

Towards a value-based approach in hemophilia: indications from the FAR-BENE study

Paolo Angelo Cortesi^{1,2}



¹Research Centre on Public Health (CESP), University of Milano-Bicocca, Monza, Italy;

²Laboratory of Public Health, IRCCS Istituto Auxologico Italiano, Milan, Italy

The management of hemophilia has undergone a remarkable transformation in recent years^{1,2}. The advent of Extended Half-Life (EHL) factor concentrates, non-factor replacement therapies, and, more recently, gene therapies have fundamentally altered the diseases treatment and management and changed expectations of hemophilia community in terms of achievable health status³⁻⁵.

However, this progress is associated with a series of questions related to the impact in real-world clinical practice and the implication from the economic point of view. To address these issues, the focus of clinical and economic evaluations must shift beyond simple efficacy metrics to a more holistic concept of value. The concept of value in healthcare has been deeply discussed in the past, moving from quality-of-care assessment based on structures and process indicators to outcome assessment, ending in the current concept of value in healthcare, defined as the health outcomes achieved per dollar spent⁶⁻⁸ (Figure 1). Achieving high value must become the overarching goal of healthcare delivery, and this goal is what matters for patients and unites the interests of all actors in the system. If value improves, patients, payers, providers, and suppliers can all benefit, while the economic sustainability of the healthcare system could improve⁶⁻⁸. Therefore, to assess the value in the field of hemophilia, new indicators for the desired health outcomes made achievable by the transformation of treatment are required. Some possible set of outcome indicators have been already proposed in the last years^{3,4,9,10}, highlighting the importance of including indicators from both patients' and clinicians' points of view.

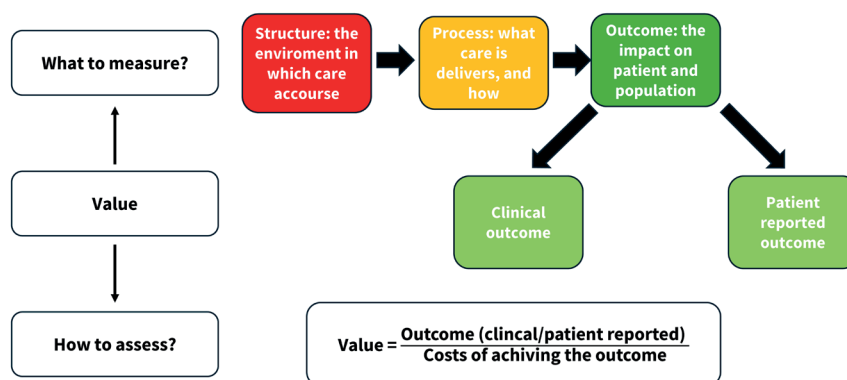


Figure 1 - The framework of value in health care

Correspondence: Paolo Angelo Cortesi
e-mail: paolo.cortesi@unimib.it

The use of systematic measurement of outcome indicators throughout the full cycle of treatment of a specific condition can provide the information needed to activate the positive loop that drives practice improvement and economic efficiency of healthcare system. The FAR-BENE (Pharmacoeconomic and Well-Being in Hemophilia) study¹², recently published, represents an important and timely effort to bridge this gap. By simultaneously monitoring pharmaceutical expenditure, clinical outcomes, and patient-reported outcomes (PROMs) in patients undergoing therapeutic switches, FAR-BENE provides real-world data to show the value produced at the Regional Reference Center for Inherited Bleeding Disorders, University Hospital of Turin, Italy, between 2017 and 2023, in a large cohort of patients with hemophilia (PwH).

First of all, looking at economic impact associated with the changes on treatment and management approaches, the study reported an overall cost stability over time, with a change in total expenditure of only € 19,996.48 (from € 12,947,580.44 in 2017 to € 12,967,576.92 to 2023) and a change in median cost per kilogram per year (€/kg/year) of € 3.00 (from € 2,458.00 in 2017 to € 2,461.00 in 2023) in all patients managed at the center. These economic data provide an indication of cost neutrality associated with the treatment and management innovations adopted in the center during the study period.

Further, regarding the impact on clinical and PROs, the study focused on PwH who switched medication during the observation period. In the 45 patients analyzed, the median

number of infusions per year significantly decreased from 156 to 91 ($p < 0.001$), the annualized bleeding rate (ABR) from 1 to 0 ($p < 0.001$) and pain numeric rating scale (NRS) from 3.5 to 0 ($p < 0.001$), with the median trough level increased from 3 IU/mL to 5 IU/mL ($p = 0.181$). Joint health did not show improvement, with a slight but not statistically significant increase (HJHS from 10 to 15, $p = 0.629$; HEAD-US from 7 to 8, $p = 0.774$), as expected once joint damage was already established. These outcome changes are reported alongside a stable median annual cost per patient, amounting to €194,376.00 in 2017 and €197,460.00 in 2023, while the median cost per kg per year shows a slight increase from €2,456.00 to €2,886.00.

These data can be used to assess the first series of value indicators to show how the center performed in terms of value produced for the patients who switched treatment over the time 2017-2023 (Table I). The value estimated with this data showed an increased efficiency with stable cost and significant improvement in ABR and NRS. The study also shows greater value created in the 35 patients with hemophilia A (-972.00 €/pts/y for an ABR reduction of 1 and -972.00 €/pts/y for an NRS reduction of 4). Finally, the study analyzed six different sub-populations to provide a picture of the values created in each of them and suggesting possible reasons for the differences observed within these sub-groups.

Even if FAR-BENE study is a first important step towards a value-based approach in hemophilia, it still misses some aspects that are needed to move this concept from a research topic to a health management approach.

Table I - Costs and outcomes from FAR-BENE study in the overall switcher population (No.=45) and the associated value¹²

No.=45 PwH	T ₀	Value indicators T ₀	T ₁	Value indicators T ₁	Delta	Value indicators T ₁ -T ₀
€/pts/y	€ 194,376.00	-	€ 197,460.00	-	€ 3,084.00	Cost stable
€/kg/y	€ 2,456.00	-	€ 2,886.00	-	€ 384.00	Cost slightly increase
ABR	1	€ 194,376.00 €/pts/y for a median ABR of 1	0	€ 197,460.00 €/pts/y for a median ABR of 0	-1	€ 3,084.00 €/pts/y for an ABR reduction of 1
NRS	3.5	€ 194,376.00 €/pts/y for a median NRS of 3.5	0	€ 197,460.00 €/pts/y for a median NRS of 0	-3.5	€ 3,084.00 €/pts/y for an NRS reduction of 3.5 points
HEAD-US	7	€ 194,376.00 €/pts/y for a median HEAD-US of 7	8	€ 197,460.00 €/pts/y for a median HEAD-US of 8	1	€ 3,084.00 €/pts/y for a HEAD-US increase of 1 point

*€/pts/y: median cost per patient per year; €/kg/y: median cost per kilogram per year; ABR: annualized bleeding rate; NRS: numeric rating scale; HEAD-US: Hemophilia Early Arthropathy Detection with Ultra Sound; T₀: pre-switch; T₁: post-switch.

First, to implement a value-based approach for healthcare management, indicators should be measured in real-time (e.g., during every outpatient follow-up visit or every hospital admission) and “online” in a prospective, and not just retrospective, manner, using purpose-built “ad-hoc” IT systems⁸. Second, the analysis of outcomes should be performed routinely at a shorter time interval (e.g. every year) as proposed by previous studies^{5,10}. Third, the analysis must initially be performed on the entire population (switchers and non-switchers) and not only on patients who change treatment. However, it should be noted that the sub-populations analyses are important and must be conducted to define the impact of each sub-group on the overall value produced by the center and to implement specific interventions where the value is low. Fourth, the study uses a set of outcome indicators already available in the center and lacks some recommended ones that could be helpful to better describe the health and value changes over time and understand where interventions are needed^{5,10}. Fifth, the FAR-BENE study is a single-center analysis and does not allow to compare the value produced by this center with what was obtained by others in Italy. Assessing value within centers that manage the same condition can help the system identify approaches and organization that are more efficient and reorganize healthcare following the high-value approach, considering the differences in geographical areas of the centers and in their case-mix.

Despite these limitations, the FAR-BENE study offers a clear signal of the need and possibility to move beyond the measure of factor consumption and bleeds. The complexity and costs of modern hemophilia treatments and management require a value-based approach that integrates economics aspects with comprehensive, clinical and patient-centric outcomes. A further effort is now required by the healthcare system to create the appropriate conditions to adopt and implement a standardized value-based approach, ensuring the possibility of improving the patients’ health by maximizing the healthcare resources available. The hemophilia community has undertaken significant work in recent years to define relevant outcome indicators aimed at implementing a value-based healthcare approach. We are now faced with the necessity of taking a further step by transforming this research work into

a useful tool to guide the management of patients with hemophilia using a value-based approach.

The Author declares no conflicts of interest.

REFERENCES

1. Srivastava A, Santagostino E, Dougall A, Kitchen S, Sutherland M, Pipe SW, et al. WFH guidelines for the management of hemophilia. *Haemophilia*. 2020; 26 (Suppl 6): 1-158. doi: 10.1111/hae.14046.
2. Mancuso ME, Mahlangu JN, Pipe SW. The changing treatment landscape in haemophilia: from standard half-life clotting factor concentrates to gene editing. *Lancet*. 2021; 397(10274): 630-640. doi:10.1016/S0140-6736(20)32722-7.
3. Manco-Johnson MJ, Warren BB, Buckner TW, Funk SM, Wang M. Outcome measures in Haemophilia: Beyond ABR (Annualized Bleeding Rate). *Haemophilia*. 2021; 27(S3): 87-95. doi: 10.1111/hae.14099.
4. Hermans C, Noone D, Benson G, Dolan G, Eichler H, Jiménez-Yuste V, et al. Hemophilia treatment in 2021: Choosing the “optimal” treatment using an integrative, patient-oriented approach to shared decision-making between patients and clinicians. *Blood Rev*. 2022; 52: 100890. doi: 10.1016/j.blre.2021.100890.
5. Cortesi PA, Rocino A, Preti D, Fragomeno A, Cucuzza F, Ceresi N, et al. Haemophilia management and treatment: an Italian survey on patients’, caregivers’ and clinicians’ point of view. *Haemophilia*. 2022; 28(2): 254-263. doi: 10.1111/hae.14504.
6. Landon SN, Padikkala J, Horwitz LI. Defining value in health care: a scoping review of the literature. *Int J Qual Health Care*. 2021; 33(4): mzab140. doi: 10.1093/intqhc/mzab140.
7. Donabedian A. The quality of care. How can it be assessed? *JAMA*. 1988; 260(12): 1743-1748. doi: 10.1001/jama.260.12.1743.
8. Porter ME, Teisberg EO. *Redefining health care: creating value-based competition on results*. Boston: Harvard Business School Press, 2006.
9. Porter ME. What is value in health care? *N Engl J Med*. 2010; 363(26): 2477-81.
10. van Balen EC, O’Mahony B, Cnossen MH, et al. Patient-relevant health outcomes for hemophilia care: development of an international standard outcomes set. *Res Pract Thromb Haemost*. 2021; 5(4): e12488.
11. Cortesi PA, Fornari C, Conti S, Pollio B, Boccalandro E, Buzzzi A, et al. The value-based healthcare approach to haemophilia: development of outcome measures for the evaluation of care of people with haemophilia. *Haemophilia*. 2024; 30(2): 437-448. doi: 10.1111/hae.14943.
12. Sella C, Valeri F, Dainese C, Porreca A, Scaldaferrri M, Cestino D, et al. FAR-BENE Study: pharmacoeconomics and well-being in hemophilia. Monitoring outcomes in light of pharmaceutical expenditure with focus on patients undergoing therapeutic switch. *Blood Transfus*. 2026; 24(1): 77-85. doi: 10.2450/BloodTransfus.1035.