.9%)	230 (1.0%)	230 (1.0%)	0.004	0.000
Prior stroke (any)	3,270 (11.5%)	9,610 (12.1%)	2,780 (11.7%)	2,800 (11.8%)	0.019	0.002
Prior ischaemic stroke	3,180 (11.2%)	9,400 (11.9%)	2,710 (11.4%)	2,730 (11.5%)	0.021	0.003
Prior haemorrhagic stroke	190 (0.7%)	520 (0.7%)	160 (0.7%)	150 (0.6%)	0.000	0.005
Prior systemic embolism	130 (0.5%)	760 (1.0%)	130 (0.5%)	130 (0.5%)	0.058	0.000
Prior transient ischaemic attack	1,010 (3.5%)	3,120 (3.9%)	860 (3.6%)	880 (3.7%)	0.021	0.005
Chronic kidney disease	450 (1.6%)	6,530 (8.2%)	450 (1.9%)	530 (2.2%)	0.312	0.025
Heart failure	3,770 (13.3%)	18,010 (22.7%)	3,510 (14.8%)	3,550 (15.0%)	0.248	0.005
Coronary artery disease	4,930 (17.4%)	21,450 (27.1%)	4,450 (18.8%)	4,510 (19.0%)	0.236	0.007
Peripheral arterial disease	1,650 (5.8%)	6,030 (7.6%)	1,440 (6.1%)	1,480 (6.2%)	0.072	0.006
Hypertension	17,780 (62.7%)	54,110 (68.3%)	15,060 (63.5%)	15,190 (64.1%)	0.119	0.012
Diabetes	4,240 (14.9%)	14,680 (18.5%)	3,700 (15.6%)	3,780 (15.9%)	0.096	0.009
Chronic obstructive pulmonary disease	3,300 (11.6%)	10,120 (12.8%)	2,820 (11.9%)	2,920 (12.3%)	0.035	0.012
Liver disease	240 (0.8%)	820 (1.0%)	210 (0.9%)	220 (0.9%)	0.021	0.004
Alcoholism	820 (2.9%)	1,790 (2.3%)	690 (2.9%)	660 (2.8%)	0.040	0.006
Dementia	460 (1.6%)	1,220 (1.5%)	400 (1.7%)	410 (1.7%)	0.007	0.006
Cancer 6 months before and including index date	870 (3.1%)	2,140 (2.7%)	740 (3.1%)	760 (3.2%)	0.022	0.005
Platelet inhibitors (excluding heparin)	9,850 (34.7%)	30,840 (39.0%)	8,370 (35.3%)	8,590 (36.2%)	0.087	0.019

Low -dose aspirin	8,660 (30.5%)	27,180 (34.3%)	7,290 (30.8%)	7,460 (31.5%)	0.081	0.015
ADP receptor blockers	1,490 (5.3%)	7,100 (9.0%)	1,400 (5.9%)	1,440 (6.1%)	0.145	0.008
Renin -angiotensin system inhibitors	12,190 (43.0%)	38,070 (48.1%)	10,330 (43.6%)	10,350 (43.7%)	0.102	0.001
Angiotensin -converting enzyme inhibitors	5,260 (18.6%)	20,500 (25.9%)	4,760 (20.1%)	4,730 (20.0%)	0.177	0.002
Angiotensin II antagonists, plain	3,940 (13.9%)	11,850 (15.0%)	3,290 (13.9%)	3,340 (14.1%)	0.031	0.007
Angiotensin II antagonists, combinations	2,610 (9.2%)	5,210 (6.6%)	1,960 (8.3%)	1,950 (8.2%)	0.097	0.003
Beta-blockers	18,990 (67.0%)	56,980 (72.0%)	16,070 (67.8%)	15,940 (67.2%)	0.109	0.012
Proton pump inhibitors	5,150 (18.2%)	17,350 (21.9%)	4,500 (19.0%)	4,490 (19.0%)	0.094	0.001
Non-steroidal anti-inflammatory drugs	2,460 (8.7%)	5,860 (7.4%)	1,960 (8.3%)	1,910 (8.1%)	0.046	0.007
Statins	9,290 (32.8%)	28,740 (36.3%)	7,870 (33.2%)	7,950 (33.5%)	0.075	0.007
Antidiabetic agents	3,070 (10.8%)	10,410 (13.1%)	2,670 (11.3%)	2,740 (11.5%)	0.072	0.009
Loop diuretics	4,600 (16.2%)	22,170 (28.0%)	4,310 (18.2%)	4,410 (18.6%)	0.287	0.011
Non-loop diuretics	320 (1.1%)	1,230 (1.6%)	270 (1.1%)	280 (1.2%)	0.038	0.005
Alpha adrenergic blockers	4,380 (15.4%)	15,810 (20.0%)	3,930 (16.6%)	3,960 (16.7%)	0.119	0.002
Amiodarone	490 (1.7%)	2,560 (3.2%)	480 (2.0%)	510 (2.1%)	0.097	0.009
Dronedarone	120 (0.4%)	600 (0.8%)	110 (0.5%)	110 (0.5%)	0.043	0.001
Antihypertensive, combination drugs	3,580 (12.6%)	7,700 (9.7%)	2,800 (11.8%)	2,780 (11.7%)	0.092	0.003
Calcium channel blockers	6,340 (22.4%)	19,680 (24.9%)	5,390 (22.7%)	5,410 (22.8%)	0.059	0.002
Selective serotonin reuptake inhibitors	1,510 (5.3%)	4,790 (6.1%)	1,300 (5.5%)	1,290 (5.4%)	0.032	0.002
Drugs used in alcohol dependence	70 (0.2%)	120 (0.2%)	50 (0.2%)	50 (0.2%)	0.019	0.002
CHA2DS2-VASc, mean(SD)	2.9 (1.63)	3.4 (1.76)	3.0 (1.65)	3.0 (1.70)	0.293	0.013
CHA2DS2-VASc:0 -1	5,750 (20.3%)	11,520 (14.6%)	4,370 (18.5%)	4,620 (19.5%)	0.151	0.026
CHA2DS2-VASc:2 -3	13,100 (46.2%)	30,330 (38.3%)	10,780 (45.5%)	10,130 (42.7%)	0.160	0.055
CHA2DS2-VASc:>=4	9,520 (33.6%)	37,330 (47.1%)	8,550 (36.1%)	8,960 (37.8%)	0.279	0.036
CHADS2, mean(SD)	1.8 (1.39)	2.4 (1.51)	1.9 (1.40)	1.9 (1.43)	0.383	0.010
CHADS2:0	4,980 (17.5%)	8,300 (10.5%)	3,530 (14.9%)	3,960 (16.7%)	0.204	0.050
CHADS2:1	8,230 (29.0%)	15,840 (20.0%)	6,680 (28.2%)	6,040 (25.5%)	0.210	0.060
CHADS2:>=2	15,160 (53.4%)	55,030 (69.5%)	13,500 (56.9%)	13,710 (57.8%)	0.335	0.018
HAS-BLED, mean(SD)	1.9 (1.01)	2.0 (1.05)	1.9 (1.01)	1.9 (1.04)	0.152	0.007
HAS-BLED:<3	21,630 (76.2%)	56,150 (70.9%)	17,900 (75.5%)	17,570 (74.1%)	0.121	0.033
HAS-BLED:>=3	6,740 (23.8%)	23,020 (29.1%)	5,800 (24.5%)	6,140 (25.9%)	0.121	0.033
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.221	0.012
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.006	0.011
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.001	0.001

Table 15.60 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin in Denmark, Norway, or Sweden and standardised mean differences before and after matching – REDUCED DOSE

Characteristic	Rivaroxaban (rounded) before matching N= 9214	Warfarin (rou nded) before matching N=79171	Rivaroxaban (rounded) after matching N= 9088	Warfarin (rou nded) after matching N= 9088	Standardised mean difference before matchi ng (max= 0.74)	Standardised mean difference after matching (max= 0.05)
index_year:2013	2,190 (23.8%)	35,000 (44.2%)	2,180 (24.0%)	2,150 (23.6%)	0.442	0.009
index_year:2014	2,330 (25.3%)	23,330 (29.5%)	2,330 (25.6%)	2,320 (25.5%)	0.094	0.002
index_year:2015	2,510 (27.2%)	13,390 (16.9%)	2,480 (27.3%)	2,540 (27.9%)	0.250	0.014
index_year:2016	2,190 (23.7%)	7,460 (9.4%)	2,100 (23.1%)	2,090 (23.0%)	0.393	0.003
Time from AF diag:< 1 month	5,250 (57.0%)	47,550 (60.1%)	5,190 (57.1%)	5,160 (56.8%)	0.063	0.006
Time from AF diag:1 - 6 month	1,010 (11.0%)	7,970 (10.1%)	1,000 (11.0%)	1,050 (11.5%)	0.029	0.016
Time from AF diag:6 - 60 months	2,960 (32.1%)	23,650 (29.9%)	2,900 (31.9%)	2,880 (31.7%)	0.048	0.005
Sex:Female	4,990 (54.1%)	32,980 (41.7%)	4,890 (53.8%)	4,860 (53.4%)	0.252	0.006
Sex:Male	4,230 (45.9%)	46,190 (58.3%)	4,200 (46.2%)	4,230 (46.6%)	0.252	0.006
Age, median(IQR)	83.1 (76.2 - 88.3)	75.0 (67.5 - 82.2)	82.9 (76.0 - 88.1)	82.9 (76.0 - 88.0)	0.735	0.004
Age -group:< 55 years	80 (0.9%)	4,480 (5.7%)	80 (0.9%)	80 (0.9%)	0.270	0.002
Age -group:55-<65 years	400 (4.3%)	10,100 (12.8%)	400 (4.4%)	400 (4.4%)	0.307	0.003
Age -group:65-<75 years	1,570 (17.0%)	25,060 (31.6%)	1,570 (17.2%)	1,550 (17.1%)	0.346	0.004
Age -group:75-<85 years	3,390 (36.8%)	26,700 (33.7%)	3,390 (37.3%)	3,460 (38.0%)	0.065	0.015
Age -group:>= 85 years	3,770 (41.0%)	12,830 (16.2%)	3,650 (40.2%)	3,600 (39.6%)	0.570	0.013
CCI-group:0	2,670 (28.9%)	29,610 (37.4%)	2,640 (29.1%)	2,760 (30.3%)	0.180	0.027
CCI-group:1-2	3,120 (33.8%)	25,600 (32.3%)	3,070 (33.7%)	2,870 (31.6%)	0.031	0.046
CCI-group:>=3	3,430 (37.2%)	23,960 (30.3%)	3,380 (37.2%)	3,460 (38.1%)	0.148	0.020
Prior bleeding (any)	1,310 (14.2%)	8,870 (11.2%)	1,300 (14.3%)	1,270 (14.0%)	0.089	0.008
Prior gastrointestinal bleeding	150 (1.6%)	820 (1.0%)	150 (1.6%)	140 (1.6%)	0.047	0.002
Prior intracranial bleeding	150 (1.6%)	710 (0.9%)	150 (1.6%)	140 (1.5%)	0.067	0.007
Prior stroke (any)	1,590 (17.2%)	9,610 (12.1%)	1,540 (17.0%)	1,570 (17.3%)	0.144	0.009
Prior ischaemic stroke	1,540 (16.7%)	9,400 (11.9%)	1,490 (16.4%)	1,530 (16.9%)	0.138	0.012
Prior haemorrhagic stroke	110 (1.2%)	520 (0.7%)	110 (1.2%)	110 (1.2%)	0.056	0.002
Prior systemic embolism	90 (1.0%)	760 (1.0%)	90 (1.0%)	80 (0.9%)	0.001	0.006
Prior transient ischaemic attack	460 (5.0%)	3,120 (3.9%)	460 (5.0%)	430 (4.8%)	0.052	0.011
Chronic kidney disease	880 (9.5%)	6,530 (8.2%)	870 (9.6%)	980 (10.7%)	0.044	0.039
Heart failure	2,390 (25.9%)	18,010 (22.7%)	2,350 (25.9%)	2,360 (25.9%)	0.075	0.001
Coronary artery disease	2,610 (28.3%)	21,450 (27.1%)	2,580 (28.4%)	2,560 (28.1%)	0.027	0.006
Peripheral arterial disease	810 (8.8%)	6,030 (7.6%)	810 (8.9%)	740 (8.1%)	0.044	0.028
Hypertension	6,550 (71.1%)	54,110 (68.3%)	6,460 (71.1%)	6,410 (70.6%)	0.060	0.012
Diabetes	1,750 (19.0%)	14,680 (18.5%)	1,730 (19.1%)	1,760 (19.4%)	0.011	0.008
Chronic obstructive pulmonary disease	1,320 (14.3%)	10,120 (12.8%)	1,310 (14.4%)	1,340 (14.7%)	0.046	0.009
Liver disease	90 (1.0%)	820 (1.0%)	90 (1.0%)	90 (1.0%)	0.005	0.002
Alcoholism	210 (2.3%)	1,790 (2.3%)	200 (2.2%)	210 (2.3%)	0.000	0.002
Dementia	440 (4.7%)	1,220 (1.5%)	400 (4.4%)	430 (4.7%)	0.184	0.013
Cancer 6 months before and including index date	370 (4.1%)	2,140 (2.7%)	370 (4.1%)	370 (4.1%)	0.075	0.001
Platelet inhibitors (excluding heparin)	4,260 (46.2%)	30,840 (39.0%)	4,190 (46.1%)	4,240 (46.7%)	0.147	0.011

Low -dose aspirin	3,670 (39.8%)	27,180 (34.3%)	3,620 (39.8%)	3,650 (40.2%)	0.113	0.008
ADP receptor blockers	880 (9.6%)	7,100 (9.0%)	860 (9.4%)	880 (9.7%)	0.022	0.007
Renin -angiotensin system inhibitors	4,290 (46.5%)	38,070 (48.1%)	4,240 (46.7%)	4,260 (46.8%)	0.031	0.003
Angiotensin -converting enzyme inhibitors	2,050 (22.2%)	20,500 (25.9%)	2,030 (22.3%)	2,020 (22.2%)	0.085	0.003
Angiotensin II antagonists, plain	1,380 (14.9%)	11,850 (15.0%)	1,360 (15.0%)	1,350 (14.9%)	0.001	0.003
Angiotensin II antagonists, combinations	810 (8.8%)	5,210 (6.6%)	800 (8.8%)	790 (8.7%)	0.084	0.005
Beta-blockers	6,200 (67.3%)	56,980 (72.0%)	6,130 (67.5%)	6,140 (67.6%)	0.102	0.003
Proton pump inhibitors	2,350 (25.5%)	17,350 (21.9%)	2,320 (25.5%)	2,380 (26.2%)	0.085	0.016
Non-steroidal anti-inflammatory drugs	650 (7.1%)	5,860 (7.4%)	650 (7.1%)	630 (6.9%)	0.012	0.008
Statins	3,240 (35.2%)	28,740 (36.3%)	3,200 (35.3%)	3,220 (35.4%)	0.024	0.003
Antidiabetic agents	1,210 (13.2%)	10,410 (13.1%)	1,200 (13.2%)	1,190 (13.1%)	0.001	0.003
Loop diuretics	3,240 (35.2%)	22,170 (28.0%)	3,170 (34.9%)	3,190 (35.1%)	0.154	0.004
Non-loop diuretics	130 (1.4%)	1,230 (1.6%)	130 (1.4%)	140 (1.6%)	0.011	0.012
Alpha adrenergic blockers	1,780 (19.3%)	15,810 (20.0%)	1,760 (19.3%)	1,760 (19.3%)	0.016	0.001
Amiodarone	240 (2.6%)	2,560 (3.2%)	230 (2.6%)	230 (2.6%)	0.040	0.001
Dronedarone	40 (0.4%)	600 (0.8%)	40 (0.4%)	30 (0.3%)	0.047	0.013
Antihypertensive, combination drugs	1,100 (11.9%)	7,700 (9.7%)	1,090 (12.0%)	1,110 (12.2%)	0.071	0.008
Calcium channel blockers	2,260 (24.5%)	19,680 (24.9%)	2,230 (24.5%)	2,260 (24.8%)	0.008	0.008
Selective serotonin reuptake inhibitors	800 (8.7%)	4,790 (6.1%)	780 (8.6%)	790 (8.6%)	0.101	0.002
Drugs used in alcohol dependence	10 (0.1%)	120 (0.2%)	10 (0.1%)	10 (0.1%)	0.022	0.000
CHA2DS2-VASc, mean(SD)	4.1 (1.61)	3.4 (1.76)	4.1 (1.61)	4.1 (1.64)	0.413	0.006
CHA2DS2-VASc:0 -1	410 (4.4%)	11,520 (14.6%)	410 (4.5%)	490 (5.4%)	0.351	0.043
CHA2DS2-VASc:2 -3	2,920 (31.7%)	30,330 (38.3%)	2,910 (32.0%)	2,810 (30.9%)	0.138	0.023
CHA2DS2-VASc:>=4	5,880 (63.8%)	37,330 (47.1%)	5,780 (63.5%)	5,790 (63.7%)	0.341	0.003
CHADS2, mean(SD)	2.7 (1.45)	2.4 (1.51)	2.7 (1.45)	2.7 (1.47)	0.190	0.002
CHADS2:0	450 (4.9%)	8,300 (10.5%)	450 (5.0%)	530 (5.9%)	0.209	0.039
CHADS2:1	1,540 (16.7%)	15,840 (20.0%)	1,530 (16.8%)	1,530 (16.9%)	0.085	0.002
CHADS2:>=2	7,220 (78.3%)	55,030 (69.5%)	7,110 (78.2%)	7,020 (77.2%)	0.202	0.023
HAS-BLED, mean(SD)	2.4 (1.02)	2.0 (1.05)	2.4 (1.02)	2.4 (1.05)	0.344	0.001
HAS-BLED:<3	5,430 (58.9%)	56,150 (70.9%)	5,380 (59.2%)	5,330 (58.7%)	0.253	0.010
HAS-BLED:>=3	3,780 (41.1%)	23,020 (29.1%)	3,710 (40.8%)	3,760 (41.3%)	0.253	0.010
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.100	0.015
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.6)	0.030	0.001
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.057	0.007

Table 15.61 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin and standardised mean differences before and after matching, Denmark – STANDARD DOSE

Characteristic	Rivaroxaban (rounded) before matching N= 9559	Warfarin (rou nded) before matching N=20070	Rivaroxaban (rounded) after matching N= 8362	Warfarin (rou nded) after matching N= 8362	Standardised mean difference before matchi ng (max= 0.58)	Standardised mean difference after matching (max= 0.07)
index_year:2013	1,540 (16.1%)	6,810 (33.9%)	1,540 (18.4%)	1,460 (17.5%)	0.421	0.023
index_year:2014	1,330 (13.9%)	5,400 (26.9%)	1,330 (15.9%)	1,350 (16.2%)	0.326	0.007
index_year:2015	2,720 (28.5%)	4,580 (22.8%)	2,630 (31.5%)	2,740 (32.8%)	0.129	0.028
index_year:2016	3,970 (41.5%)	3,280 (16.4%)	2,860 (34.2%)	2,810 (33.6%)	0.578	0.014
Time from AF diag:< 1 month	6,420 (67.1%)	12,620 (62.9%)	5,520 (66.0%)	5,480 (65.5%)	0.090	0.011
Time from AF diag:1 - 6 month	1,130 (11.8%)	2,410 (12.0%)	1,000 (11.9%)	1,040 (12.4%)	0.005	0.016
Time from AF diag:6 - 60 months	2,010 (21.0%)	5,040 (25.1%)	1,840 (22.1%)	1,850 (22.1%)	0.098	0.000
Sex:Female	3,980 (41.6%)	7,950 (39.6%)	3,450 (41.3%)	3,480 (41.6%)	0.041	0.006
Sex:Male	5,580 (58.4%)	12,120 (60.4%)	4,910 (58.7%)	4,890 (58.4%)	0.041	0.006
Age, median(IQR)	71.7 (65.7 - 78.5)	73.3 (66.1 - 80.6)	72.0 (65.7 - 78.9)	72.2 (65.8 - 79.1)	0.086	0.012
Age -group:< 55 years	600 (6.2%)	1,520 (7.6%)	560 (6.7%)	580 (6.9%)	0.053	0.010
Age -group:55-<65 years	1,560 (16.3%)	2,870 (14.3%)	1,330 (15.9%)	1,300 (15.6%)	0.056	0.008
Age -group:65-<75 years	3,850 (40.3%)	6,820 (34.0%)	3,260 (39.0%)	3,190 (38.1%)	0.130	0.018
Age -group:75-<85 years	2,680 (28.0%)	6,280 (31.3%)	2,390 (28.6%)	2,440 (29.1%)	0.071	0.013
Age -group:>= 85 years	880 (9.2%)	2,580 (12.9%)	830 (9.9%)	860 (10.3%)	0.119	0.012
CCI-group:0	4,810 (50.4%)	8,600 (42.8%)	4,130 (49.4%)	4,230 (50.6%)	0.151	0.024
CCI-group:1-2	3,190 (33.3%)	6,000 (29.9%)	2,800 (33.4%)	2,530 (30.3%)	0.073	0.068
CCI-group:>=3	1,560 (16.3%)	5,470 (27.2%)	1,430 (17.1%)	1,600 (19.1%)	0.267	0.050
Prior bleeding (any)	730 (7.7%)	1,940 (9.7%)	660 (7.9%)	670 (8.0%)	0.071	0.006
Prior gastrointestinal bleeding	70 (0.7%)	270 (1.4%)	60 (0.8%)	70 (0.8%)	0.067	0.005
Prior intracranial bleeding	80 (0.8%)	140 (0.7%)	70 (0.8%)	70 (0.8%)	0.014	0.001
Prior stroke (any)	1,150 (12.1%)	1,980 (9.8%)	950 (11.3%)	940 (11.2%)	0.071	0.004
Prior ischaemic stroke	1,130 (11.8%)	1,940 (9.7%)	930 (11.1%)	920 (11.0%)	0.068	0.003
Prior haemorrhagic stroke	50 (0.5%)	90 (0.4%)	40 (0.5%)	40 (0.5%)	0.013	0.002
Prior systemic embolism	30 (0.3%)	110 (0.5%)	30 (0.3%)	20 (0.3%)	0.043	0.002
Prior transient ischaemic attack	300 (3.2%)	600 (3.0%)	270 (3.2%)	270 (3.2%)	0.009	0.001
Chronic kidney disease	110 (1.1%)	1,690 (8.4%)	110 (1.3%)	120 (1.4%)	0.346	0.012
Heart failure	1,120 (11.7%)	3,570 (17.8%)	1,050 (12.6%)	1,040 (12.4%)	0.172	0.005
Coronary artery disease	1,390 (14.6%)	4,590 (22.9%)	1,300 (15.6%)	1,300 (15.6%)	0.214	0.000
Peripheral arterial disease	510 (5.3%)	1,630 (8.1%)	480 (5.7%)	500 (5.9%)	0.113	0.009
Hypertension	5,690 (59.5%)	12,270 (61.1%)	4,950 (59.1%)	4,980 (59.6%)	0.033	0.009
Diabetes	1,360 (14.2%)	3,490 (17.4%)	1,230 (14.7%)	1,260 (15.0%)	0.086	0.009
Chronic obstructive pulmonary disease	1,050 (11.0%)	2,570 (12.8%)	940 (11.2%)	1,000 (11.9%)	0.055	0.022
Liver disease	80 (0.8%)	240 (1.2%)	80 (0.9%)	80 (1.0%)	0.040	0.006
Alcoholism	310 (3.3%)	590 (2.9%)	280 (3.4%)	270 (3.2%)	0.018	0.009
Dementia	150 (1.6%)	220 (1.1%)	130 (1.5%)	120 (1.5%)	0.041	0.003
Cancer 6 months before and including index date	350 (3.7%)	930 (4.6%)	330 (3.9%)	330 (4.0%)	0.048	0.001
Platelet inhibitors (excluding heparin)	2,660 (27.8%)	6,760 (33.7%)	2,390 (28.6%)	2,420 (29.0%)	0.128	0.008
Low -dose aspirin	1,960 (20.5%)	5,110 (25.5%)	1,770 (21.1%)	1,770 (21.1%)	0.117	0.000
ADP receptor blockers	760 (7.9%)	2,260 (11.2%)	690 (8.3%)	710 (8.5%)	0.113	0.006
Renin -angiotensin system inhibitors	3,790 (39.7%)	8,420 (42.0%)	3,330 (39.8%)	3,300 (39.4%)	0.047	0.007
Angiotensin -converting enzyme inhibitors	1,850 (19.3%)	4,510 (22.5%)	1,660 (19.9%)	1,630 (19.5%)	0.078	0.011
Angiotensin II antagonists, plain	1,020 (10.6%)	2,220 (11.0%)	870 (10.5%)	890 (10.7%)	0.013	0.008
Angiotensin II antagonists, combinations	700 (7.3%)	1,210 (6.0%)	570 (6.8%)	550 (6.6%)	0.049	0.011
Beta-blockers	5,980 (62.6%)	12,420 (61.9%)	5,190 (62.1%)	5,090 (60.8%)	0.014	0.027
Proton pump inhibitors	1,760 (18.4%)	4,510 (22.5%)	1,600 (19.2%)	1,550 (18.5%)	0.101	0.017
Non-steroidal anti-inflammatory drugs	990 (10.3%)	1,980 (9.9%)	820 (9.8%)	830 (9.9%)	0.016	0.003
Statins	3,100 (32.4%)	6,990 (34.8%)	2,710 (32.5%)	2,690 (32.2%)	0.052	0.006
Antidiabetic agents	1,050 (11.0%)	2,650 (13.2%)	950 (11.3%)	980 (11.7%)	0.067	0.013
Loop diuretics	1,730 (18.1%)	5,800 (28.9%)	1,630 (19.5%)	1,630 (19.5%)	0.256	0.001

Non-loop diuretics	110 (1.1%)	350 (1.7%)	100 (1.2%)	110 (1.3%)	0.050	0.007
Alpha adrenergic blockers	1,600 (16.7%)	3,670 (18.3%)	1,420 (17.0%)	1,420 (16.9%)	0.040	0.002
Amiodarone	230 (2.4%)	970 (4.9%)	220 (2.7%)	240 (2.8%)	0.133	0.010
Dronedarone	20 (0.2%)	30 (0.1%)	10 (0.2%)	20 (0.2%)	0.011	0.003
Antihypertensive, combination drugs	1,110 (11.6%)	2,110 (10.5%)	950 (11.3%)	920 (11.0%)	0.035	0.012
Calcium channel blockers	2,180 (22.8%)	4,790 (23.9%)	1,890 (22.7%)	1,930 (23.1%)	0.026	0.011
Selective serotonin reuptake inhibitors	540 (5.6%)	1,150 (5.7%)	470 (5.6%)	480 (5.7%)	0.005	0.006
Drugs used in alcohol dependence	30 (0.3%)	50 (0.2%)	20 (0.3%)	20 (0.3%)	0.009	0.007
CHA2DS2-VASc, mean(SD)	2.9 (1.58)	3.1 (1.67)	2.9 (1.59)	2.9 (1.64)	0.133	0.008
CHA2DS2-VASc:0 -1	1,880 (19.6%)	3,580 (17.8%)	1,620 (19.3%)	1,690 (20.2%)	0.046	0.021
CHA2DS2-VASc:2 -3	4,530 (47.4%)	8,410 (41.9%)	3,940 (47.1%)	3,720 (44.5%)	0.111	0.053
CHA2DS2-VASc:>=4	3,150 (32.9%)	8,080 (40.2%)	2,810 (33.5%)	2,950 (35.3%)	0.152	0.038
CHADS2, mean(SD)	1.5 (1.18)	1.6 (1.21)	1.5 (1.17)	1.5 (1.20)	0.115	0.007
CHADS2:0	1,880 (19.6%)	3,470 (17.3%)	1,600 (19.1%)	1,740 (20.8%)	0.061	0.044
CHADS2:1	3,450 (36.0%)	6,320 (31.5%)	3,010 (36.0%)	2,720 (32.5%)	0.097	0.075
CHADS2:>=2	4,240 (44.3%)	10,280 (51.2%)	3,750 (44.9%)	3,900 (46.7%)	0.139	0.036
HAS-BLED, mean(SD)	2.0 (1.06)	2.1 (1.17)	2.0 (1.07)	2.0 (1.11)	0.131	0.006
HAS-BLED:<3	6,670 (69.8%)	12,660 (63.1%)	5,830 (69.7%)	5,700 (68.2%)	0.142	0.033
HAS-BLED:>=3	2,890 (30.2%)	7,410 (36.9%)	2,540 (30.3%)	2,660 (31.8%)	0.142	0.033
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.113	0.007
log_beddays, median(IQR)	1.1 (0.0 - 1.6)	1.1 (0.0 - 1.9)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.8)	0.198	0.007
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.053	0.009
income, median(IQR), k€	137.1 (96.7 - 218.8)	122.8 (88.9 - 187.6)	132.8 (94.8 - 210.0)	131.8 (94.4 - 209.4)	0.094	0.011
education:Secondary compulsory	3,480 (36.4%)	8,430 (42.0%)	3,160 (37.8%)	3,170 (37.9%)	0.114	0.003
education:Vocational / High school	3,990 (41.8%)	8,140 (40.6%)	3,490 (41.7%)	3,450 (41.3%)	0.024	0.009
education:Higher education	1,870 (19.6%)	2,980 (14.8%)	1,520 (18.1%)	1,540 (18.4%)	0.126	0.007
education:Unknown	210 (2.2%)	520 (2.6%)	200 (2.3%)	200 (2.4%)	0.024	0.001
employment:Employed or self - employed	2,070 (21.6%)	3,720 (18.5%)	1,750 (20.9%)	1,720 (20.6%)	0.078	0.009
employment:Unemployed	520 (5.5%)	1,190 (5.9%)	460 (5.5%)	460 (5.5%)	0.020	0.001
employment:Retired	6,890 (72.1%)	15,010 (74.8%)	6,090 (72.8%)	6,120 (73.2%)	0.062	0.009
employment:Unknown	80 (0.8%)	150 (0.7%)	70 (0.8%)	70 (0.8%)	0.010	0.005

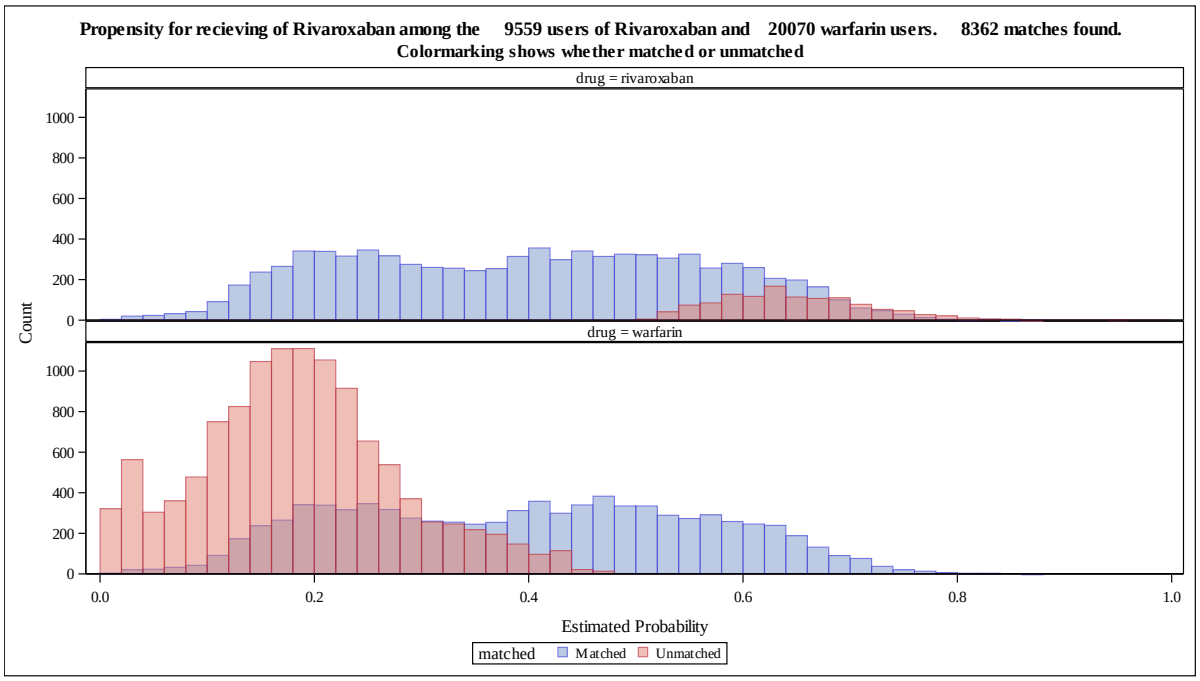

Table 15.62 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin and standardised mean differences before and after matching, Denmark – REDUCED DOSE

Characteristic	Rivaroxaban (rounded) before matching N= 3123	Warfarin (rou nded) before matching N=20070	Rivaroxaban (rounded) after matching N= 3010	Warfarin (rou nded) after matching N= 3010	Standardised mean difference before matchi ng (max= 0.89)	Standardised mean difference after matching (max= 0.09)
index_year:2013	810 (26.0%)	6,810 (33.9%)	800 (26.6%)	780 (25.9%)	0.174	0.017
index_year:2014	550 (17.6%)	5,400 (26.9%)	550 (18.2%)	540 (17.9%)	0.225	0.008
index_year:2015	790 (25.2%)	4,580 (22.8%)	770 (25.4%)	790 (26.2%)	0.056	0.018
index_year:2016	980 (31.3%)	3,280 (16.4%)	900 (29.7%)	900 (30.0%)	0.355	0.005
Time from AF diag:< 1 month	1,950 (62.4%)	12,620 (62.9%)	1,890 (62.8%)	1,880 (62.4%)	0.010	0.009
Time from AF diag:1 - 6 month	340 (10.8%)	2,410 (12.0%)	330 (11.1%)	360 (12.1%)	0.037	0.032
Time from AF diag:6 - 60 months	840 (26.8%)	5,040 (25.1%)	790 (26.1%)	770 (25.5%)	0.038	0.014
Sex:Female	1,730 (55.4%)	7,950 (39.6%)	1,640 (54.4%)	1,650 (54.8%)	0.320	0.009
Sex:Male	1,390 (44.6%)	12,120 (60.4%)	1,370 (45.6%)	1,360 (45.2%)	0.320	0.009
Age, median(IQR)	83.4 (76.3 - 88.6)	73.3 (66.1 - 80.6)	82.9 (76.0 - 88.2)	82.9 (76.1 - 88.0)	0.892	0.003
Age -group:< 55 years	40 (1.2%)	1,520 (7.6%)	40 (1.2%)	30 (1.1%)	0.319	0.009
Age -group:55-<65 years	140 (4.4%)	2,870 (14.3%)	140 (4.6%)	110 (3.5%)	0.344	0.054
Age -group:65-<75 years	520 (16.6%)	6,820 (34.0%)	520 (17.2%)	530 (17.6%)	0.409	0.012
Age -group:75-<85 years	1,080 (34.7%)	6,280 (31.3%)	1,080 (35.8%)	1,130 (37.5%)	0.073	0.034
Age -group:>= 85 years	1,350 (43.2%)	2,580 (12.9%)	1,240 (41.2%)	1,210 (40.3%)	0.717	0.019
CCI-group:0	940 (29.9%)	8,600 (42.8%)	910 (30.4%)	1,010 (33.7%)	0.271	0.071
CCI-group:1-2	1,100 (35.1%)	6,000 (29.9%)	1,050 (35.0%)	930 (30.8%)	0.111	0.089
CCI-group:>=3	1,090 (35.0%)	5,470 (27.2%)	1,040 (34.6%)	1,070 (35.5%)	0.167	0.019
Prior bleeding (any)	360 (11.7%)	1,940 (9.7%)	360 (11.9%)	340 (11.3%)	0.064	0.018
Prior gastrointestinal bleeding	60 (2.0%)	270 (1.4%)	60 (2.1%)	60 (2.1%)	0.051	0.002
Prior intracranial bleeding	50 (1.5%)	140 (0.7%)	40 (1.4%)	40 (1.2%)	0.074	0.018
Prior stroke (any)	590 (18.9%)	1,980 (9.8%)	540 (18.0%)	560 (18.5%)	0.259	0.012
Prior ischaemic stroke	580 (18.5%)	1,940 (9.7%)	530 (17.7%)	550 (18.3%)	0.256	0.016
Prior haemorrhagic stroke	30 (0.9%)	90 (0.4%)	30 (0.8%)	20 (0.8%)	0.058	0.004
Prior systemic embolism	20 (0.6%)	110 (0.5%)	20 (0.6%)	10 (0.4%)	0.014	0.028
Prior transient ischaemic attack	120 (3.8%)	600 (3.0%)	110 (3.8%)	110 (3.6%)	0.042	0.012
Chronic kidney disease	250 (8.0%)	1,690 (8.4%)	240 (8.0%)	280 (9.3%)	0.016	0.044
Heart failure	730 (23.4%)	3,570 (17.8%)	690 (23.0%)	700 (23.3%)	0.139	0.006
Coronary artery disease	740 (23.8%)	4,590 (22.9%)	720 (23.9%)	710 (23.5%)	0.022	0.009
Peripheral arterial disease	270 (8.7%)	1,630 (8.1%)	270 (8.9%)	270 (8.8%)	0.020	0.005
Hypertension	2,140 (68.4%)	12,270 (61.1%)	2,060 (68.3%)	2,000 (66.5%)	0.152	0.038
Diabetes	610 (19.4%)	3,490 (17.4%)	590 (19.6%)	580 (19.4%)	0.051	0.006
Chronic obstructive pulmonary disease	490 (15.6%)	2,570 (12.8%)	480 (15.9%)	500 (16.5%)	0.080	0.017
Liver disease	40 (1.1%)	240 (1.2%)	30 (1.1%)	30 (0.9%)	0.006	0.023
Alcoholism	100 (3.2%)	590 (2.9%)	90 (3.1%)	80 (2.8%)	0.013	0.020
Dementia	160 (5.2%)	220 (1.1%)	140 (4.5%)	130 (4.4%)	0.236	0.005
Cancer 6 months before and including index date	160 (5.0%)	930 (4.6%)	160 (5.2%)	150 (5.0%)	0.019	0.008
Platelet inhibitors (excluding heparin)	1,300 (41.7%)	6,760 (33.7%)	1,240 (41.3%)	1,260 (41.8%)	0.165	0.010
Low -dose aspirin	950 (30.4%)	5,110 (25.5%)	910 (30.3%)	910 (30.1%)	0.109	0.003
ADP receptor blockers	440 (14.1%)	2,260 (11.2%)	420 (13.8%)	450 (15.0%)	0.087	0.033
Renin -angiotensin system inhibitors	1,380 (44.1%)	8,420 (42.0%)	1,330 (44.3%)	1,310 (43.6%)	0.042	0.014
Angiotensin -converting enzyme inhibitors	700 (22.5%)	4,510 (22.5%)	680 (22.7%)	680 (22.6%)	0.001	0.002
Angiotensin II antagonists, plain	390 (12.4%)	2,220 (11.0%)	380 (12.5%)	340 (11.2%)	0.043	0.040
Angiotensin II antagonists, combinations	220 (7.0%)	1,210 (6.0%)	210 (7.0%)	200 (6.7%)	0.039	0.012
Beta-blockers	1,900 (60.8%)	12,420 (61.9%)	1,840 (61.1%)	1,830 (60.7%)	0.022	0.007
Proton pump inhibitors	860 (27.5%)	4,510 (22.5%)	830 (27.6%)	850 (28.1%)	0.117	0.010
Non-steroidal anti-inflammatory drugs	290 (9.1%)	1,980 (9.9%)	280 (9.4%)	260 (8.6%)	0.025	0.028
Statins	1,070 (34.4%)	6,990 (34.8%)	1,040 (34.7%)	1,050 (34.9%)	0.010	0.006
Antidiabetic agents	450 (14.4%)	2,650 (13.2%)	440 (14.7%)	430 (14.4%)	0.036	0.008

Loop diuretics	1,290 (41.3%)	5,800 (28.9%)	1,230 (40.7%)	1,230 (41.0%)	0.262	0.005
Non-loop diuretics	50 (1.5%)	350 (1.7%)	40 (1.5%)	50 (1.5%)	0.020	0.005
Alpha adrenergic blockers	680 (21.6%)	3,670 (18.3%)	650 (21.6%)	640 (21.2%)	0.084	0.011
Amiodarone	140 (4.5%)	970 (4.9%)	140 (4.6%)	140 (4.7%)	0.016	0.006
Dronedarone	<5	30 (0.1%)	<5	<5	0.033	0.000
Antihypertensive, combination drugs	360 (11.6%)	2,110 (10.5%)	350 (11.7%)	360 (12.0%)	0.034	0.008
Calcium channel blockers	760 (24.3%)	4,790 (23.9%)	730 (24.4%)	730 (24.1%)	0.010	0.005
Selective serotonin reuptake inhibitors	290 (9.2%)	1,150 (5.7%)	270 (8.9%)	270 (8.9%)	0.132	0.000
Drugs used in alcohol dependence	<5	50 (0.2%)	<5	<5	0.036	0.026
CHA2DS2-VASc, mean(SD)	4.1 (1.53)	3.1 (1.67)	4.1 (1.52)	4.1 (1.58)	0.628	0.002
CHA2DS2-VASc:0 -1	120 (3.9%)	3,580 (17.8%)	120 (4.1%)	140 (4.5%)	0.458	0.020
CHA2DS2-VASc:2 -3	950 (30.3%)	8,410 (41.9%)	930 (31.0%)	940 (31.4%)	0.245	0.009
CHA2DS2-VASc:>=4	2,060 (65.8%)	8,080 (40.2%)	1,960 (65.0%)	1,930 (64.2%)	0.530	0.017
CHADS2, mean(SD)	2.3 (1.23)	1.6 (1.21)	2.3 (1.22)	2.3 (1.26)	0.552	0.013
CHADS2:0	150 (4.7%)	3,470 (17.3%)	150 (4.9%)	180 (6.1%)	0.412	0.054
CHADS2:1	590 (19.0%)	6,320 (31.5%)	580 (19.4%)	610 (20.2%)	0.290	0.019
CHADS2:>=2	2,380 (76.3%)	10,280 (51.2%)	2,280 (75.7%)	2,220 (73.8%)	0.540	0.046
HAS-BLED, mean(SD)	2.5 (1.06)	2.1 (1.17)	2.5 (1.06)	2.5 (1.10)	0.367	0.008
HAS-BLED:<3	1,570 (50.2%)	12,660 (63.1%)	1,530 (50.7%)	1,520 (50.6%)	0.262	0.002
HAS-BLED:>=3	1,560 (49.8%)	7,410 (36.9%)	1,480 (49.3%)	1,490 (49.4%)	0.262	0.002
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.193	0.014
log_beddays, median(IQR)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.9)	1.1 (0.0 - 1.8)	1.1 (0.0 - 1.8)	0.169	0.007
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.0 (0.0 - 0.0)	0.097	0.015
income, median(IQR), k€	99.5 (77.7 - 134.3)	122.8 (88.9 - 187.6)	100.7 (78.1 - 135.6)	100.0 (77.7 - 136.8)	0.242	0.018
education:Secondary compulsory	1,520 (48.6%)	8,430 (42.0%)	1,460 (48.6%)	1,490 (49.6%)	0.132	0.019
education:Vocational / High school	990 (31.7%)	8,140 (40.6%)	970 (32.2%)	960 (31.9%)	0.184	0.008
education:Higher education	380 (12.3%)	2,980 (14.8%)	370 (12.4%)	370 (12.1%)	0.074	0.009
education:Unknown	230 (7.4%)	520 (2.6%)	200 (6.7%)	190 (6.4%)	0.222	0.012
employment:Employed or self - employed	180 (5.6%)	3,720 (18.5%)	170 (5.8%)	180 (6.0%)	0.405	0.010
employment:Unemployed	70 (2.1%)	1,190 (5.9%)	70 (2.2%)	50 (1.8%)	0.194	0.033
employment:Retired	2,880 (92.1%)	15,010 (74.8%)	2,760 (91.8%)	2,770 (91.9%)	0.478	0.004
employment:Unknown	10 (0.2%)	150 (0.7%)	10 (0.2%)	10 (0.3%)	0.086	0.028

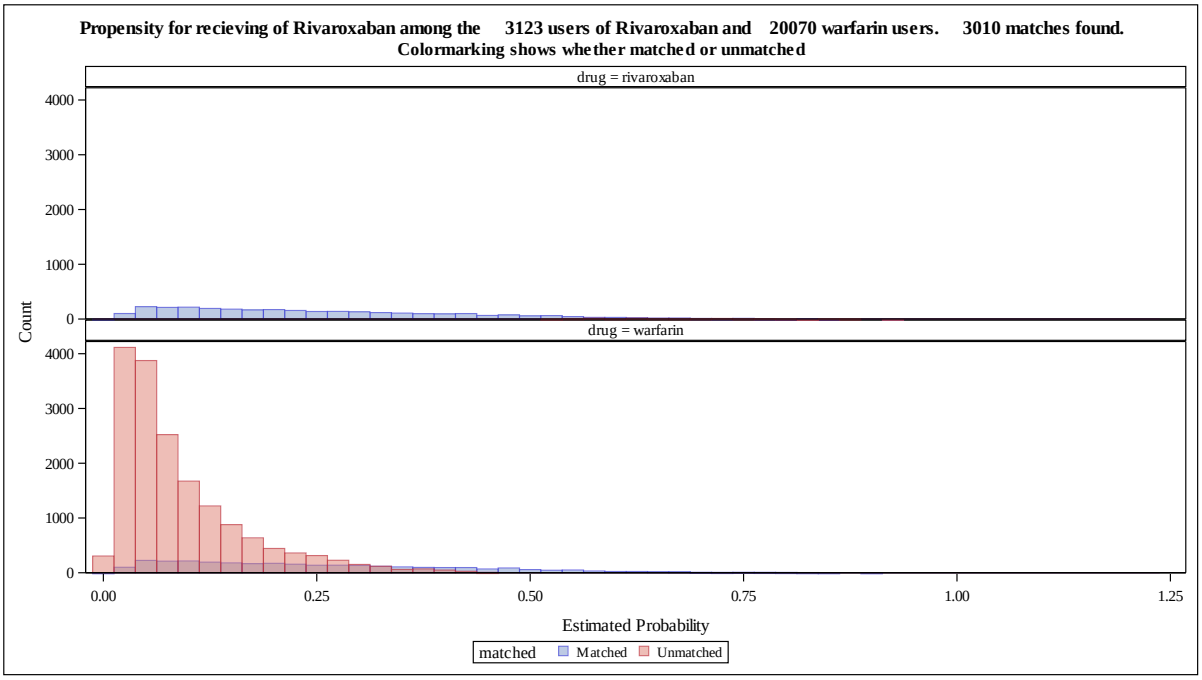

Table 15.63 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin and standardised mean differences before and after matching, Norway – STANDARD DOSE

Characteristic	Rivaroxaban (rounded) before matching N= 7916	Warfarin (rounded) before matching N=11949	Rivaroxaban (rounded) after matching N= 5466	Warfarin (rounded) after matching N= 5466	Standardised mean difference before matching (max= 0.55)	Standardised mean difference after matching (max= 0.08)
index_year:2013	1,840 (23.3%)	5,810 (48.6%)	1,840 (33.6%)	1,790 (32.7%)	0.547	0.019
index_year:2014	1,880 (23.8%)	3,450 (28.8%)	1,730 (31.6%)	1,710 (31.2%)	0.115	0.008
index_year:2015	2,210 (27.9%)	1,760 (14.8%)	1,250 (22.9%)	1,240 (22.7%)	0.324	0.004
index_year:2016	1,990 (25.1%)	930 (7.8%)	650 (11.9%)	730 (13.4%)	0.480	0.043
Time from AF diag:< 1 month	4,960 (62.6%)	6,410 (53.6%)	3,160 (57.9%)	3,200 (58.5%)	0.182	0.011
Time from AF diag:1 - 6 month	660 (8.4%)	1,340 (11.2%)	530 (9.7%)	550 (10.1%)	0.095	0.014
Time from AF diag:6 - 60 months	2,300 (29.0%)	4,200 (35.2%)	1,770 (32.4%)	1,720 (31.4%)	0.132	0.021
Sex:Female	3,150 (39.8%)	4,740 (39.7%)	2,210 (40.5%)	2,230 (40.8%)	0.003	0.007
Sex:Male	4,760 (60.2%)	7,210 (60.3%)	3,260 (59.5%)	3,240 (59.2%)	0.003	0.007
Age, median(IQR)	71.2 (65.3 - 77.8)	75.3 (66.7 - 83.2)	72.4 (65.3 - 79.7)	72.5 (65.6 - 80.1)	0.261	0.024
Age -group:< 55 years	530 (6.6%)	830 (7.0%)	400 (7.3%)	370 (6.7%)	0.013	0.024
Age -group:55-<65 years	1,390 (17.5%)	1,690 (14.2%)	910 (16.6%)	920 (16.8%)	0.092	0.004
Age -group:65-<75 years	3,240 (41.0%)	3,360 (28.1%)	1,930 (35.3%)	1,920 (35.2%)	0.273	0.003
Age -group:75-<85 years	2,090 (26.4%)	3,860 (32.3%)	1,600 (29.2%)	1,600 (29.2%)	0.129	0.001
Age -group:>= 85 years	670 (8.5%)	2,210 (18.5%)	630 (11.5%)	660 (12.1%)	0.296	0.019
CCI-group:0	3,320 (42.0%)	3,340 (27.9%)	2,030 (37.0%)	2,040 (37.3%)	0.298	0.005
CCI-group:1-2	2,870 (36.2%)	3,810 (31.9%)	2,020 (37.0%)	1,900 (34.7%)	0.090	0.048
CCI-group:>=3	1,730 (21.9%)	4,800 (40.2%)	1,420 (25.9%)	1,530 (28.0%)	0.404	0.047
Prior bleeding (any)	820 (10.4%)	1,780 (14.9%)	640 (11.7%)	670 (12.2%)	0.137	0.016
Prior gastrointestinal bleeding	70 (0.9%)	190 (1.6%)	60 (1.1%)	70 (1.2%)	0.061	0.012
Prior intracranial bleeding	70 (0.9%)	160 (1.3%)	60 (1.0%)	70 (1.2%)	0.045	0.016
Prior stroke (any)	870 (11.0%)	1,440 (12.0%)	670 (12.3%)	660 (12.1%)	0.030	0.007
Prior ischaemic stroke	860 (10.8%)	1,380 (11.5%)	660 (12.0%)	640 (11.8%)	0.024	0.007
Prior haemorrhagic stroke	40 (0.5%)	110 (0.9%)	40 (0.7%)	40 (0.7%)	0.048	0.000
Prior systemic embolism	30 (0.4%)	140 (1.2%)	30 (0.6%)	30 (0.6%)	0.085	0.002
Prior transient ischaemic attack	290 (3.7%)	460 (3.9%)	220 (4.0%)	210 (3.9%)	0.009	0.005
Chronic kidney disease	200 (2.5%)	1,560 (13.1%)	200 (3.6%)	240 (4.3%)	0.404	0.039
Heart failure	970 (12.2%)	3,110 (26.0%)	830 (15.2%)	860 (15.7%)	0.358	0.012
Coronary artery disease	1,660 (20.9%)	4,410 (36.9%)	1,360 (24.8%)	1,420 (25.9%)	0.358	0.025
Peripheral arterial disease	660 (8.4%)	1,370 (11.5%)	500 (9.2%)	500 (9.1%)	0.104	0.003
Hypertension	4,520 (57.1%)	7,270 (60.8%)	3,180 (58.3%)	3,190 (58.3%)	0.076	0.001
Diabetes	1,080 (13.6%)	2,100 (17.6%)	790 (14.4%)	800 (14.7%)	0.111	0.007
Chronic obstructive pulmonary disease	1,030 (13.0%)	1,850 (15.5%)	750 (13.7%)	760 (14.0%)	0.070	0.008
Liver disease	80 (1.0%)	150 (1.3%)	60 (1.0%)	60 (1.0%)	0.031	0.002
Alcoholism	190 (2.5%)	170 (1.4%)	120 (2.2%)	110 (2.1%)	0.075	0.005
Dementia	100 (1.2%)	230 (1.9%)	80 (1.5%)	80 (1.5%)	0.054	0.000
Cancer 6 months before and including index date	440 (5.6%)	810 (6.8%)	340 (6.2%)	360 (6.5%)	0.048	0.015
Platelet inhibitors (excluding heparin)	3,160 (39.9%)	5,400 (45.2%)	2,270 (41.6%)	2,300 (42.1%)	0.107	0.011
Low -dose aspirin	3,040 (38.4%)	5,060 (42.4%)	2,180 (39.8%)	2,190 (40.1%)	0.080	0.005
ADP receptor blockers	190 (2.4%)	1,130 (9.5%)	190 (3.4%)	220 (3.9%)	0.303	0.029
Renin -angiotensin system inhibitors	3,250 (41.1%)	5,500 (46.0%)	2,280 (41.7%)	2,290 (41.8%)	0.101	0.003
Angiotensin -converting enzyme inhibitors	950 (12.0%)	2,500 (20.9%)	770 (14.2%)	800 (14.6%)	0.241	0.012
Angiotensin II antagonists, plain	1,080 (13.6%)	1,640 (13.7%)	740 (13.5%)	730 (13.4%)	0.002	0.003
Angiotensin II antagonists, combinations	1,220 (15.4%)	1,450 (12.2%)	770 (14.1%)	760 (13.9%)	0.094	0.007
Beta-blockers	4,980 (62.9%)	8,410 (70.4%)	3,540 (64.8%)	3,570 (65.3%)	0.159	0.010
Proton pump inhibitors	1,340 (16.9%)	2,690 (22.5%)	1,000 (18.3%)	1,020 (18.6%)	0.143	0.008
H2-receptor antagonists	110 (1.4%)	170 (1.4%)	70 (1.3%)	80 (1.4%)	0.003	0.009
Non-steroidal anti-inflammatory drugs	750 (9.5%)	910 (7.6%)	490 (8.9%)	460 (8.4%)	0.069	0.020
Statins	2,790 (35.2%)	5,020 (42.0%)	2,010 (36.8%)	2,030 (37.1%)	0.140	0.006
Antidiabetic agents	730 (9.2%)	1,400 (11.7%)	530 (9.7%)	550 (10.1%)	0.082	0.013
Loop diuretics	1,010 (12.8%)	3,390 (28.4%)	880 (16.1%)	910 (16.7%)	0.393	0.017
Non-loop diuretics	100 (1.3%)	230 (1.9%)	80 (1.4%)	70 (1.3%)	0.048	0.005
Alpha adrenergic blockers	390 (4.9%)	960 (8.0%)	300 (5.5%)	310 (5.7%)	0.127	0.010

Amiodarone	160 (2.0%)	700 (5.9%)	150 (2.8%)	160 (3.0%)	0.197	0.011
Dronedarone	50 (0.7%)	130 (1.1%)	50 (0.9%)	40 (0.7%)	0.048	0.017
Antihypertensive, combination drugs	1,410 (17.8%)	1,740 (14.6%)	910 (16.6%)	900 (16.4%)	0.087	0.004
Calcium channel blockers	1,580 (20.0%)	2,640 (22.1%)	1,110 (20.3%)	1,100 (20.1%)	0.052	0.007
Selective serotonin reuptake inhibitors	310 (3.9%)	530 (4.5%)	230 (4.2%)	220 (4.0%)	0.027	0.008
Drugs used in alcohol dependence	20 (0.2%)	20 (0.1%)	10 (0.2%)	10 (0.2%)	0.027	0.004
CHA2DS2-VASc, mean(SD)	2.7 (1.64)	3.3 (1.86)	2.9 (1.68)	2.9 (1.79)	0.345	0.000
CHA2DS2-VASc:0 -1	2,030 (25.7%)	2,240 (18.7%)	1,200 (21.9%)	1,330 (24.4%)	0.168	0.058
CHA2DS2-VASc:2 -3	3,670 (46.3%)	4,370 (36.6%)	2,470 (45.1%)	2,250 (41.1%)	0.199	0.080
CHA2DS2-VASc:>=4	2,220 (28.0%)	5,340 (44.7%)	1,800 (33.0%)	1,880 (34.5%)	0.352	0.032
CHADS2, mean(SD)	1.3 (1.21)	1.7 (1.35)	1.4 (1.24)	1.4 (1.29)	0.333	0.016
CHADS2:0	2,490 (31.5%)	2,530 (21.1%)	1,420 (26.0%)	1,590 (29.1%)	0.236	0.071
CHADS2:1	2,680 (33.8%)	3,480 (29.1%)	1,860 (34.1%)	1,690 (31.0%)	0.100	0.066
CHADS2:>=2	2,750 (34.8%)	5,940 (49.7%)	2,180 (40.0%)	2,180 (39.9%)	0.307	0.002
HAS-BLED, mean(SD)	1.8 (1.12)	2.1 (1.26)	1.9 (1.14)	1.9 (1.19)	0.253	0.007
HAS-BLED:<3	5,850 (73.9%)	7,410 (62.0%)	3,880 (71.0%)	3,800 (69.4%)	0.256	0.035
HAS-BLED:>=3	2,070 (26.1%)	4,540 (38.0%)	1,580 (29.0%)	1,670 (30.6%)	0.256	0.035
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.7 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.7 - 1.1)	0.421	0.019
log_beddays, median(IQR)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	0.049	0.003
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.079	0.002

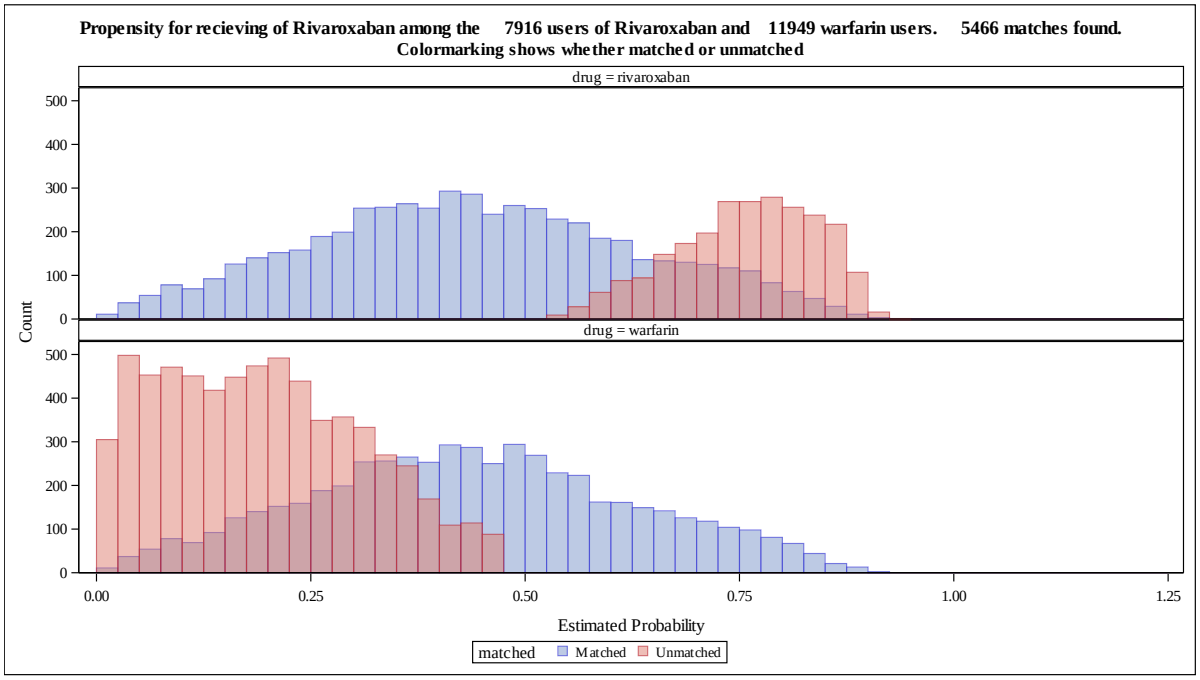

Table 15.64 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin and standardised mean differences before and after matching, Norway – REDUCED DOSE

Characteristic	Rivaroxaban (rounded) before matching N= 2649	Warfarin (rou nded) before matching N=11949	Rivaroxaban (rounded) after matching N= 2641	Warfarin (rou nded) after matching N= 2641	Standardised mean difference before matchi ng (max= 0.61)	Standardised mean difference after matching (max= 0.08)
index_year:2013	860 (32.6%)	5,810 (48.6%)	860 (32.7%)	860 (32.6%)	0.329	0.002
index_year:2014	710 (26.8%)	3,450 (28.8%)	710 (26.9%)	680 (25.8%)	0.045	0.025
index_year:2015	640 (24.2%)	1,760 (14.8%)	640 (24.2%)	670 (25.3%)	0.241	0.026
index_year:2016	430 (16.3%)	930 (7.8%)	430 (16.2%)	430 (16.2%)	0.263	0.001
Time from AF diag:< 1 month	1,480 (55.9%)	6,410 (53.6%)	1,480 (56.0%)	1,490 (56.4%)	0.046	0.008
Time from AF diag:1 - 6 month	290 (11.0%)	1,340 (11.2%)	290 (11.0%)	290 (10.8%)	0.006	0.005
Time from AF diag:6 - 60 months	880 (33.0%)	4,200 (35.2%)	870 (33.0%)	870 (32.8%)	0.045	0.005
Sex:Female	1,360 (51.3%)	4,740 (39.7%)	1,350 (51.3%)	1,330 (50.2%)	0.236	0.020
Sex:Male	1,290 (48.7%)	7,210 (60.3%)	1,290 (48.7%)	1,310 (49.8%)	0.236	0.020
Age, median(IQR)	82.0 (74.7 - 87.6)	75.3 (66.7 - 83.2)	82.0 (74.7 - 87.6)	82.1 (74.3 - 87.6)	0.608	0.010
Age -group:< 55 years	30 (1.1%)	830 (7.0%)	30 (1.1%)	30 (1.0%)	0.304	0.004
Age -group:55-<65 years	140 (5.2%)	1,690 (14.2%)	140 (5.2%)	170 (6.3%)	0.306	0.046
Age -group:65-<75 years	510 (19.4%)	3,360 (28.1%)	510 (19.5%)	500 (19.0%)	0.205	0.011
Age -group:75-<85 years	1,000 (37.6%)	3,860 (32.3%)	1,000 (37.7%)	1,000 (37.7%)	0.111	0.000
Age -group:>= 85 years	970 (36.8%)	2,210 (18.5%)	970 (36.6%)	950 (36.0%)	0.417	0.013
CCI-group:0	720 (27.3%)	3,340 (27.9%)	720 (27.3%)	720 (27.1%)	0.015	0.004
CCI-group:1-2	880 (33.3%)	3,810 (31.9%)	880 (33.2%)	810 (30.5%)	0.030	0.058
CCI-group:>=3	1,050 (39.4%)	4,800 (40.2%)	1,040 (39.5%)	1,120 (42.4%)	0.015	0.059
Prior bleeding (any)	440 (16.4%)	1,780 (14.9%)	440 (16.5%)	450 (16.8%)	0.042	0.010
Prior gastrointestinal bleeding	50 (1.8%)	190 (1.6%)	50 (1.9%)	50 (1.9%)	0.019	0.000
Prior intracranial bleeding	40 (1.5%)	160 (1.3%)	40 (1.6%)	50 (1.8%)	0.018	0.021
Prior stroke (any)	390 (14.6%)	1,440 (12.0%)	390 (14.7%)	400 (15.3%)	0.077	0.018
Prior ischaemic stroke	370 (14.0%)	1,380 (11.5%)	370 (14.0%)	390 (14.6%)	0.073	0.016
Prior haemorrhagic stroke	30 (1.1%)	110 (0.9%)	30 (1.1%)	30 (1.3%)	0.017	0.021
Prior systemic embolism	20 (0.9%)	140 (1.2%)	20 (0.9%)	20 (0.6%)	0.030	0.031
Prior transient ischaemic attack	140 (5.3%)	460 (3.9%)	140 (5.3%)	130 (5.0%)	0.069	0.012
Chronic kidney disease	380 (14.5%)	1,560 (13.1%)	380 (14.5%)	440 (16.7%)	0.042	0.058
Heart failure	640 (24.1%)	3,110 (26.0%)	640 (24.1%)	610 (23.0%)	0.045	0.026
Coronary artery disease	860 (32.4%)	4,410 (36.9%)	860 (32.4%)	840 (31.9%)	0.096	0.011
Peripheral arterial disease	310 (11.5%)	1,370 (11.5%)	300 (11.5%)	270 (10.3%)	0.001	0.040
Hypertension	1,740 (65.6%)	7,270 (60.8%)	1,730 (65.6%)	1,750 (66.1%)	0.100	0.011
Diabetes	410 (15.5%)	2,100 (17.6%)	410 (15.5%)	410 (15.6%)	0.057	0.003
Chronic obstructive pulmonary disease	390 (14.9%)	1,850 (15.5%)	390 (14.9%)	400 (15.0%)	0.017	0.002
Liver disease	30 (1.2%)	150 (1.3%)	30 (1.2%)	40 (1.4%)	0.011	0.017
Alcoholism	50 (2.0%)	170 (1.4%)	50 (2.0%)	50 (2.0%)	0.045	0.000
Dementia	90 (3.2%)	230 (1.9%)	90 (3.2%)	100 (3.7%)	0.086	0.027
Cancer 6 months before and including index date	200 (7.4%)	810 (6.8%)	190 (7.3%)	200 (7.6%)	0.024	0.010
Platelet inhibitors (excluding heparin)	1,300 (48.9%)	5,400 (45.2%)	1,290 (48.8%)	1,260 (47.8%)	0.075	0.020
Low -dose aspirin	1,230 (46.5%)	5,060 (42.4%)	1,220 (46.3%)	1,200 (45.4%)	0.083	0.018
ADP receptor blockers	140 (5.3%)	1,130 (9.5%)	140 (5.3%)	140 (5.5%)	0.160	0.005
Renin -angiotensin system inhibitors	1,180 (44.7%)	5,500 (46.0%)	1,180 (44.6%)	1,190 (44.9%)	0.028	0.005
Angiotensin -converting enzyme inhibitors	440 (16.6%)	2,500 (20.9%)	440 (16.7%)	440 (16.5%)	0.110	0.004
Angiotensin II antagonists, plain	380 (14.3%)	1,640 (13.7%)	380 (14.4%)	390 (14.8%)	0.019	0.013
Angiotensin II antagonists, combinations	380 (14.3%)	1,450 (12.2%)	380 (14.3%)	380 (14.2%)	0.064	0.002
Beta-blockers	1,750 (66.0%)	8,410 (70.4%)	1,750 (66.1%)	1,750 (66.3%)	0.094	0.005
Proton pump inhibitors	650 (24.5%)	2,690 (22.5%)	650 (24.5%)	690 (25.9%)	0.047	0.032
H2-receptor antagonists	40 (1.5%)	170 (1.4%)	40 (1.5%)	50 (1.8%)	0.011	0.021
Non-steroidal anti-inflammatory drugs	200 (7.7%)	910 (7.6%)	200 (7.7%)	210 (8.0%)	0.004	0.011
Statins	1,020 (38.4%)	5,020 (42.0%)	1,010 (38.4%)	1,010 (38.3%)	0.074	0.001
Antidiabetic agents	270 (10.2%)	1,400 (11.7%)	270 (10.3%)	270 (10.0%)	0.048	0.008
Loop diuretics	740 (28.0%)	3,390 (28.4%)	740 (28.1%)	730 (27.5%)	0.008	0.014
Non-loop diuretics	50 (1.8%)	230 (1.9%)	50 (1.8%)	60 (2.1%)	0.011	0.025
Alpha adrenergic blockers	220 (8.4%)	960 (8.0%)	220 (8.3%)	240 (9.2%)	0.013	0.031

Amiodarone	60 (2.4%)	700 (5.9%)	60 (2.4%)	60 (2.2%)	0.174	0.015
Dronedarone	20 (0.7%)	130 (1.1%)	20 (0.7%)	20 (0.6%)	0.041	0.019
Antihypertensive, combination drugs	440 (16.7%)	1,740 (14.6%)	440 (16.7%)	450 (16.8%)	0.060	0.005
Calcium channel blockers	610 (23.0%)	2,640 (22.1%)	610 (22.9%)	600 (22.7%)	0.022	0.005
Selective serotonin reuptake inhibitors	180 (6.6%)	530 (4.5%)	180 (6.6%)	180 (6.6%)	0.095	0.000
Drugs used in alcohol dependence	<5	20 (0.1%)	<5	<5	0.031	0.000
CHA2DS2-VASc, mean(SD)	3.8 (1.62)	3.3 (1.86)	3.8 (1.62)	3.7 (1.70)	0.283	0.012
CHA2DS2-VASc:0 -1	180 (6.9%)	2,240 (18.7%)	180 (6.9%)	240 (9.0%)	0.359	0.078
CHA2DS2-VASc:2 -3	1,020 (38.6%)	4,370 (36.6%)	1,020 (38.5%)	970 (36.8%)	0.042	0.035
CHA2DS2-VASc:>=4	1,440 (54.5%)	5,340 (44.7%)	1,440 (54.5%)	1,430 (54.1%)	0.197	0.008
CHADS2, mean(SD)	2.0 (1.29)	1.7 (1.35)	2.0 (1.29)	2.0 (1.32)	0.209	0.004
CHADS2:0	280 (10.5%)	2,530 (21.1%)	280 (10.6%)	310 (11.8%)	0.294	0.040
CHADS2:1	790 (29.9%)	3,480 (29.1%)	790 (29.8%)	770 (29.3%)	0.016	0.010
CHADS2:>=2	1,580 (59.6%)	5,940 (49.7%)	1,580 (59.7%)	1,560 (58.9%)	0.199	0.016
HAS-BLED, mean(SD)	2.4 (1.15)	2.1 (1.26)	2.4 (1.15)	2.4 (1.20)	0.219	0.017
HAS-BLED:<3	1,510 (56.9%)	7,410 (62.0%)	1,500 (56.8%)	1,440 (54.4%)	0.106	0.049
HAS-BLED:>=3	1,140 (43.1%)	4,540 (38.0%)	1,140 (43.2%)	1,210 (45.6%)	0.106	0.049
log_n_hosp, median(IQR)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.7 (0.7 - 1.1)	0.111	0.025
log_beddays, median(IQR)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	1.4 (0.7 - 1.8)	0.080	0.006
log_n_outpatient, median(IQR)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.027	0.008

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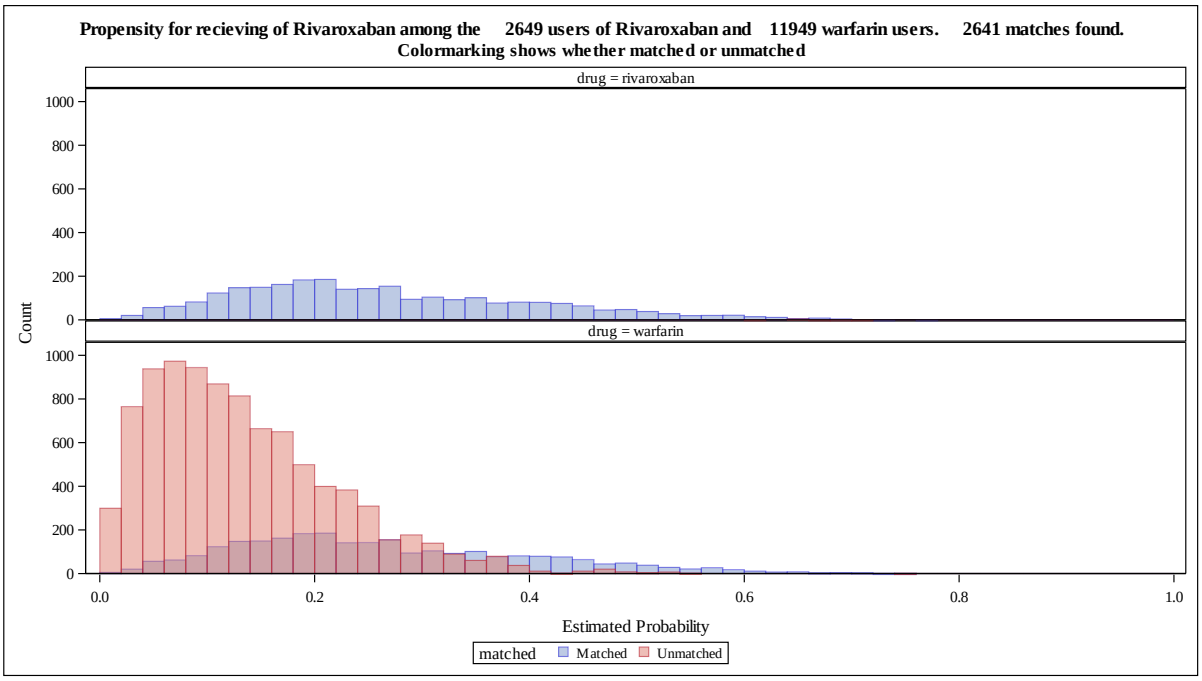


Table 15.65 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin and standardised mean differences before and after matching, Sweden – STANDARD DOSE

Characteristic	Rivaroxaban (rounded) before matching N=10891	Warfarin (rou nded) before matching N=47152	Rivaroxaban (rounded) after matching N= 9875	Warfarin (rou nded) after matching N= 9875	Standardised mean difference before matchi ng (max= 0.82)	Standardised mean difference after matching (max= 0.05)
index_year:2013	1,380 (12.7%)	22,380 (47.5%)	1,380 (14.0%)	1,430 (14.5%)	0.820	0.014
index_year:2014	2,740 (25.2%)	14,490 (30.7%)	2,740 (27.7%)	2,620 (26.5%)	0.124	0.027
index_year:2015	3,660 (33.6%)	7,040 (14.9%)	3,500 (35.5%)	3,540 (35.8%)	0.446	0.008
index_year:2016	3,110 (28.5%)	3,240 (6.9%)	2,250 (22.8%)	2,290 (23.2%)	0.592	0.008
Time from AF diag:< 1 month	6,620 (60.8%)	28,530 (60.5%)	6,080 (61.5%)	5,960 (60.4%)	0.006	0.024
Time from AF diag:1 - 6 month	930 (8.5%)	4,220 (9.0%)	840 (8.5%)	920 (9.3%)	0.016	0.025
Time from AF diag:6 - 60 months	3,350 (30.7%)	14,400 (30.5%)	2,960 (29.9%)	3,000 (30.4%)	0.004	0.010
Sex:Female	4,550 (41.8%)	20,290 (43.0%)	4,150 (42.0%)	4,120 (41.7%)	0.025	0.006
Sex:Male	6,340 (58.2%)	26,860 (57.0%)	5,720 (58.0%)	5,750 (58.3%)	0.025	0.006
Age, median(IQR)	72.4 (66.4 - 79.1)	75.6 (68.4 - 82.6)	72.9 (66.7 - 79.6)	73.2 (66.8 - 80.0)	0.245	0.026
Age -group:< 55 years	570 (5.2%)	2,130 (4.5%)	510 (5.2%)	460 (4.6%)	0.033	0.026
Age -group:55-<65 years	1,620 (14.9%)	5,540 (11.8%)	1,390 (14.1%)	1,450 (14.7%)	0.092	0.017
Age -group:65-<75 years	4,370 (40.1%)	14,880 (31.6%)	3,830 (38.8%)	3,740 (37.9%)	0.179	0.018
Age -group:75-<85 years	3,300 (30.3%)	16,570 (35.1%)	3,120 (31.6%)	3,140 (31.8%)	0.104	0.003
Age -group:>= 85 years	1,030 (9.5%)	8,030 (17.0%)	1,030 (10.4%)	1,090 (11.1%)	0.224	0.023
CCI-group:0	5,240 (48.1%)	17,670 (37.5%)	4,620 (46.7%)	4,480 (45.4%)	0.217	0.027
CCI-group:1-2	3,590 (33.0%)	15,790 (33.5%)	3,300 (33.4%)	3,280 (33.2%)	0.011	0.005
CCI-group:>=3	2,060 (18.9%)	13,700 (29.0%)	1,960 (19.8%)	2,120 (21.4%)	0.239	0.039
Prior bleeding (any)	1,010 (9.2%)	5,150 (10.9%)	930 (9.4%)	910 (9.2%)	0.056	0.006
Prior gastrointestinal bleeding	40 (0.4%)	360 (0.8%)	40 (0.4%)	40 (0.4%)	0.048	0.013
Prior intracranial bleeding	120 (1.1%)	410 (0.9%)	100 (1.0%)	90 (1.0%)	0.021	0.009
Prior stroke (any)	1,240 (11.4%)	6,200 (13.1%)	1,160 (11.7%)	1,200 (12.1%)	0.053	0.012
Prior ischaemic stroke	1,200 (11.0%)	6,080 (12.9%)	1,130 (11.4%)	1,170 (11.8%)	0.058	0.013
Prior haemorrhagic stroke	100 (0.9%)	330 (0.7%)	80 (0.8%)	80 (0.8%)	0.022	0.009
Prior systemic embolism	80 (0.7%)	510 (1.1%)	70 (0.7%)	70 (0.7%)	0.041	0.002
Prior transient ischaemic attack	410 (3.8%)	2,050 (4.3%)	370 (3.8%)	400 (4.1%)	0.030	0.015
Chronic kidney disease	140 (1.3%)	3,280 (7.0%)	140 (1.4%)	170 (1.7%)	0.286	0.023
Heart failure	1,690 (15.5%)	11,330 (24.0%)	1,630 (16.5%)	1,660 (16.8%)	0.216	0.008
Coronary artery disease	1,880 (17.3%)	12,460 (26.4%)	1,790 (18.1%)	1,800 (18.2%)	0.223	0.002
Peripheral arterial disease	480 (4.4%)	3,030 (6.4%)	460 (4.7%)	480 (4.9%)	0.090	0.010
Hypertension	7,580 (69.6%)	34,570 (73.3%)	6,930 (70.2%)	7,030 (71.1%)	0.083	0.021
Diabetes	1,810 (16.6%)	9,090 (19.3%)	1,680 (17.0%)	1,720 (17.4%)	0.070	0.010
Chronic obstructive pulmonary disease	1,220 (11.2%)	5,700 (12.1%)	1,140 (11.5%)	1,160 (11.7%)	0.028	0.006
Liver disease	80 (0.8%)	430 (0.9%)	80 (0.8%)	80 (0.8%)	0.014	0.002
Alcoholism	310 (2.9%)	1,030 (2.2%)	290 (2.9%)	280 (2.8%)	0.045	0.004
Dementia	220 (2.0%)	770 (1.6%)	190 (1.9%)	210 (2.1%)	0.026	0.014
Cancer 6 months before and including index date	70 (0.7%)	400 (0.9%)	70 (0.7%)	70 (0.7%)	0.020	0.000
Platelet inhibitors (excluding heparin)	4,040 (37.1%)	18,680 (39.6%)	3,700 (37.5%)	3,860 (39.1%)	0.052	0.033
Low -dose aspirin	3,660 (33.6%)	17,010 (36.1%)	3,350 (33.9%)	3,500 (35.5%)	0.052	0.033

ADP receptor blockers	540 (5.0%)	3,710 (7.9%)	520 (5.2%)	520 (5.3%)	0.118	0.000
Renin -angiotensin system inhibitors	5,150 (47.3%)	24,140 (51.2%)	4,730 (47.9%)	4,770 (48.3%)	0.078	0.008
Angiotensin -converting enzyme inhibitors	2,470 (22.6%)	13,490 (28.6%)	2,320 (23.5%)	2,310 (23.4%)	0.137	0.002
Angiotensin II antagonists, plain	1,850 (17.0%)	8,000 (17.0%)	1,680 (17.0%)	1,720 (17.4%)	0.000	0.012
Angiotensin II antagonists, combinations	700 (6.4%)	2,540 (5.4%)	620 (6.3%)	640 (6.5%)	0.043	0.009
Beta-blockers	8,030 (73.7%)	36,150 (76.7%)	7,330 (74.3%)	7,280 (73.7%)	0.068	0.012
Proton pump inhibitors	2,050 (18.9%)	10,150 (21.5%)	1,900 (19.2%)	1,930 (19.5%)	0.066	0.008
H2-receptor antagonists	40 (0.4%)	210 (0.4%)	40 (0.4%)	40 (0.4%)	0.014	0.003
Non-steroidal anti-inflammatory drugs	710 (6.6%)	2,970 (6.3%)	650 (6.6%)	620 (6.3%)	0.010	0.010
Statins	3,410 (31.3%)	16,730 (35.5%)	3,150 (31.9%)	3,230 (32.7%)	0.088	0.017
Antidiabetic agents	1,290 (11.8%)	6,350 (13.5%)	1,190 (12.1%)	1,200 (12.2%)	0.050	0.003
Loop diuretics	1,850 (17.0%)	12,990 (27.5%)	1,800 (18.2%)	1,870 (18.9%)	0.255	0.017
Non-loop diuretics	110 (1.0%)	650 (1.4%)	100 (1.0%)	110 (1.1%)	0.039	0.010
Alpha adrenergic blockers	2,390 (21.9%)	11,180 (23.7%)	2,210 (22.4%)	2,230 (22.6%)	0.042	0.004
Amiodarone	100 (0.9%)	890 (1.9%)	100 (1.0%)	110 (1.1%)	0.080	0.007
Dronedarone	50 (0.5%)	440 (0.9%)	50 (0.5%)	60 (0.6%)	0.053	0.008
Antihypertensive, combination drugs	1,070 (9.8%)	3,850 (8.2%)	950 (9.6%)	970 (9.8%)	0.057	0.007
Calcium channel blockers	2,580 (23.7%)	12,240 (26.0%)	2,390 (24.2%)	2,390 (24.2%)	0.053	0.000
Selective serotonin reuptake inhibitors	660 (6.1%)	3,110 (6.6%)	600 (6.1%)	590 (6.0%)	0.021	0.005
Drugs used in alcohol dependence	20 (0.2%)	60 (0.1%)	20 (0.2%)	10 (0.1%)	0.015	0.016
CHA2DS2-VASc, mean(SD)	3.1 (1.65)	3.6 (1.75)	3.2 (1.66)	3.2 (1.69)	0.274	0.025
CHA2DS2-VASc:0 -1	1,840 (16.8%)	5,700 (12.1%)	1,560 (15.8%)	1,600 (16.2%)	0.135	0.010
CHA2DS2-VASc:2 -3	4,900 (45.0%)	17,540 (37.2%)	4,380 (44.3%)	4,160 (42.1%)	0.159	0.044
CHA2DS2-VASc:>=4	4,160 (38.2%)	23,910 (50.7%)	3,940 (39.9%)	4,120 (41.7%)	0.255	0.036
CHADS2, mean(SD)	2.5 (1.41)	2.9 (1.47)	2.6 (1.41)	2.6 (1.44)	0.251	0.026
CHADS2:0	610 (5.6%)	2,300 (4.9%)	510 (5.2%)	620 (6.3%)	0.031	0.047
CHADS2:1	2,110 (19.4%)	6,040 (12.8%)	1,800 (18.3%)	1,630 (16.5%)	0.179	0.046
CHADS2:>=2	8,180 (75.1%)	38,810 (82.3%)	7,560 (76.6%)	7,620 (77.2%)	0.177	0.015
HAS-BLED, mean(SD)	1.8 (0.86)	1.9 (0.92)	1.8 (0.86)	1.8 (0.87)	0.197	0.018
HAS-BLED:<3	9,110 (83.6%)	36,080 (76.5%)	8,190 (83.0%)	8,070 (81.8%)	0.179	0.032
HAS-BLED:>=3	1,780 (16.4%)	11,080 (23.5%)	1,680 (17.0%)	1,800 (18.2%)	0.179	0.032
log_n_hosp, median(IQR)	0.7 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.275	0.024
log_beddays, median(IQR)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.075	0.022
log_n_outpatient, median(IQR)	0.7 (0.0 - 0.7)	0.0 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.7 (0.0 - 0.7)	0.229	0.000
income, median(IQR), k€	55.0 (43.0 - 84.6)	49.8 (40.5 - 72.3)	54.1 (42.6 - 81.9)	53.7 (42.4 - 81.5)	0.078	0.004
education:Secondary compulsory	3,710 (34.1%)	18,850 (40.0%)	3,460 (35.0%)	3,450 (34.9%)	0.122	0.002
education:Vocational / High school	4,330 (39.7%)	18,480 (39.2%)	3,950 (40.0%)	3,920 (39.7%)	0.011	0.008
education:Higher education	2,750 (25.3%)	9,340 (19.8%)	2,380 (24.1%)	2,410 (24.4%)	0.131	0.009
education:Unknown	100 (0.9%)	490 (1.0%)	90 (0.9%)	100 (1.0%)	0.013	0.009

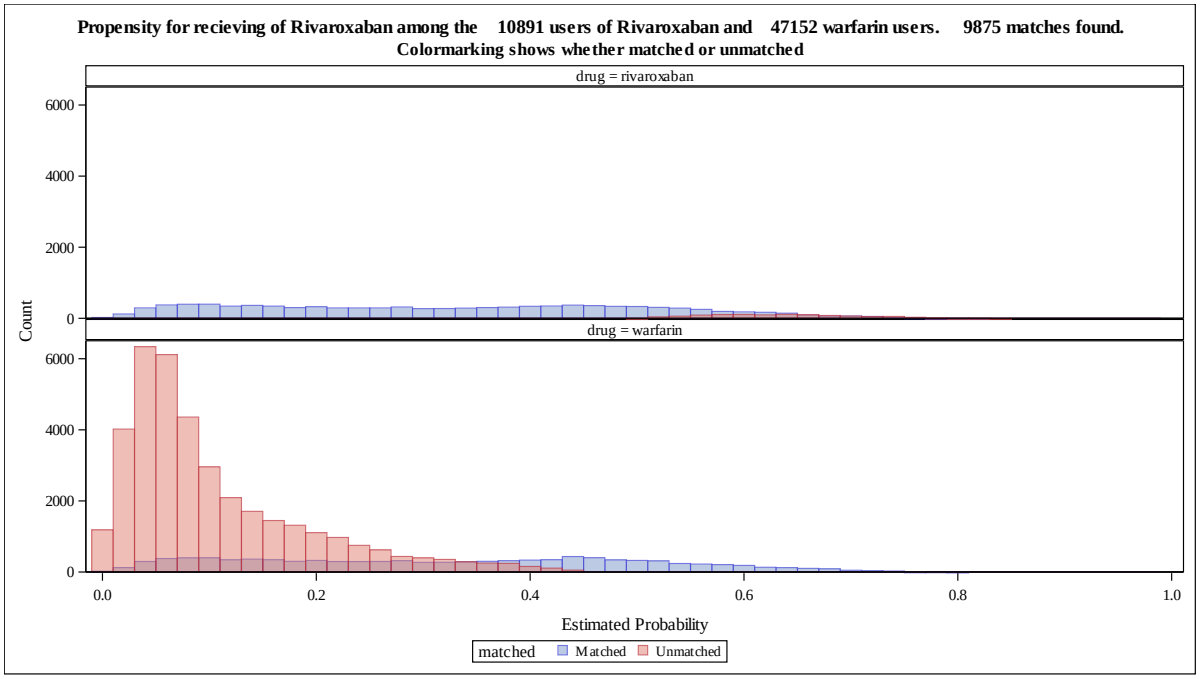

Propensity for recieving of Rivaroxaban among the 10891 users of Rivaroxaban and 47152 warfarin users. 9875 matches found.
Colormarking shows whether matched or unmatched
drug = rivaroxaban
drug = warfarin
Count
6000
4000
2000
0
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.66 Baseline characteristics of patients with non-valvular atrial fibrillation initiating rivaroxaban or warfarin and standardised mean differences before and after matching, Sweden – REDUCED DOSE

Characteristic	Rivaroxaban (rounded) before matching N= 3442	Warfarin (rou nded) before matching N=47152	Rivaroxaban (rounded) after matching N= 3437	Warfarin (rou nded) after matching N= 3437	Standardised mean difference before matchi ng (max= 0.76)	Standardised mean difference after matching (max= 0.04)
index_year:2013	520 (15.0%)	22,380 (47.5%)	520 (15.0%)	500 (14.6%)	0.749	0.010
index_year:2014	1,070 (31.1%)	14,490 (30.7%)	1,070 (31.1%)	1,100 (32.0%)	0.007	0.019
index_year:2015	1,080 (31.3%)	7,040 (14.9%)	1,080 (31.4%)	1,080 (31.4%)	0.396	0.001
index_year:2016	780 (22.7%)	3,240 (6.9%)	780 (22.5%)	760 (22.0%)	0.457	0.013
Time from AF diag:< 1 month	1,820 (52.8%)	28,530 (60.5%)	1,820 (52.9%)	1,790 (52.2%)	0.155	0.014
Time from AF diag:1 - 6 month	380 (11.0%)	4,220 (9.0%)	380 (11.0%)	400 (11.6%)	0.069	0.018
Time from AF diag:6 - 60 months	1,250 (36.2%)	14,400 (30.5%)	1,240 (36.1%)	1,240 (36.2%)	0.119	0.002
Sex:Female	1,900 (55.2%)	20,290 (43.0%)	1,900 (55.1%)	1,880 (54.7%)	0.245	0.009
Sex:Male	1,540 (44.8%)	26,860 (57.0%)	1,540 (44.9%)	1,560 (45.3%)	0.245	0.009
Age, median(IQR)	83.5 (77.1 - 88.4)	75.6 (68.4 - 82.6)	83.5 (77.1 - 88.4)	83.4 (77.1 - 88.2)	0.755	0.004
Age -group:< 55 years	20 (0.6%)	2,130 (4.5%)	20 (0.6%)	20 (0.6%)	0.254	0.008
Age -group:55-<65 years	120 (3.5%)	5,540 (11.8%)	120 (3.5%)	130 (3.8%)	0.315	0.016
Age -group:65-<75 years	540 (15.6%)	14,880 (31.6%)	540 (15.6%)	520 (15.1%)	0.384	0.013
Age -group:75-<85 years	1,320 (38.2%)	16,570 (35.1%)	1,320 (38.3%)	1,330 (38.8%)	0.063	0.010
Age -group:>= 85 years	1,450 (42.2%)	8,030 (17.0%)	1,450 (42.1%)	1,430 (41.7%)	0.573	0.008
CCI-group:0	1,010 (29.3%)	17,670 (37.5%)	1,010 (29.4%)	1,030 (29.9%)	0.173	0.011
CCI-group:1-2	1,140 (33.1%)	15,790 (33.5%)	1,140 (33.1%)	1,140 (33.1%)	0.009	0.000
CCI-group:>=3	1,290 (37.6%)	13,700 (29.0%)	1,290 (37.6%)	1,270 (37.1%)	0.182	0.010
Prior bleeding (any)	510 (14.7%)	5,150 (10.9%)	500 (14.7%)	490 (14.1%)	0.114	0.016
Prior gastrointestinal bleeding	30 (1.0%)	360 (0.8%)	30 (1.0%)	30 (0.9%)	0.022	0.003
Prior intracranial bleeding	70 (1.9%)	410 (0.9%)	70 (1.9%)	60 (1.6%)	0.088	0.020
Prior stroke (any)	610 (17.8%)	6,200 (13.1%)	610 (17.8%)	610 (17.8%)	0.128	0.001
Prior ischaemic stroke	590 (17.1%)	6,080 (12.9%)	590 (17.1%)	600 (17.3%)	0.118	0.005
Prior haemorrhagic stroke	50 (1.6%)	330 (0.7%)	50 (1.6%)	50 (1.5%)	0.082	0.007
Prior systemic embolism	50 (1.3%)	510 (1.1%)	50 (1.3%)	50 (1.6%)	0.023	0.019
Prior transient ischaemic attack	200 (5.9%)	2,050 (4.3%)	200 (5.8%)	190 (5.6%)	0.069	0.009
Chronic kidney disease	240 (7.0%)	3,280 (7.0%)	240 (7.0%)	260 (7.4%)	0.003	0.016
Heart failure	1,020 (29.7%)	11,330 (24.0%)	1,020 (29.7%)	1,050 (30.4%)	0.129	0.016
Coronary artery disease	1,010 (29.3%)	12,460 (26.4%)	1,010 (29.3%)	1,010 (29.3%)	0.063	0.000
Peripheral arterial disease	240 (6.9%)	3,030 (6.4%)	240 (6.9%)	200 (5.9%)	0.017	0.041
Hypertension	2,680 (77.8%)	34,570 (73.3%)	2,670 (77.7%)	2,660 (77.5%)	0.104	0.006
Diabetes	730 (21.3%)	9,090 (19.3%)	730 (21.3%)	760 (22.2%)	0.050	0.022
Chronic obstructive pulmonary disease	440 (12.8%)	5,700 (12.1%)	440 (12.8%)	450 (13.0%)	0.021	0.007
Liver disease	20 (0.7%)	430 (0.9%)	20 (0.7%)	30 (0.8%)	0.023	0.013
Alcoholism	60 (1.6%)	1,030 (2.2%)	60 (1.6%)	70 (2.0%)	0.040	0.028
Dementia	190 (5.4%)	770 (1.6%)	180 (5.4%)	200 (5.8%)	0.207	0.018
Cancer 6 months before and including index date	20 (0.6%)	400 (0.9%)	20 (0.6%)	20 (0.5%)	0.025	0.015
Platelet inhibitors (excluding heparin)	1,660 (48.3%)	18,680 (39.6%)	1,660 (48.3%)	1,720 (50.0%)	0.176	0.036
Low -dose aspirin	1,490 (43.2%)	17,010 (36.1%)	1,480 (43.1%)	1,550 (45.0%)	0.146	0.038
ADP receptor blockers	300 (8.8%)	3,710 (7.9%)	300 (8.8%)	280 (8.3%)	0.033	0.019

Renin -angiotensin system inhibitors	1,730 (50.2%)	24,140 (51.2%)	1,730 (50.3%)	1,760 (51.1%)	0.020	0.016
Angiotensin -converting enzyme inhibitors	910 (26.3%)	13,490 (28.6%)	910 (26.4%)	900 (26.3%)	0.051	0.002
Angiotensin II antagonists, plain	610 (17.6%)	8,000 (17.0%)	610 (17.7%)	620 (18.2%)	0.018	0.013
Angiotensin II antagonists, combinations	210 (6.2%)	2,540 (5.4%)	210 (6.2%)	210 (6.2%)	0.034	0.001
Beta-blockers	2,550 (74.1%)	36,150 (76.7%)	2,550 (74.1%)	2,560 (74.5%)	0.060	0.011
Proton pump inhibitors	840 (24.4%)	10,150 (21.5%)	840 (24.4%)	850 (24.8%)	0.069	0.009
H2-receptor antagonists	20 (0.6%)	210 (0.4%)	20 (0.6%)	20 (0.6%)	0.026	0.011
Non-steroidal anti-inflammatory drugs	160 (4.8%)	2,970 (6.3%)	160 (4.8%)	160 (4.7%)	0.067	0.004
Statins	1,150 (33.4%)	16,730 (35.5%)	1,150 (33.4%)	1,160 (33.6%)	0.043	0.005
Antidiabetic agents	490 (14.3%)	6,350 (13.5%)	490 (14.3%)	500 (14.4%)	0.024	0.003
Loop diuretics	1,210 (35.1%)	12,990 (27.5%)	1,210 (35.1%)	1,230 (35.8%)	0.163	0.015
Non-loop diuretics	40 (1.1%)	650 (1.4%)	40 (1.1%)	40 (1.2%)	0.026	0.005
Alpha adrenergic blockers	880 (25.7%)	11,180 (23.7%)	880 (25.7%)	880 (25.5%)	0.046	0.005
Amiodarone	30 (0.9%)	890 (1.9%)	30 (0.9%)	30 (1.0%)	0.083	0.009
Dronedarone	20 (0.5%)	440 (0.9%)	20 (0.5%)	10 (0.4%)	0.052	0.013
Antihypertensive, combination drugs	290 (8.5%)	3,850 (8.2%)	290 (8.6%)	310 (8.9%)	0.014	0.011
Calcium channel blockers	890 (25.8%)	12,240 (26.0%)	890 (25.8%)	930 (27.1%)	0.003	0.028
Selective serotonin reuptake inhibitors	340 (9.8%)	3,110 (6.6%)	340 (9.8%)	340 (9.9%)	0.117	0.005
Drugs used in alcohol dependence	<5	60 (0.1%)	<5	10 (0.1%)	0.010	0.017
CHA2DS2-VASc, mean(SD)	4.3 (1.62)	3.6 (1.75)	4.3 (1.62)	4.3 (1.60)	0.464	0.005
CHA2DS2-VASc:0 -1	100 (2.9%)	5,700 (12.1%)	100 (2.9%)	120 (3.4%)	0.353	0.027
CHA2DS2-VASc:2 -3	960 (27.8%)	17,540 (37.2%)	960 (27.8%)	890 (25.9%)	0.202	0.043
CHA2DS2-VASc:>=4	2,390 (69.3%)	23,910 (50.7%)	2,380 (69.2%)	2,430 (70.7%)	0.386	0.032
CHADS2, mean(SD)	3.5 (1.35)	2.9 (1.47)	3.5 (1.35)	3.5 (1.34)	0.455	0.001
CHADS2:0	30 (0.8%)	2,300 (4.9%)	30 (0.8%)	40 (1.1%)	0.244	0.029
CHADS2:1	160 (4.5%)	6,040 (12.8%)	160 (4.5%)	150 (4.5%)	0.297	0.004
CHADS2:>=2	3,260 (94.6%)	38,810 (82.3%)	3,250 (94.6%)	3,250 (94.4%)	0.393	0.009
HAS-BLED, mean(SD)	2.2 (0.83)	1.9 (0.92)	2.2 (0.83)	2.2 (0.83)	0.294	0.014
HAS-BLED:<3	2,360 (68.4%)	36,080 (76.5%)	2,350 (68.5%)	2,370 (69.1%)	0.181	0.013
HAS-BLED:>=3	1,090 (31.6%)	11,080 (23.5%)	1,080 (31.5%)	1,060 (30.9%)	0.181	0.013
log_n_hosp, median(IQR)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.080	0.009
log_beddays, median(IQR)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.7 (0.0 - 1.4)	0.023	0.005
log_n_outpatient, median(IQR)	0.7 (0.0 - 1.1)	0.0 (0.0 - 0.7)	0.7 (0.0 - 1.1)	0.7 (0.0 - 1.1)	0.324	0.005
income, median(IQR), k€	46.3 (39.4 - 59.8)	49.8 (40.5 - 72.3)	46.3 (39.4 - 59.8)	46.5 (39.7 - 59.3)	0.042	0.002
education:Secondary compulsory	1,640 (47.5%)	18,850 (40.0%)	1,630 (47.5%)	1,650 (47.9%)	0.152	0.008
education:Vocational / High school	1,150 (33.3%)	18,480 (39.2%)	1,140 (33.3%)	1,100 (32.1%)	0.123	0.025
education:Higher education	590 (17.0%)	9,340 (19.8%)	580 (17.0%)	610 (17.7%)	0.072	0.020
education:Unknown	80 (2.2%)	490 (1.0%)	80 (2.2%)	80 (2.3%)	0.094	0.002

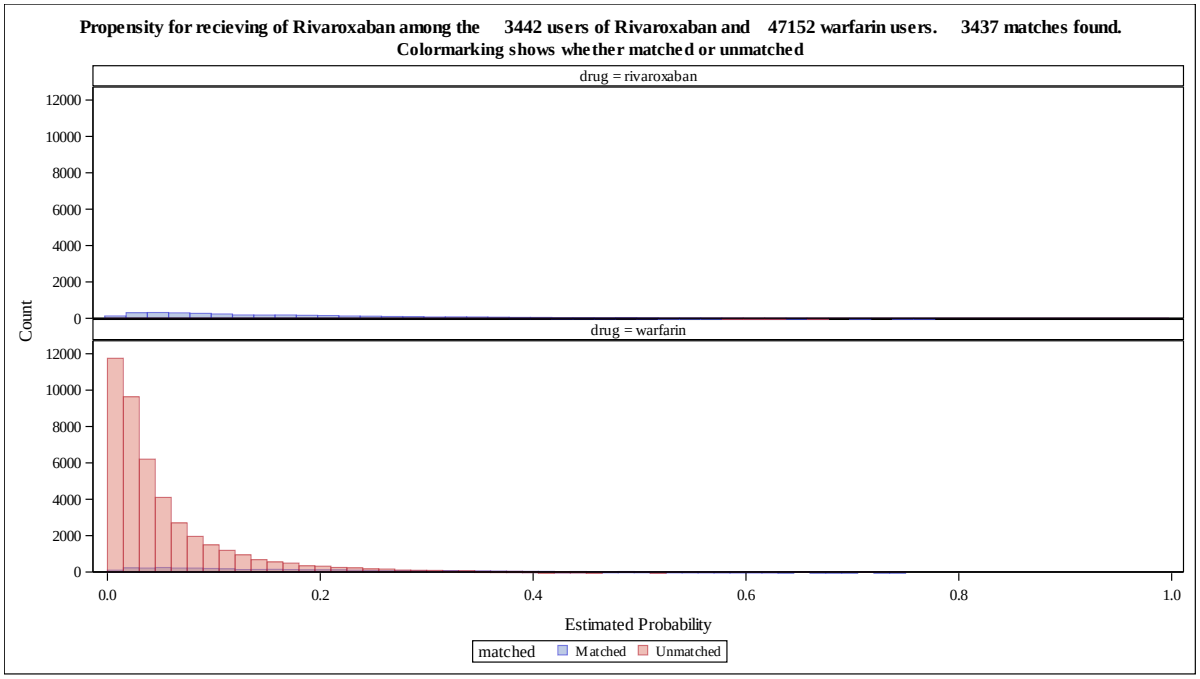
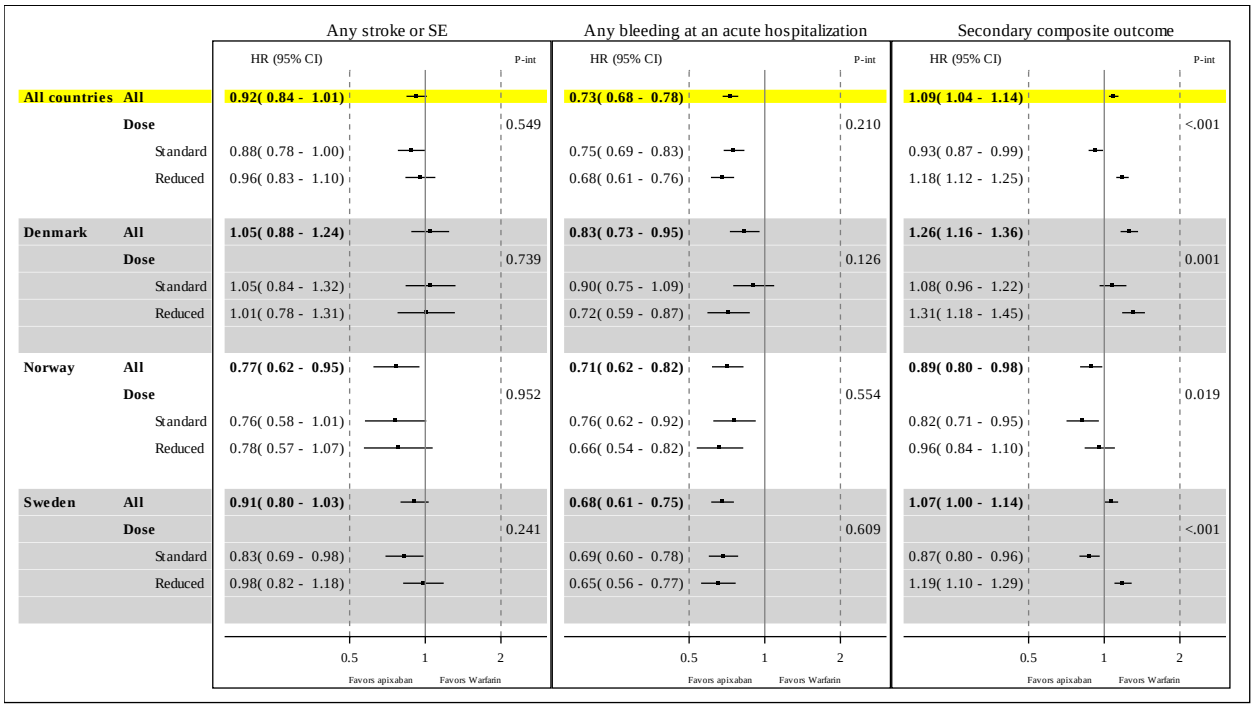
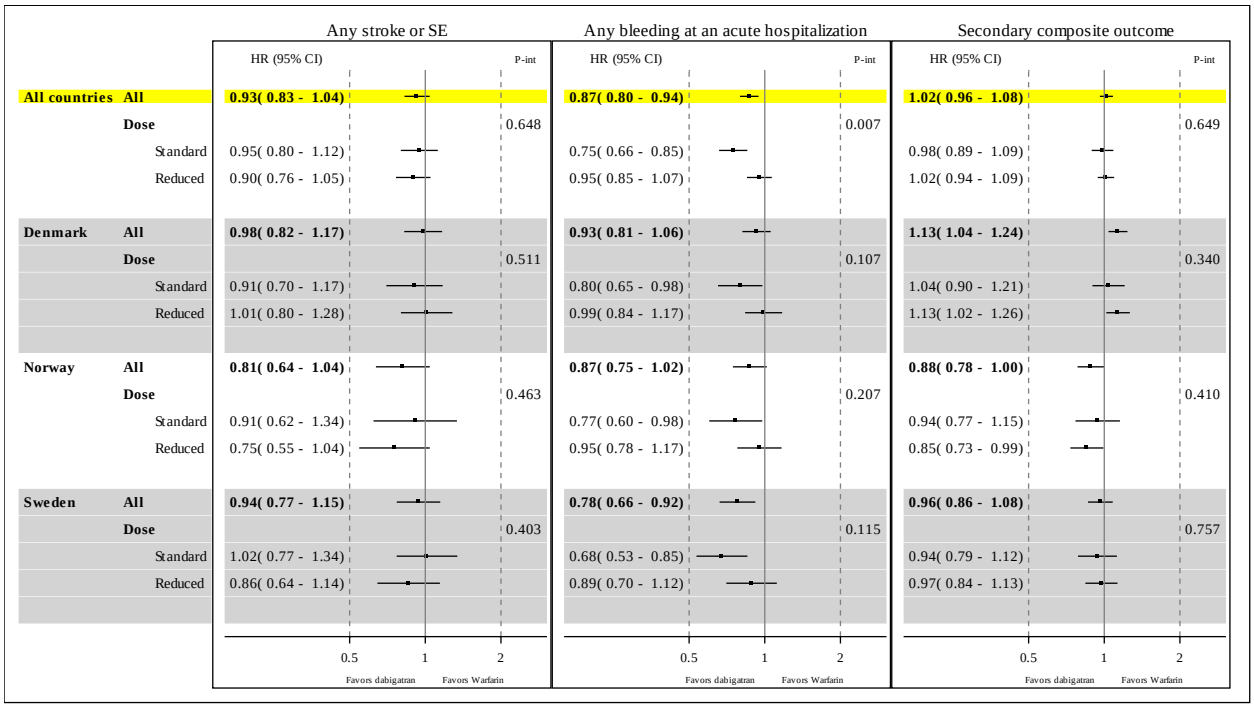

Propensity for recieving of Rivaroxaban among the 3442 users of Rivaroxaban and 47152 warfarin users. 3437 matches found.
Colormarking shows whether matched or unmatched
drug = rivaroxaban
drug = warfarin
Count
0
2000
4000
6000
8000
10000
12000
0.0
0.2
0.4
0.6
0.8
1.0
Estimated Probability
matched
Matched
Unmatched

Table 15.67 Sensitivity analysis (after re -matching within subgroups defined by initial dose): pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of apixaban vs. warfarin, overall and by country



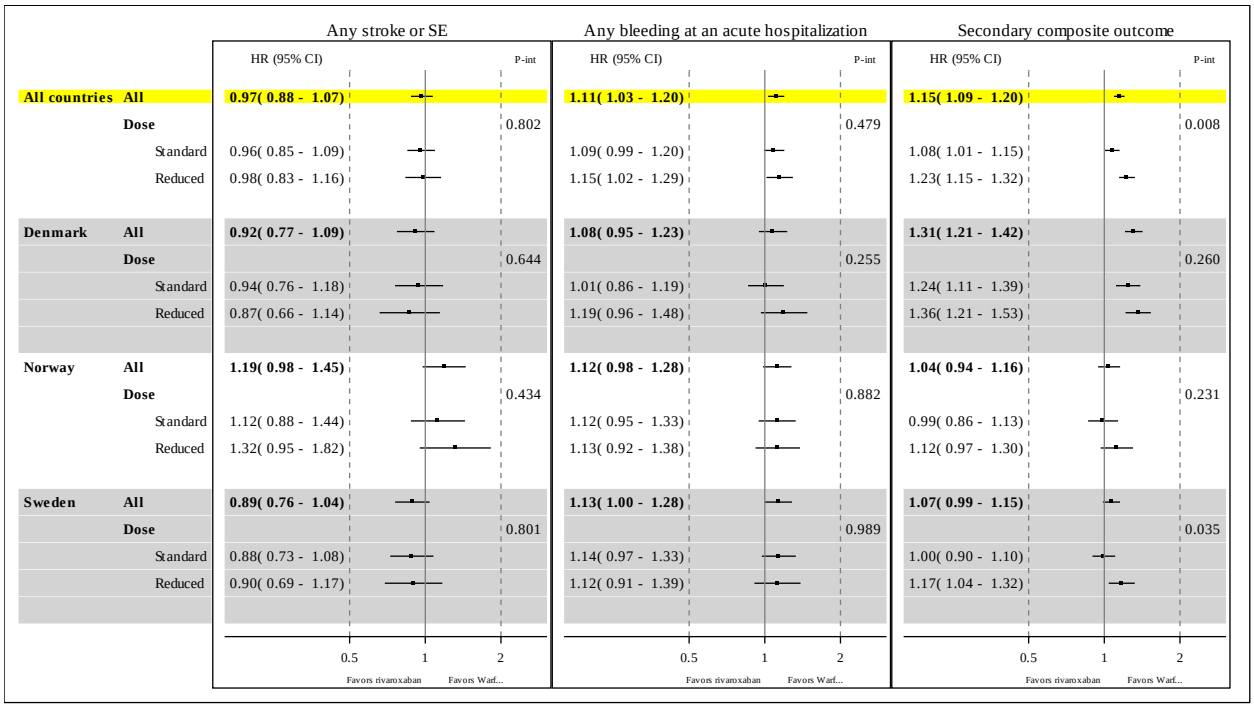
CI confidence interval; HR hazard ratio; NVAV non-valvular atrial fibrillation; SE systemic embolism

Table 15.68 Sensitivity subgroup analysis for initial dose: pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of dabigatran vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAV non-valvular atrial fibrillation; SE systemic embolism

Table 15.69 Sensitivity subgroup analysis for initial dose: pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of rivaroxaban vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAV non-valvular atrial fibrillation; SE systemic embolism

Table 15.70 Health care resource utilisation (HCRU) and associated costs related to bleeding and stroke/systemic embolism among patients with NVAF treated with apixaban and warfarin, Denmark (propensity -score matched population)

cost_EP_year=1

Endpoint	apixaban: #patients available for year	apixaban: mean (SD)	apixaban: proportion of patients with any	apixaban: proportion of patients with >1	apixaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	8092	0.047(0.282)	3.39%	0.95%	0.00%		11024	0.065(0.352)	4.39%	1.46%	0.03%
Bleeding BedDays	8092	0.252(4.586)	2.88%	2.19%	1.01%		11024	0.255(2.193)	3.80%	2.88%	1.31%
Bleeding hospitalisation costs	8092	135(2464)	.	.	.		11024	137(1178)	.	.	.
Bleeding outpat. visits	8092	0.029(0.191)	2.60%	0.30%	0.00%		11024	0.037(0.220)	3.24%	0.42%	0.00%
Bleeding outpat. costs	8092	3(18)	.	.	.		11024	4(21)	.	.	.
Stroke/se hospitalisations	8092	0.029(0.215)	2.21%	0.48%	0.00%		11024	0.030(0.214)	2.23%	0.60%	0.00%
Stroke/se BedDays	8092	0.176(1.933)	2.04%	1.74%	0.93%		11024	0.183(2.081)	2.02%	1.64%	0.93%
Stroke/se hospitalisation costs	8092	95(1038)	.	.	.		11024	98(1118)	.	.	.
Stroke/se outpat. visits	8092	0.032(0.211)	2.63%	0.54%	0.00%		11024	0.026(0.191)	2.20%	0.36%	0.00%
Stroke/se outpat. costs	8092	3(20)	.	.	.		11024	2(18)	.	.	.

cost_EP_year=2

Endpoint	apixaban: #patients available for year	apixaban: mean (SD)	apixaban: proportion of patients with any	apixaban: proportion of patients with >1	apixaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	2157	0.032(0.245)	2.23%	0.65%	0.00%		3413	0.041(0.280)	2.75%	0.94%	0.00%
Bleeding BedDays	2157	0.163(1.743)	1.95%	1.62%	0.93%		3413	0.149(1.486)	2.31%	1.73%	0.94%
Bleeding hospitalisation costs	2157	87(937)	.	.	.		3413	80(798)	.	.	.
Bleeding outpat. visits	2157	0.022(0.179)	1.85%	0.28%	0.00%		3413	0.030(0.194)	2.61%	0.26%	0.00%
Bleeding outpat. costs	2157	2(17)	.	.	.		3413	3(18)	.	.	.
Stroke/se hospitalisations	2157	0.017(0.170)	1.21%	0.42%	0.00%		3413	0.014(0.145)	1.08%	0.29%	0.00%
Stroke/se BedDays	2157	0.136(2.366)	1.16%	1.02%	0.60%		3413	0.080(1.078)	0.97%	0.82%	0.44%
Stroke/se hospitalisation costs	2157	73(1271)	.	.	.		3413	43(579)	.	.	.
Stroke/se outpat. visits	2157	0.011(0.117)	0.97%	0.14%	0.00%		3413	0.008(0.109)	0.70%	0.12%	0.00%
Stroke/se outpat. costs	2157	1(11)	.	.	.		3413	1(10)	.	.	.

Table 15.71 Health care resource utilisation (HCRU) and associated costs related to bleeding and stroke/systemic embolism among patients with NVAF treated with dabigatran and warfarin, Denmark (propensity -score matched population)

cost_EP_year=1

Endpoint	dabigatran: #patients available for year	dabigatran: mean (SD)	dabigatran: proportion of patients with any	dabigatran: proportion of patients with >1	dabigatran: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	10402	0.045(0.277)	3.27%	0.96%	0.00%		10403	0.057(0.334)	3.81%	1.30%	0.03%
Bleeding BedDays	10402	0.150(1.363)	2.76%	2.11%	0.91%		10403	0.225(2.128)	3.25%	2.51%	1.14%
Bleeding hospitalisation costs	10402	81(733)	.	.	.		10403	121(1143)	.	.	.
Bleeding outpat. visits	10402	0.033(0.199)	2.91%	0.37%	0.00%		10403	0.038(0.227)	3.24%	0.46%	0.00%
Bleeding outpat. costs	10402	3(19)	.	.	.		10403	4(21)	.	.	.
Stroke/se hospitalisations	10402	0.024(0.202)	1.78%	0.47%	0.01%		10403	0.025(0.195)	1.85%	0.56%	0.00%
Stroke/se BedDays	10402	0.126(1.612)	1.62%	1.34%	0.70%		10403	0.156(1.968)	1.68%	1.43%	0.83%
Stroke/se hospitalisation costs	10402	67(866)	.	.	.		10403	84(1057)	.	.	.
Stroke/se outpat. visits	10402	0.021(0.173)	1.75%	0.34%	0.00%		10403	0.023(0.181)	1.86%	0.37%	0.00%
Stroke/se outpat. costs	10402	2(16)	.	.	.		10403	2(17)	.	.	.

cost_EP_year=2

Endpoint	dabigatran: #patients available for year	dabigatran: mean (SD)	dabigatran: proportion of patients with any	dabigatran: proportion of patients with >1	dabigatran: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	4941	0.033(0.265)	2.21%	0.67%	0.02%		3929	0.031(0.238)	2.21%	0.56%	0.00%
Bleeding BedDays	4941	0.097(1.040)	1.76%	1.32%	0.57%		3929	0.112(1.331)	1.86%	1.27%	0.61%
Bleeding hospitalisation costs	4941	52(559)	.	.	.		3929	60(715)	.	.	.
Bleeding outpat. visits	4941	0.028(0.188)	2.39%	0.32%	0.00%		3929	0.031(0.196)	2.72%	0.28%	0.00%
Bleeding outpat. costs	4941	3(18)	.	.	.		3929	3(19)	.	.	.
Stroke/se hospitalisations	4941	0.013(0.139)	0.97%	0.22%	0.00%		3929	0.012(0.137)	0.94%	0.23%	0.00%
Stroke/se BedDays	4941	0.076(1.279)	0.97%	0.75%	0.45%		3929	0.063(0.925)	0.87%	0.74%	0.36%
Stroke/se hospitalisation costs	4941	41(687)	.	.	.		3929	34(497)	.	.	.
Stroke/se outpat. visits	4941	0.006(0.083)	0.51%	0.06%	0.00%		3929	0.006(0.097)	0.51%	0.10%	0.00%
Stroke/se outpat. costs	4941	1(8)	.	.	.		3929	1(9)	.	.	.

Table 15.72 Health care resource utilisation (HCRU) and associated costs related to bleeding and stroke/systemic embolism among patients with NVAF treated with rivaroxaban and warfarin, Denmark (propensity -score matched population)

cost_EP_year=1

Endpoint	rivaroxaban: #patients available for year	rivaroxaban: mean (SD)	rivaroxaban: proportion of patients with any	rivaroxaban: proportion of patients with >1	rivaroxaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	7389	0.064(0.363)	4.11%	1.52%	0.05%		7494	0.066(0.376)	4.20%	1.44%	0.05%
Bleeding BedDays	7389	0.238(1.907)	3.63%	2.99%	1.37%		7494	0.246(2.125)	3.67%	2.80%	1.32%
Bleeding hospitalisation costs	7389	128(1024)	.	.	.		7494	132(1142)	.	.	.
Bleeding outpat. visits	7389	0.042(0.239)	3.56%	0.57%	0.00%		7494	0.039(0.228)	3.34%	0.49%	0.00%
Bleeding outpat. costs	7389	4(23)	.	.	.		7494	4(21)	.	.	.
Stroke/se hospitalisations	7389	0.027(0.207)	2.02%	0.49%	0.00%		7494	0.032(0.224)	2.39%	0.71%	0.00%
Stroke/se BedDays	7389	0.158(1.915)	1.83%	1.39%	0.76%		7494	0.195(2.088)	2.26%	1.77%	1.03%
Stroke/se hospitalisation costs	7389	85(1029)	.	.	.		7494	105(1122)	.	.	.
Stroke/se outpat. visits	7389	0.018(0.144)	1.60%	0.15%	0.00%		7494	0.028(0.200)	2.30%	0.44%	0.00%
Stroke/se outpat. costs	7389	2(14)	.	.	.		7494	3(19)	.	.	.

cost_EP_year=2

Endpoint	rivaroxaban: #patients available for year	rivaroxaban: mean (SD)	rivaroxaban: proportion of patients with any	rivaroxaban: proportion of patients with >1	rivaroxaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	2544	0.048(0.284)	3.50%	0.98%	0.00%		1735	0.036(0.242)	2.71%	0.58%	0.00%
Bleeding BedDays	2544	0.119(0.945)	2.87%	2.24%	0.59%		1735	0.139(1.403)	2.36%	1.61%	0.98%
Bleeding hospitalisation costs	2544	64(508)	.	.	.		1735	75(754)	.	.	.
Bleeding outpat. visits	2544	0.037(0.222)	3.07%	0.47%	0.00%		1735	0.029(0.191)	2.59%	0.29%	0.00%
Bleeding outpat. costs	2544	3(21)	.	.	.		1735	3(18)	.	.	.
Stroke/se hospitalisations	2544	0.020(0.173)	1.65%	0.24%	0.00%		1735	0.011(0.129)	0.86%	0.17%	0.00%
Stroke/se BedDays	2544	0.119(1.618)	1.65%	1.30%	0.51%		1735	0.080(1.160)	0.81%	0.69%	0.40%
Stroke/se hospitalisation costs	2544	64(869)	.	.	.		1735	43(623)	.	.	.
Stroke/se outpat. visits	2544	0.006(0.084)	0.59%	0.04%	0.00%		1735	0.009(0.110)	0.69%	0.17%	0.00%
Stroke/se outpat. costs	2544	1(8)	.	.	.		1735	1(10)	.	.	.

Table 15.73 Health care resource utilisation (HCRU) and associated costs related to bleeding and stroke/systemic embolism among patients with NVAF treated with apixaban and warfarin, Norway (propensity -score matched population)

Exploratory analysis - costs. Country no. Comparing drug apixaban with warfarin

For patients included at least 1 and 2 years before end of study, (and for the latter not censored before start of that year).

Using price per hospital bed -day=1627.99 € and price per outpatient visit=54.03 €.

cost_EP_year=1

Endpoint	apixaban: #patients available for year	apixaban: mean (SD)	apixaban: proportion of patients with any	apixaban: proportion of patients with >1	apixaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	5980	0.054(0.308)	3.86%	1.07%	0.00%		9759	0.076(0.393)	5.09%	1.46%	0.07%
Bleeding BedDays	5980	0.463(4.176)	3.86%	3.46%	2.22%		9759	0.548(4.076)	5.09%	4.57%	2.78%
Bleeding hospitalisation costs	5980	753(6798)	.	.	.		9759	892(6635)	.	.	.
Bleeding outpat. visits	5980	0.052(0.315)	3.60%	1.02%	0.03%		9759	0.055(0.329)	3.87%	0.99%	0.04%
Bleeding outpat. costs	5980	3(17)	.	.	.		9759	3(18)	.	.	.
Stroke/se hospitalisations	5980	0.027(0.193)	2.27%	0.33%	0.00%		9759	0.026(0.194)	2.11%	0.30%	0.00%
Stroke/se BedDays	5980	0.238(2.691)	2.27%	2.09%	1.27%		9759	0.237(2.651)	2.11%	2.00%	1.25%
Stroke/se hospitalisation costs	5980	388(4381)	.	.	.		9759	386(4316)	.	.	.
Stroke/se outpat. visits	5980	0.028(0.290)	1.81%	0.42%	0.03%		9759	0.024(0.316)	1.39%	0.40%	0.05%
Stroke/se outpat. costs	5980	2(16)	.	.	.		9759	1(17)	.	.	.

cost_EP_year=2

Endpoint	apixaban: #patients available for year	apixaban: mean (SD)	apixaban: proportion of patients with any	apixaban: proportion of patients with >1	apixaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	1458	0.047(0.300)	3.29%	0.82%	0.00%		3530	0.051(0.328)	3.34%	1.08%	0.06%
Bleeding BedDays	1458	0.374(3.330)	3.29%	3.09%	1.99%		3530	0.338(2.901)	3.34%	3.06%	2.04%
Bleeding hospitalisation costs	1458	609(5421)	.	.	.		3530	550(4723)	.	.	.
Bleeding outpat. visits	1458	0.046(0.270)	3.57%	0.69%	0.00%		3530	0.050(0.300)	3.60%	0.88%	0.00%
Bleeding outpat. costs	1458	2(15)	.	.	.		3530	3(16)	.	.	.
Stroke/se hospitalisations	1458	0.017(0.163)	1.37%	0.21%	0.00%		3530	0.016(0.147)	1.36%	0.23%	0.00%
Stroke/se BedDays	1458	0.139(1.529)	1.37%	1.23%	0.89%		3530	0.117(1.278)	1.36%	1.22%	0.85%
Stroke/se hospitalisation costs	1458	226(2489)	.	.	.		3530	191(2080)	.	.	.
Stroke/se outpat. visits	1458	0.003(0.052)	0.27%	0.00%	0.00%		3530	0.002(0.053)	0.20%	0.03%	0.00%
Stroke/se outpat. costs	1458	0(3)	.	.	.		3530	0(3)	.	.	.

Table 15.74 Health care resource utilisation (HCRU) and associated costs related to bleeding and stroke/systemic embolism among patients with NVAF treated with dabigatran and warfarin, Norway (propensity -score matched population)

Exploratory analysis - costs. Country no. Comparing drug dabigatran with warfarin

For patients included at least 1 and 2 years before end of study, (and for the latter not censored before start of that year).

Using price per hospital bed -day=1627.99 € and price per outpatient visit=54.03 €.

cost_EP_year=1

Endpoint	dabigatran: #patients available for year	dabigatran: mean (SD)	dabigatran: proportion of patients with any	dabigatran: proportion of patients with >1	dabigatran: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	6634	0.047(0.281)	3.56%	0.80%	0.02%		6663	0.057(0.325)	4.07%	1.08%	0.02%
Bleeding BedDays	6634	0.345(2.857)	3.56%	3.33%	1.85%		6663	0.418(3.489)	4.07%	3.60%	2.15%
Bleeding hospitalisation costs	6634	562(4651)	.	.	.		6663	680(5681)	.	.	.
Bleeding outpat. visits	6634	0.045(0.281)	3.33%	0.71%	0.02%		6663	0.051(0.314)	3.62%	0.92%	0.05%
Bleeding outpat. costs	6634	2(15)	.	.	.		6663	3(17)	.	.	.
Stroke/se hospitalisations	6634	0.023(0.206)	1.67%	0.36%	0.02%		6663	0.022(0.181)	1.80%	0.27%	0.00%
Stroke/se BedDays	6634	0.191(2.410)	1.67%	1.61%	1.01%		6663	0.194(2.521)	1.80%	1.68%	1.01%
Stroke/se hospitalisation costs	6634	311(3924)	.	.	.		6663	315(4104)	.	.	.
Stroke/se outpat. visits	6634	0.030(0.340)	1.67%	0.50%	0.06%		6663	0.025(0.358)	1.34%	0.36%	0.08%
Stroke/se outpat. costs	6634	2(18)	.	.	.		6663	1(19)	.	.	.

cost_EP_year=2

Endpoint	dabigatran: #patients available for year	dabigatran: mean (SD)	dabigatran: proportion of patients with any	dabigatran: proportion of patients with >1	dabigatran: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	3009	0.041(0.338)	2.59%	0.70%	0.10%		2622	0.041(0.298)	2.48%	0.99%	0.00%
Bleeding BedDays	3009	0.278(2.489)	2.59%	2.39%	1.40%		2622	0.286(2.858)	2.48%	2.29%	1.60%
Bleeding hospitalisation costs	3009	453(4051)	.	.	.		2622	465(4652)	.	.	.
Bleeding outpat. visits	3009	0.042(0.276)	3.22%	0.56%	0.07%		2622	0.045(0.291)	3.28%	0.76%	0.00%
Bleeding outpat. costs	3009	2(15)	.	.	.		2622	2(16)	.	.	.
Stroke/se hospitalisations	3009	0.012(0.118)	1.10%	0.10%	0.00%		2622	0.013(0.127)	1.11%	0.11%	0.00%
Stroke/se BedDays	3009	0.092(1.157)	1.10%	1.00%	0.56%		2622	0.102(1.245)	1.11%	1.03%	0.72%
Stroke/se hospitalisation costs	3009	150(1883)	.	.	.		2622	166(2026)	.	.	.
Stroke/se outpat. visits	3009	0.007(0.105)	0.53%	0.13%	0.00%		2622	0.002(0.055)	0.19%	0.04%	0.00%
Stroke/se outpat. costs	3009	0(6)	.	.	.		2622	0(3)	.	.	.

Table 15.75 Health care resource utilisation (HCRU) and associated costs related to bleeding and stroke/systemic embolism among patients with NVAF treated with rivaroxaban and warfarin, Norway (propensity -score matched population)

Exploratory analysis - costs. Country no. Comparing drug rivaroxaban with warfarin

For patients included at least 1 and 2 years before end of study, (and for the latter not censored before start of that year).

Using price per hospital bed -day=1627.99 € and price per outpatient visit=54.03 €.

cost_EP_year=1

Endpoint	rivaroxaban: #patients available for year	rivaroxaban: mean (SD)	rivaroxaban: proportion of patients with any	rivaroxaban: proportion of patients with >1	rivaroxaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	6484	0.077(0.378)	5.41%	1.60%	0.03%		6421	0.067(0.359)	4.67%	1.28%	0.03%
Bleeding BedDays	6484	0.539(3.821)	5.41%	4.86%	2.87%		6421	0.456(3.132)	4.67%	4.16%	2.59%
Bleeding hospitalisation costs	6484	877(6220)	.	.	.		6421	743(5099)	.	.	.
Bleeding outpat. visits	6484	0.066(0.380)	4.66%	1.08%	0.09%		6421	0.059(0.349)	4.13%	1.03%	0.06%
Bleeding outpat. costs	6484	4(21)	.	.	.		6421	3(19)	.	.	.
Stroke/se hospitalisations	6484	0.032(0.221)	2.56%	0.52%	0.00%		6421	0.023(0.180)	1.98%	0.23%	0.00%
Stroke/se BedDays	6484	0.328(3.741)	2.56%	2.27%	1.48%		6421	0.200(2.212)	1.98%	1.90%	1.09%
Stroke/se hospitalisation costs	6484	534(6090)	.	.	.		6421	326(3600)	.	.	.
Stroke/se outpat. visits	6484	0.031(0.309)	2.02%	0.43%	0.05%		6421	0.025(0.256)	1.59%	0.42%	0.05%
Stroke/se outpat. costs	6484	2(17)	.	.	.		6421	1(14)	.	.	.

cost_EP_year=2

Endpoint	rivaroxaban: #patients available for year	rivaroxaban: mean (SD)	rivaroxaban: proportion of patients with any	rivaroxaban: proportion of patients with >1	rivaroxaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (SD)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalisations	3174	0.055(0.302)	4.06%	1.07%	0.00%		2187	0.054(0.339)	3.34%	1.37%	0.05%
Bleeding BedDays	3174	0.335(2.301)	4.06%	3.62%	2.11%		2187	0.375(3.199)	3.34%	3.16%	2.15%
Bleeding hospitalisation costs	3174	545(3745)	.	.	.		2187	610(5209)	.	.	.
Bleeding outpat. visits	3174	0.059(0.316)	4.47%	1.07%	0.03%		2187	0.052(0.305)	3.70%	0.96%	0.00%
Bleeding outpat. costs	3174	3(17)	.	.	.		2187	3(16)	.	.	.
Stroke/se hospitalisations	3174	0.022(0.186)	1.70%	0.32%	0.00%		2187	0.018(0.156)	1.55%	0.23%	0.00%
Stroke/se BedDays	3174	0.203(2.607)	1.70%	1.61%	0.95%		2187	0.138(1.372)	1.55%	1.42%	1.01%
Stroke/se hospitalisation costs	3174	330(4244)	.	.	.		2187	224(2234)	.	.	.
Stroke/se outpat. visits	3174	0.012(0.224)	0.57%	0.32%	0.03%		2187	0.003(0.064)	0.27%	0.05%	0.00%
Stroke/se outpat. costs	3174	1(12)	.	.	.		2187	0(3)	.	.	.

Table 15.76 Health care resource utilisation (HCRU) and associated costs related to bleeding and stroke/systemic embolism among patients with NVAF treated with apixaban and warfarin, Sweden (propensity -score matched population)

Exploratory analysis - costs. Country se. Comparing drug apixaban with warfarin
For patients included at least 1 and 2 years before end of study, (and for the latter not censored before start of that year).
Using price per hospital bed-day=1009.83 € and price per outpatient visit=36.87 €.

cost_EP_year=1

cost_ep_type_text	apixaban: #patients available for year	apixaban: mean (sd)	apixaban: proportion of patients with any	apixaban: proportion of patients with >1	apixaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (sd)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalizations	18315	0.035(0.238)	2.79%	0.52%	0.01%		29240	0.046(0.283)	3.45%	0.76%	0.01%
Bleeding BedDays	18315	0.254(2.274)	2.77%	2.68%	1.44%		29240	0.323(2.548)	3.44%	3.35%	1.80%
Bleeding hospitalization costs	18315	257(2296)	.	.	.		29240	326(2573)	.	.	.
Bleeding outpat. visits	18315	0.063(0.352)	4.24%	1.34%	0.02%		29240	0.073(0.404)	4.70%	1.46%	0.08%
Bleeding outpat. costs	18315	2(13)	.	.	.		29240	3(15)	.	.	.
Stroke/se hospitalizations	18315	0.022(0.171)	1.90%	0.28%	0.00%		29240	0.024(0.186)	1.96%	0.35%	0.00%
Stroke/se BedDays	18315	0.226(2.233)	1.93%	1.90%	1.24%		29240	0.251(2.530)	2.00%	1.97%	1.29%
Stroke/se hospitalization costs	18315	229(2255)	.	.	.		29240	253(2555)	.	.	.
Stroke/se outpat. visits	18315	0.035(0.287)	2.41%	0.54%	0.04%		29240	0.039(0.606)	2.15%	0.52%	0.08%
Stroke/se outpat. costs	18315	1(11)	.	.	.		29240	1(22)	.	.	.

cost_EP_year=2

cost_ep_type_text	apixaban: #patients available for year	apixaban: mean (sd)	apixaban: proportion of patients with any	apixaban: proportion of patients with >1	apixaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (sd)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalizations	5086	0.027(0.194)	2.26%	0.28%	0.00%		12679	0.035(0.247)	2.63%	0.56%	0.02%
Bleeding BedDays	5086	0.188(1.678)	2.24%	2.14%	1.04%		12679	0.242(2.314)	2.59%	2.50%	1.30%
Bleeding hospitalization costs	5086	190(1695)	.	.	.		12679	244(2336)	.	.	.
Bleeding outpat. visits	5086	0.050(0.303)	3.58%	0.88%	0.02%		12679	0.062(0.363)	4.05%	1.25%	0.05%
Bleeding outpat. costs	5086	2(11)	.	.	.		12679	2(13)	.	.	.
Stroke/se hospitalizations	5086	0.012(0.125)	1.00%	0.16%	0.00%		12679	0.011(0.118)	0.91%	0.13%	0.00%
Stroke/se BedDays	5086	0.126(1.770)	0.96%	0.96%	0.65%		12679	0.095(1.293)	0.88%	0.88%	0.62%
Stroke/se hospitalization costs	5086	127(1787)	.	.	.		12679	96(1305)	.	.	.
Stroke/se outpat. visits	5086	0.011(0.148)	0.90%	0.06%	0.02%		12679	0.008(0.106)	0.63%	0.09%	0.00%
Stroke/se outpat. costs	5086	0(5)	.	.	.		12679	0(4)	.	.	.

Table 15.77 Health care resource utilisation (HCRU) and associated costs related to bleeding and stroke/systemic embolism among patients with NVAF treated with dabigatran and warfarin, Sweden (propensity -score matched population)

Exploratory analysis - costs. Country se. Comparing drug dabigatran with warfarin
For patients included at least 1 and 2 years before end of study, (and for the latter not censored before start of that year).
Using price per hospital bed-day=1009.83 € and price per outpatient visit=36.87 €.

cost_EP_year=1

cost_ep_type_text	dabigatran: #patients available for year	dabigatran: mean (sd)	dabigatran: proportion of patients with any	dabigatran: proportion of patients with >1	dabigatran: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (sd)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalizations	7926	0.031(0.233)	2.31%	0.57%	0.01%		7890	0.036(0.256)	2.66%	0.61%	0.03%
Bleeding BedDays	7926	0.254(2.657)	2.31%	2.23%	1.31%		7890	0.240(2.146)	2.64%	2.55%	1.29%
Bleeding hospitalization costs	7926	257(2684)	.	.	.		7890	243(2167)	.	.	.
Bleeding outpat. visits	7926	0.062(0.387)	3.86%	1.30%	0.08%		7890	0.069(0.411)	4.35%	1.36%	0.08%
Bleeding outpat. costs	7926	2(14)	.	.	.		7890	3(15)	.	.	.
Stroke/se hospitalizations	7926	0.019(0.160)	1.59%	0.26%	0.00%		7890	0.020(0.178)	1.58%	0.27%	0.00%
Stroke/se BedDays	7926	0.169(1.973)	1.64%	1.64%	1.01%		7890	0.198(2.174)	1.56%	1.55%	1.03%
Stroke/se hospitalization costs	7926	170(1993)	.	.	.		7890	200(2196)	.	.	.
Stroke/se outpat. visits	7926	0.054(0.536)	2.75%	0.86%	0.16%		7890	0.054(0.947)	2.17%	0.66%	0.14%
Stroke/se outpat. costs	7926	2(20)	.	.	.		7890	2(35)	.	.	.

cost_EP_year=2

cost_ep_type_text	dabigatran: #patients available for year	dabigatran: mean (sd)	dabigatran: proportion of patients with any	dabigatran: proportion of patients with >1	dabigatran: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (sd)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalizations	3750	0.021(0.200)	1.55%	0.35%	0.03%		3443	0.025(0.187)	2.03%	0.32%	0.00%
Bleeding BedDays	3750	0.149(1.994)	1.52%	1.44%	0.88%		3443	0.138(1.280)	2.00%	1.92%	0.78%
Bleeding hospitalization costs	3750	150(2013)	.	.	.		3443	139(1292)	.	.	.
Bleeding outpat. visits	3750	0.047(0.292)	3.41%	0.80%	0.03%		3443	0.067(0.420)	4.04%	1.28%	0.12%
Bleeding outpat. costs	3750	2(11)	.	.	.		3443	2(15)	.	.	.
Stroke/se hospitalizations	3750	0.008(0.098)	0.72%	0.08%	0.00%		3443	0.007(0.101)	0.61%	0.09%	0.00%
Stroke/se BedDays	3750	0.074(1.115)	0.72%	0.72%	0.45%		3443	0.064(1.096)	0.61%	0.61%	0.38%
Stroke/se hospitalization costs	3750	75(1126)	.	.	.		3443	64(1106)	.	.	.
Stroke/se outpat. visits	3750	0.007(0.094)	0.56%	0.11%	0.00%		3443	0.018(0.365)	0.73%	0.26%	0.06%
Stroke/se outpat. costs	3750	0(3)	.	.	.		3443	1(13)	.	.	.

Table 15.78 Health care resource utilisation (HCRU) and associated costs related to bleeding and stroke/systemic embolism among patients with NVAF treated with rivaroxaban and warfarin, Sweden (propensity -score matched population)

Exploratory analysis - costs. Country se. Comparing drug rivaroxaban with warfarin
For patients included at least 1 and 2 years before end of study, (and for the latter not censored before start of that year).
Using price per hospital bed-day=1009.83 € and price per outpatient visit=36.87 €.

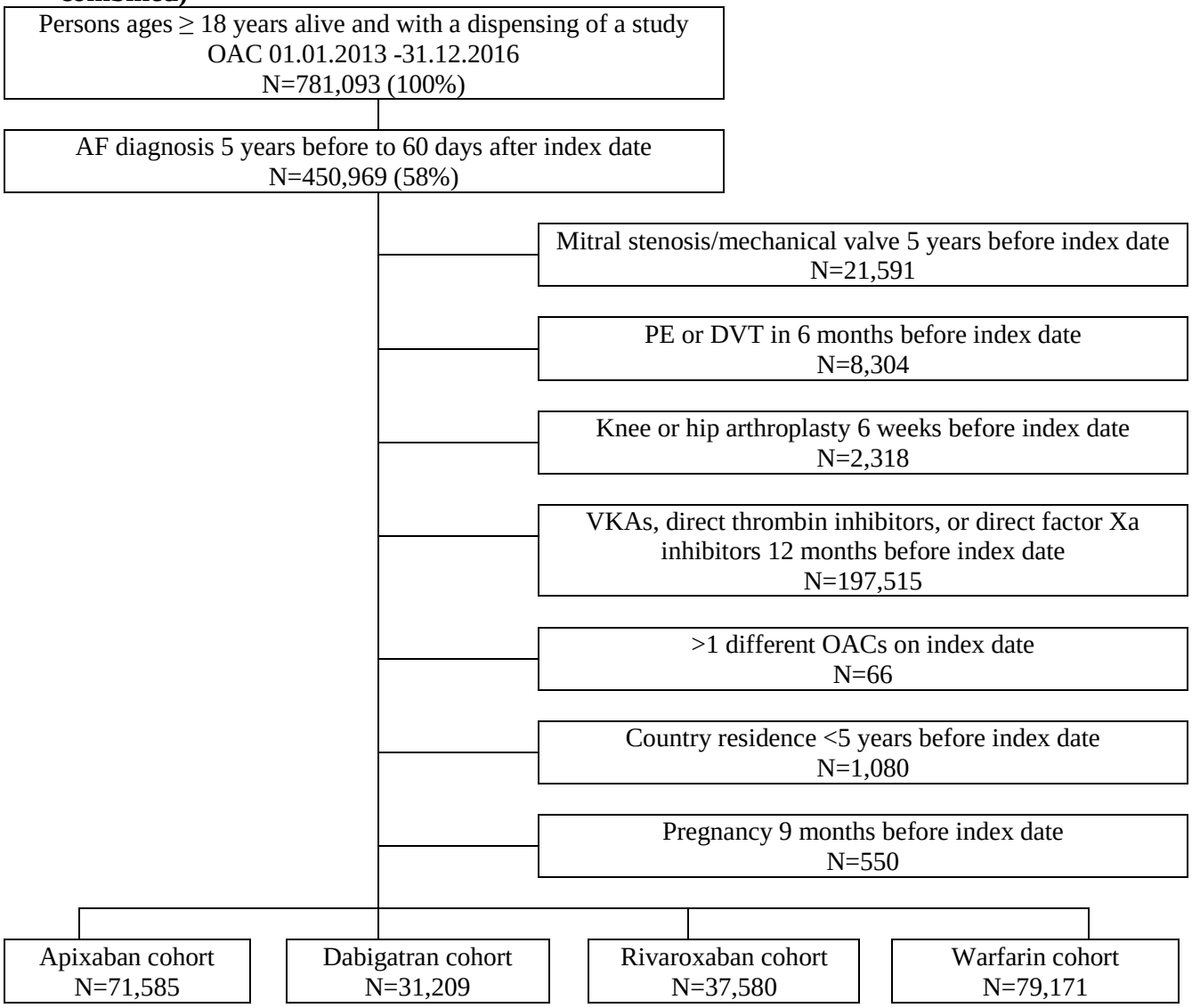
cost_EP_year=1

cost_ep_type_text	rivaroxaban: #patients available for year	rivaroxaban: mean (sd)	rivaroxaban: proportion of patients with any	rivaroxaban: proportion of patients with >1	rivaroxaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (sd)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalizations	10177	0.048(0.265)	3.85%	0.72%	0.00%		10137	0.043(0.286)	3.22%	0.65%	0.02%
Bleeding BedDays	10177	0.308(2.260)	3.83%	3.67%	1.78%		10137	0.284(2.279)	3.24%	3.18%	1.63%
Bleeding hospitalization costs	10177	311(2282)	.	.	.		10137	287(2301)	.	.	.
Bleeding outpat. visits	10177	0.108(0.490)	7.04%	2.10%	0.13%		10137	0.075(0.407)	4.89%	1.40%	0.08%
Bleeding outpat. costs	10177	4(18)	.	.	.		10137	3(15)	.	.	.
Stroke/se hospitalizations	10177	0.023(0.180)	1.84%	0.34%	0.00%		10137	0.021(0.168)	1.81%	0.26%	0.00%
Stroke/se BedDays	10177	0.218(2.307)	1.85%	1.81%	1.18%		10137	0.207(2.208)	1.82%	1.81%	1.09%
Stroke/se hospitalization costs	10177	220(2330)	.	.	.		10137	209(2230)	.	.	.
Stroke/se outpat. visits	10177	0.037(0.569)	2.02%	0.44%	0.07%		10137	0.040(0.513)	2.39%	0.47%	0.07%
Stroke/se outpat. costs	10177	1(21)	.	.	.		10137	1(19)	.	.	.

cost_EP_year=2

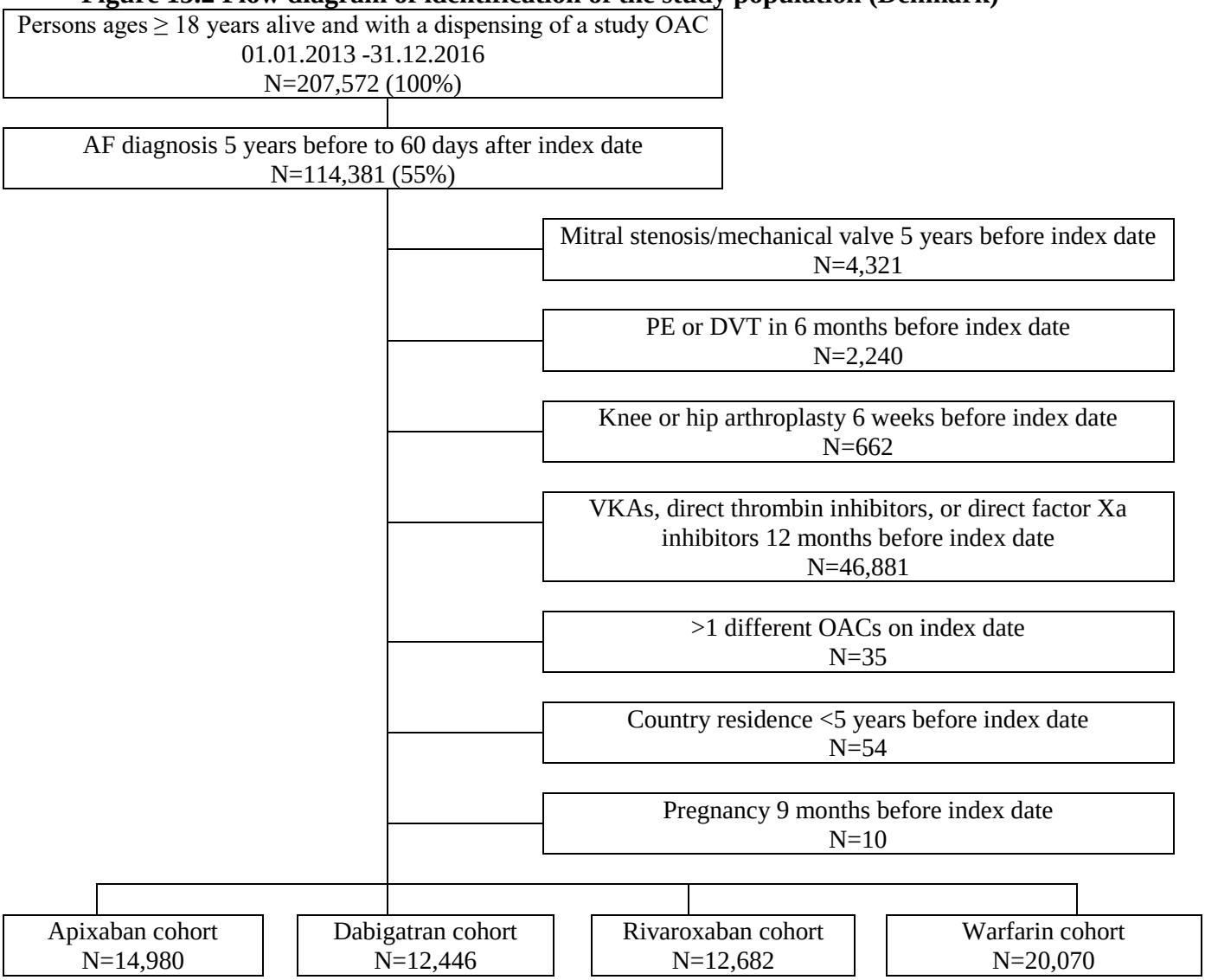
cost_ep_type_text	rivaroxaban: #patients available for year	rivaroxaban: mean (sd)	rivaroxaban: proportion of patients with any	rivaroxaban: proportion of patients with >1	rivaroxaban: proportion of patients with >5	-	warfarin: #patients available for year	warfarin: mean (sd)	warfarin: proportion of patients with any	warfarin: proportion of patients with >1	warfarin: proportion of patients with >5
Bleeding hospitalizations	3955	0.034(0.229)	2.73%	0.53%	0.00%		3014	0.032(0.233)	2.36%	0.53%	0.00%
Bleeding BedDays	3955	0.221(1.854)	2.68%	2.58%	1.39%		3014	0.189(1.922)	2.42%	2.32%	1.00%
Bleeding hospitalization costs	3955	223(1872)	.	.	.		3014	191(1941)	.	.	.
Bleeding outpat. visits	3955	0.089(0.436)	5.94%	1.77%	0.08%		3014	0.069(0.389)	4.35%	1.46%	0.03%
Bleeding outpat. costs	3955	3(16)	.	.	.		3014	3(14)	.	.	.
Stroke/se hospitalizations	3955	0.018(0.172)	1.39%	0.30%	0.00%		3014	0.008(0.103)	0.66%	0.13%	0.00%
Stroke/se BedDays	3955	0.145(1.650)	1.37%	1.29%	0.94%		3014	0.079(1.146)	0.70%	0.70%	0.56%
Stroke/se hospitalization costs	3955	146(1666)	.	.	.		3014	79(1157)	.	.	.
Stroke/se outpat. visits	3955	0.010(0.117)	0.88%	0.13%	0.00%		3014	0.007(0.085)	0.63%	0.03%	0.00%
Stroke/se outpat. costs	3955	0(4)	.	.	.		3014	0(3)	.	.	.

Figure 15.1 Flow diagram of identification of the study population (all countries combined)



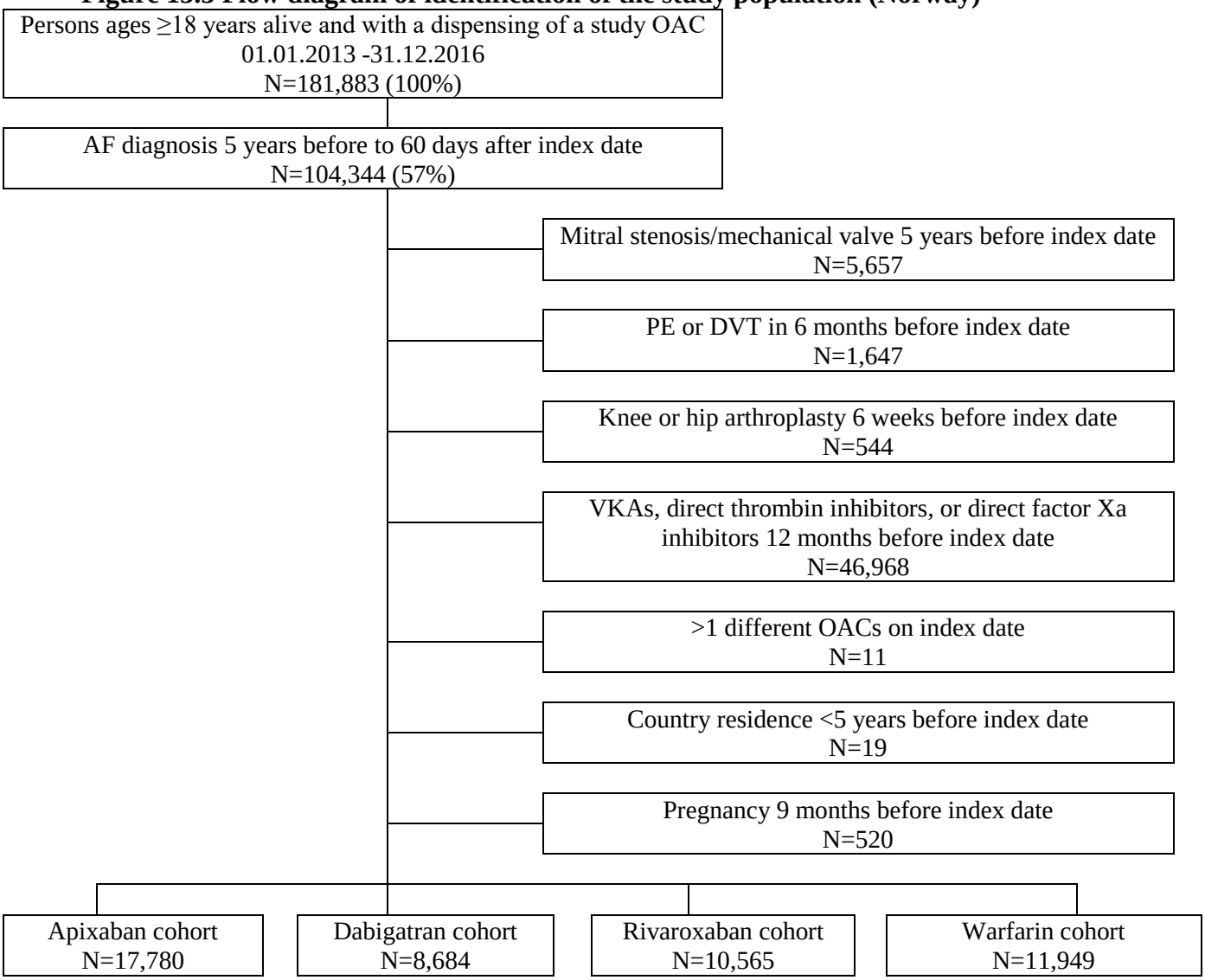
Abbreviations: AF atrial fibrillation, DVT deep vein thrombosis, OAC oral anticoagulant, PE pulmonary embolism, VKA vitamin K antagonist

Figure 15.2 Flow diagram of identification of the study population (Denmark)



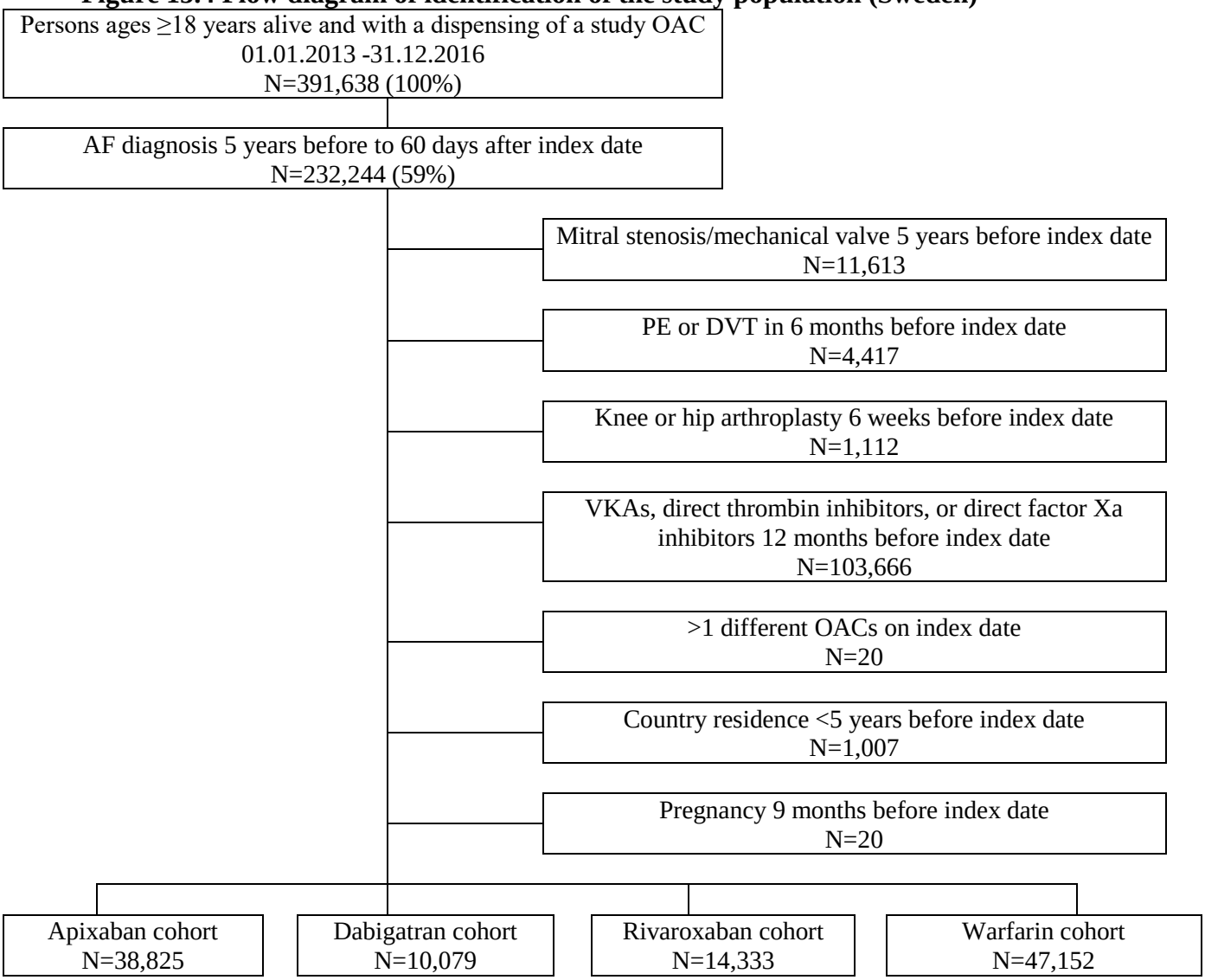
Abbreviations: AF atrial fibrillation, DVT deep vein thrombosis, OAC oral anticoagulant, PE pulmonary embolism, VKA vitamin K antagonist

Figure 15.3 Flow diagram of identification of the study population (Norway)



Abbreviations: AF atrial fibrillation, DVT deep vein thrombosis, OAC oral anticoagulant, PE pulmonary embolism, VKA vitamin K antagonist

Figure 15.4 Flow diagram of identification of the study population (Sweden)



Abbreviations: AF atrial fibrillation, DVT deep vein thrombosis, OAC oral anticoagulant, PE pulmonary embolism, VKA vitamin K antagonist

Figure 15.5 Crude cumulative incidence of any stroke or systemic embolism at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

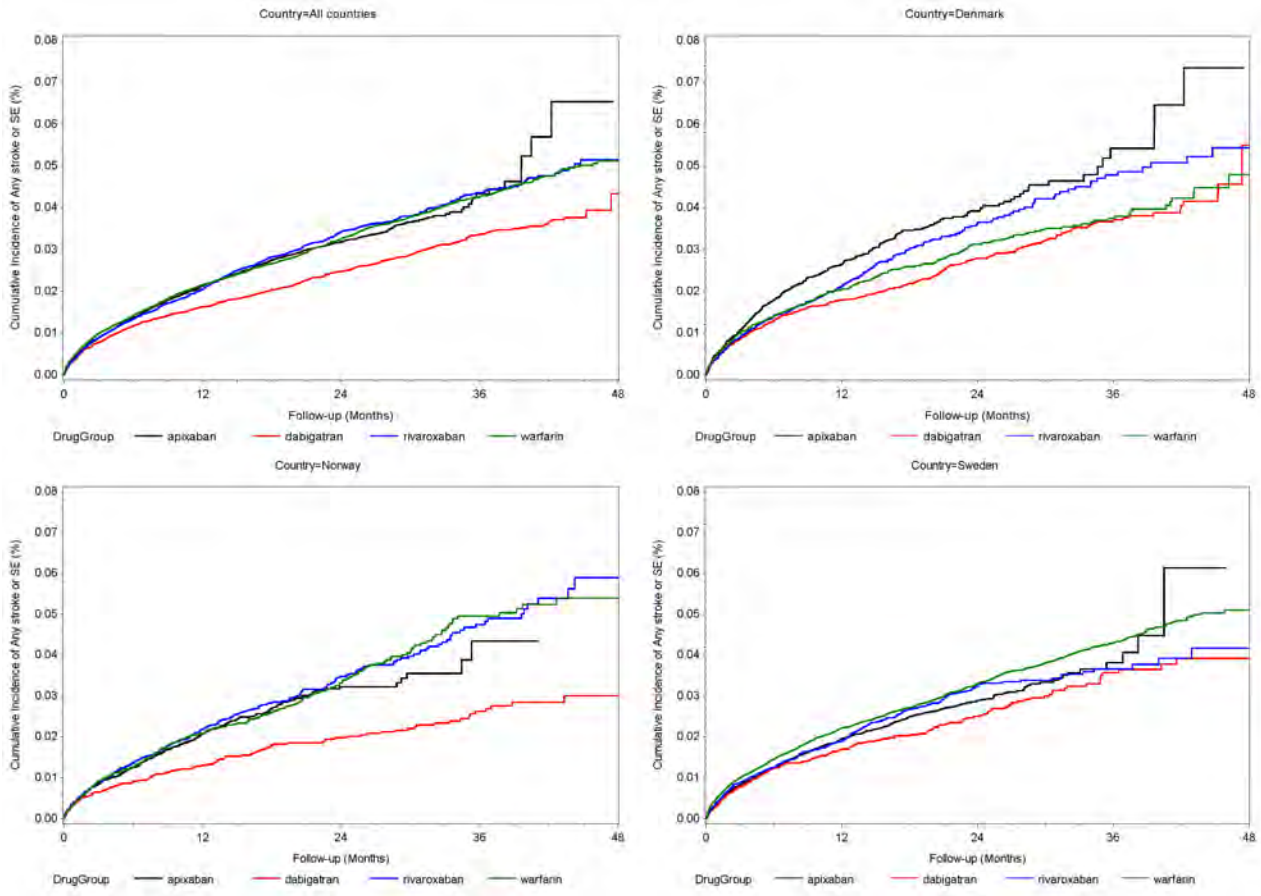


Figure 15.6 Crude cumulative incidence of any bleeding at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

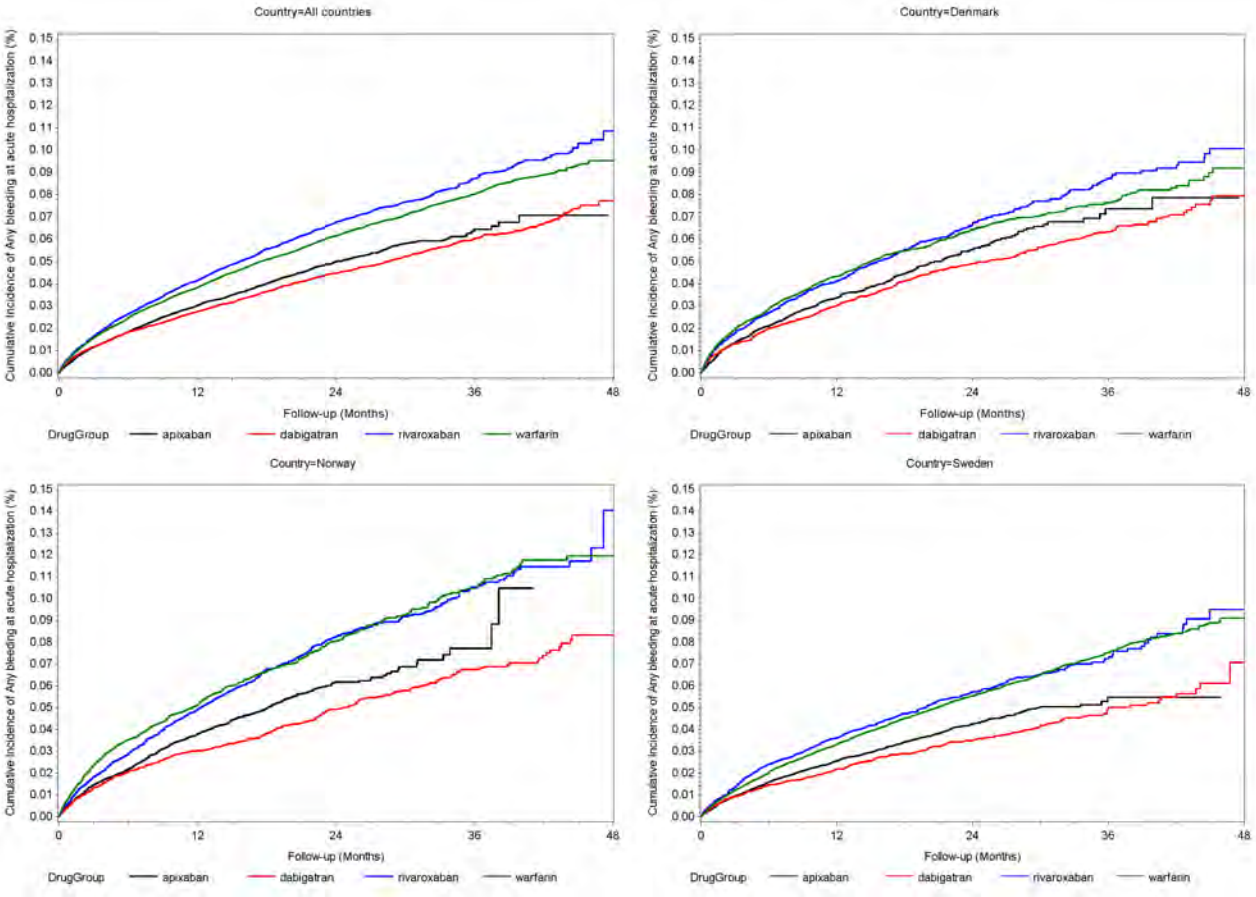


Figure 15.7 Crude cumulative incidence of ischaemic stroke at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

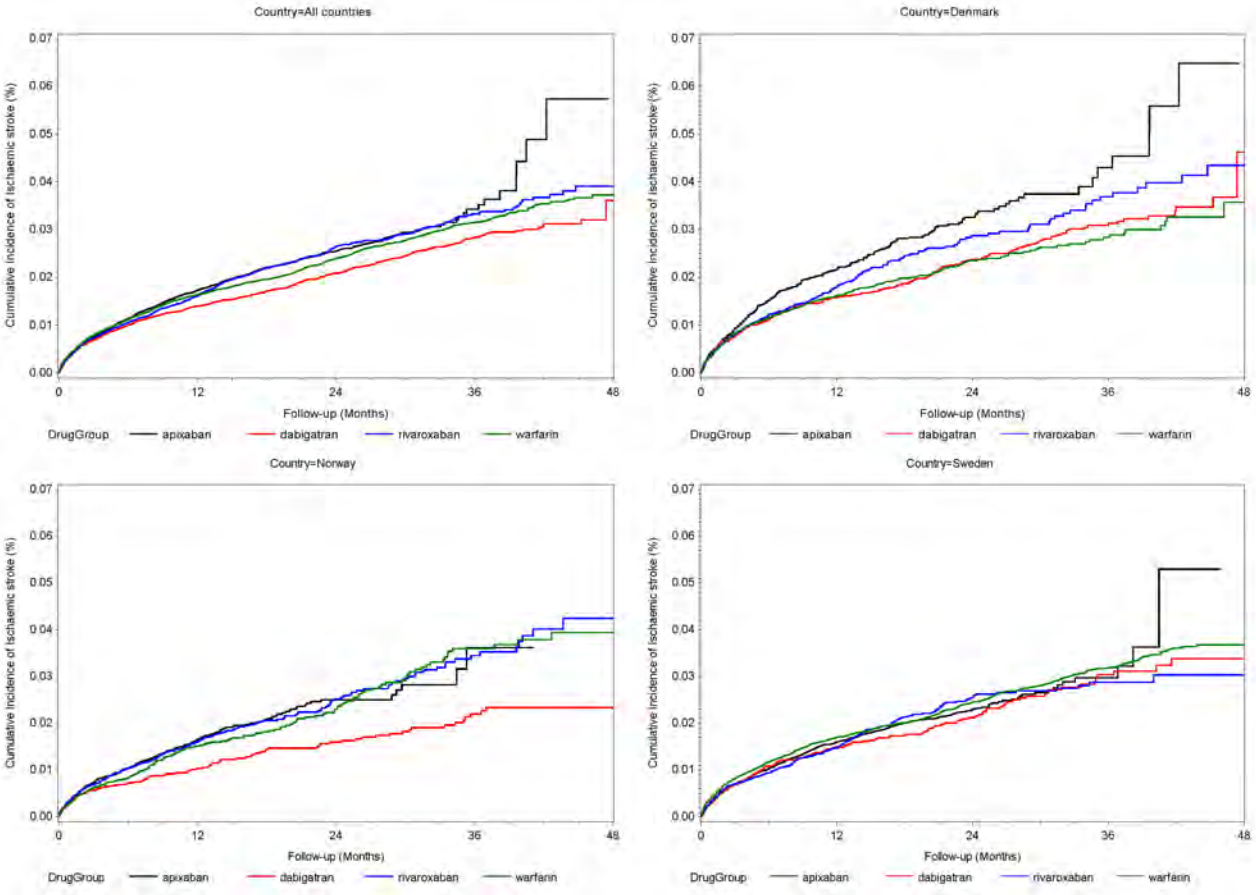


Figure 15.8 Crude cumulative incidence of haemorrhagic stroke at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

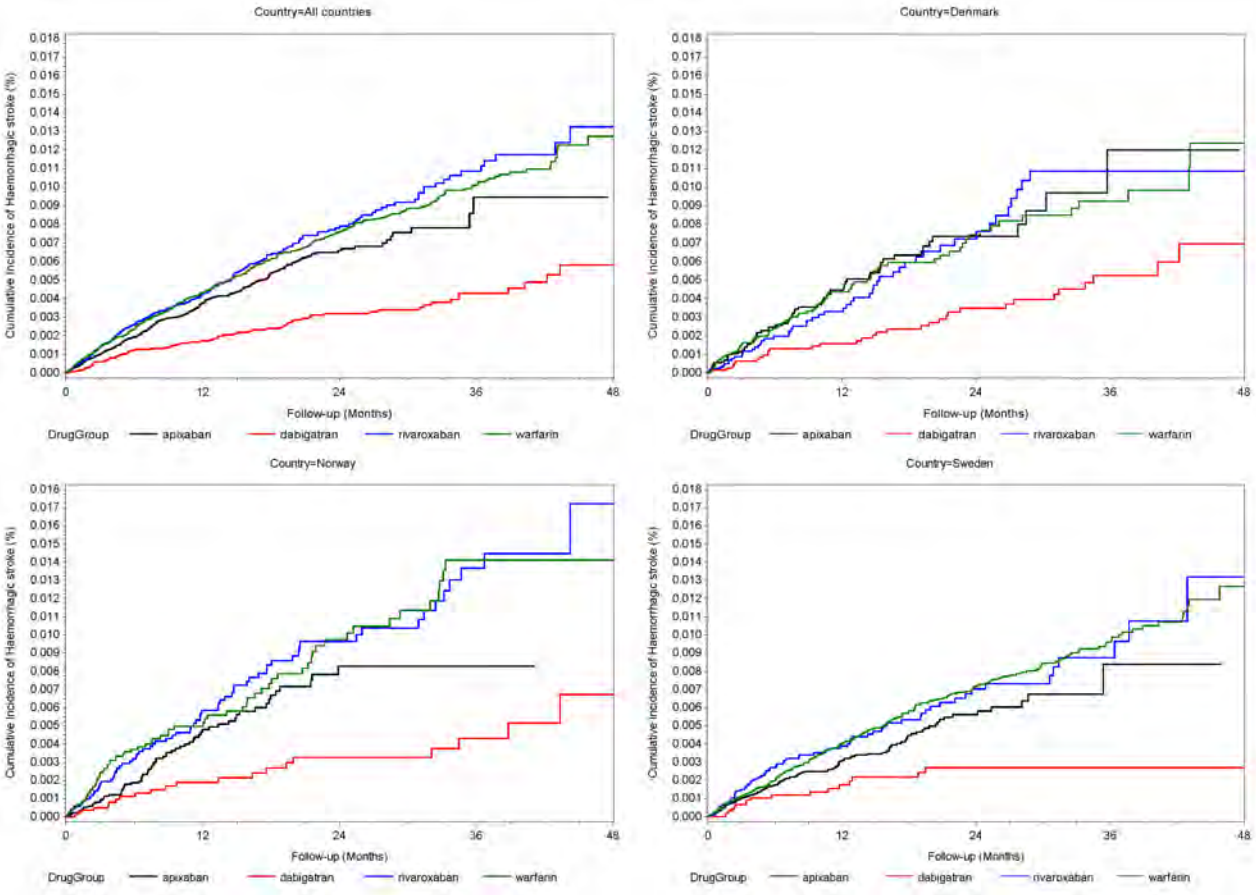


Figure 15.9 Crude cumulative incidence of intracranial bleeding at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

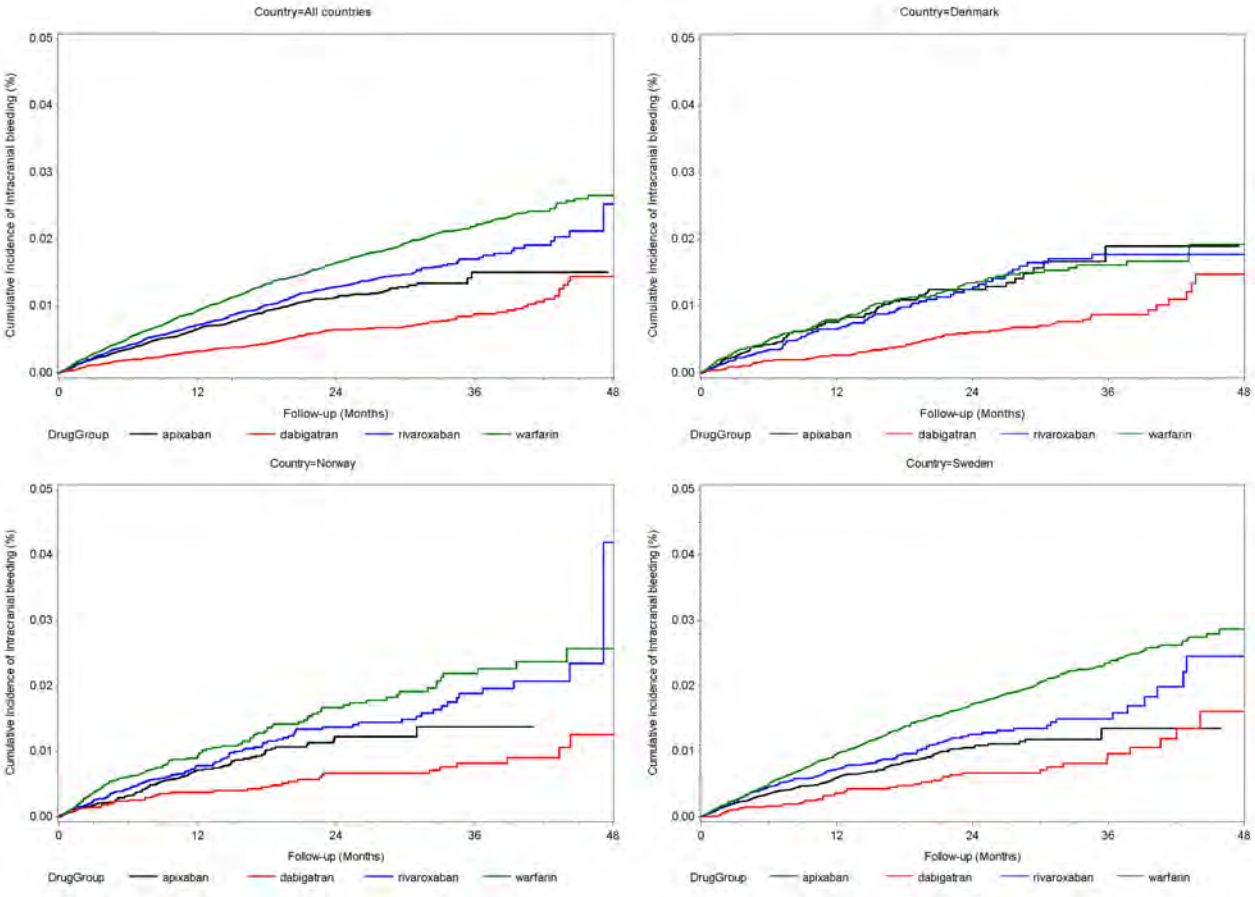


Figure 15.10 Crude cumulative incidence of gastrointestinal bleeding at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

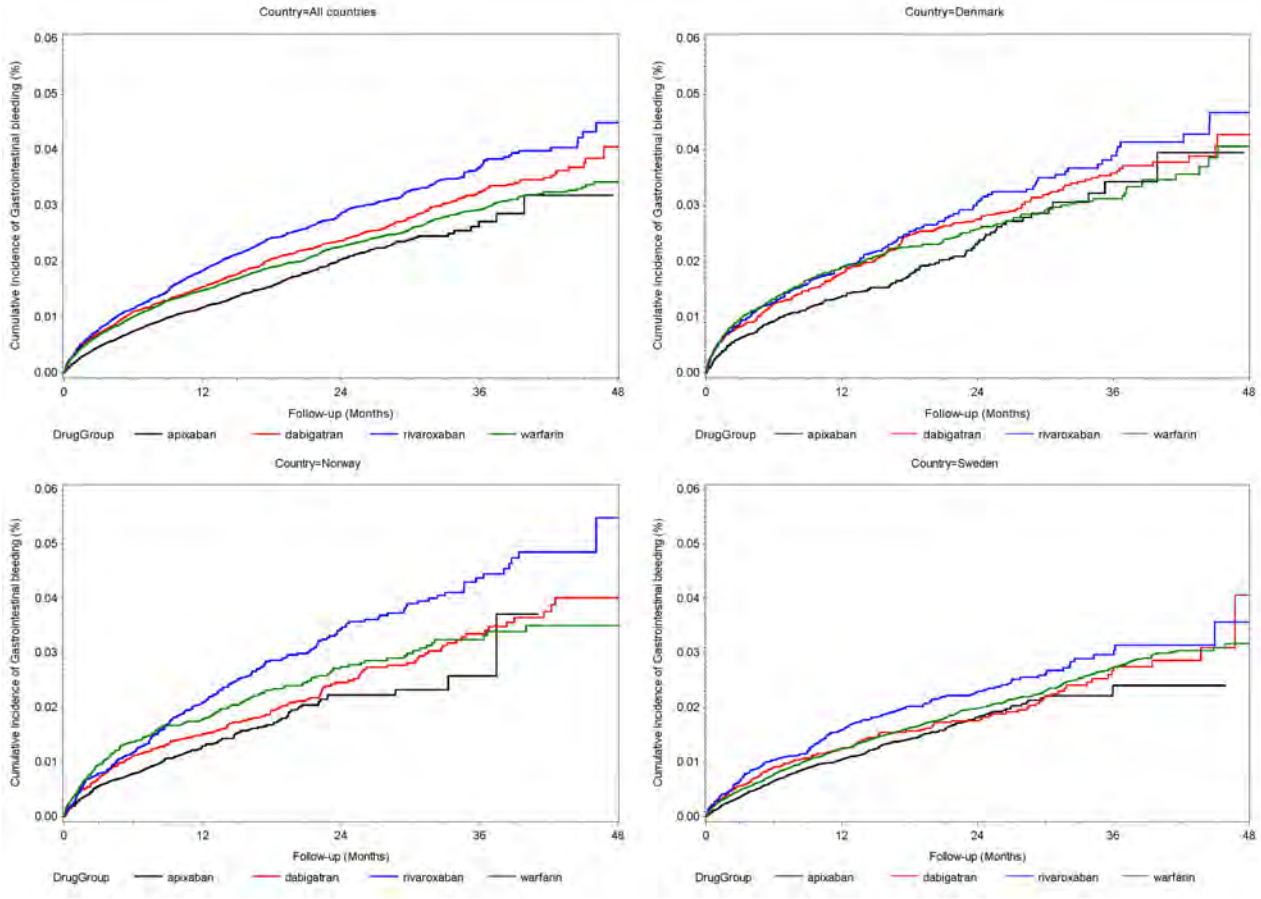


Figure 15.11 Crude cumulative incidence of acute myocardial infarction at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

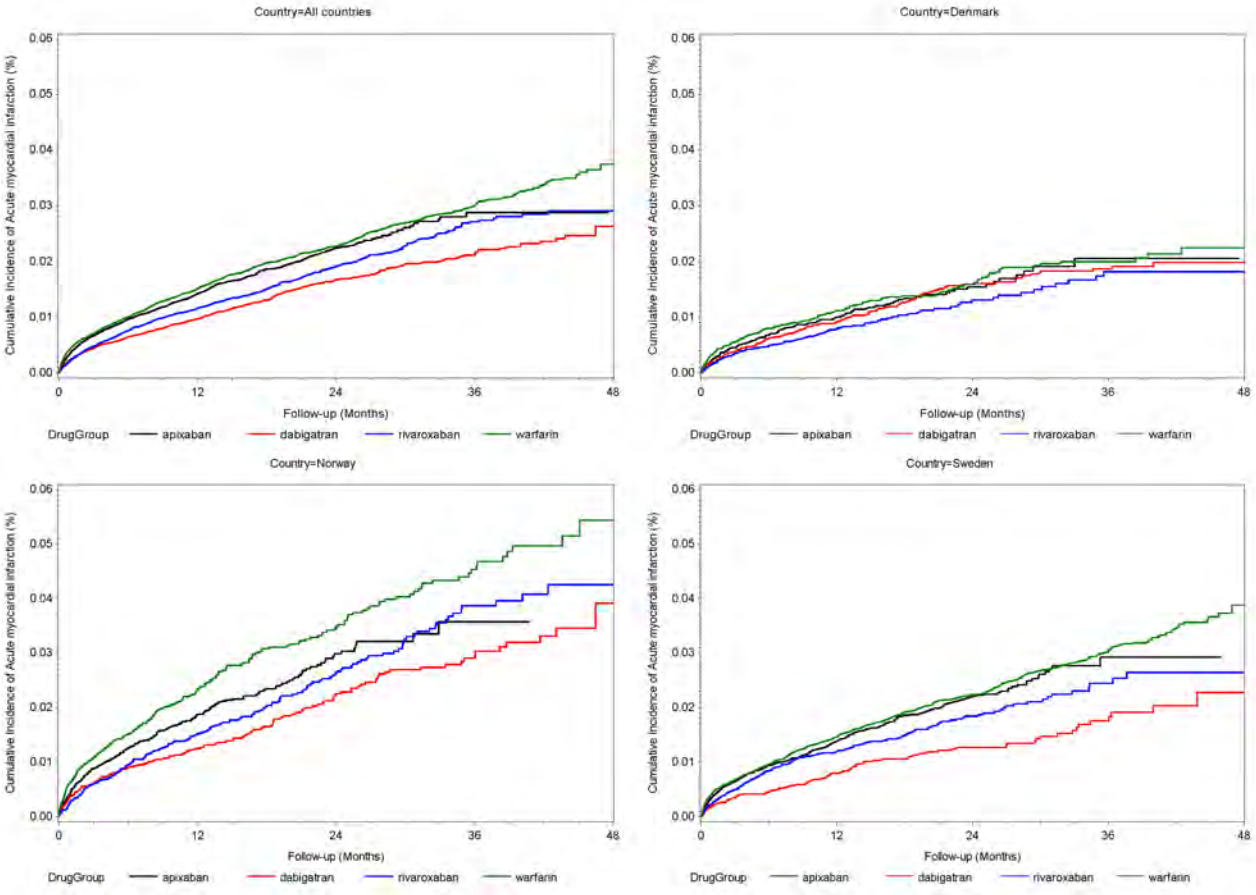
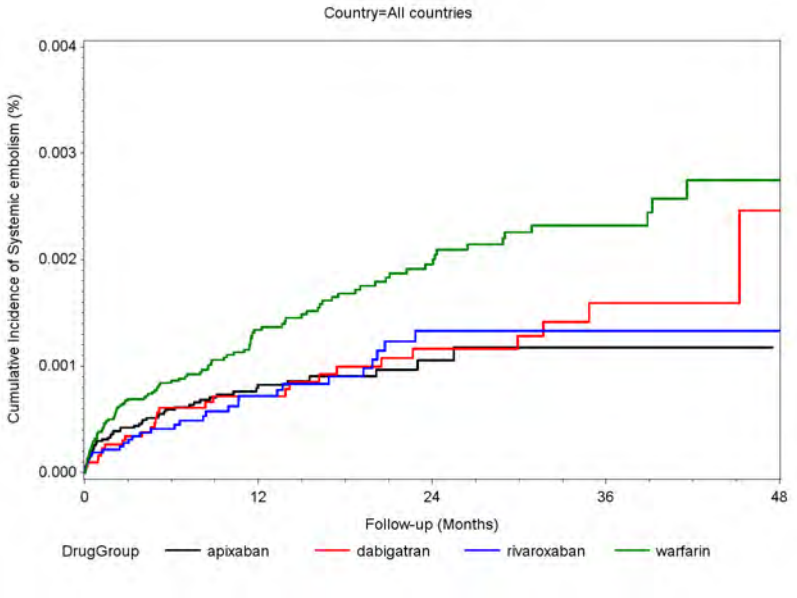


Figure 15.12 Crude cumulative incidence of systemic embolism at an acute hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country*



*Country-specific data too sparse to report

Figure 15.13 Cumulative mortality among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

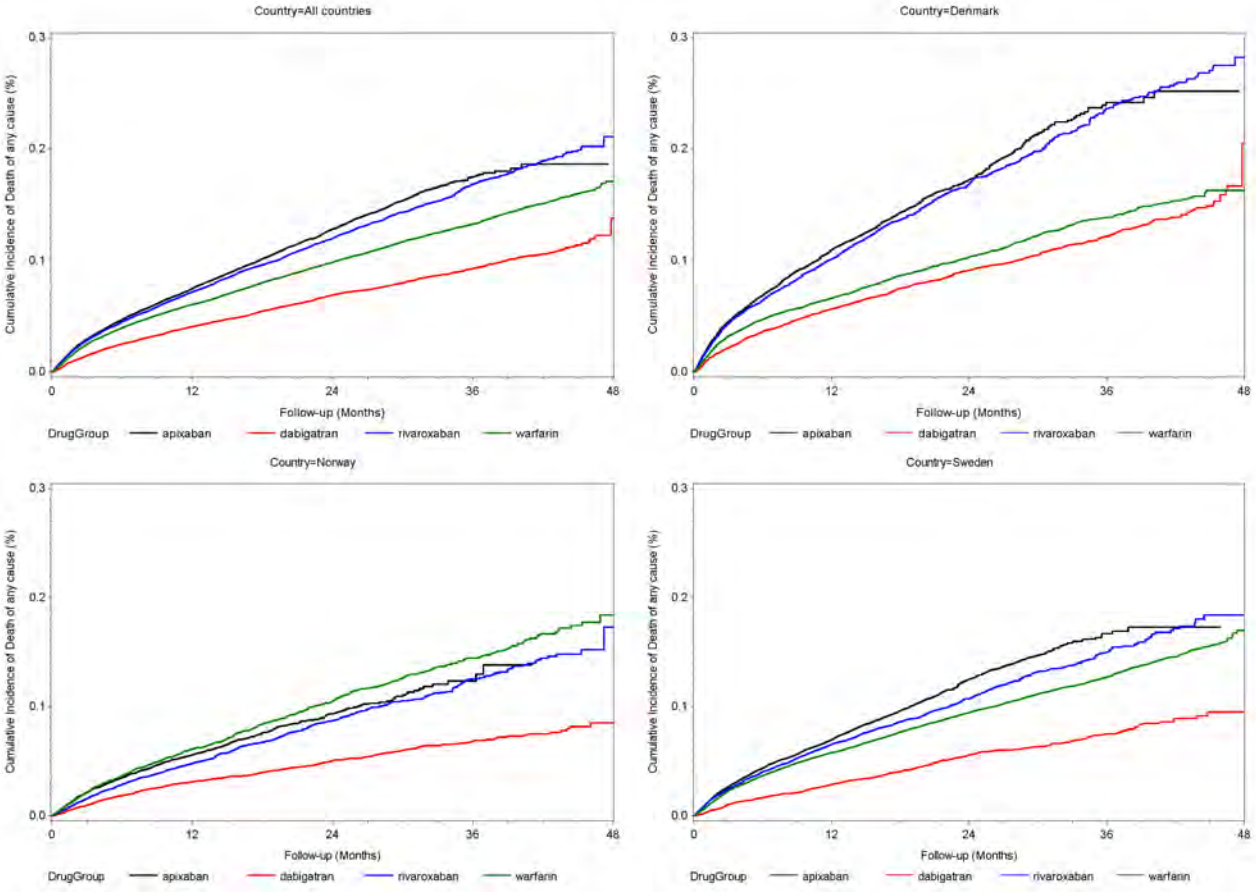


Figure 15.14 Crude cumulative incidence of ischaemic stroke at an acute hospitalisation with an overnight stay, systemic embolism at an acute hospitalisation with an overnight stay, acute myocardial infarction at an acute hospitalisation with an overnight stay, or death of any cause among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

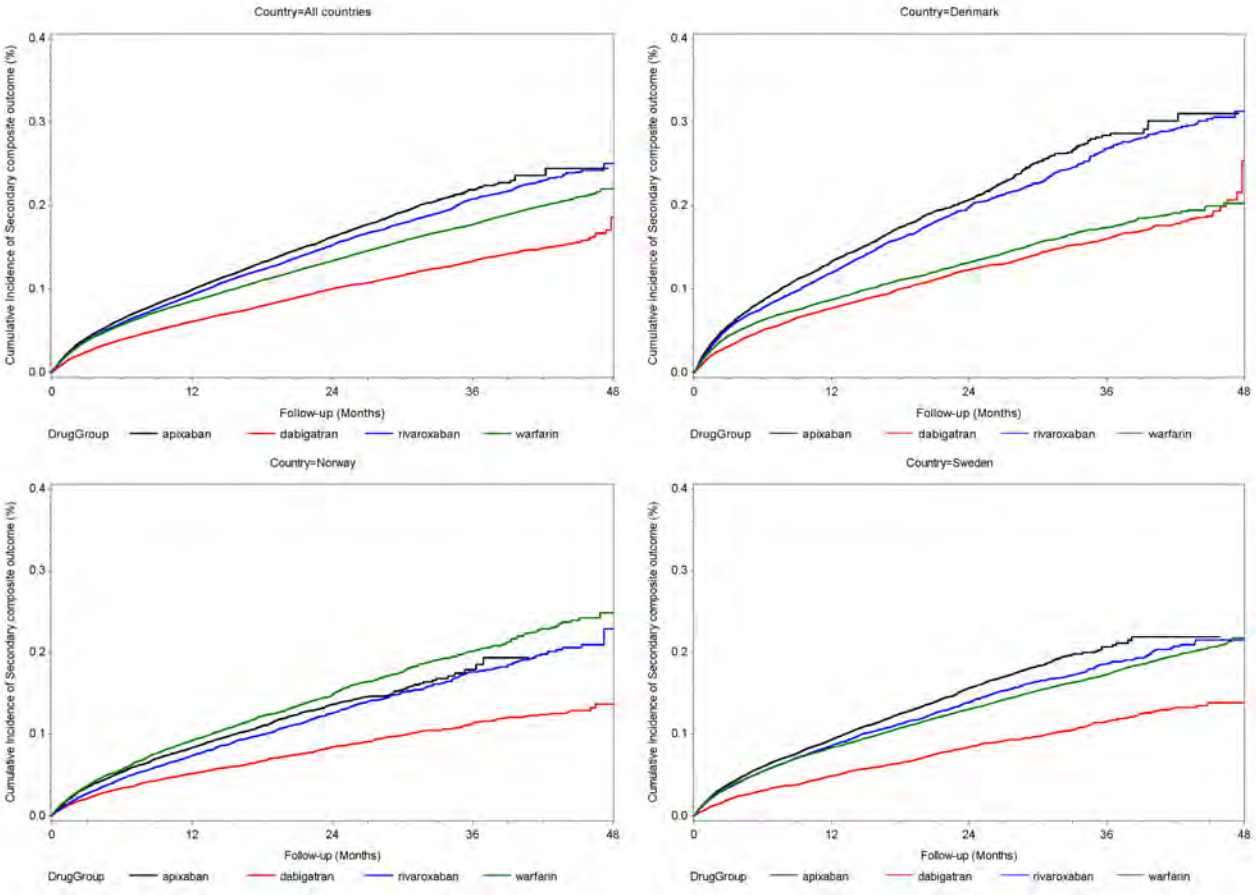


Figure 15.15 Crude cumulative incidence of any bleeding at an acute or planned hospitalisation with an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban, or warfarin, overall and by country

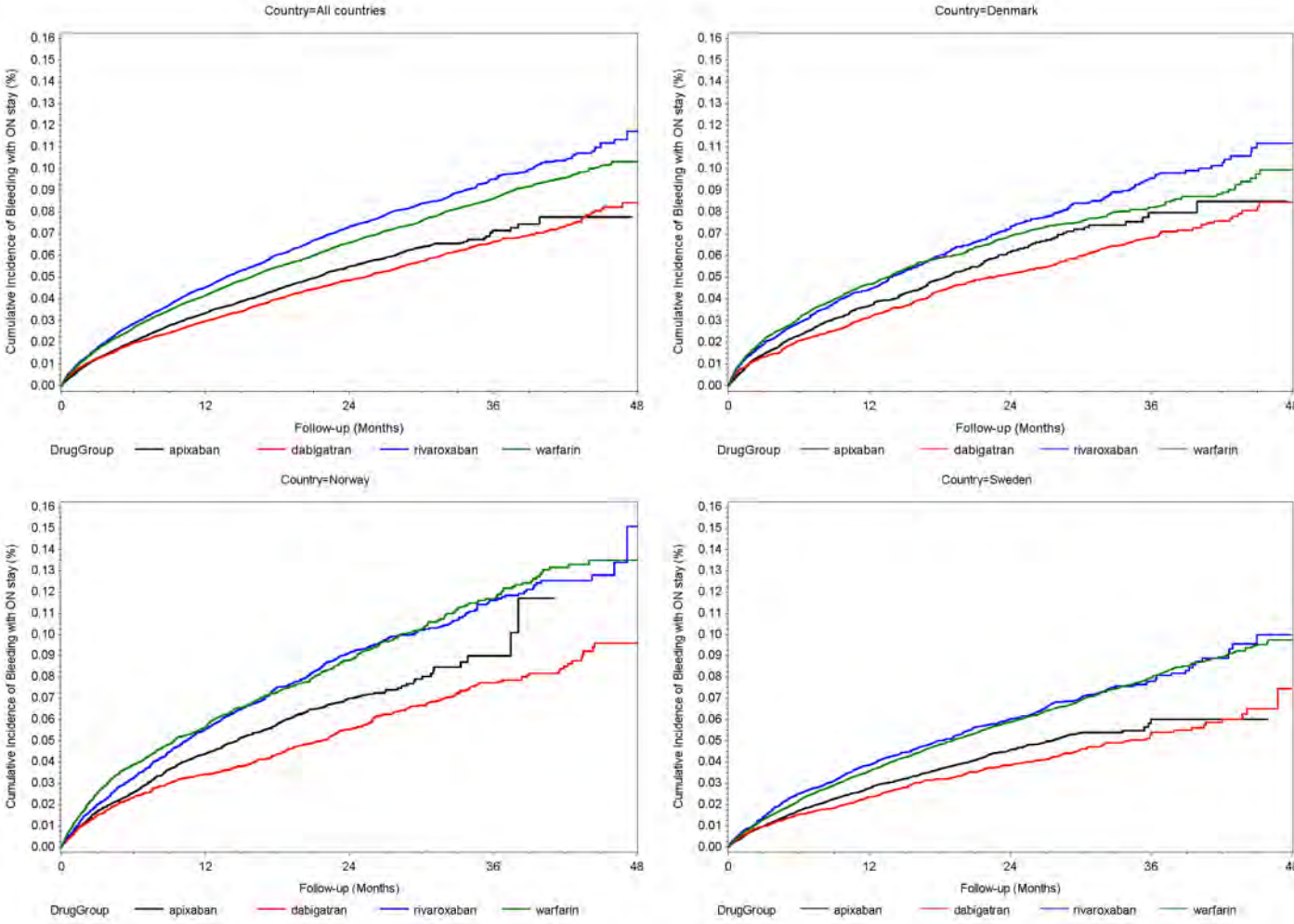


Figure 15.16 Crude cumulative incidence of any bleeding at an acute hospital contact without an overnight stay among patients with NVAF initiating apixaban, dabigatran, rivaroxaban vs. warfarin, overall and by country

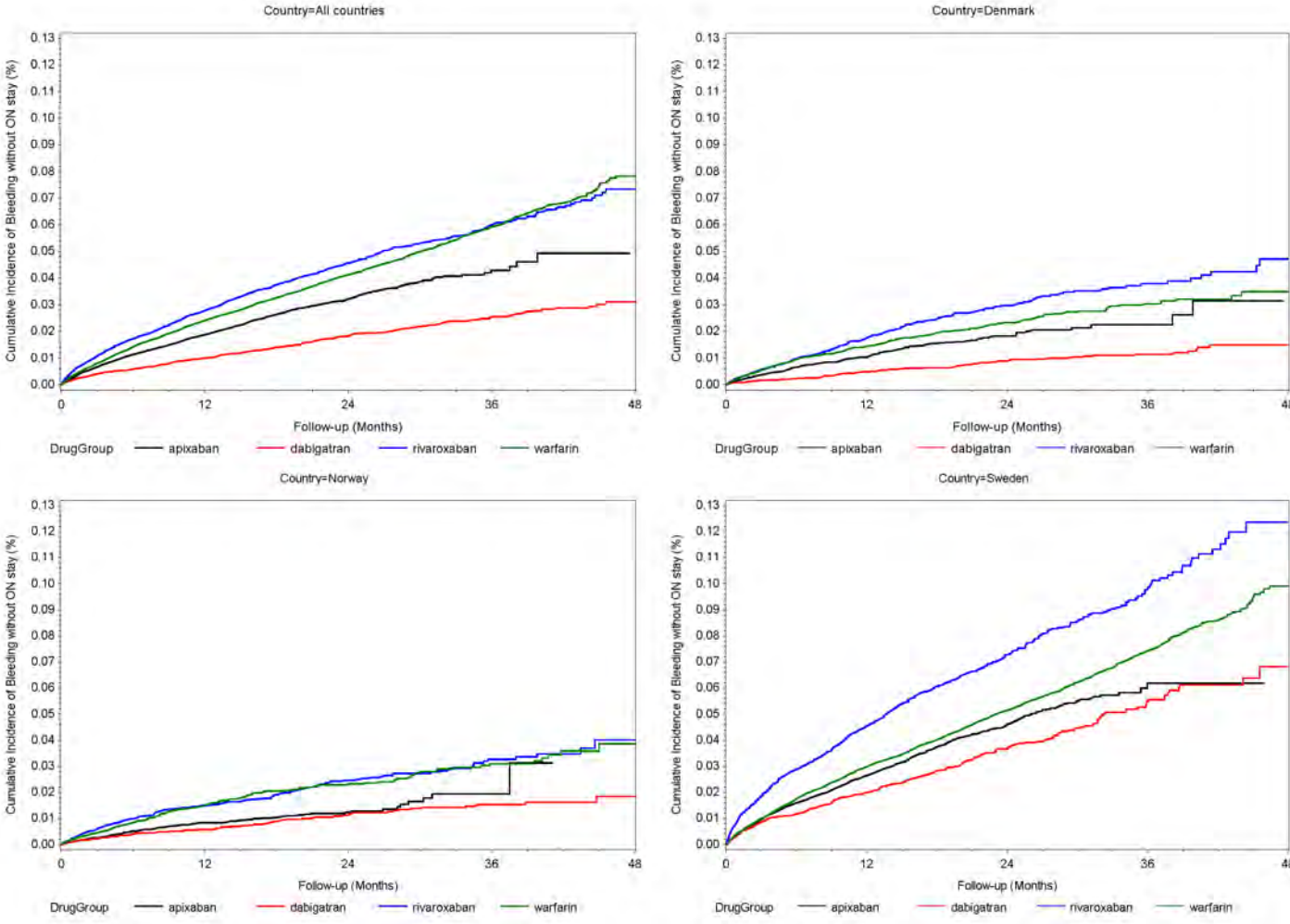


Figure 15.17 Crude cumulative incidence of <u>any bleeding</u> <u>recorded as the primary diagnosis at an acute hospitalisation with an overnight stay (sensitivity analysis)</u> among patients with NVAF initiating apixaban, dabigatran, rivaroxaban

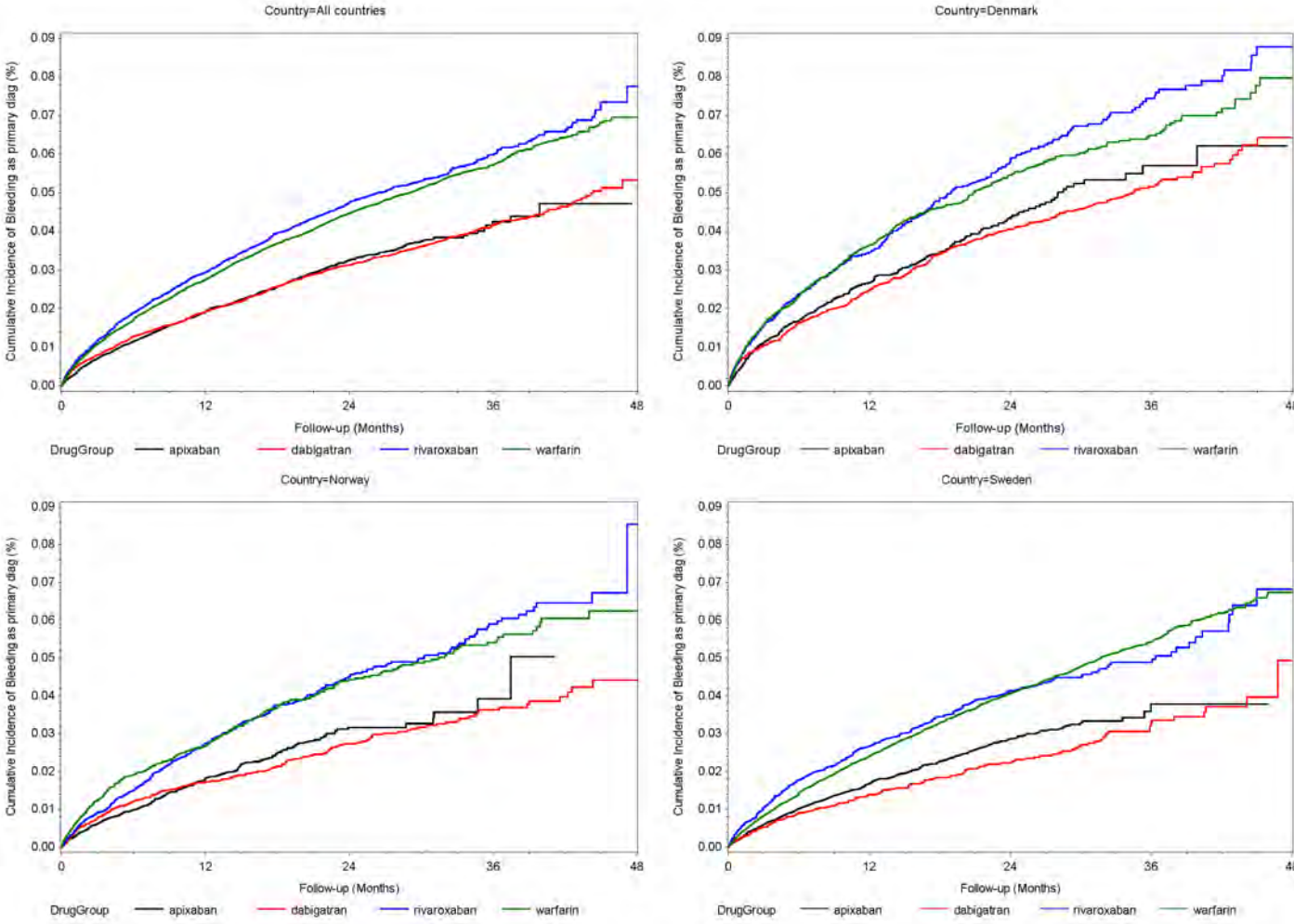
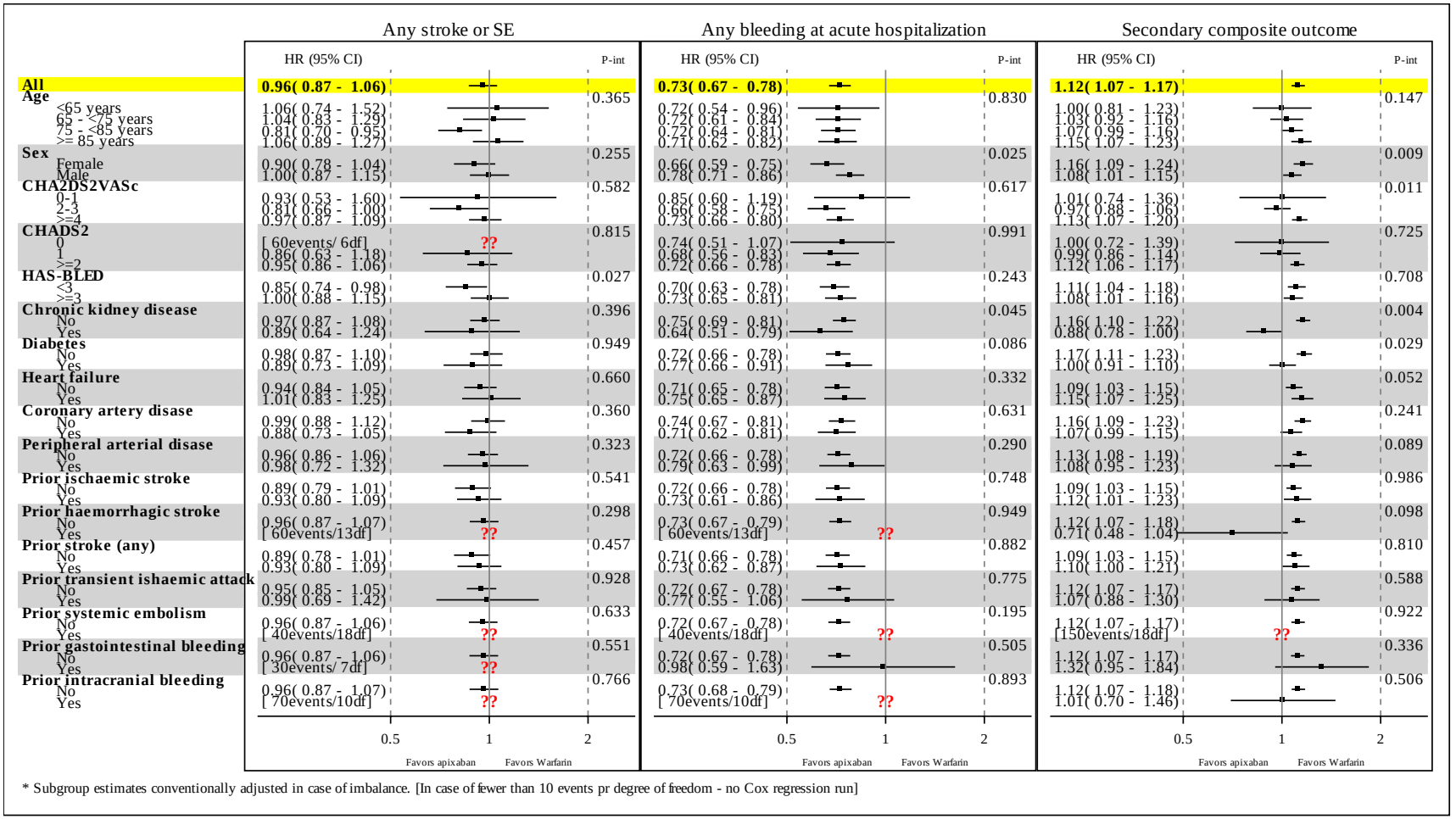


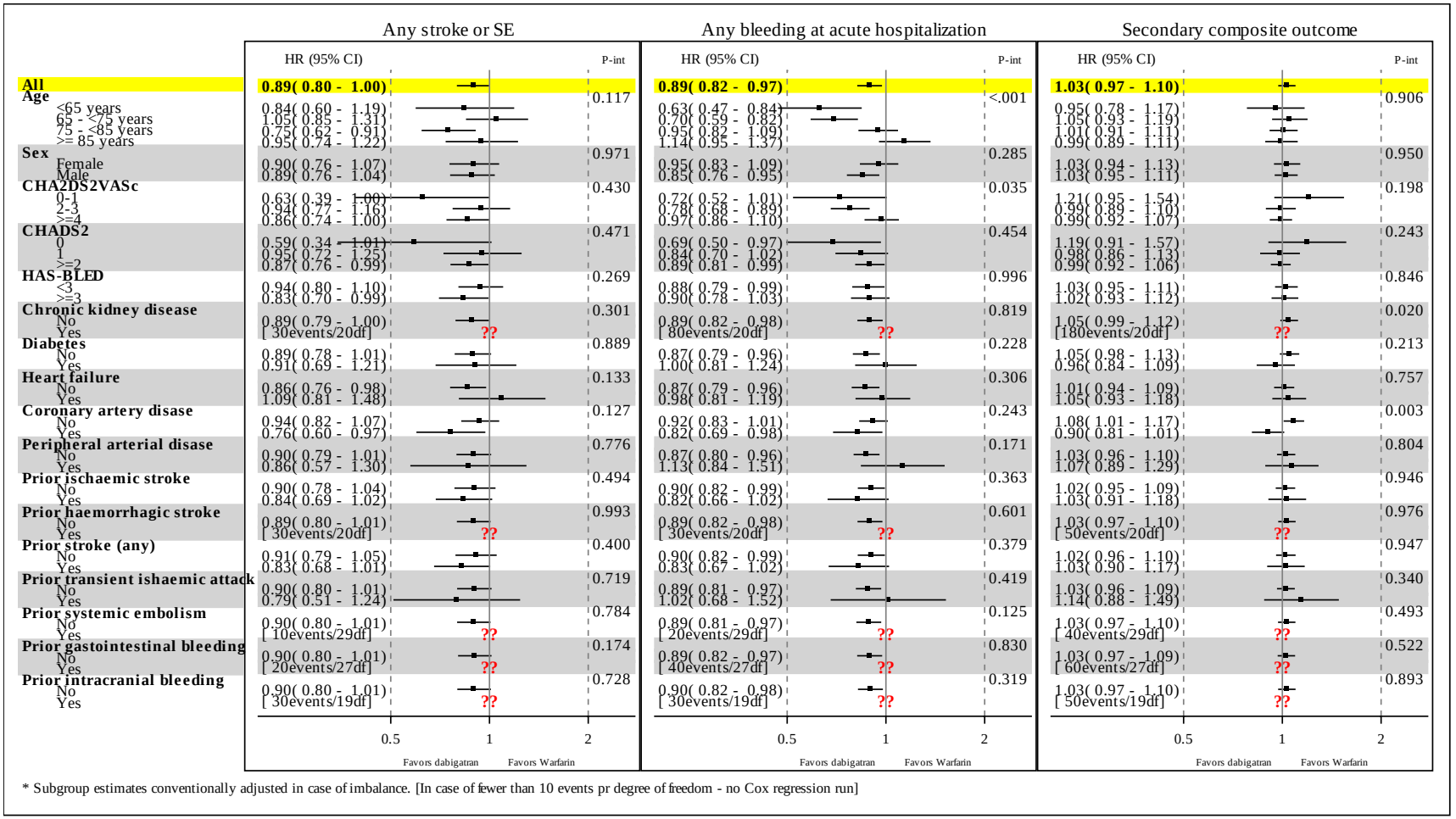
Figure 15.18 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of apixaban vs. warfarin overall and in the subgroups – all countries combined



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

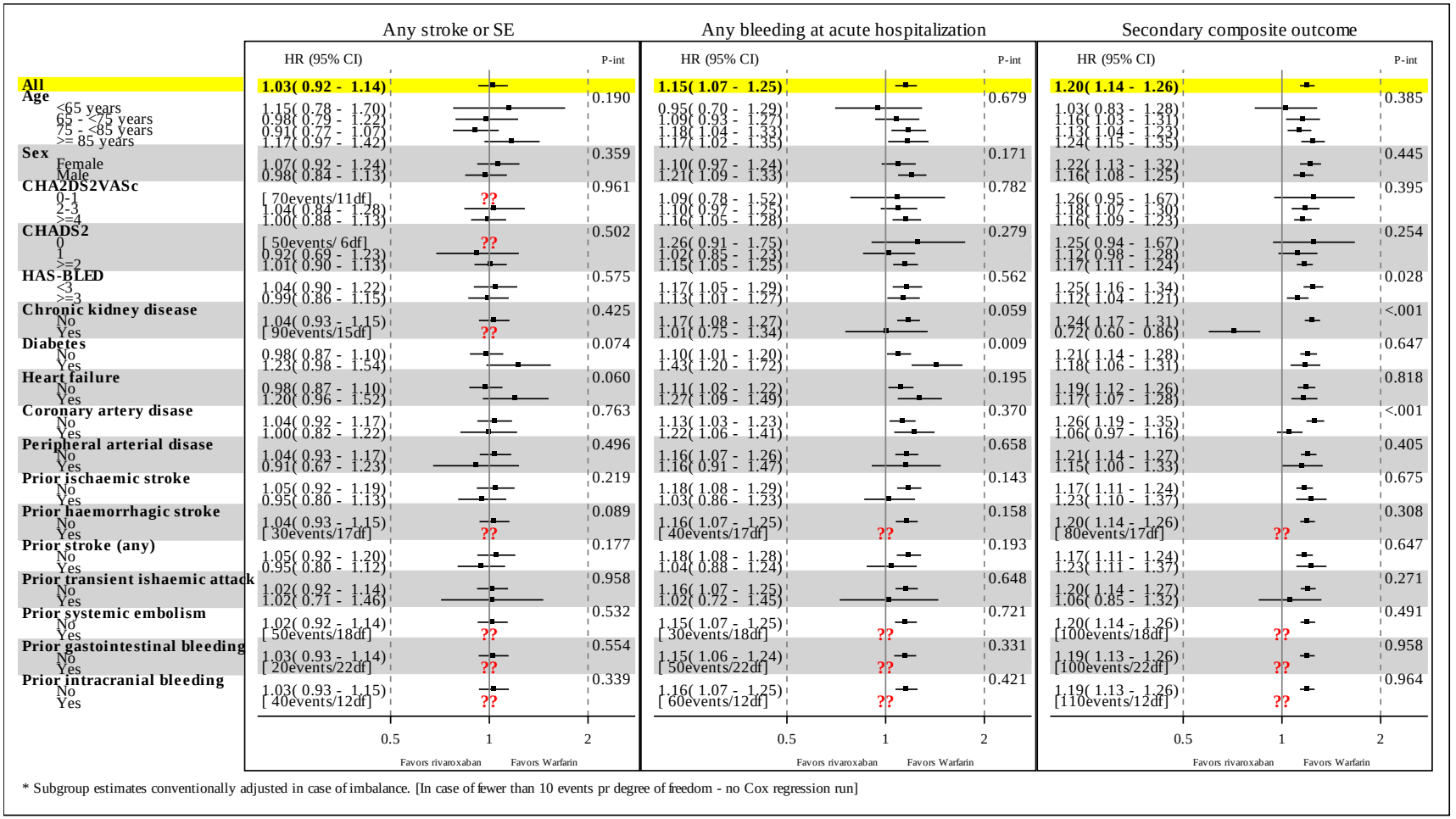
Figure 15.19 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of dabigatran vs. warfarin overall and in the subgroups – all countries combined



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

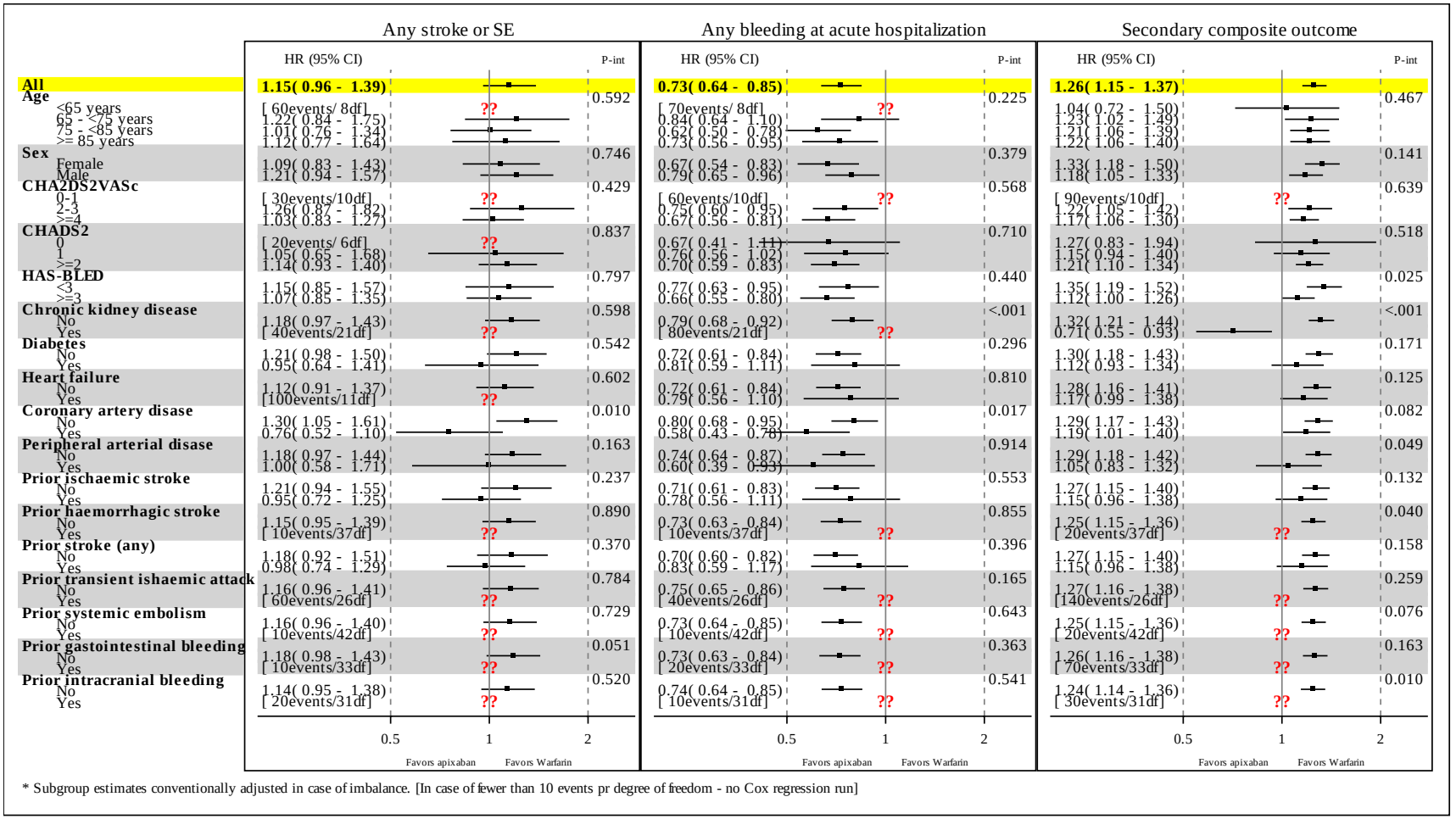
Figure 15.20 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of rivaroxaban vs. warfarin overall and in the subgroups – all countries combined



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

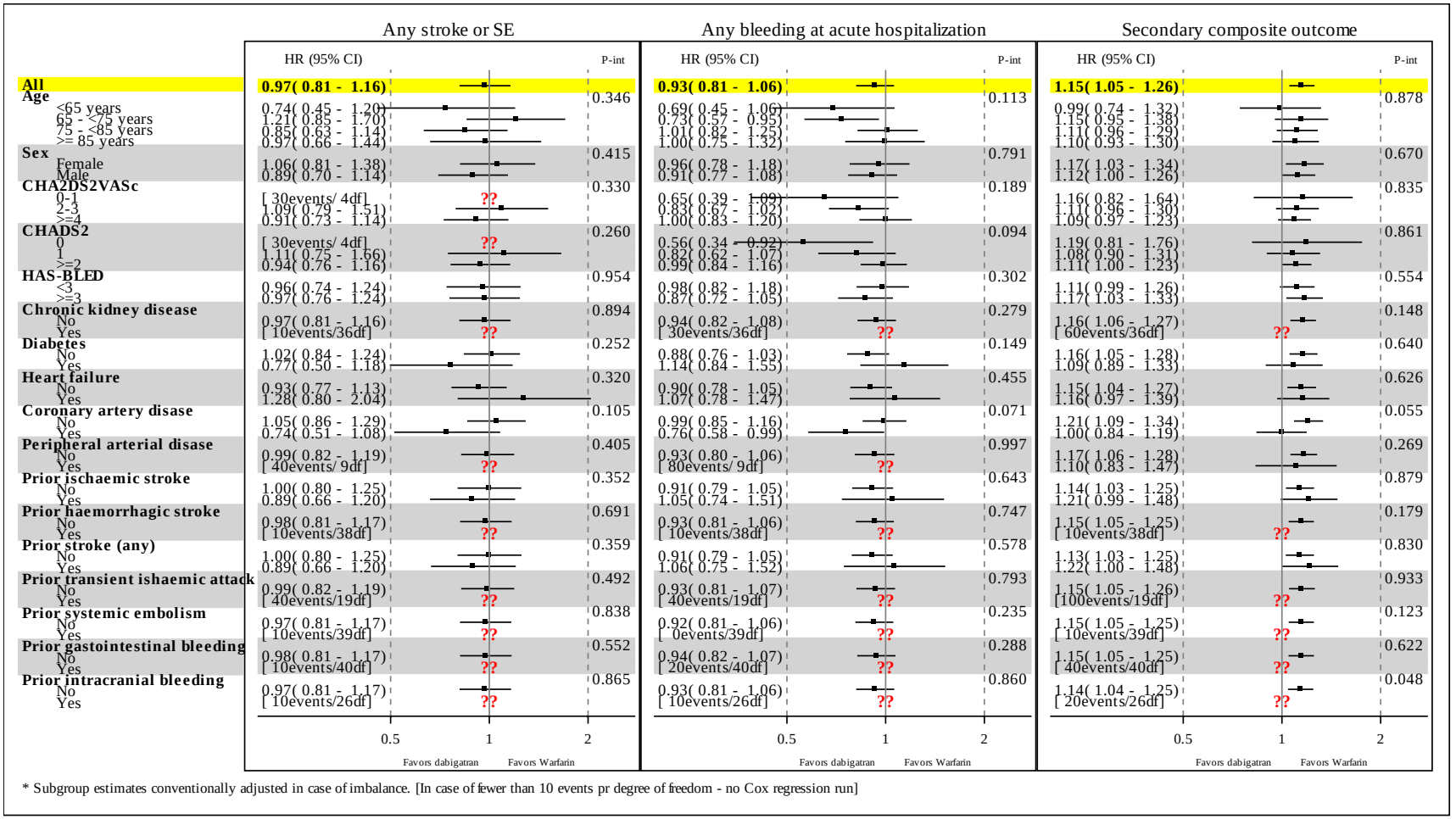
Figure 15.21 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of apixaban vs. warfarin overall and in the subgroups – *Denmark*



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

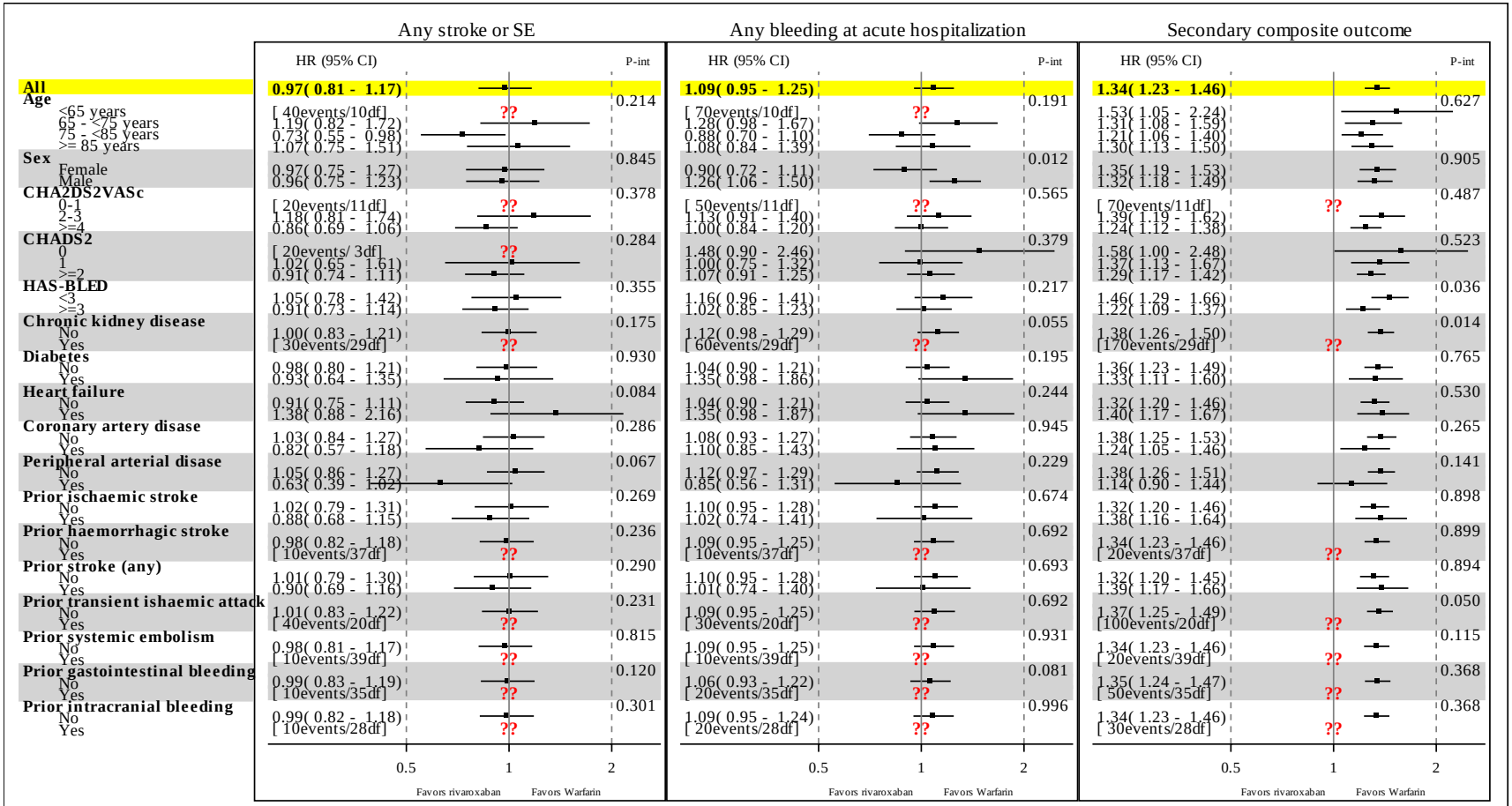
Figure 15.22 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of dabigatran vs. warfarin overall and in the subgroups – *Denmark*



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

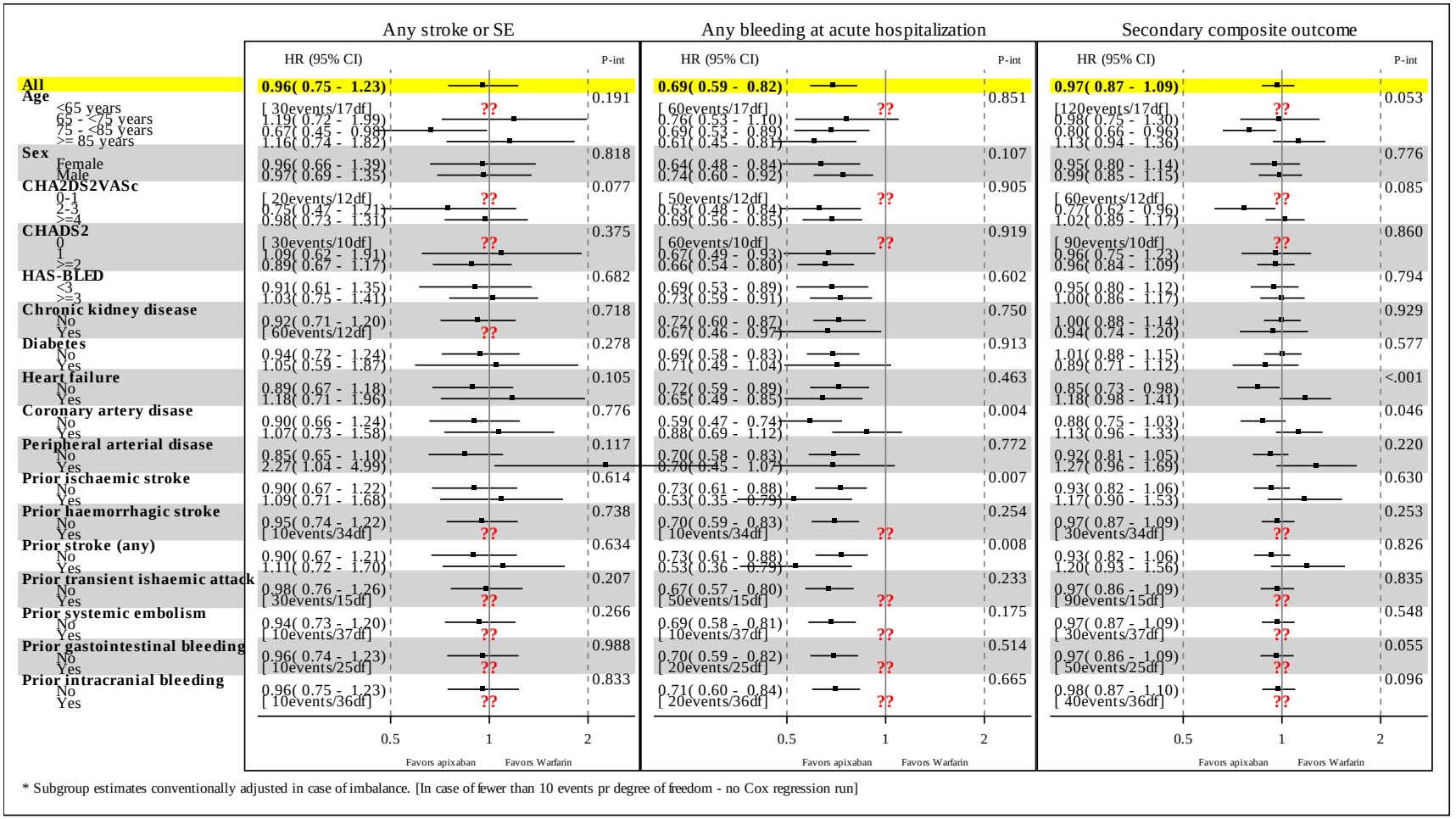
Figure 15.23 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of rivaroxaban vs. warfarin overall and in the subgroups – *Denmark*



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

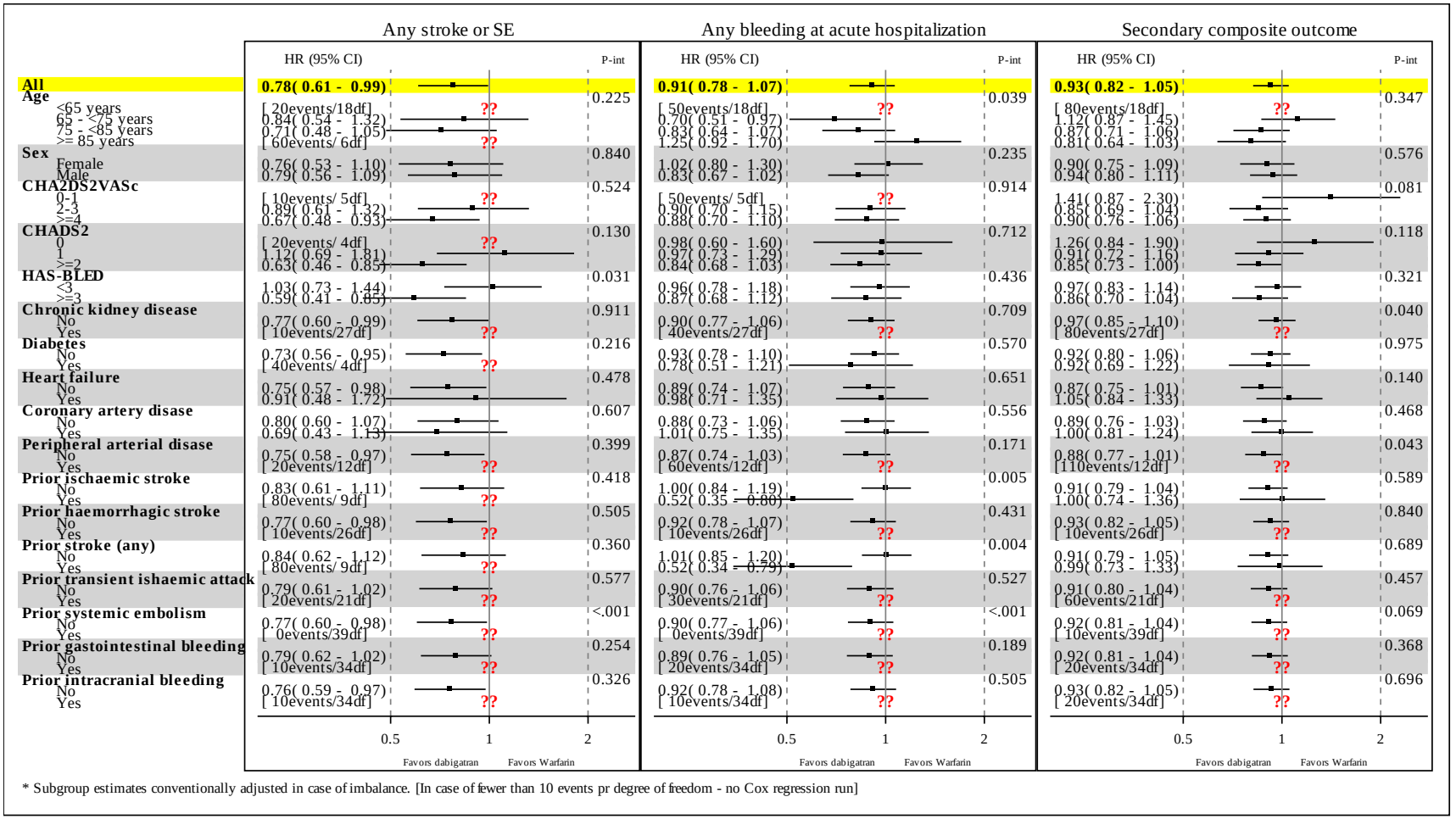
Figure 15.24 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of apixaban vs. warfarin overall and in the subgroups – *Norway*



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

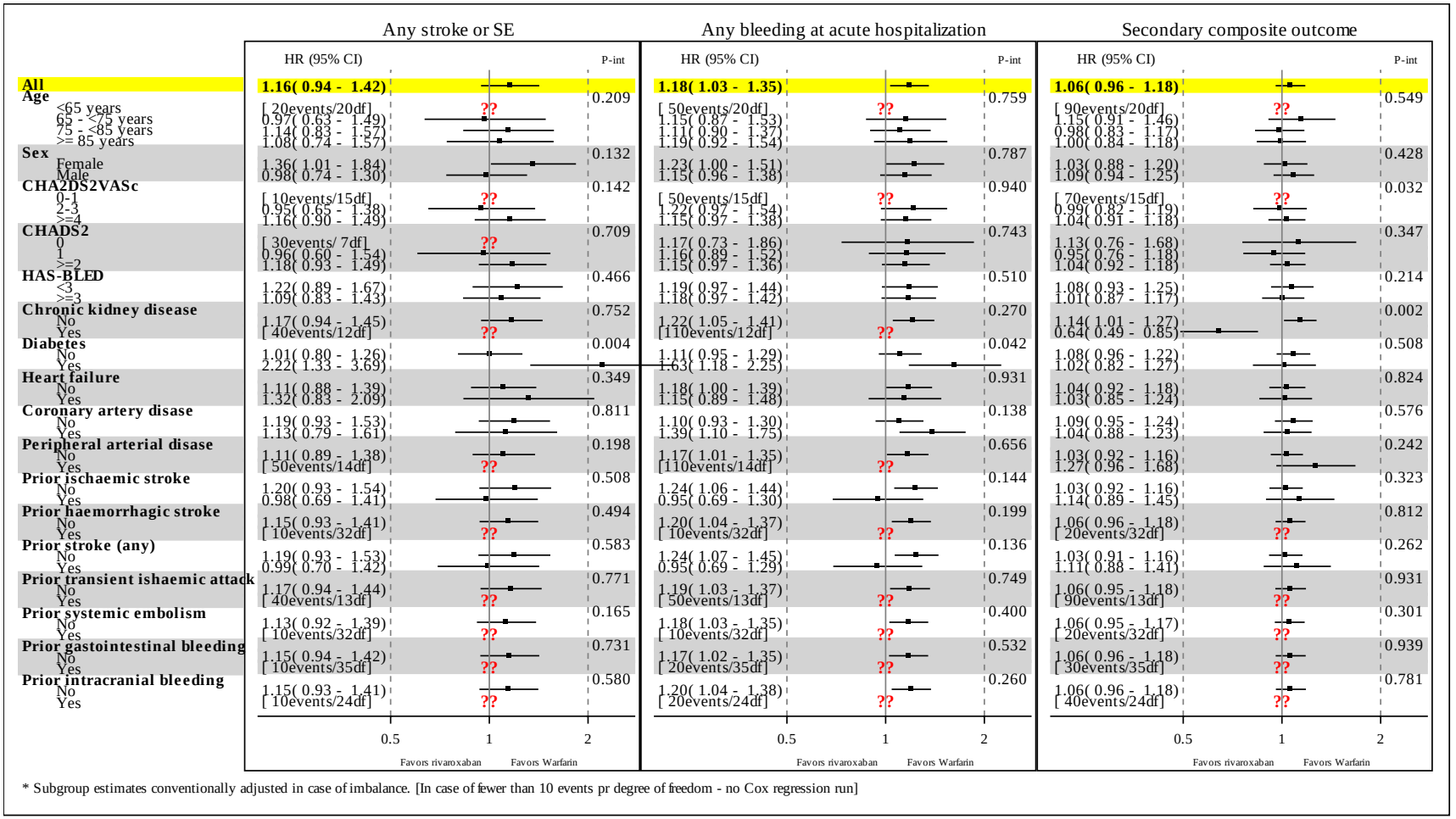
Figure 15.25 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of dabigatran vs. warfarin overall and in the subgroups – *Norway*



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

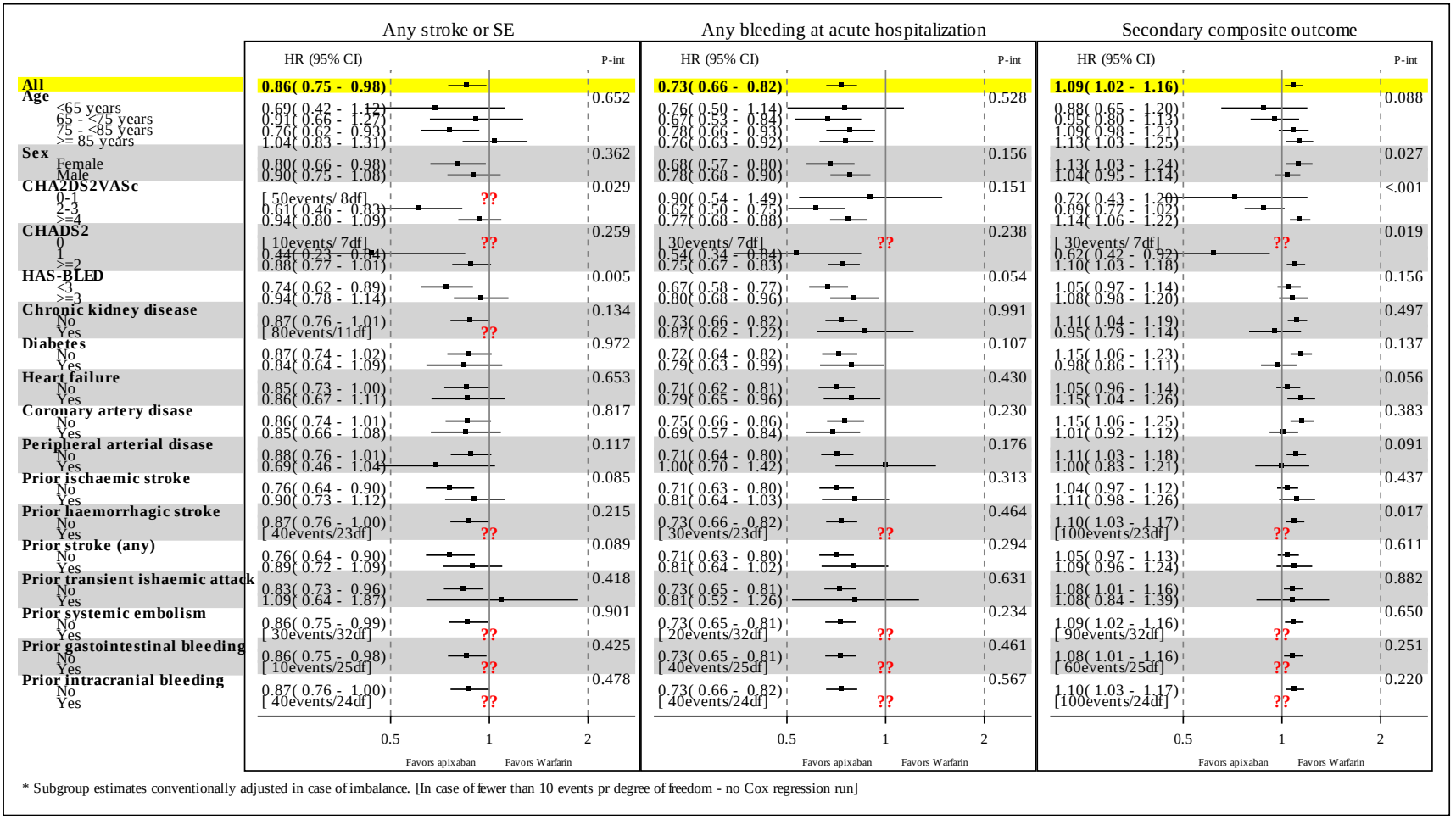
Figure 15.26 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of rivaroxaban vs. warfarin overall and in the subgroups – *Norway*



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

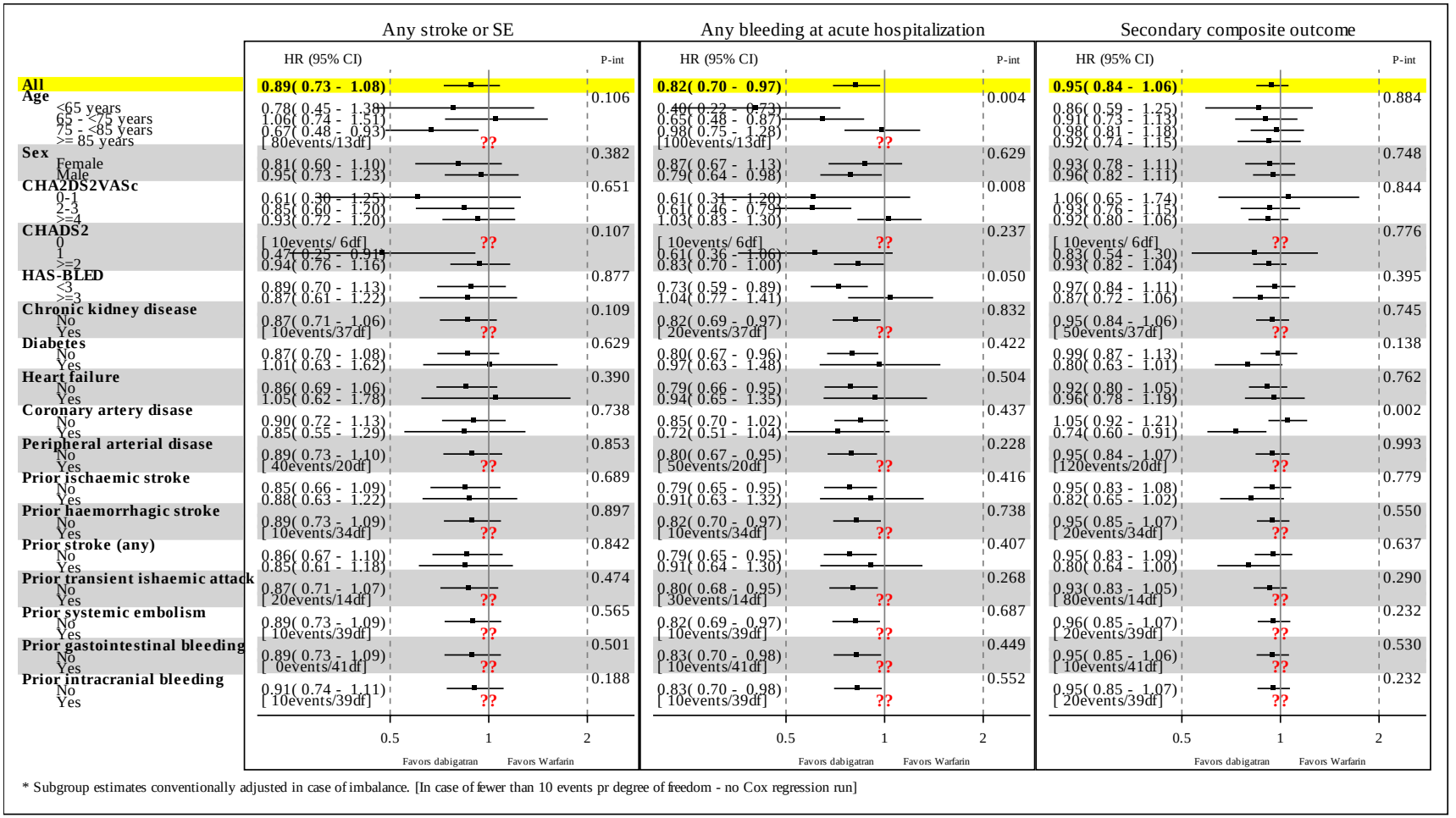
Figure 15.27 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of apixaban vs. warfarin overall and in the subgroups – *Sweden*



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

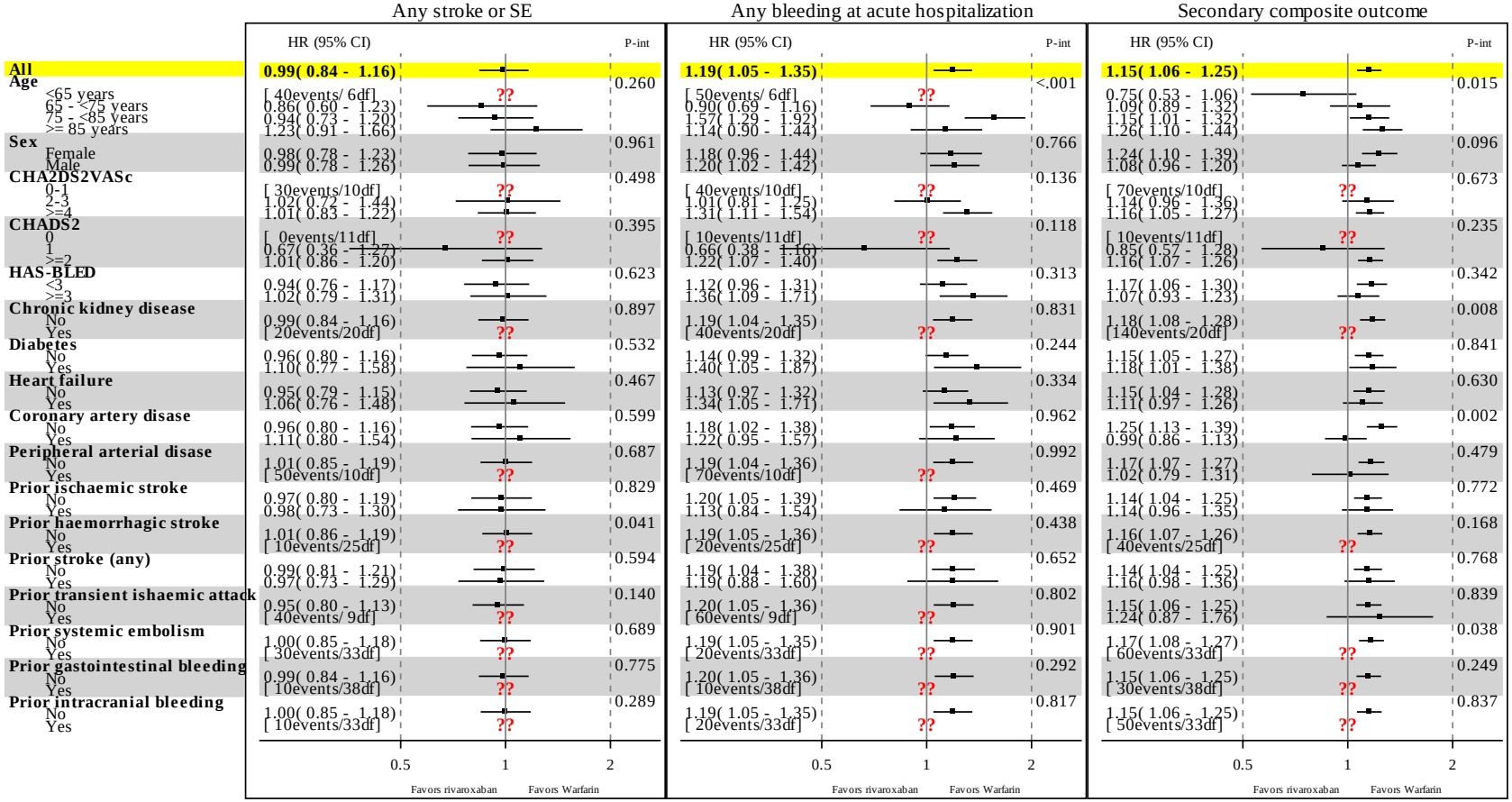
Figure 15.28 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of dabigatran vs. warfarin overall and in the subgroups – *Sweden*



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

Question marks indicate estimates not provided due to <10 events per degree of freedom.

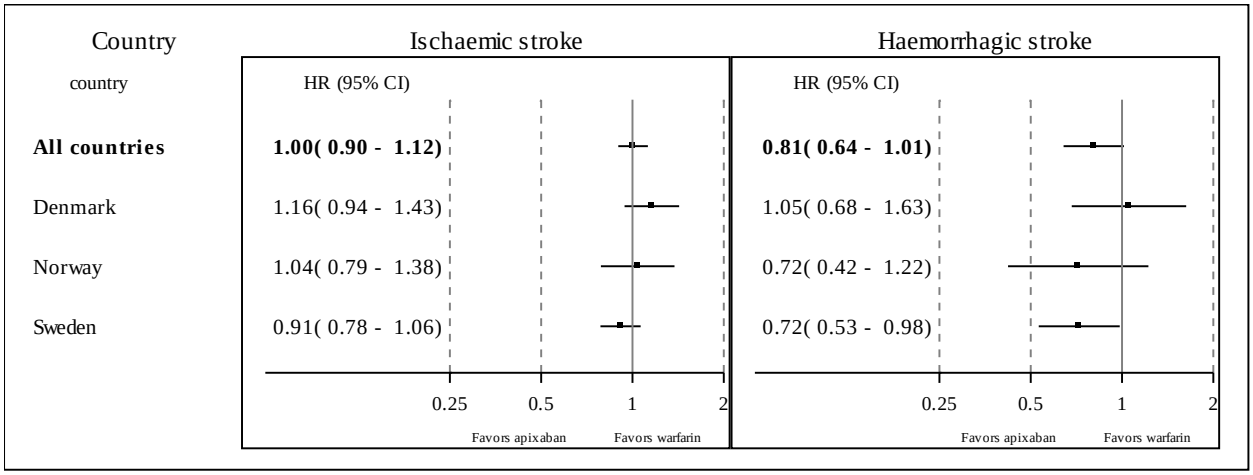
Figure 15.29 Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of rivaroxaban vs. warfarin overall and in the subgroups – *Sweden*



* Subgroup estimates conventionally adjusted in case of imbalance. [In case of fewer than 10 events pr degree of freedom - no Cox regression run]

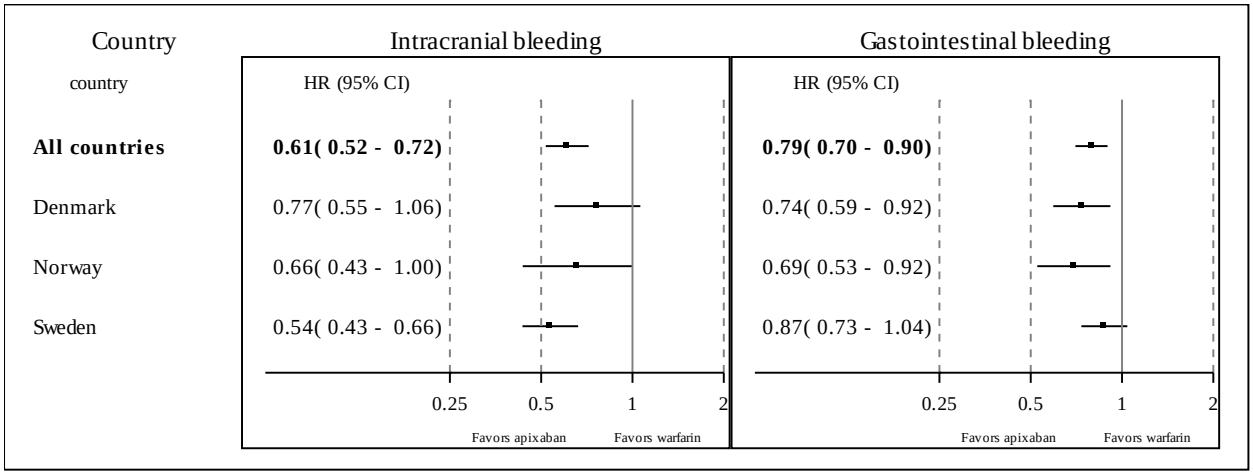
Question marks indicate estimates not provided due to <10 events per degree of freedom.

Figure 15.30 Pairwise propensity -score matched adjusted hazard ratios for the secondary stroke endpoints among patients with NVAF comparing initiators of apixaban vs. warfarin, overall and by country



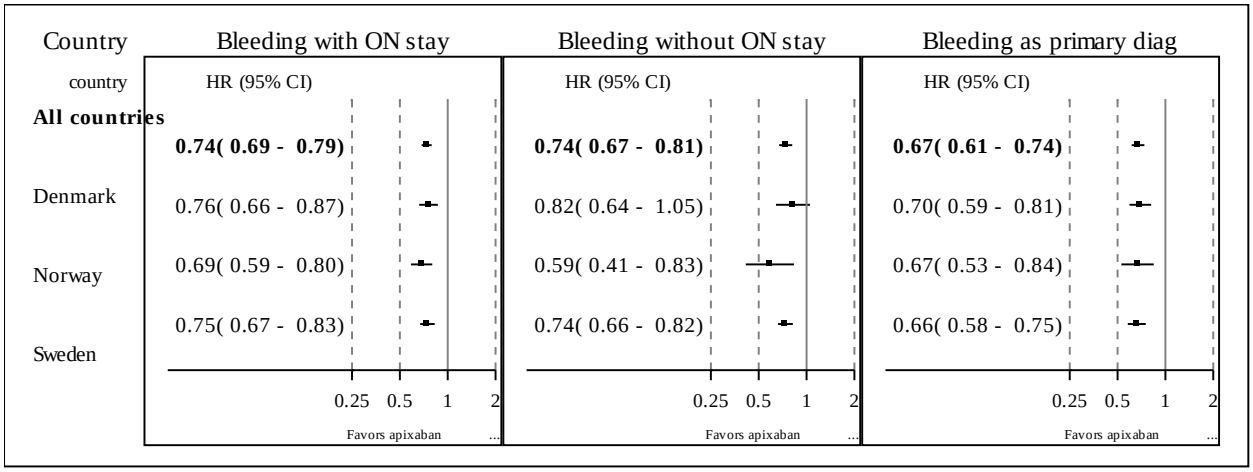
CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation

Figure 15.31 Pairwise propensity -score matched adjusted hazard ratios for the secondary site -specific bleeding endpoints among patients with NVAF comparing initiators of apixaban vs. warfarin, overall and by country



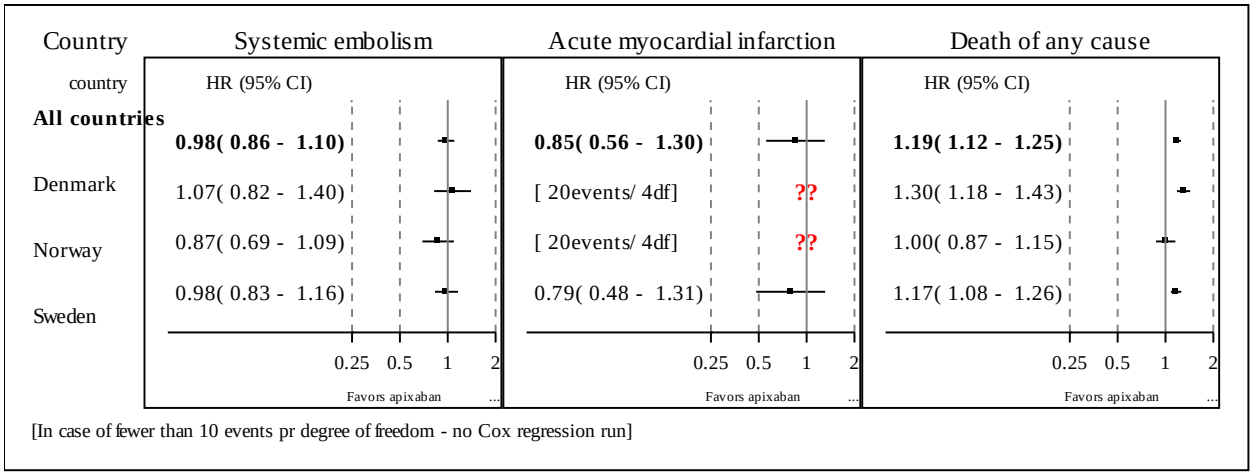
CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation

Figure 15.32 Pairwise propensity -score matched adjusted hazard ratios for the secondary and sensitivity analysis of any bleeding endpoints among patients with NVAF comparing initiators of apixaban vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; ON overnight

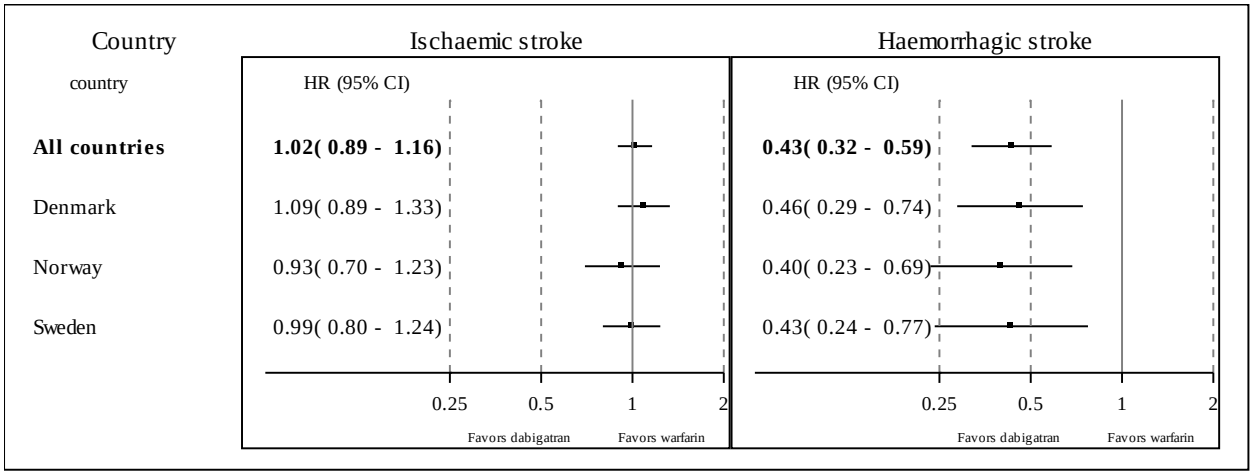
Figure 15.33 Pairwise propensity -score matched adjusted hazard ratios for the secondary endpoints systemic embolism, acute myocardial infarction and death of any cause among patients with NVAF comparing initiators of apixaban vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; ON overnight

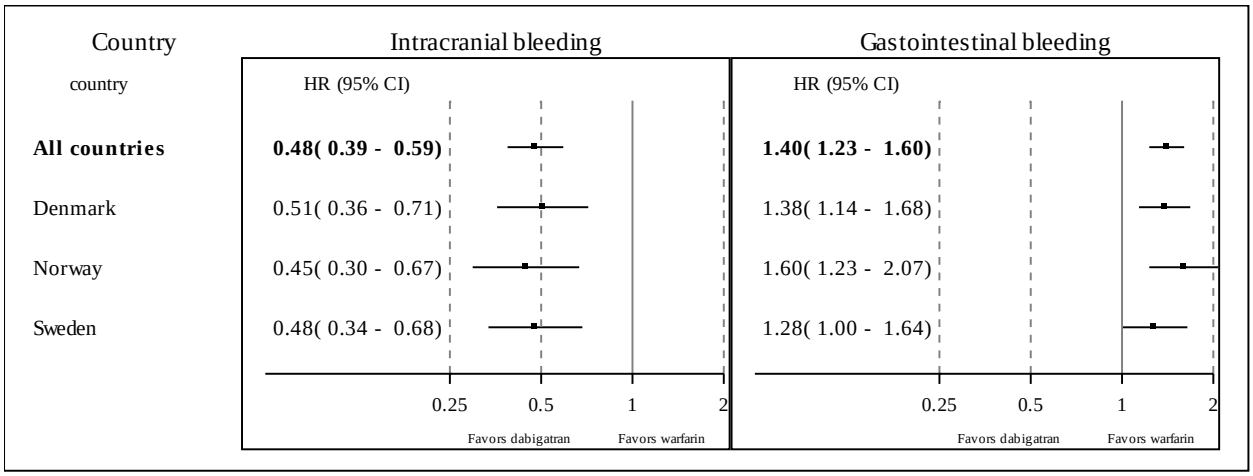
Question marks indicate estimates not provided due to <10 events per degree of freedom.

Figure 15.34 Pairwise propensity -score matched adjusted hazard ratios for the secondary stroke endpoints among patients with NVAF comparing initiators of dabigatran vs. warfarin, overall and by country, overall and by country



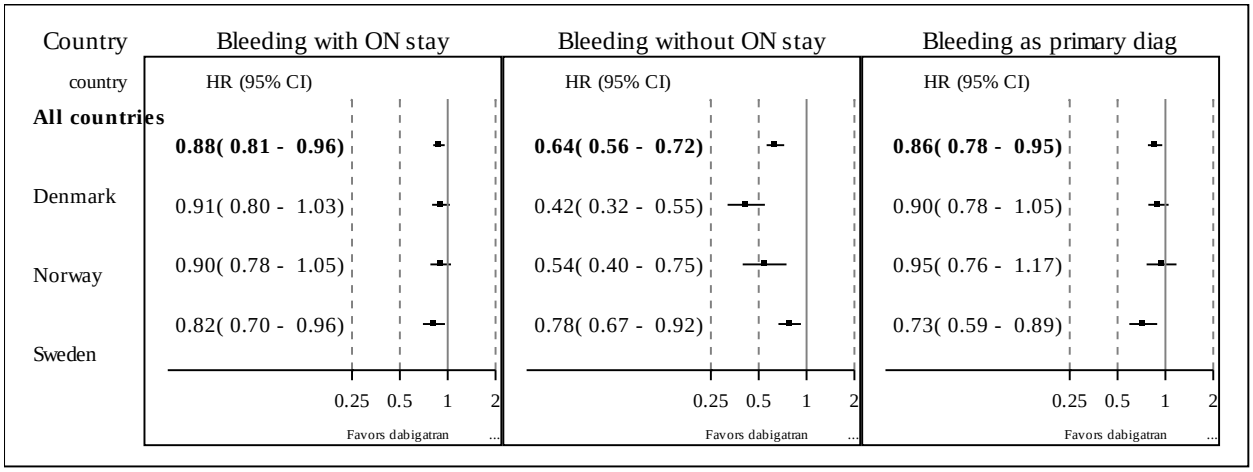
CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation

Figure 15.35 Pairwise propensity -score matched adjusted hazard ratios for the secondary site -specific bleeding endpoints among patients with NVAF comparing initiators of dabigatran vs. warfarin, overall and by country



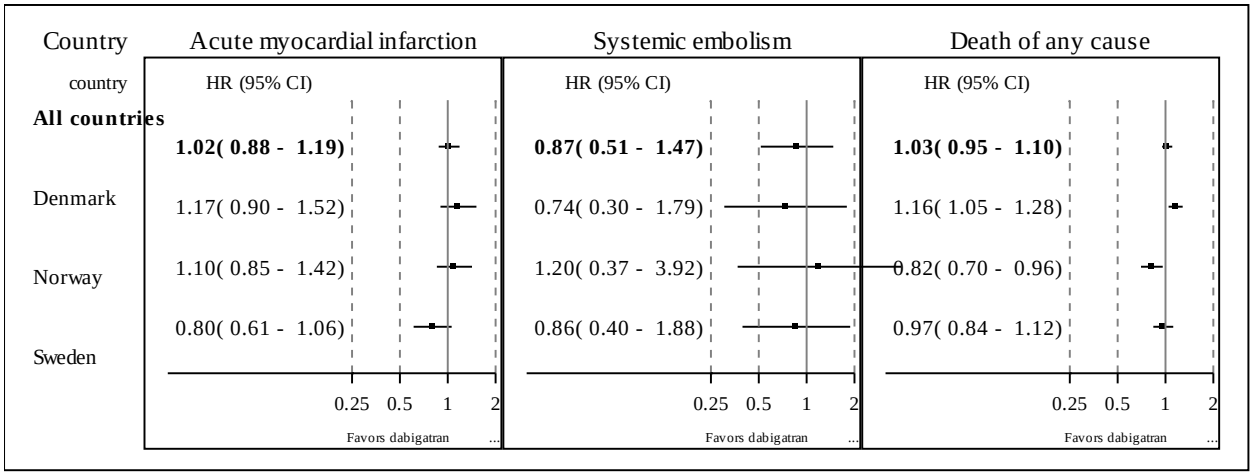
CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation

Figure 15.36 Pairwise propensity -score matched adjusted hazard ratios for the secondary and sensitivity analysis of any bleeding endpoints among patients with NVAF comparing initiators of dabigatran vs. warfarin, overall and by country



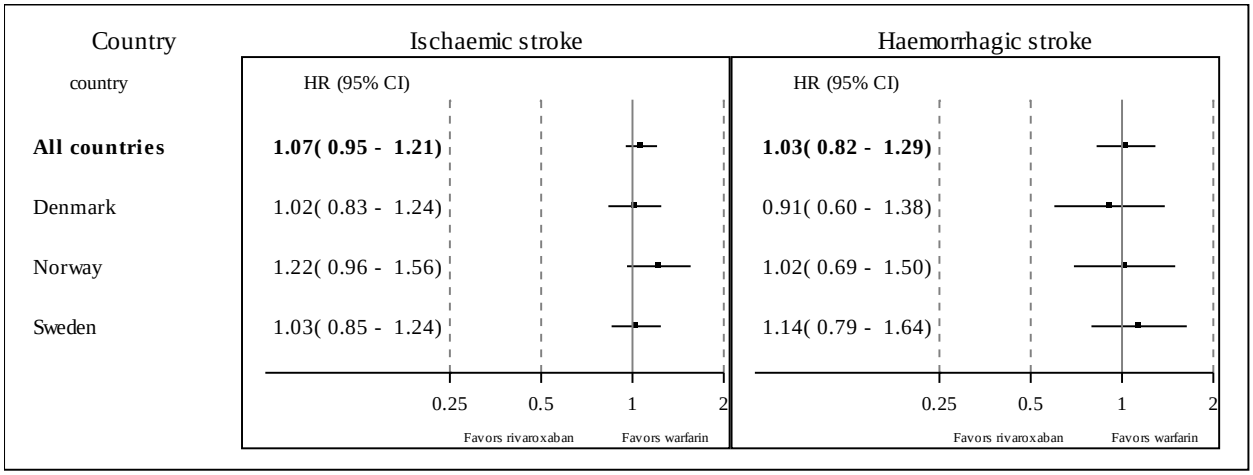
CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; ON overnight

Figure 15.37 Pairwise propensity -score matched adjusted hazard ratios for the secondary endpoints systemic embolism, acute myocardial infarction and death of any cause among patients with NVAF comparing initiators of dabigatran vs. warfarin, overall and by country



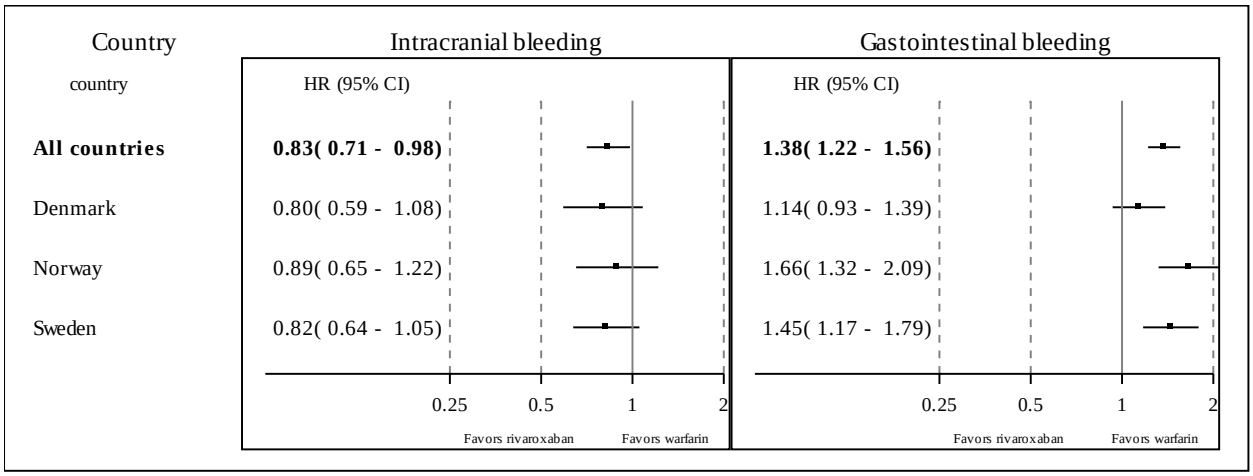
CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation

Figure 15.38 Pairwise propensity -score matched adjusted hazard ratios for the secondary stroke endpoints among patients with NVAF comparing initiators of rivaroxaban vs. warfarin, overall and by country



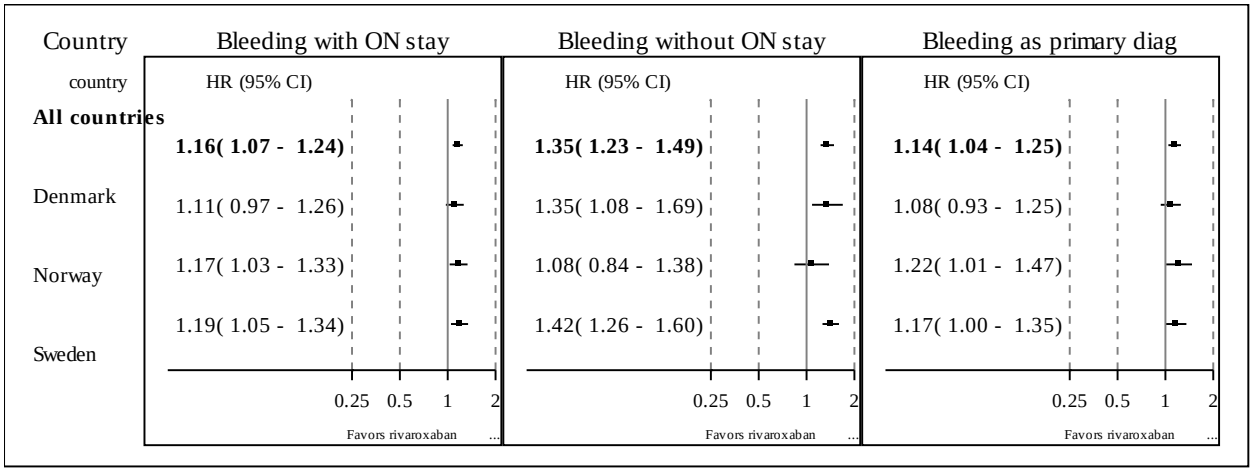
CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation

Figure 15.39 Pairwise propensity -score matched adjusted hazard ratios for the secondary site -specific bleeding endpoints among patients with NVAF comparing initiators of rivaroxaban vs. warfarin, overall and by country



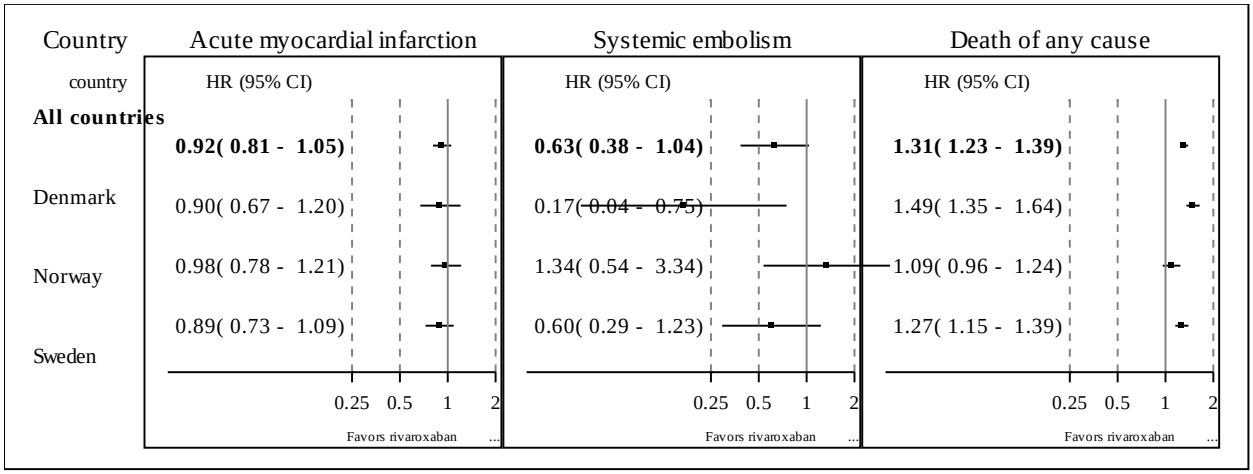
CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation

Figure 15.40 Pairwise propensity -score matched adjusted hazard ratios for the secondary and sensitivity analysis of any bleeding endpoints among patients with NVAF comparing initiators of rivaroxaban vs. warfarin, overall and by country



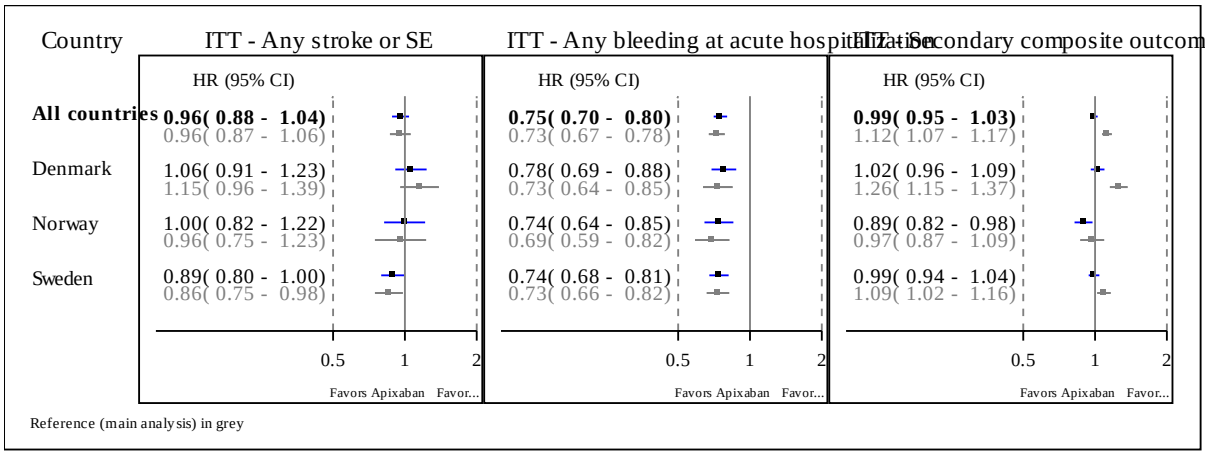
CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; ON overnight

Figure 15.41 Pairwise propensity -score matched adjusted hazard ratios for the secondary endpoints systemic embolism, acute myocardial infarction and death of any cause among patients with NVAF comparing initiators of rivaroxaban vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation

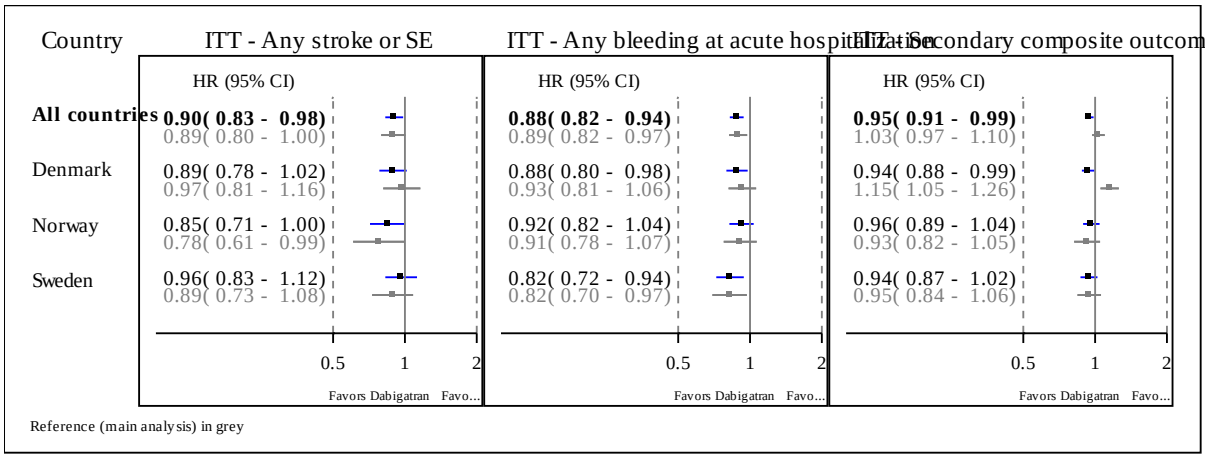
Figure 15.42 Sensitivity analysis (intention to treat): Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of apixaban vs. warfarin, overall and by country



CI confidence interval; ITT intention to treat like analysis; HR hazard ratio; NVAF non-valvular atrial fibrillation; SE systemic embolism

For main analyses of apixaban vs. warfarin see Figure 15.18 (all countries); Figure 15.21 (Denmark); Figure 15.24 (Norway); Figure 15.27 (Sweden).

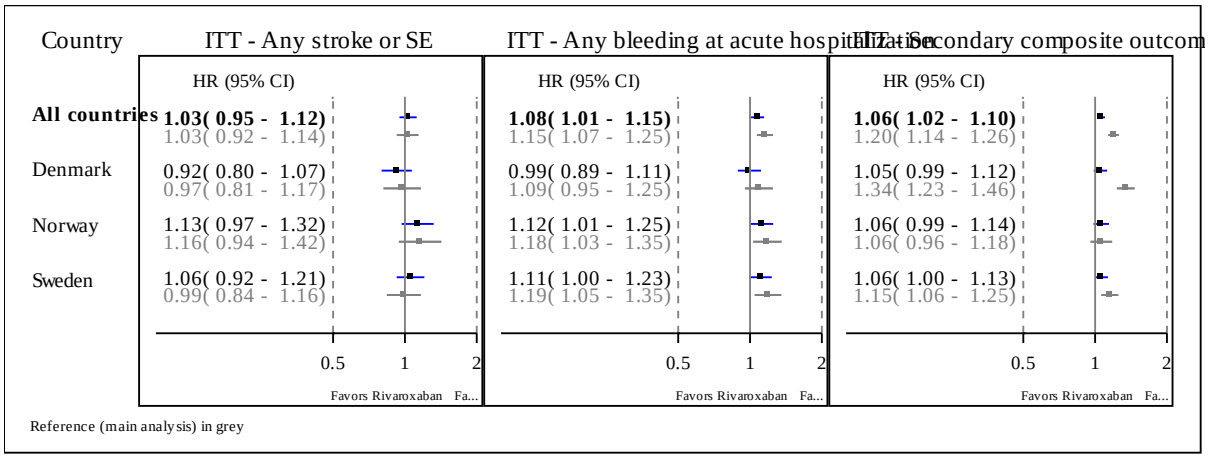
Figure 15.43 Sensitivity analysis (intention to treat): Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of dabigatran vs. warfarin, overall and by country



CI confidence interval; ITT intention to treat like analysis; HR hazard ratio; NVAF non-valvular atrial fibrillation; SE systemic embolism

For main analyses of dabigatran vs. warfarin see Figure 15.19 (all countries); Figure 15.22 (Denmark); Figure 15.25 (Norway); Figure 15.28 (Sweden).

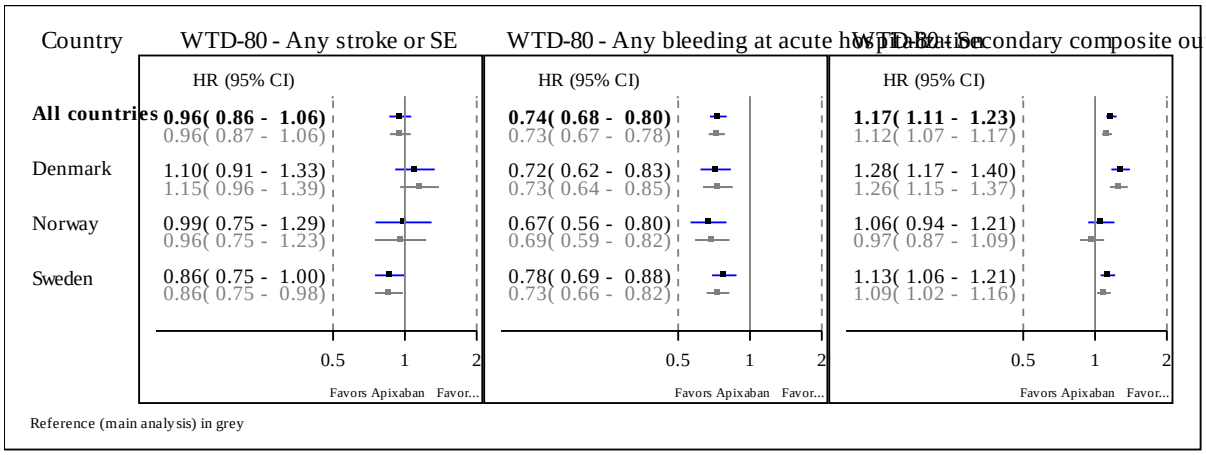
Figure 15.44 Sensitivity analysis (intention to treat): Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of rivaroxaban vs. warfarin, overall and by country



CI confidence interval; ITT intention to treat like analysis; HR hazard ratio; NVAF non-valvular atrial fibrillation; SE systemic embolism

For main analyses of rivaroxaban vs. warfarin see Figure 15.20 (all countries); Figure 15.23 (Denmark); Figure 15.26 (Norway); Figure 15.29 (Sweden).

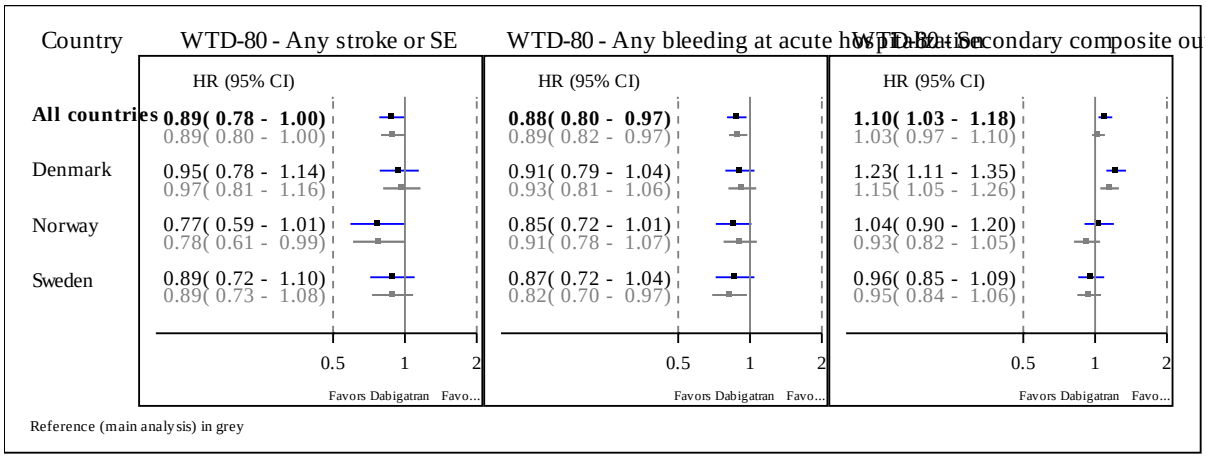
Figure 15.45 Sensitivity analysis (alternative definition of on -treatment time for warfarin): Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of apixaban vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; SE systemic embolism; WDT -80 80th percentile of the waiting time distribution

For main analyses of apixaban vs. warfarin see Figure 15.18 (all countries); Figure 15.21 (Denmark); Figure 15.24 (Norway); Figure 15.27 (Sweden).

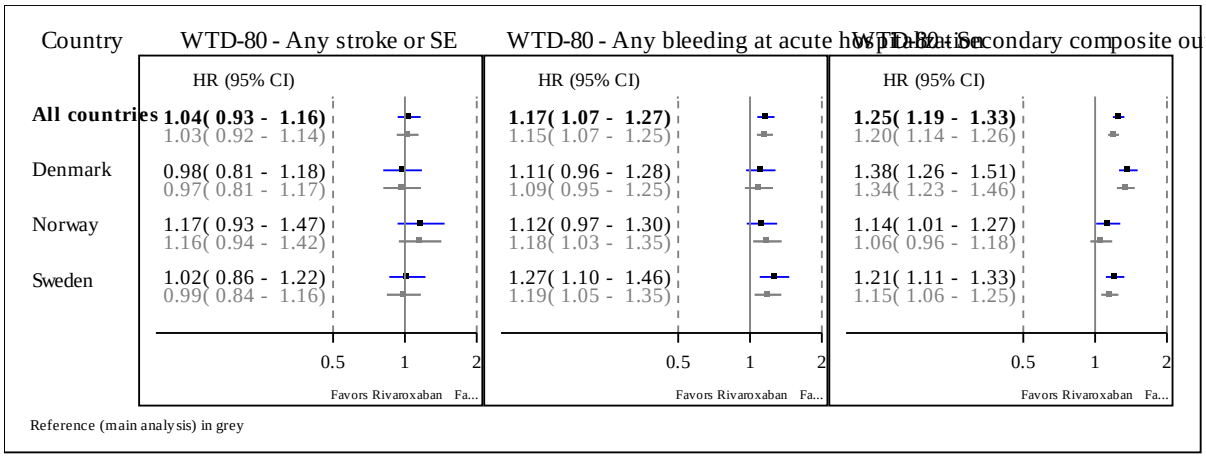
Figure 15.46 Sensitivity analysis (alternative definition of on -treatment time for warfarin): Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of dabigatran vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; SE systemic embolism; WDT -80 80th percentile of the waiting time distribution

For main analyses of dabigatran vs. warfarin see Figure 15.19 (all countries); Figure 15.22 (Denmark); Figure 15.25 (Norway); Figure 15.28 (Sweden).

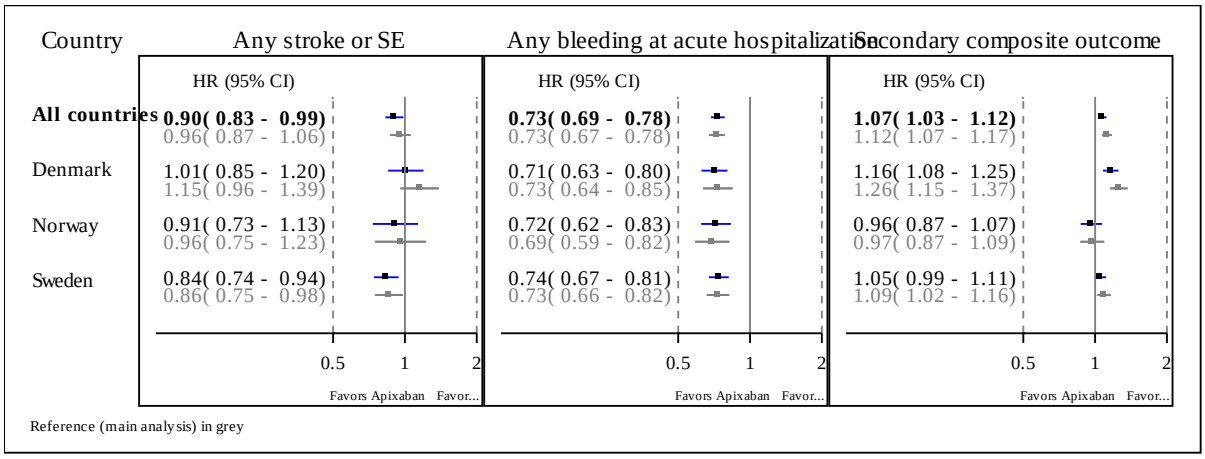
Figure 15.47 Sensitivity analysis (alternative definition of on -treatment time for warfarin): Pairwise propensity -score matched adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of rivaroxaban vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; SE systemic embolism; WDT -80 80th percentile of the waiting time distribution

For main analyses of rivaroxaban vs. warfarin see Figure 15.20 (all countries); Figure 15.23 (Denmark); Figure 15.26 (Norway); Figure 15.29 (Sweden).

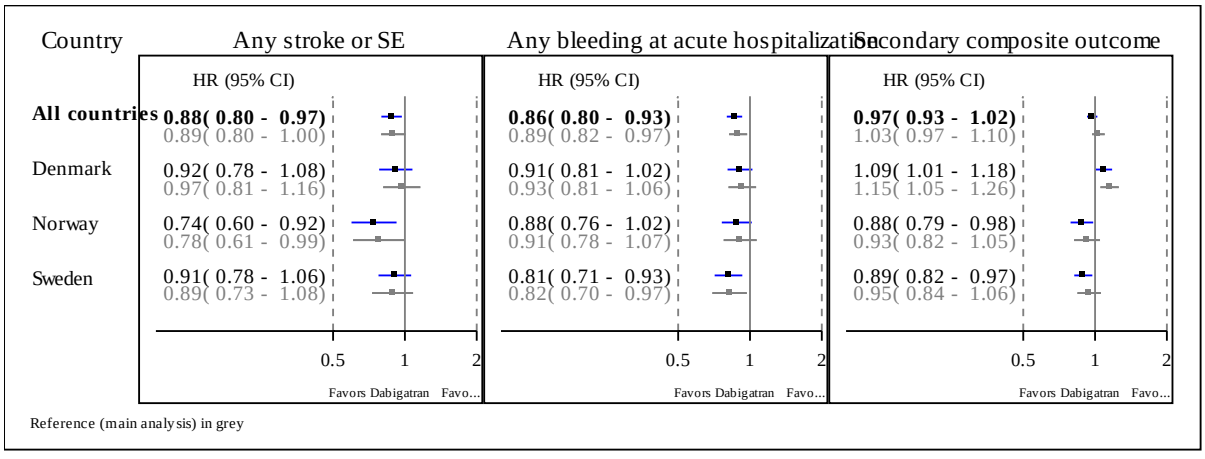
Figure 15.48 Sensitivity analysis (conventional adjustment): Pairwise conventionally adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of apixaban vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; SE systemic embolism

For main analyses of apixaban vs. warfarin see Figure 15.18 (all countries); Figure 15.21 (Denmark); Figure 15.24 (Norway); Figure 15.27 (Sweden).

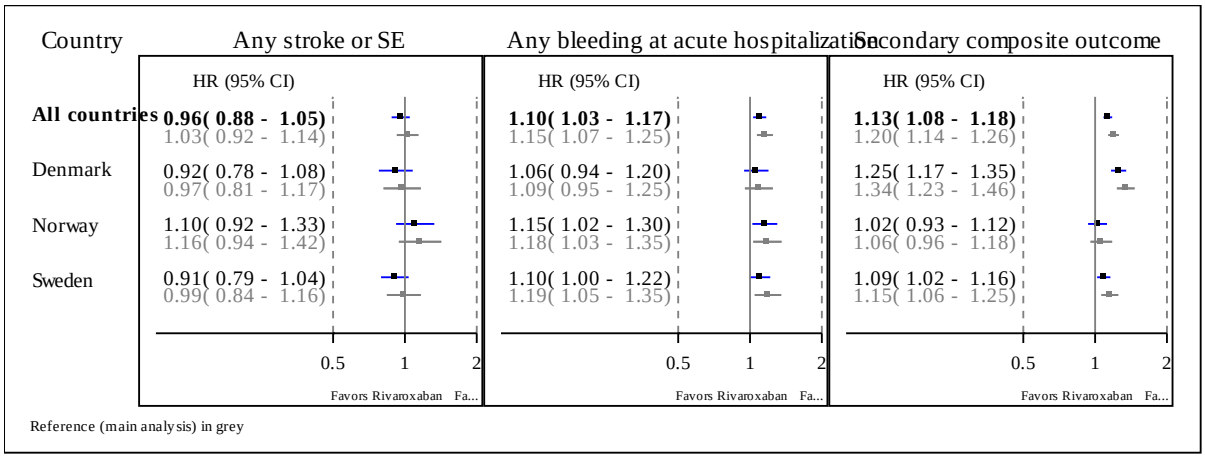
Figure 15.49 Sensitivity analysis (conventional adjustment): Pairwise conventionally adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of dabigatran vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; SE systemic embolism

For main analyses of dabigatran vs. warfarin see Figure 15.19 (all countries); Figure 15.22 (Denmark); Figure 15.25 (Norway); Figure 15.28 (Sweden).

Figure 15.50 Sensitivity analysis (conventional adjustment): Pairwise conventionally adjusted hazard ratios of the primary endpoints and the composite secondary endpoint among patients with NVAF comparing initiators of rivaroxaban vs. warfarin, overall and by country



CI confidence interval; HR hazard ratio; NVAF non-valvular atrial fibrillation; SE systemic embolism

For main analyses of rivaroxaban vs. warfarin see Figure 15.20 (all countries); Figure 15.23 (Denmark); Figure 15.26 (Norway); Figure 15.29 (Sweden).