

## BACKGROUND

Approximately three million blood donations are carried out annually by *Etablissement Français du sang* (EFS) to treat one million patients. As whole blood (WB) donation leads to a 1 g/dL decrease of hemoglobin (Hb) levels [1], various measures are needed in France to prevent anemia in WB donors.

Implementing a ferritin testing policy for whole-blood (WB) donors may prevent iron deficiency (ID, ferritin < 26 ng/ml) and anemia, but may induce donation losses.

Iron deficiency in French WB donors was investigated in the FERRIDON research study [2], and 4 subgroups of donors at high risk of ID were determined for ferritin testing management.

As part of a national prevention plan in France, we aimed to estimate the impact of ferritin testing policy on ID, anemias and WB donations among donors at high-risk of ID.

## METHOD

A dynamic micro-simulation model was developed to evaluate different scenarios compared to the current situation without ferritin testing as a reference scenario:

**Reference scenario:** current situation without ferritin testing, and a minimum mandatory inter-donation interval of 8 weeks

**Minimum scenario:** implementation of ferritin testing for every donor of each risk group, with 6-month deferral for donors with ferritin levels <15 ng/ml. No specific intervention is planned for donors at 15-25 ng/ml

**Main scenario:** minimum scenario, plus an additional intervention for donors at 15-25 ng/ml, with a minimum return interval of 3 and 4 months for male and female donors, respectively

**Supplementation scenario:** main scenario, plus an oral iron supplementation for 50% of donors with ferritin levels < 15 ng/ml

**Model data :** the model used data from the FERRIDON study [2] for most parameters and the literature for the necessary time for ferritin recovery [3] in the different subgroups

**Structure of the model (Figure 1) :**

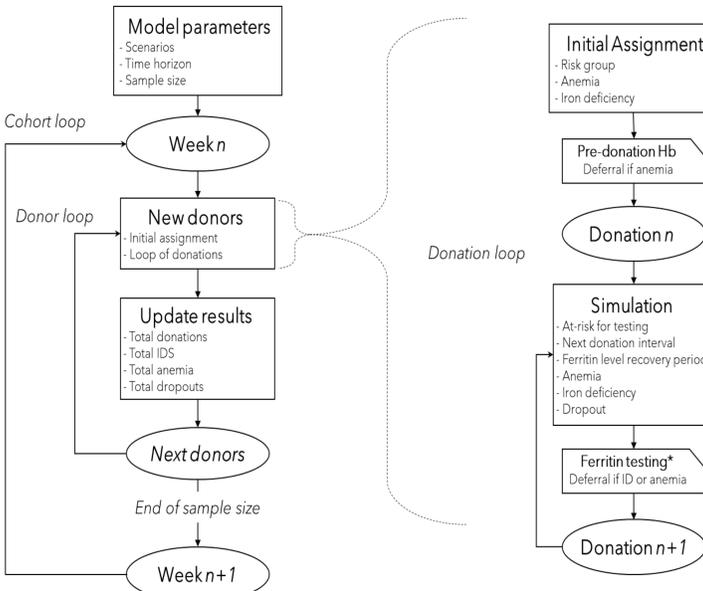
- **weekly cohort loop**, simulating new high-risk donors every week, and updating results, and
- **individual donor loop**, simulating the course of donations and various time-dependent states for each donor. An ID was assumed when the time to donation occurred before the ferritin recovery period.

### Statistical analysis

The model was simulated over a 5-year period. Results were calculated separately for each risk group and aggregated for the 1st, and 5th year in terms of WB donations, IDs and anemias. Sensitivity analyses were conducted to assess uncertainty associated to key parameters.

**Table 1 - Definition of groups of whole blood donors at high risk of iron deficiency (< 26 ng/ml)**

Group	Population	Definition of high risk subgroups	Proportion among all donors
G1	Repeat female donors	Women with last donation under 4.5 months ago, TCMH at last donation ≥30 pg and aged <31.5 years old	1.21%
G2	New female donors	Women with last donation under 4.5 months ago and TCMH at last donation <30 pg	9.65%
G3	Repeat male donors	Men with at least 2 donations within last year and: - Last donation under 3.5 months ago and TCMH at last donation <29.5 pg - Or last donation more than 3.5 months ago and TCMH at last donation <27.4 pg	7.23%



**Figure 1 Structure of the patient-level micro-simulation model**

## RESULTS

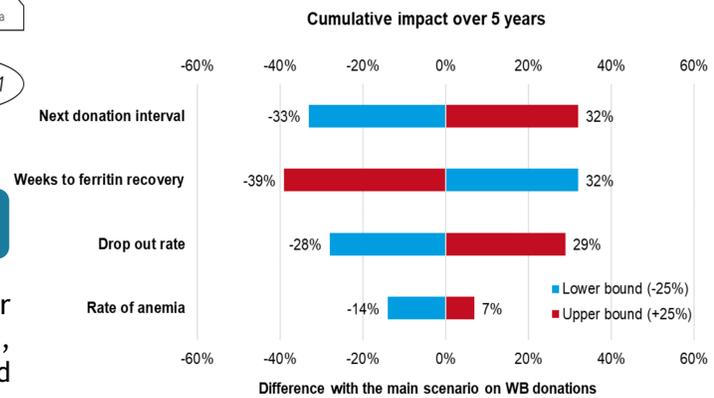
In the main scenario, 52,699 WB donations per year were estimated to be lost after one year (-8%), falling to 27,687 (-4.7%) after 5 years. IDs and anemias were reduced by 13.6% and 29.3%, respectively, after one year. The supplementation scenario increased the number of prevented IDs and anemias to 24.1% and 35.4%, respectively, after one year, and halved the number of anemias at 5 years. The latter scenario also had the least impact on the number of donations (-3.2% after 5 years).

**Table 2 - Estimated results in high-risk donors eligible for ferritin testing over a 5-year time-period**

Difference versus reference scenario	Reference scenario	Minimum scenario	Main scenario	Iron supp. <15 ng/ml
<b>Whole Blood donations loss</b>				
1 <sup>st</sup> year Change	662,286	-46,313	-52,699	-30,164
% Change	-	-7.0%	-8.0%	-4.6%
5 <sup>th</sup> year Change	594,627	-27,418	-27,687	-19,232
% Change	-	-4.6%	-4.7%	-3.2%
<b>Iron deficiency avoided</b>				
1 <sup>st</sup> year Change	369,847	-41,733	-50,315	-89,235
% Change	-	-11.3%	-13.6%	-24.1%
5 <sup>th</sup> year Change	296,411	-45,952	-53,333	-74,406
% Change	-	-15.5%	-18.0%	-25.1%
<b>Anemia avoided</b>				
1 <sup>st</sup> year Change	60,215	-16,460	-17,626	-21,339
% Change	-	-27.3%	-29.3%	-35.4%
5 <sup>th</sup> year Change	44,115	-10,666	-11,406	-13,295
% Change	-	-24.2%	-25.9%	-30.1%

Our study highlighted that after five years, donations recovered from donors in whom ID and anemia have been prevented do not compensate for the loss of donations resulting from deferral and drop-out. The maximum of WB donation loss occurred during the first year, decreasing thereafter over time, while the reduction in ID was stable over time (~50,000 IDs per year). Our study also showed that the impact of iron supplementation in 50% of donors with very low ferritin levels (<15 ng/ml) had a substantial positive impact on donations (+20,000) and IDs (-40,000) in the first year

**Figure 2 - Changes in the loss of donations after implementation of ferritin testing (main scenario)**



**Figure 3 - Sensitivity analysis of key parameters**

Sensitivity analyses showed that a shorter inter-donation interval (-25%) and a lower drop-out rate (-25%) had a more adverse impact on WB donation from repeat donors. This was confirmed by the 8% reduction in the average number of annual donations for repeat donors for all risk groups.

Due to extended inter-donation intervals, prolonged deferral periods and changes in donor behavior, its implementation will reduce the amount of WB collected from 5% to 8% in the high-risk subgroups after one year.

## Conclusion

**A ferritin testing policy resulting in delayed donations for ID donors is effective in reducing IDs and anemias, but significantly impacts the number of donations, thereby posing a self-sufficiency challenge.**

### References

1. Boulton F. Evidence-based criteria for the care and selection of blood donors, with some comments on the relationship to blood supply, and emphasis on the management of donation-induced iron depletion. *Transfus Med.* 2008;18:13-27
2. Fillet A, Martinlaud C, Malard L, Le Cam S, Hejl C, Chenus F, et al. Iron deficiency among French whole-blood donors: first assessment and identification of predictive factors. *Vox Sang.* 2021;116:42-52
3. Kiss JE, Brambilla D, Glynn SA, Mast AE, Spencer BR, Stone M, et al. Oral iron supplementation after blood donation: a randomized clinical trial. *JAMA.* 2015;313:575-83.