haematologica
Journal of the Ferrata Storti Foundation

Carbon footprint of direct oral anticoagulants in atrial fibrillation and venous thromboembolism

by Laurence Chery, Zahra Hassani, Lise Durand, Dorothée Boisseau, Victorien Monguillon, David Grimaldi, Sebastien Taillemite, Benjamin de Sainte Marie and Nicolas Gendron

Received: November 11, 2025.
Accepted: December 4, 2025.

Citation: Laurence Chery, Zahra Hassani, Lise Durand, Dorothée Boisseau, Victorien Monguillon, David Grimaldi, Sebastien Taillemite, Benjamin de Sainte Marie and Nicolas Gendron. Carbon footprint of direct oral anticoagulants in atrial fibrillation and venous thromboembolism. Haematologica. 2025 Dec 11. doi: 10.3324/haematol.2025.300204 [Epub ahead of print]

Carbon footprint of direct oral anticoagulants in atrial fibrillation and venous thromboembolism

Laurence Chery[1,2], Zahra Hassani[2,3], Lise Durand[2,4], Dorothée Boisseau[2,5], Victorien Monguillon[6], David Grimaldi[7], Sebastien Taillemite[8], Benjamin de Sainte Marie[9], Nicolas Gendron[2,10,11,12]

1. Pharmacy department, Groupe Hospitalier UNEOS, Metz-Vantoux, France.
2. The Shifters association, Cercle Thématique Santé, Paris, France
3. SESAME, One Health Medical Education, Prades-le-Lez, France
4. Pharmacy department, Centre Hospitalier Universitaire de Rennes, Rennes, France
5. Department of infectious disease, St Nazaire Hospital, Saint-Nazaire, France
6. Sorbonne Université, ACTION Study Group, INSERM UMRS 1166, Institut de Cardiologie, Hôpital Pitié-Salpêtrière (AP-HP), 47 boulevard de l'Hôpital, Paris 75013, France
7. The Shift Project, Paris, France
8. Ecovamed, Paris, France
9. Department of Internal Medicine, Centre Hospitalier Universitaire de La Timone, Marseille, France.
10. Hematology Department, Hôpital européen Georges Pompidou, Assistance Publique Hôpitaux de Paris-Centre Université Paris Cité (APHP-CUP), F-75015, Paris, France.
11. Paris Cité University, INSERM, Paris Cardiovascular Research Centre, Team Endotheliopathy and Hemostasis disorders, Paris, France.
12. Investigation Network on Venous Thrombo-Embolism–French Clinical Research Infrastructure Network, Saint-Étienne, France

Corresponding author: Dr Nicolas Gendron (PharmD, PhD), Hematology department, Hôpital européen Georges-Pompidou, 20 rue Leblanc 75015 Paris, France

Tel: +33 156093938. Fax: +33 156093393

E-mail: nicolas.gendron@aphp.fr

Acknowledgment: We thank Ecovamed (Paris, France) for providing free access to the Ecovamed database. We thank SESAME (Paris, France) for funding access to the MCF Classifier.

Funding: None

Disclosure: NG discloses consulting fees or travel awards by Bayer, Bristol-Myers Squibb/Pfizer, LEO-Pharma, Werfen and Diagnostica Stago, without any relation with the current manuscript. All other authors have nothing to disclose.

Authorship contributions: LR, ZH, ST and NG collected data, analyzed data and wrote the manuscript. LR, ZH, LD, DB, VM, DG, ST, BST, and NG contributed to data analysis and manuscript revision.

Data Sharing statement: The datasets generated and/or analyzed during the current study are not publicly available due to contractual restrictions with data providers. Data cannot be shared.

Anticoagulant therapies are used for the treatment and the prevention of venous thromboembolism (VTE) and stroke or systemic embolic events in atrial fibrillation (AF). Direct oral anticoagulants (DOACs) are now recommended by all major scientific guidelines as a first line therapy.[1,2] DOACs including dabigatran, which inhibits thrombin; rivaroxaban, apixaban and edoxaban which inhibit factor Xa (FXa), are now widely used for oral anticoagulation due to their ease of administration, favorable pharmacological and safety profiles, and the absence of need for biological monitoring[3]. DOACs, and in particular apixaban, are among the most prescribed drugs worldwide. DOACs have shown similar clinical efficacy and risk profiles in phase III trials in both VTE and AF indications[4,5]. However, no randomized prospective trial has directly compared one DOAC with another and therefore a head-to-head comparison is not yet available. Available evidence is limited to registry-based studies, healthcare claims databases, and meta-analyses extrapolating data from trials using warfarin as a comparator and, confirms an overall reduced risk of bleeding but suggests an increased risk of bleeding with rivaroxaban compared with apixaban[6–9]. In the absence of robust evidence-based superiority, international guidelines do not recommend one specific DOAC over another neither for AF nor for VTE. As a result, treatment choice depends largely on cost, dosing frequency (once-daily vs twice-daily regimen), and physicians preferences, explaining national and international discrepancies in prescribing. In AF, patients usually receive lifelong treatment whereas in VTE, patients are usually treated for 3 to 6 months, or with long-term or indefinite anticoagulation in some cases of unprovoked VTE at high risk of recurrence, or in the context of cancer-associated VTE[1,10]. Reduced-dose DOAC are recommended in AF in the context of renal impairment, low body weight, older age, or drug–drug interactions and according to each drug[2]. For VTE, recently, two randomized multicentric trials demonstrated the benefit of reduced-dose oral FXa inhibitors compared with standard-dose therapy after at least 6 months of full-dose anticoagulation, both in patients at high risk of recurrence and in those with cancer-associated thrombosis[11,12].

Recently, Fan Bingwen et al.[13], in an international collaborative viewpoint, highlighted the importance of incorporating sustainability into anticoagulation care, aligning clinical excellence with climate responsibility, and suggested transitioning to lower-carbon anticoagulants. Given the near equivalence in efficacy and safety, and to provide an environmental perspective in treatment selection, the objective of this study was to compare greenhouse gas (GHG) emissions of three DOAC (dabigatran, apixaban and rivaroxaban) for use in VTE and AF, analyzed per molecule and

per indication. The second objective was to compare the GHG emissions of reduced dose in the context of extended VTE treatment. For each DOAC, we calculated GHG emissions in carbon dioxide equivalents (CO_2eq) using procurement data and published CO_2eq values from the latest life cycle assessments (LCA) available. Evaluated treatment durations included 1 year for AF and 6 months to 10 years for VTE, based on standard dosing regimens. Carbon footprint data were retrieved from two databases, respectively: Ecovamed (France, accessed April 17, 2025 and previously described here[14]) and MCF Classifier (United Kingdom, UK, accessed March 13, 2025 and previously described here[15]). No human or animal data were used. Ethics approval was not required, and all procedures adhered to national ethical standards. Continuous data were expressed as median and range (min–max) according to methods of calculation. Descriptive analyses were performed using Prism (version 10.0; GraphPad).

After extracting the estimation of carbon footprint data of DOAC regimens from the Ecovamed and MCF Classifier databases, we calculated the carbon footprint for each daily dose of rivaroxaban, apixaban, and dabigatran (**Table 1**). We observed differences in the total carbon footprint between the two databases, but a similar trend: a higher carbon footprint for dabigatran compared with apixaban and rivaroxaban, and a lower daily carbon footprint with reduced-dose regimens of each molecule. Using the Ecovamed database, we were able to analyze the partitioning of the carbon footprint of DOACs by emission source (**Figure 1**). We observed that, for oral FXa inhibitors, about 70% of emissions originated from corporate activities, compared with 22.0% for dabigatran. Regarding emissions from the active pharmaceutical ingredient (API), these accounted for 67.4% for dabigatran, versus 10.2% for rivaroxaban and 5.5% for apixaban. In terms of manufacturing, emissions represented 18.5% for apixaban, compared with 9.9% for rivaroxaban and 7.2% for dabigatran. Partitioning of the carbon footprint was not available in the MCF due to the method. Next, we analyzed the carbon footprint of DOACs for one year of treatment in AF. According to the Ecovamed database, the median carbon footprints per year at standard dose of rivaroxaban, apixaban, and dabigatran were 33.7 kg CO_2eq (6.7–60.7), 36.8 kg CO_2eq (10.3–63.3), and 123.7 kg CO_2eq (74.2–173.2), respectively (**Figure 2A**). The median carbon footprints per year of the reduced-dose rivaroxaban, apixaban, and dabigatran were 32.4 kg CO_2eq (5.5–59.3), 35.3 kg CO_2eq (7.8–62.8), and 99.9 kg CO_2eq (59.9–139.9), respectively. According to the MCF Classifier database, the median carbon footprints per year at standard dose were 6.2 kg CO_2eq (3.5–8.9) for rivaroxaban, 2.9 kg CO_2eq (1.9–3.9) for apixaban, and 106.1 kg CO_2eq (69.0–143.2) for

dabigatran, respectively (**Figure 2B**). The median carbon footprints per year of the reduced-dose rivaroxaban, apixaban, and dabigatran were 4.8 kg CO_2eq (3.1–6.5), 2.0 kg CO_2eq (1.3–2.7), and 78.1 kg CO_2eq (50.8–105.4), respectively. Both databases showed no notable difference between the two oral anti–FXa inhibitors. However, dabigatran exhibited a significant environmental disadvantage, with carbon emissions 3 to 36 times higher than those of rivaroxaban or apixaban for one year of AF treatment. The large discrepancies between the Ecovamed and MCF Classifier results, particularly for the two oral anti-FXa inhibitors, are explained by the different LCA system boundaries. Notably, the MCF Classifier does not include corporate activities (such as R&D, sales, marketing, administration, or regulatory processes). When both datasets are adjusted to the same boundaries, the results are consistent (**Figure 2C**). Next, we analyzed the carbon footprint of rivaroxaban and apixaban for the 6 first months of treatment for VTE. According to the Ecovamed database, the median carbon footprints of rivaroxaban was 18.4 kg CO_2eq (3.4–33.4) and for apixaban was 18.8 kg CO_2eq (5.3–32.3), respectively (**Figure 2D**). According to the MCF Classifier database, the median carbon footprints was 3.2 kg CO_2eq (2.1–4.3) for rivaroxaban and 1.5 kg CO_2eq (1.0–2.0) for apixaban, respectively (**Figure 2E**). The carbon footprint after six months of initial VTE treatment and over 6 months, 2, 5, and 10 years with both databases is shown in **Figure 2F- G.** After 1 year and 10 years of treatment, the use of reduced-dose rivaroxaban, following 6 months of initial therapy, reduced CO_2eq emission by 21.9% and 43.1% with the MCF Classifier, and by 3.1% and 6.4% with Ecovamed. After 1 year and 10 years of treatment the use of reduced-dose apixaban following 6 months of initial therapy, reduced CO_2eq emission by 15.0% and 29.1% with the MCF Classifier, and by 2.2% and 3.9% with Ecovamed.

In this study, we provide an environmental perspective based on GHG emissions to help guide clinicians in the choice between DOAC in both AF and VTE indication at equivalent doses. Using two methods, we observed that dabigatran has a clearly higher GHG impact compared with apixaban and rivaroxaban in both AF and VTE. The carbon footprint of dabigatran is mainly linked to the API, in contrast to other DOACs. Conversely, corporate activities account for approximately 70% of the total impact of oral FXa inhibitors. The GHG impact of apixaban and rivaroxaban appears to be similar across indications. Reduced-dose DOAC for extended VTE treatment decreases bleeding risk while maintaining similar efficacy in preventing recurrent events[11,12], thereby improving the environmental impact. As expected, reduced-dose DOAC for extended treatment duration lowered the GHG emissions of each drug. GHG emissions were reduced by

about 30% when using the MCF Classifier and by around 3–5% with Ecovamed. The smaller reductions observed with Ecovamed, compared with MCF, are due to the high contribution of corporate activities, which remain stable across doses, unlike API, excipients, and manufacturing, and are not reported in the MCF Classifier. Our results should encourage guidelines to promote low carbon footprint therapies (oral FXa inhibitors) in clinical decision making, encourage reduced-dose strategies when clinically indicated and encourage manufacturers to provide more transparency in their carbon footprint. To the best of our knowledge, this is the first study evaluating the carbon footprint of DOACs. We acknowledge some limitations. First, both methods are validated for DOAC prescriptions in France (Ecovamed) and in UK (MCF), which limits the applicability of our observations beyond Western Europe. Second, the carbon footprint values in the MCF Data Extract are modeled predictions rather than measured emissions using a cradle-to-gate carbon footprint assessment that follows the principles of ISO 14040–14044 and complies with the GHG Protocol. Third, our data do not include edoxaban, which is not available in France, nor account for the use of parenteral heparin therapy recommended for five days prior to dabigatran initiation in VTE.

References

1. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41(4):543-603.

2. Van Gelder IC, Rienstra M, Bunting KV, et al. 2024 ESC Guidelines for the management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2024;45(36):3314-3414.

3. Gendron N, Billoir P, Siguret V, et al. Is there a role for the laboratory monitoring in the management of specific antidotes of direct oral anticoagulants? Thromb Res. 2024;237:171-180.

4. Ruff CT, Giugliano RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet. 2014;383(9921):955-962.

5. van Es N, Coppens M, Schulman S, Middeldorp S, Büller HR. Direct oral anticoagulants compared with vitamin K antagonists for acute venous thromboembolism: evidence from phase 3 trials. Blood. 2014;124(12):1968-1975.

6. López-López JA, Sterne JAC, Thom HHZ, et al. Oral anticoagulants for prevention of stroke in atrial fibrillation: systematic review, network meta-analysis, and cost effectiveness analysis. BMJ. 2017;359:j5058.

7. Bai Y, Deng H, Shantsila A, Lip GYH. Rivaroxaban Versus Dabigatran or Warfarin in Real-World Studies of Stroke Prevention in Atrial Fibrillation: Systematic Review and Meta-Analysis. Stroke. 2017;48(4):970-976.

8. Bonde AN, Martinussen T, Lee CJ-Y, et al. Rivaroxaban Versus Apixaban for Stroke Prevention in Atrial Fibrillation: An Instrumental Variable Analysis of a Nationwide Cohort. Circ Cardiovasc Qual Outcomes. 2020;13(4):e006058.

9. Fralick M, Colacci M, Schneeweiss S, Huybrechts KF, Lin KJ, Gagne JJ. Effectiveness and Safety of Apixaban Compared With Rivaroxaban for Patients With Atrial Fibrillation in Routine Practice: A Cohort Study. Ann Intern Med. 2020;172(7):463-473.

10. Sanchez O, Benhamou Y, Bertoletti L, et al. [Recommendations of good practice for the management of thromboembolic venous disease in adults. Short version]. Rev Mal Respir. 2019;36(2):249-283.

11. Couturaud F, Schmidt J, Sanchez O, et al. Extended treatment of venous thromboembolism with reduced-dose versus full-dose direct oral anticoagulants in patients at high risk of recurrence: a non-inferiority, multicentre, randomised, open-label, blinded endpoint trial. The Lancet. 2025;405(10480):725-735.

12. Mahé I, Carrier M, Mayeur D, et al. Extended Reduced-Dose Apixaban for Cancer-Associated Venous Thromboembolism. N Engl J Med. 2025;392(14):1363-1373.

13. Fan BE, Milla K, McAlister S, et al. Sustainable anticoagulation for climate resilient care. Lancet Haematol. 2025;12(11):e918-e925.

14. Piffoux M, Le Tellier A, Taillemite Z, Ducrot C, Taillemite S. Carbon footprint of oral medicines using hybrid life cycle assessment. J Clean Prod. 2024;475:143576.

15. Taylor H, Mahamdallie S, Sawyer M, Rahman N. MCF classifier: Estimating, standardizing, and stratifying medicine carbon footprints, at scale. Br J Clin Pharmacol. 2024;90(11):2713-2723.

Table 1. Daily Carbon Footprint of DOAC regimens Using Ecovamed and MCF Classifier Databases

Median daily carbon footprint (g CO_2eq) of DOAC regimens according to the Ecovamed and MCF Classifier databases.

*For the treatment of VTE, dabigatran requires an initial 5 to 10 days of parenteral anticoagulation, the carbon footprint of which is not included here; calculations are based on AF treatment.

DOAC: direct oral anticoagulant; BID: Twice daily; OD: Once daily; VTE: venous thromboembolism; AF: atrial fibrillation; g CO_2e: grams of carbon dioxide equivalent.

Direct oral anticoagulant	Dose	Dosing regimen	Indication	Daily Carbon Footprint (g CO_2eq)	
				Ecovamed	MCF classifier
Apixaban	10 mg	BID	VTE	201.6	16.0
Apixaban	5 mg	BID	AF & VTE	100.8	8.0
Apixaban	2.5 mg	BID	AF & VTE	96.6	5.5
Rivaroxaban	20 mg	OD	AF & VTE	92.3	16.9
Rivaroxaban	15 mg	OD	AF	88.8	13.0
Rivaroxaban	15 mg	BID	VTE	177.6	26.0
Rivaroxaban	10 mg	OD	VTE	86.1	9.2
Dabigatran	150 mg	BID	AF & VTE*	338.8	290.8
Dabigatran	110 mg	BID	AF & VTE*	273.8	214.0

Figure 1. Distribution of the carbon footprint of direct oral anticoagulants by emission source (Ecovamed data)

API: active pharmaceutical ingredient

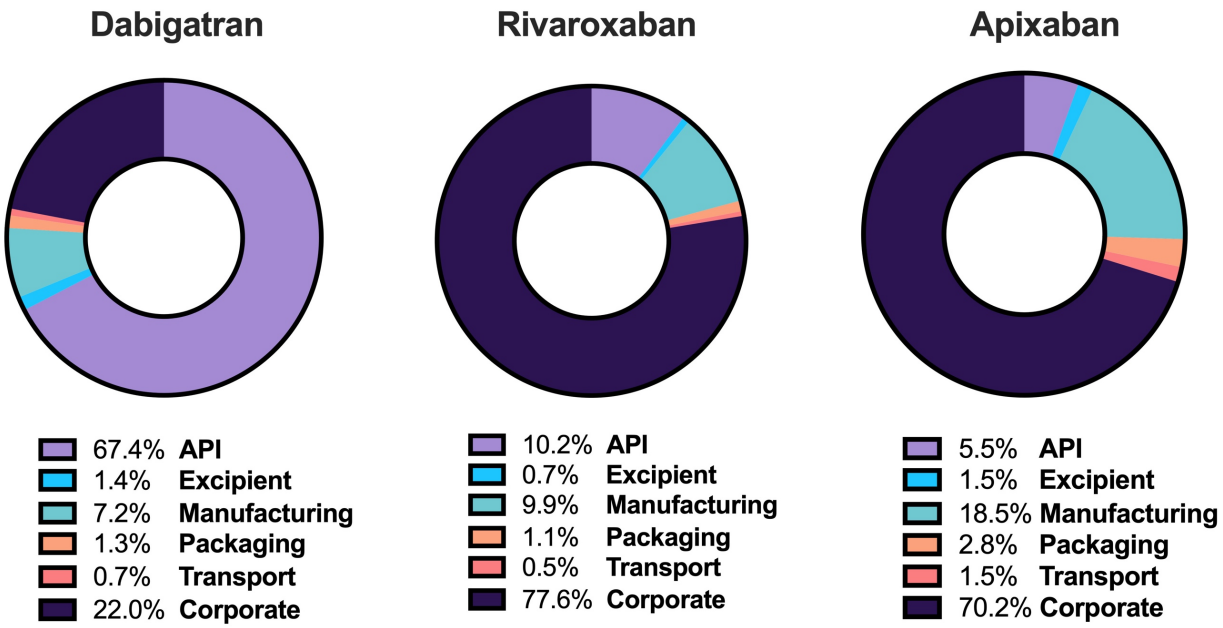


Figure 2. **Carbon footprint of one year of DOAC treatment across indications and dose regimens**

A) Carbon footprint of one year of DOAC treatment for AF according to Ecovamed

B) Carbon footprint of one year of DOAC treatment for AF according to MCF classifier

C) Carbon footprint of one year of DOAC treatment for AF according to Ecovamed with corporate emission and others.

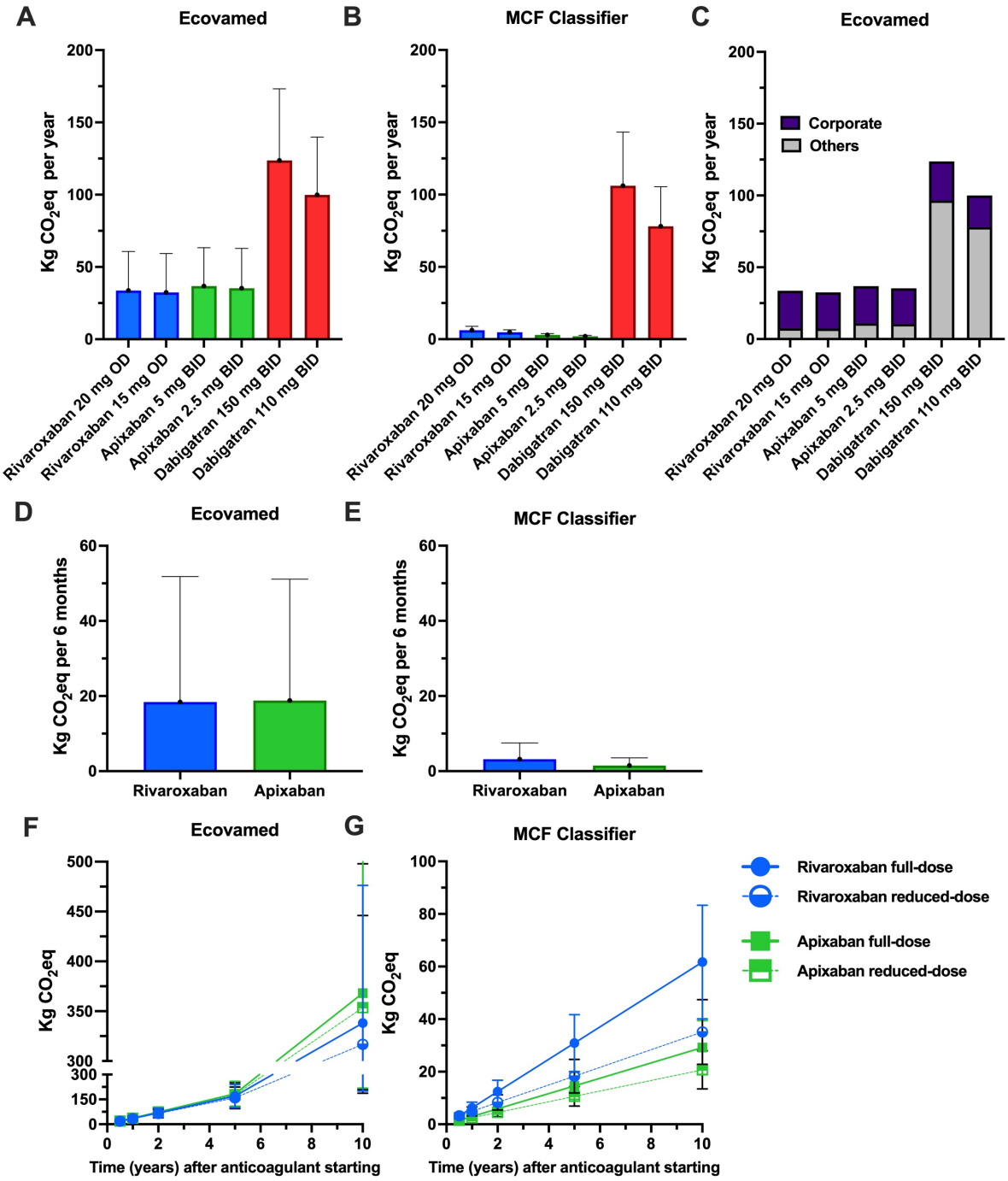
D) Carbon footprint of 6 months of oral factor Xa inhibitors for VTE according to Ecovamed

E) Carbon footprint of 6 months of oral factor Xa inhibitors for VTE according to MCF classifier.

F) 10-year carbon footprint of standard- vs reduced-dose oral factor Xa inhibitors for VTE (Ecovamed)

G) 10-year carbon footprint of standard- vs reduced-dose oral factor Xa inhibitors for VTE (MCF classifier)

OD: once daily; BID: twice daily. Kg CO2eq: Carbon footprint expressed in kg CO_2eq per year.


A
Ecovamed
B
MCF Classifier
C
Ecovamed
Kg CO_2eq per year
200
150
100
50
0
Corporate
Others
Rivaroxaban 20 mg OD
Rivaroxaban 15 mg OD
Apixaban 5 mg BID
Apixaban 2.5 mg BID
Dabigatran 150 mg BID
Dabigatran 110 mg BID
D
Ecovamed
E
MCF Classifier
Kg CO_2eq per 6 months
60
40
20
0
Rivaroxaban
Apixaban
F
Ecovamed
G
MCF Classifier
Kg CO_2eq
500
450
400
350
300
150
100
80
60
40
20
0
2
4
6
8
10
Time (years) after anticoagulant starting
Rivaroxaban full-dose
Rivaroxaban reduced-dose
Apixaban full-dose
Apixaban reduced-dose