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Environmental assessment of hemophilia therapies. Comment on: "Carbon footprint of direct oral anticoagulants in atrial fibrillation and venous thromboembolism"

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Environmental footprint in hemophilia

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Author contributions

MRL: Conceptualization (lead), investigation, writing – original draft (lead), writing – review and editing.

MCS: Conceptualization (supporting), investigation, writing – review and editing.
Both authors contributed to the scientific discussion and interpretation of the literature, critically revised the manuscript, and approved the final version.

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Chery et al. quantified the carbon footprint of the direct oral anticoagulants used in atrial fibrillation and venous thromboembolic disease.[1] Their work answers the call by Fan et al. to bring environmental sustainability into the care of the anticoagulated patient.[2] It is a useful and timely contribution. We would like to highlight one finding that, in our opinion, conditions any extension of this approach to other areas of hematology, and specifically to hemophilia.

The authors used two estimation tools, Ecovamed and the MCF Classifier.[3,4] For the same molecules and the same regimens, the results differed considerably. Why? Simple. The MCF Classifier did not include certain corporate activities, which accounted for 70% of total footprint of the oral factor Xa inhibitors. When both estimates were adjusted to equivalent boundaries, the results agreed.[1] Two estimates of the environmental impact of the same drug can differ substantially without either of them being necessarily wrong.

The consequence matters. Comparability does not depend only on having figures. It depends on those figures answering to the same functional unit and to equivalent analytical boundaries. Chery et al. were able to show this because the methods were described and accessible. In hemophilia, that possibility remains limited.

The published information on the environmental footprint of treatments, for example in hemophilia A, is scarce and heterogeneous. For the recombinant factor VIII concentrates (rFVIII) NovoEight® and Esperoct®, annual estimates of 128.7 and 108.8 kg CO_2e have been reported.[6] For Mim8 (denecimig), values between 4.0 and 14.7 kg CO_2e per year have been described, depending on the administration regimen.[7] These figures do not allow direct comparison. They come from assessments with different assumptions, functional units and system boundaries. Nor do they always provide disaggregated information on manufacturing, transport, cold chain, administration or waste. Arranging them in a table might produce an apparent hierarchy, but not a scientifically defensible one.

The French experience with Emicizumab adds another perspective. The HemiValue study estimated an annual reduction of 52 tonnes of CO_2 linked to the reorganisation of the dispensing circuit.[8] A later analysis, published as an abstract for ISPOR Europe 2026, estimated a 38% reduction in the footprint of the care circuit between 2018 and 2025, equivalent to 3,843

tonnes of CO_2e in a modelled population of 2,270 patients.[9] These are interesting results. Even so, they are not an integral life cycle assessment of the drug. They depend on the scenarios compared, the components included and the sources used. Again, having figures does not mean we can compare them.

There is a less visible limitation. Access to the data needed to reproduce the calculations. The published annual estimates do not necessarily provide the manufacturing emissions corresponding to each commercial presentation of FVIII. Without that information, it is difficult to calculate independently the environmental impact of prophylaxis in real patients, taking into account dose, actual consumption and vial combinations. Nor can we assume that emissions are proportional to the FVIII content of each vial. An analysis verified by a third party can be methodologically valid without being reproducible by external researchers. Verification, transparency and reproducibility are related concepts, but not equivalent ones.

This distinction is important. International standards do apply. ISO 14040 and ISO 14044 set out the principles and the requirements of life cycle assessment. ISO 14067 specifically governs the quantification of the carbon footprint of products.[10] Their application, however, does not guarantee public access to disaggregated manufacturing inventories. The problem is not the absence of a methodological framework. It is the distance between having an environmental estimate and being able to reproduce it or apply it to an independent clinical cohort.

The consequences are practical. Environmental criteria are gaining weight in public procurement and in health technology assessment. An estimate with insufficient methodological information can be used in a hospital tender, or in promotional material, as an argument of environmental superiority. In hemophilia, where cost differences between alternatives are considerable and decisions affect prolonged treatments, this risk deserves attention.

We should also question an intuitive assumption. That fewer administrations necessarily mean a lower environmental impact. The number of administrations is easy to count, but it does not represent the whole life cycle. In the study by Chery et al., the active substance accounted for 67.4% of the footprint of dabigatran, compared with 5.5% for apixaban.[1] In FVIII concentrates,

manufacturing through cell culture, purification and lyophilisation, or plasma collection and fractionation, introduces processes whose environmental contribution has to be quantified. Devices and care circuits matter, but they cannot replace an integral assessment.

In our opinion, environmental assessment should be incorporated into the appraisal of therapeutic strategies in hemophilia, together with efficacy, safety and cost. Not as a dominant criterion, but as an additional dimension of therapeutic value. Minimum reporting requirements should also be established. We are talking about a functional unit, defined, for example, as one year of prophylaxis in a patient with a specified weight and regimen. We are talking about system boundaries, manufacturing emissions per commercial presentation, packaging, transport, cold chain, administration, waste and care resources. The corporate activities included, the emission allocation rules, the methodology and the reference year should also be declared. The ISO standards provide the framework. What is missing is accessible information to apply it independently.

Finally, we should avoid claims of environmental superiority while the estimates are not methodologically homogeneous. This caution includes gene therapy. In a recent paper on its environmental impact in hemophilia B we argued for incorporating this dimension into health technology assessment, while acknowledging the limitations of the available data.[5] Chery et al. call for greater transparency from manufacturers.[1] We share that request and we consider it necessary to go further. Publishing global estimates is not enough if independent researchers lack the data to reproduce them and apply them to their own patients. Environmental transparency should allow us to verify the results, not simply to accept them. Until we have public, verifiable and comparable information, any environmental ranking of these therapies will risk being a preference disguised as a measurement.

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