Copenhagen Economics

THE IMPACT OF PLASMA-DERIVED THERAPIES IN EUROPE

The health and economic case for ensuring sustainable supply

March 2026

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The report references select data from Marketing Research Bureau (MRB) reports. For full access to MRB's datasets and reports, please contact MRB.

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Plasma-derived therapies are therapies derived from human plasma. They are manufactured using a fractionation process where the relevant proteins in plasma are separated out. Plasma is the single largest component of human blood and contains water, salts, enzymes, antibodies, and other proteins. Plasma-derived therapies are used to treat a wide range of (rare) diseases from bleeding disorders and inhibitor deficiencies to primary (PID) and secondary immunodeficiencies (SID), as well as neuroimmunological conditions.

The number of patients affected by diseases that can be treated by plasma-derived therapies is large and increasing. At the same time, there are concerns over the long-term supply of plasma, and in particular Europe's heavy reliance on US imports, while growing recognition of SID is expected to increase the need for IG.

Against this background, Takeda commissioned Copenhagen Economics (CE) to inform the debate by investigating the value of plasma-derived therapies to patients and the wider economy, and on policy options to secure the supply of plasma in the future. The report focuses on three main questions:

1. How do plasma-derived therapies benefit patients?
2. How does the plasma-derived therapies industry contribute to the economy?
3. How to secure a sustainable supply across Europe that keeps pace with the growth in therapies demanded by patients' needs?

Plasma-derived therapies benefit large numbers of patients

The number of patients that can benefit from plasma-derived therapies is significant. It is estimated that between 6,000 and 8,000 rare diseases exist, affecting 27 to 36 million Europeans. We estimate that 1.12 million patients in Europe suffer from the 12 most well-known rare diseases, which can all be treated with plasma-derived therapies, such as haemophilia and PID.

Beyond these rare diseases, increasing diagnosis of SID will further raise need for IG.

Patients benefit from plasma-derived therapies through two primary channels: a better management of their disease with an associated increase in life expectancy, and increased quality of life. These better outcomes also affect society in general since well-treated patients are more able to contribute to society through, for example, labour market participation. Additionally, healthcare treatments at home with plasma-derived therapies that allow for self-administration can create value for health systems and society by reducing costs and saving resources.

For some of the rare diseases treated with plasma-derived therapies alternative therapies also exist. These are often recombinant therapies that do not rely on human plasma and are instead manufactured using animal or other living cells.

However, plasma-derived therapies continue to be important to proper disease management for patients with some rare diseases despite the existence of alternative recombinant therapies for three reasons. Firstly, there are rare diseases for which no alternatives to plasma-derived therapies exist. Secondly, even if a recombinant alternative exists for a specific condition, it does not mean it will be available in all markets. Thirdly, when both plasma-derived and recombinant therapies are available, patients with the same disease may be treated with different therapies. Doctors prefer to have access to a range of therapies to tailor an optimal treatment approach, based on individual patient needs. The widespread use and co-existence of both plasma-derived and recombinant factor VIII is an example of this. There are thus no one-size-fits-all therapies for rare diseases, and the more therapy options available to patients, the better.

There is ongoing interest in both donor health and the health of patients receiving plasma-derived therapies. We have not found any evidence on adverse side-effects related to pathogen transmission on patients in this millennium, and we found limited evidence to suggest that plasma donations have adverse effects on donors. On patient safety, the risk of pathogen transmission cases is minimised within the plasma-derived therapies industry. Through diligent quality control process, companies adhere to regulatory requirements and industry voluntary standards. Furthermore, few adverse effects have been found for plasma donors, as, e.g., even relatively frequent donors have protein levels above reference values.

The plasma-derived therapies industry supports the European economy

The plasma-derived therapies industry supports the European economy through direct, indirect, and induced effects. The direct economic effects relate to production within the plasma-derived therapies industry. The indirect effects derive from sub-contractors to the plasma-derived therapies industry, e.g., at plasma collection centres, cleaning companies, or IT solution providers. The induced effects represent the value created by employees, both in the industry and its sub-contractors. To understand the order of magnitude, we derived indicative estimates of the three types of impact. The direct impact alone can amount to 6.6 billion EUR, with indirect and induced effects increasing the total economic contribution by another 7.7 billion EUR. Our indicative analysis suggests that the overall magnitude of the three types of impact could be around 14 billion EUR. As Europe strengthens its focus on resilience and security, it is important to invest in plasma and plasma-derived therapies to ensure a secure and sustainable supply for patients. This includes investing in the plasma-derived therapies ecosystem, safeguarding the economic and health benefits created by the industry, and ensuring that plasma collection and fractionation keep pace with patient needs and support long-term security of supply.

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Furthermore, the spending of donor compensation supports an estimated 151 million EUR per year of the induced effect, and spending in the wider economy of compensations to plasma donors in Germany, Austria, the Czech Republic, and Hungary supports 2,260 full-time equivalent jobs.

Plasma collection centres can themselves have further positive effects on the local community through a number of different channels such as employing staff, using local contractors, employees spending their income and collaborative partnerships.

There is a risk that the supply of plasma will not keep pace with the increasing patient need for plasma-derived therapies

The patient need for plasma-derived therapies is increasing. This drives an increase in the demand for plasma for fractionation despite the existence of recombinant and other alternative treatments.

While the patient need is increasing, the industry is constrained due to the scarcity of donated human plasma. Given the complexity and time needed to manufacture PDTs, the industry has a fixed production capacity and cannot scale up quickly. This potentially hinders the delivery of life-saving and quality-of-life-improving therapies to patients with rare diseases.

Thus far, Europe has relied heavily on imported plasma. Europe imported around 40 per cent of its plasma need for fractionation and is reliant on plasma imports from the US.

Plasma donations in Europe are not clearly differentiated from blood donations and are governed by the principle of voluntary and unpaid donations. However, what constitutes an unpaid donation varies from one Member State to another. In most European countries it is not possible to affect donation rates by other means than small tokens, refreshments, and similar. Only four countries in Europe allow for monetary compensation of donors and for plasma collection by private entities: Germany, the Czech Republic, Austria, and Hungary.

The functioning of the plasma-derived therapy industry is further shaped by reimbursement and procurement policies which vary across countries. An important development, which we refer to as 'commoditisation', means that therapies with different properties are treated as homogenous, undifferentiated products and therefore procured and priced as such.

There can be risks of over commoditisation for plasma-derived therapies which can stem from reimbursement approaches together with the finite budgets available for healthcare systems. For example, different patient groups need immunoglobulin (IG) therapies with different characteristics. Reimbursement policies can vary depending on IG therapy, and in some countries only one specific type of product is reimbursed. This can lead to patients using a suboptimal therapy for their specific medical need, even if more optimal ones would be available.

There is a strong case for considering alternative ways to secure the supply of plasma in Europe

Recent focus on supply chain risks has sparked debate about medicine stockpiling in the EU. However, plasma-derived therapies are not suited for stockpiling, since plasma is limited, therapies have short shelf life, and cost would likely increase from stockpiling. Moreover, as Europe's need for plasma-derived therapies is projected to increase, local stockpiling could reduce global availability, undermine the principle of solidarity, and exacerbate access risks in smaller countries. Instead, resilience can be strengthened by investments in plasma collection capacity, including better use of recovered plasma by leveraging existing standards for blood and plasma collection. In the four European countries where private collection is possible, 43 new commercial centres were opened between 2022 and 2024, and the average collection volumes in these countries are substantially higher than the EU average, but still below US levels.

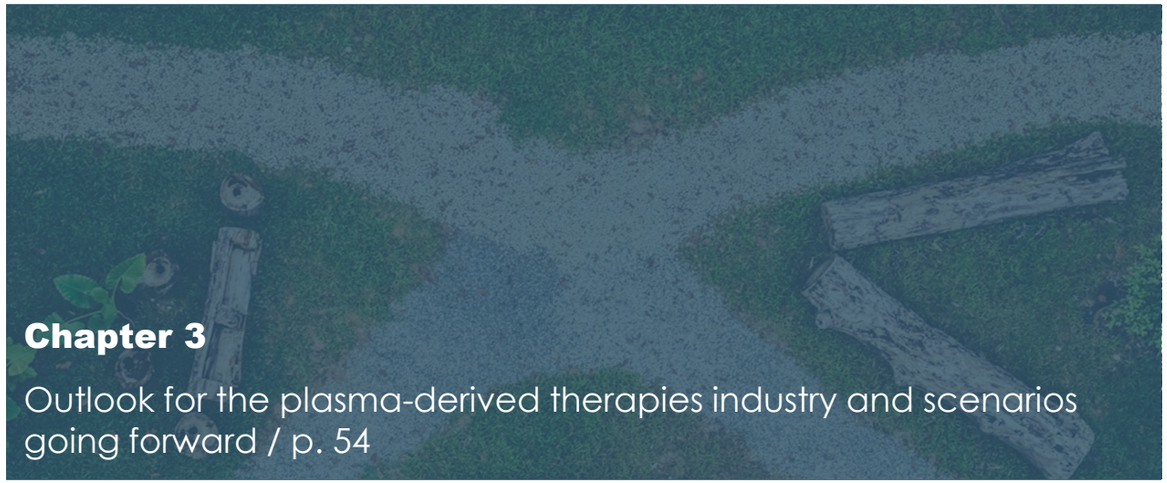
While some of the market issues surrounding the industry could be alleviated through more effective procurement, a re-evaluation of donation schemes would be needed to secure European plasma supply. We reviewed a range of options recognizing the relevant ethical considerations.

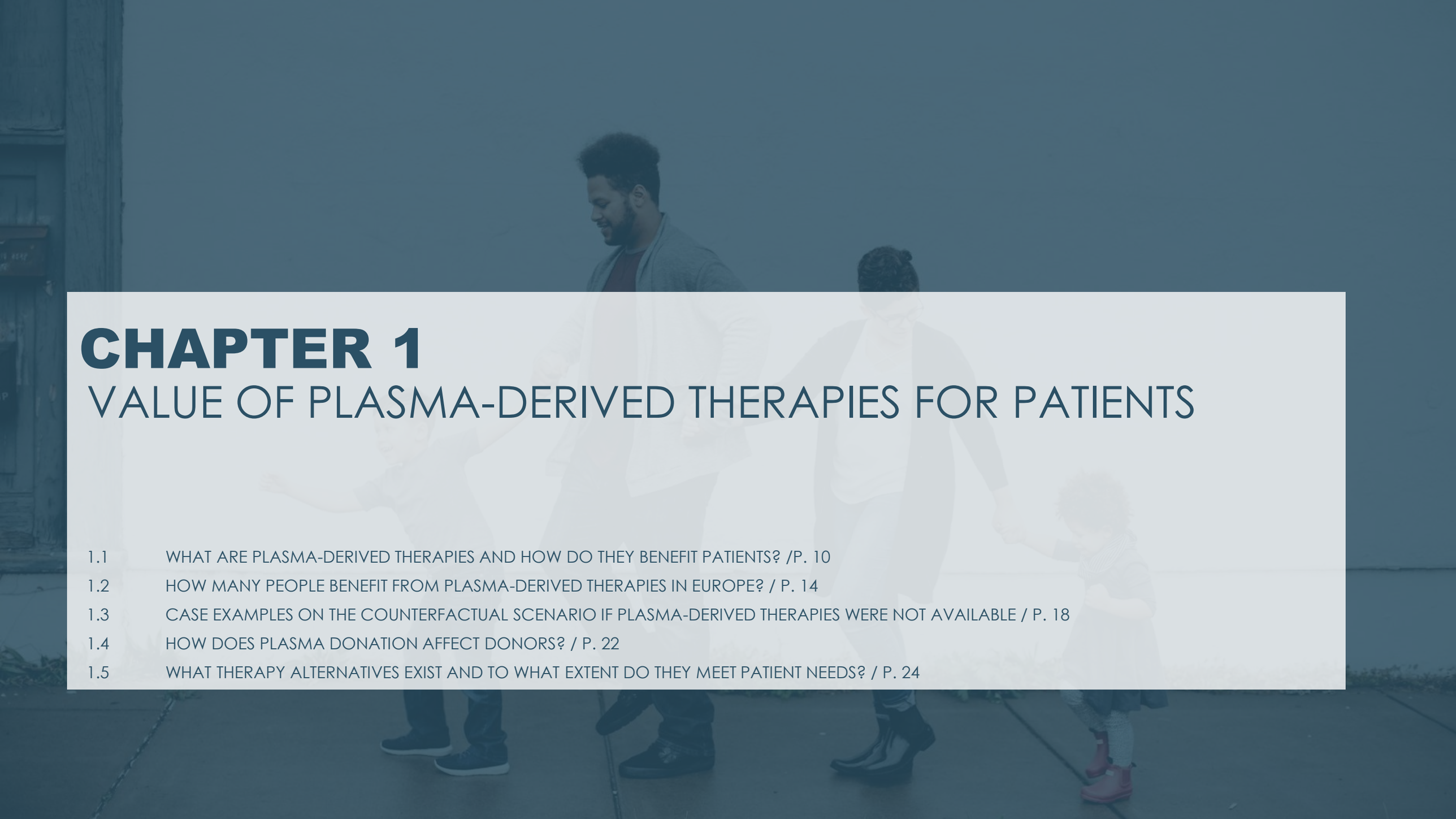
Reimbursement of donors' incurred expenses associated with the donation by a flat fee is ethically acceptable, compatible with the principle of voluntary and unpaid donations, and in line with European legislation. However, despite this, such reimbursements are not available in all European Member States. Monetary and non-monetary compensation to mitigate disincentives (e.g., time commitments) associated with donations is also ethically acceptable and compatible with the principle of voluntary and unpaid donations, insofar as the compensation does not incentivise individuals to donate who would otherwise not have chosen to do so. European countries that provide monetary compensation have substantially higher donation rates than those who do not and there is no clear evidence of a so-called crowding out effect of non-compensated blood donations in countries where plasma donors are monetarily compensated.

Overall, there appears to be a case for revisiting donation schemes and increasing the supply of plasma in Europe. A paradigm shift in the compensation of plasma donors in Europe that includes a small monetary or non-monetary compensation will be ethically acceptable, significantly increase donations, and make the European supply of plasma-derived therapies more resilient to shocks in the supply chain and dependency on US plasma, especially for indications with no synthetic alternatives. At the same time, such compensations will ensure that plasma used for fractionation in Europe abides to the principle of voluntary and unpaid donations.

Abbreviations

AI	Artificial intelligence
CAGR	Compounded average growth rate
CIDP	Chronic inflammatory demyelinating polyneuropathy
CPI	Consumer price index
cSCIG	Conventional subcutaneous immunoglobulin
EU	European Union
fSCIG	Facilitated subcutaneous immunoglobulin
GDP	Gross domestic product
HIV	Human Immunodeficiency Virus
IG	Immunoglobulin
IgG	Immunoglobulin G
IO	Input-Output
IU	International unit
IVIG	Intravenous immunoglobulin
MRB	Marketing Research Bureau
NGO	Non-governmental organisations
NHS	National Health Service
OECD	Organisation for Economic Co-operation and Development
PID	Primary immunodeficiency
PPTA	Plasma Protein Therapeutics Association
SCIG	Subcutaneous immunoglobulin
SF-36	Short Form Health Survey with 36 questions
SID	Secondary immunodeficiency
vWF	von Willebrand factor





CHAPTER 1
VALUE OF PLASMA-DERIVED THERAPIES FOR PATIENTS

Chapter 1 – Main conclusions

Plasma-derived therapies benefit patients

Plasma-derived therapies are derived from human plasma using a fractionation process where the relevant proteins in plasma are separated out. Plasma is the single largest component of human blood and contains water, salts, enzymes, antibodies, and other proteins.[1] Plasma-derived therapies are used to treat a wide range of (rare) diseases from bleeding disorders and inhibitor deficiencies to PID and SID.

Treatment with plasma-derived therapies has two main goals: to increase life expectancy and improve quality of life.[2] For example, the survival rate for patients with PID is similar to the survival rate in the general population.[3] Similarly, life expectancy of patients with severe haemophilia, for example, has increased from less than 20 years to around 63 years today, and patients treated from infancy can now expect relatively few bleedings and close to normal life expectancy.[4] Patients with rare diseases are likely to have additional conditions co-occurring with their primary condition (co-morbidities). Well-treated patients are often associated with fewer co-morbidities, which implies savings for healthcare systems.[5] For example, treating SID in patients who have undergone cancer therapy can reduce the risk of severe infections and help protect the value of prior investments in their treatment.[6]

Treatment with plasma-derived therapies significantly improves patient quality of life if the alternative is no treatment.[7] This affects both the physical and the psychological aspects of quality of life as well as social life and has large impacts on the everyday life of patients. Furthermore, improvements in quality of life not only affect the individual but also help the patient contribute to society in terms of, for example, increased labour market participation and decreased disability benefits. Additionally, plasma-derived therapies administered at home and by the patient themselves can create value for appropriate patients, health systems and society by reducing costs and saving resources.

A large patient population

There are between 6,000 and 8,000 rare diseases[8], and an estimated 27 to 36 million Europeans are affected by a rare disease.[9] We estimate that around 1.12 million patients in Europe suffer from the 12 most well-known rare diseases, such as haemophilia and PID, which can all be treated with plasma-derived therapies. Patients suffering from rare diseases frequently participate in testing new plasma-derived therapies through clinical trials.

Limited evidence on adverse health effects for donors

Plasma donors' levels of proteins are lower than that of non-donors, but not lower than a given reference level and do not imply adverse health effects for donors.

Plasma-derived therapies are safe to use for patients

Pathogen safety depends on safeguard measures, which ensure that only plasma from healthy donors is used in the manufacturing process. Further, the plasma production safety measures self-imposed by the plasma-derived therapies industry go beyond those required by regulation. With plasma-derived therapies, zero risk of pathogen transmission does not exist. However, in 2009, a study found that since 1997, there have been no new cases of disease transmissions,[10] which implies that this hypothetical risk is practically limited to new, unknown diseases.

Patients require multiple treatment options

Plasma-derived therapies are not interchangeable and a one-size-fits-all but are biological treatments that differ in terms of concentration, tolerance, and more as well as mode of administration. A wide range of plasma-derived therapies thus enable patients and clinicians to use the best possible care specifically for that patient.

Plasma-derived therapies are key to proper disease management for patients with rare diseases and co-exist with recombinant therapies in some areas for two reasons. First, there are rare diseases for which no alternatives to plasma-derived therapies exist. Second, even if a recombinant alternative exists for a specific condition, it does not mean it will be available in all markets. When both plasma-derived and recombinant therapies are available, patients with the same disease still use different treatments. Doctors prefer a range of therapies in their toolbox to be able to tailor an optimal treatment based on patient needs. The widespread use and co-existence of both plasma-derived and recombinant factor VIII is an example of this. There are thus no one-size-fits-all therapies for rare diseases, and the more therapy alternatives available to patients, the better.

Box 1. Plasma-derived therapies

- increase life expectancy ☑
- improve patients' quality of life ☑
- lower healthcare expenditures on co-morbidities and sequelae ☑
- provide socioeconomic gains ☑

Source: Copenhagen Economics.

Notes: 1) Plasma Protein Therapeutics Association (PPTA (n.d.)). / 2) Grifols (2024). / 3) Joshi et al. (2009). / 4) Aledort (2016). / 5) García-Pérez et al. (2021). / 6) Shah et al (2023) / 7) Abdou et al. (2009). / 8) A condition is defined as rare (or orphan) if it affects less than 5 in 10,000 people in the European Union. European Commission (2025d). / 9) European Rare Disease Organisation (2025). / 10) Grillberger et al. (2009).

1.1
WHAT ARE PLASMA-DERIVED THERAPIES AND HOW DO THEY BENEFIT PATIENTS?

Plasma is the source for the development and manufacturing of plasma-derived therapies

What is plasma?

Plasma is the single largest component of human blood and contains salts, enzymes, antibodies, other proteins, and water. In particular, 7 per cent of plasma consists of proteins like immunoglobulins (IG), albumin, clotting factors, C1 esterase inhibitor, and alpha-1 proteinase inhibitor.

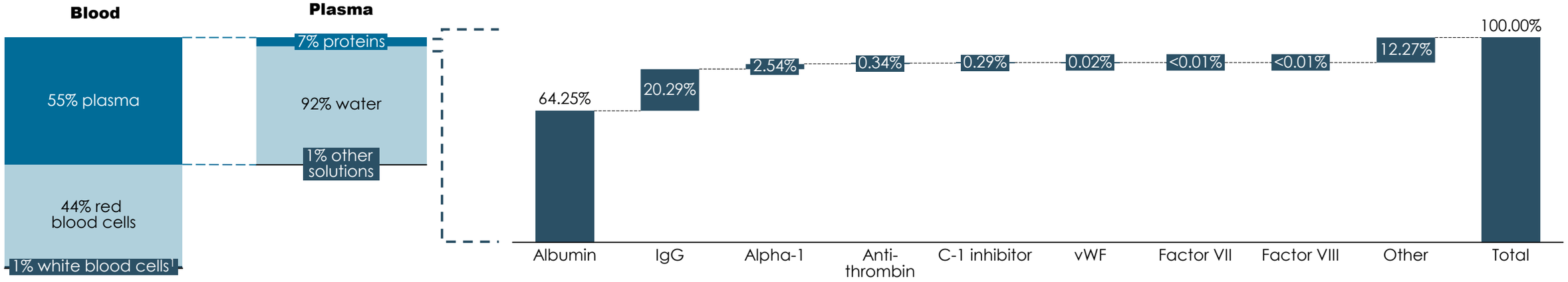
Plasma is collected using either source plasma from plasmapheresis donations or recovered plasma from whole blood donations. During plasmapheresis, plasma is separated from red blood cells and other cellular components of blood, which are then returned to the donor during the plasma donation process.[1]

What are plasma-derived therapies?

Plasma-derived therapies are treatments derived from human plasma. The relevant proteins in plasma are separated out in the fractionation process that enables the production of therapies to treat specific diseases and conditions. For example, separating out C1 esterase inhibitor from plasma in the fractionation process is part of the process to develop therapies used to treat hereditary angioedema, and precipitating out von Willebrand factor is part of the process to manufacture therapies to treat von Willebrand disease.

The patient need for plasma-derived therapies is the driver of the demand for plasma components. Furthermore, the demand for plasma is affected by the composition of plasma, see Figure 1, as the number of donations needed to treat one patient for one year differs a lot between diseases. For example, 130 donations are required to treat a patient with PID for one year, whereas 1,200 donations are required to treat a patient with haemophilia A.[2]

Figure 1. Composition of blood and plasma
Per cent of components that a litre of blood consists of



Note: IgG = immunoglobulin G, alpha-1 = alpha-1 antitrypsin, vWF = von Willebrand factor. The category 'Other' includes fibrinogen, prothrombin, alpha-2 macro, FIX, FXI, and more. / 1) White blood cells and platelets.
Source: PPTA (2020a) and Burnouf (2008).

Notes: 1) PPTA / 2) PPTA (2023a).

Plasma-derived therapies offer life-saving treatments to patients who suffer from rare diseases and other conditions

Plasma-derived therapies are vital to patients because they…

Increase life expectancy

Treatment of haemophilia is a useful example of the impact of plasma-derived therapies due to the amount of research available and the long-term use of these treatments. Today, patients with haemophilia who are treated appropriately from infancy and do not develop inhibitors can expect a normal life expectancy and relatively few bleeding episodes due to plasma-derived and recombinant factor VIII. The median lifespan for persons with severe haemophilia is 63 years.[1] Recombinant factor VIII became widely available after the completion of clinical trials in 1994. Even before then, a Swedish study found that median life expectancy for patients with severe haemophilia increased from 11 years during 1831-1920 to 56.8 years during 1961-1980.[2]

Another example of increased life expectancy is seen in patients with PIDs: the proportion of patients with PIDs who are alive 10 years after diagnosis is 93.5 per cent, which is similar to the survival rate in the general population.[3]

Improve quality of life

Significant improvements in health-related quality of life have been found.[4] For example, a study found that adverse health-related quality of life scores decreased from 49.15 before IG therapy to 15.9 after 12 months of IG infusions, indicating a substantial improvement in quality of life, which remained better than baseline even three months after treatment ended (22.1).[5] These quality of life gains were driven by fewer infections, reduced antibiotic use, and fewer infection-related hospitalisations during IG treatment.[5]

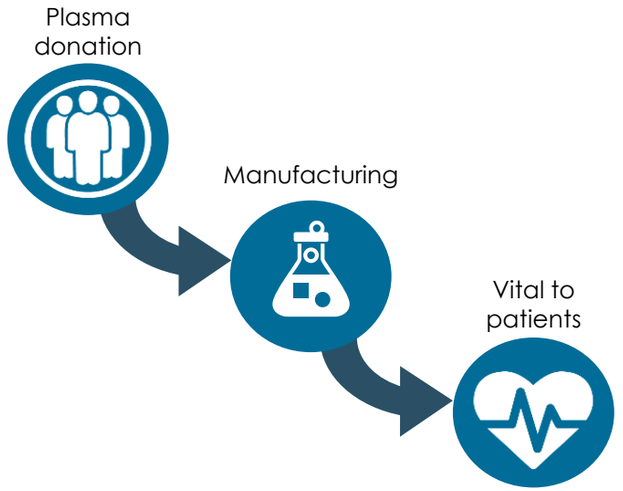
Provide economic gains and healthcare savings

Improvements in quality of life not only affect the individual, but also society more broadly through 1) fewer hospitalisations and other reductions in healthcare utilisation, which can lower healthcare expenditures and 2) socioeconomic gains such as increased labour market participation. 57 per cent of patients with PID were hospitalised prior to being diagnosed and treated with IG therapy, whereas the hospitalisation rate after being treated dropped to 25 per cent. Similarly, the number of sick days for these patients dropped from 20 to 5 days with IG therapy. [6]

Treat more than patients with rare diseases

In addition to treating rare diseases, plasma-derived therapies are used to treat critical illnesses. Albumin is commonly used for hypovolemia or shock, burns, hypoalbuminemia, surgery or trauma, cardiopulmonary bypass, acute respiratory distress syndrome, haemodialysis, and more.[7] IG therapy is generally effective in reducing the frequency and severity of severe bacterial infections in patients with SID.[8] Clotting factor concentrate is used in the management of perioperative bleeding.[9]

Figure 2. From plasma donation to value generation



Source: Copenhagen Economics.

Notes: 1) Aledort (2016). / 2) These were available from 1994 and onwards, Powell (2009). / 3) Joshi et al. (2009). / 4) Abdou et al. (2009), Routes et al. (2016), and Modell et al. (2017). / 5) Abdou et al. (2009). / 6) Boyle and Scalchunes (2008). / 7) Mendez et al. (2005). / 8) Benbrahim et al. (2019). / 9) Godier et al. (2019).

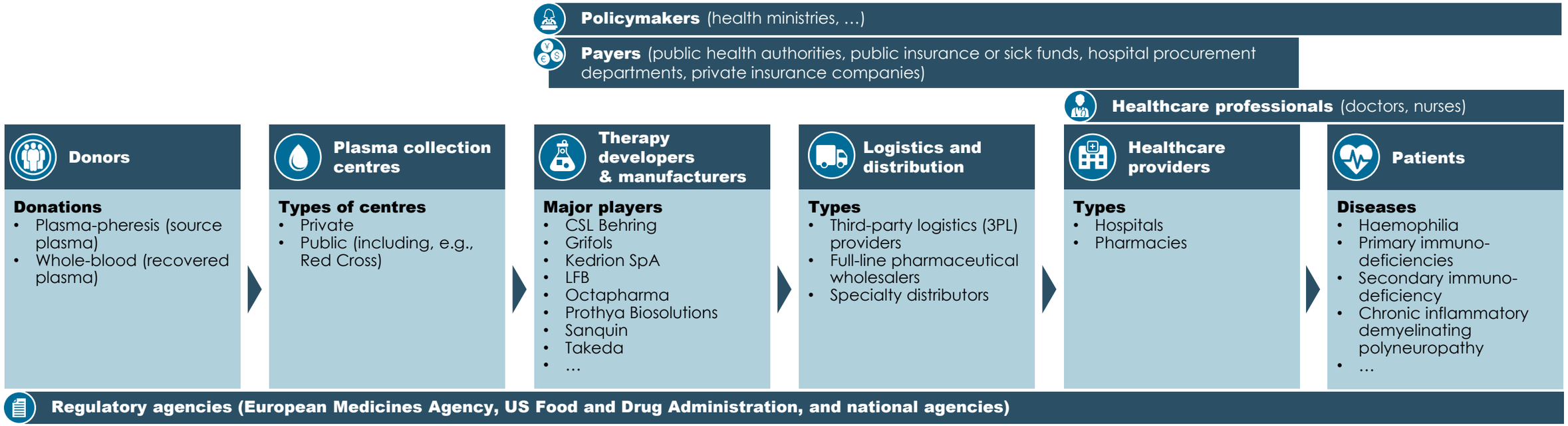
The plasma-derived therapies value chain starts and ends with people

From people to people

The value chain in the plasma-derived therapies industry starts and ends with people, see Figure 3. The key players in transforming the plasma to enable a delivery of health from one person to another are donors and the pharmaceutical companies, and regulatory agencies along with payers and policymakers play a key role throughout the entire value chain.

Plasma is collected from volunteers using either plasmapheresis, where plasma is separated from the blood during the donation, or a whole-blood donation, after which plasma is separated from the blood. The collection is done in either specialised private or public collection centres. After the collection, plasma is either sold/tendered to fractionators and/or fractionated domestically or through contract fractionation.[1] The plasma-derived therapies are produced by pharmaceutical companies or specialised fractionation centres which develop and manufacture plasma-derived therapies. After the fractionation process, the product is distributed to healthcare providers (hospitals and pharmacies) where it reaches patients after being prescribed by a healthcare professional. The flow of plasma-derived therapies from therapy developers and manufacturers to healthcare providers and patients occurs via agreements with payers governed by conditions formulated by policymakers and the overall supply chain is governed by regulatory agencies.

Figure 3. The supply chain in the plasma-derived therapies industry



Note: Major players are in alphabetical order. Arrows indicate flow of plasma-derived therapies through the supply chain. / Source: Copenhagen Economics Inspired by Creative Ceutical (2015).

Notes: 1) If a domestic or contract fractionation is in place, the product produced through manufacturing of the plasma is returned to the country where the plasma originated from. Plasma-derived therapies purchased commercially are very likely to rely on plasma sourced from donor pools outside the country.

1.2
HOW MANY PEOPLE BENEFIT FROM PLASMA-DERIVED THERAPIES IN EUROPE?

We estimate that around 1.12 million European patients are affected by rare diseases that could potentially be treated with plasma-derived therapies

Plasma-derived therapies can benefit many patients

We estimate that 1.12 million Europeans (out of 600 million people in Europe, excluding transcontinental countries) are affected by one of the 12 most common (groups of) rare diseases that can be treated with plasma-derived therapies. An overview of disease prevalence and the estimated number of patients in Europe is shown in Table 1. Using prevalence estimates implies that both patients who are diagnosed and people who are not diagnosed are included in the numbers to the extent that they are available in the literature. The table includes bleeding disorders such as haemophilia A and von Willebrand disease , PID, and immune thrombocytopenic purpura. A condition is defined as rare (or orphan) if it affects less than 5 in 10,000 people in Europe.[1] There are between 6,000 and 8,000 rare diseases, and an estimated 27 to 36 million Europeans are affected by a rare disease.[2]

The patient population in Europe suffering from one of the 12 most common rare diseases is significant. For example, it is around three times larger than the incidence of breast cancer in the European Union (EU) 27 in 2022 of 375,000 individuals[3]. Unlike cancer, full recovery is not possible for patients suffering from a rare disease. To ensure their survival and quality of life, on-going treatment is required.

In addition to rare diseases, plasma-derived therapies are used to treat several critical conditions such as severe burns, leukaemia, and paediatric human immunodeficiency virus. Furthermore, the therapies are also used to treat SIDs or as part of cancer therapy. In 2022 alone, there were 4.4 million new cases of cancer in Europe.[4] The appendix contains a table with critical conditions and the plasma-derived therapies used to treat them.

Table 1. Estimate European patients affected by rare diseases

Condition	Prevalence estimate (interval in parenthesis)	Number of patients in Europe
Haemophilia A (factor VIII deficiency)	3.5 in 50,000 [Na][1]	42,000
Haemophilia B (factor IX deficiency)	0.95 in 50,000 [0.8-1.1][2]	11,400
von Willebrand disease	2.7 in 50,000 [2.2-8.3][3]	32,400
Other factor deficiencies (e.g., factor I, II, V, V+VIII, VII, X, XI, and XIII)	Na (observation study)	9,700[4]
Antithrombin III deficiency	20.8 in 50,000 [16.6-25][5]	249,600
Alpha-1 antitrypsin deficiency	11.8 in 50,000 [Na][6]	141,600
Hereditary angioedema, types 1 and 2	0.63 in 50,000 [0.5–0.75][7]	7,560
Primary immunodeficiency (PID)	43.15 in 50,000 [25.5-60.75][8]	517,800
Chronic inflammatory demyelinating polyneuropathy (CIDP)	1.4 in 50,000 [0.34-5.12] [9]	16,800
Immune thrombocytopenic purpura	7.25 in 50,000 [4.5-10][10]	87,000
Multifocal motor neuropathy	0.3 in 50,000 [Na][11]	3,600
Kawasaki disease	1.2 in 50,000 [0.75-1,65][12]	516
Total		**1,119,976**

Note: 1) List obtained from PPTA, and industry experts. Patient numbers are mostly rounded to nearest 100. Other studies use lower patient populations for some conditions, see, e.g. Vintura (2020) on PID by relying on estimates based on registry data on diagnosed patients. The PID prevalence is estimated based on survey data, which is estimated as 1 in 2,000 children and 1 in 1,200 for all persons, see Boyle and Buckley (2007). References 1-12 on prevalence estimates, European populations, and more are available in the appendix.

Notes: 1) European Parliament and the Council (2000), Regulation (EC) No. 141/2000, Article 3.1.a. / 2) European Commission; Rare diseases. / 3) Europa Donna (n.d.). / 4) Elmadani et al. (2025).

Individuals all over Europe are treated with plasma-derived therapies, and they should have the same availability as patients treated with other medical products – case example using PID

Every country in Europe has patients with PID

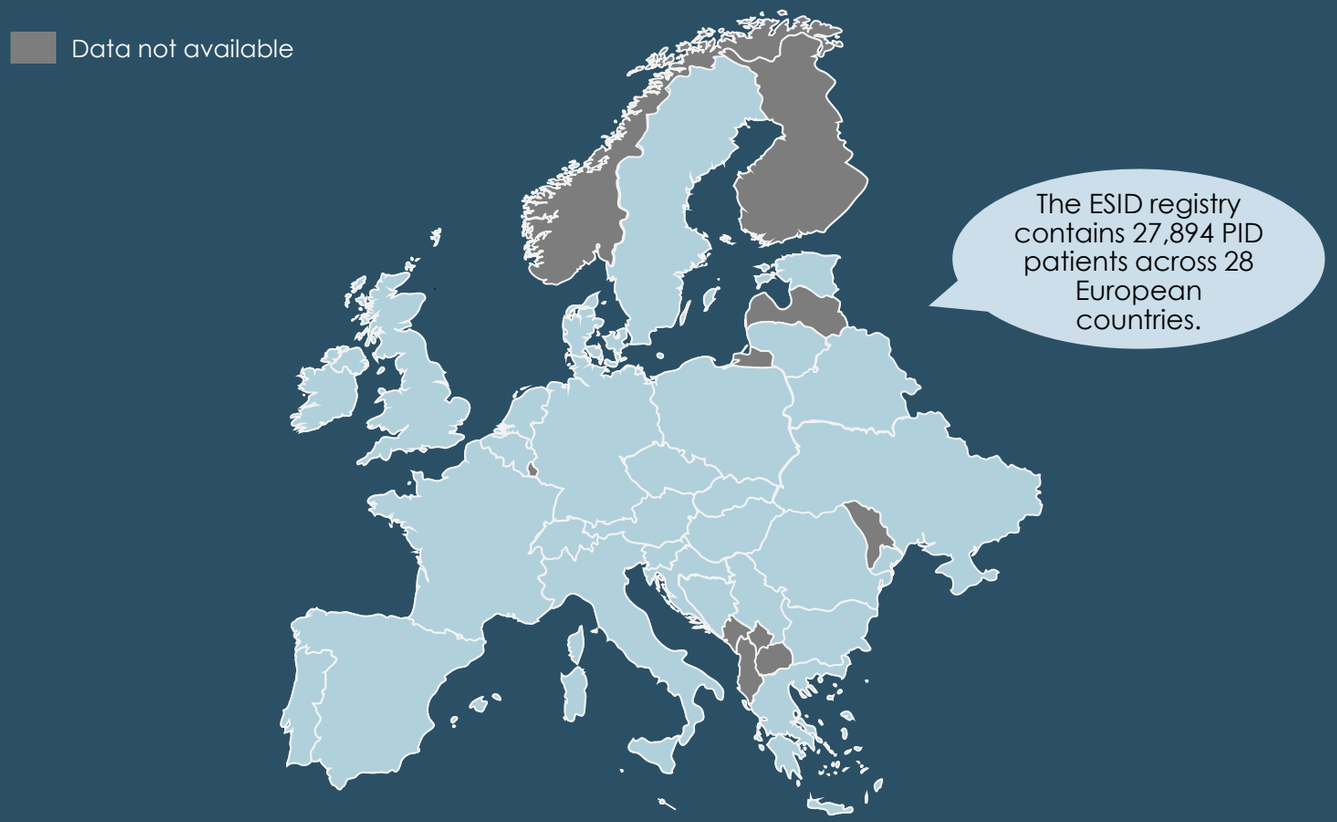
Diseases that are treated with plasma-derived therapies are found throughout Europe. Figure 4 shows a map of countries with registered PID patients. The European Society for Immunodeficiencies (ESID) registry contains 27,894 patients with PID in Europe (excluding transcontinental countries).[1] This is a lower bound since the data are not available in some countries and since the registry only includes diagnosed patients who are registered in a database. Also, research suggests that PID is heavily underdiagnosed,[2] which explains the discrepancy between the number of diagnosed PID cases and the estimated prevalence of PID, see page 15. Every country of Europe for which registry data is available – from Portugal and Spain over France and Germany to the Czech Republic, Poland and Ukraine – has citizens that require treatment. In France alone, 9,113 PID patients are registered.[1]

Box 2. Orphan drugs

> Patients with such conditions deserve the same quality, safety, and efficacy in medicinal products as other patients.
>
> (…) the Commission shall (…) support research into, and the development and availability of, orphan medicinal products.

Source: European Commission (2000).

Figure 4. European countries with registered PID patients, 2020-2025
Number of patients



Note: This number of registered patients is a conservative estimate of the true prevalence of patients with PID (see also the table on the previous page). The ESID registry contains a total of 30,628 patients including the 28 European countries included here and in addition Iran, Türkiye, Egypt, Russia, and Israel.
Source: Kindle et al. (2025).

Notes: 1) Kindle et al. (2025). The ESID registry contains a total of 30,628 patients including the 28 European countries included here and in addition Iran, Türkiye, Egypt, Russia, and Israel. / 2) Meyts et al. (2021).

An estimated 8,423 people from Europe participated in clinical trials involving the 12 most common rare diseases in the 2010s

Patients help develop and test new treatments

The industry is investing in research and development to develop plasma-derived therapies and recombinant alternatives for patients with rare diseases.

Patients with rare diseases are actively involved in helping researchers develop and test new treatments. To showcase how many patients are actively involved, we have estimated the total number of patients involved in clinical trials in the last ten years, see Table 2. These clinical trials are related to the 12 specific rare diseases but may be related to the development and testing of either plasma-derived therapies or recombinant alternatives.

There were 265 clinical trials in Europe with the 12 (groups of) conditions listed in Table 2 in the period 1 January 2015 to 1 July 2025. An estimated 8,423 Europeans participated in a clinical trial in that period, and 19,905 individuals participated world-wide (including Europe).

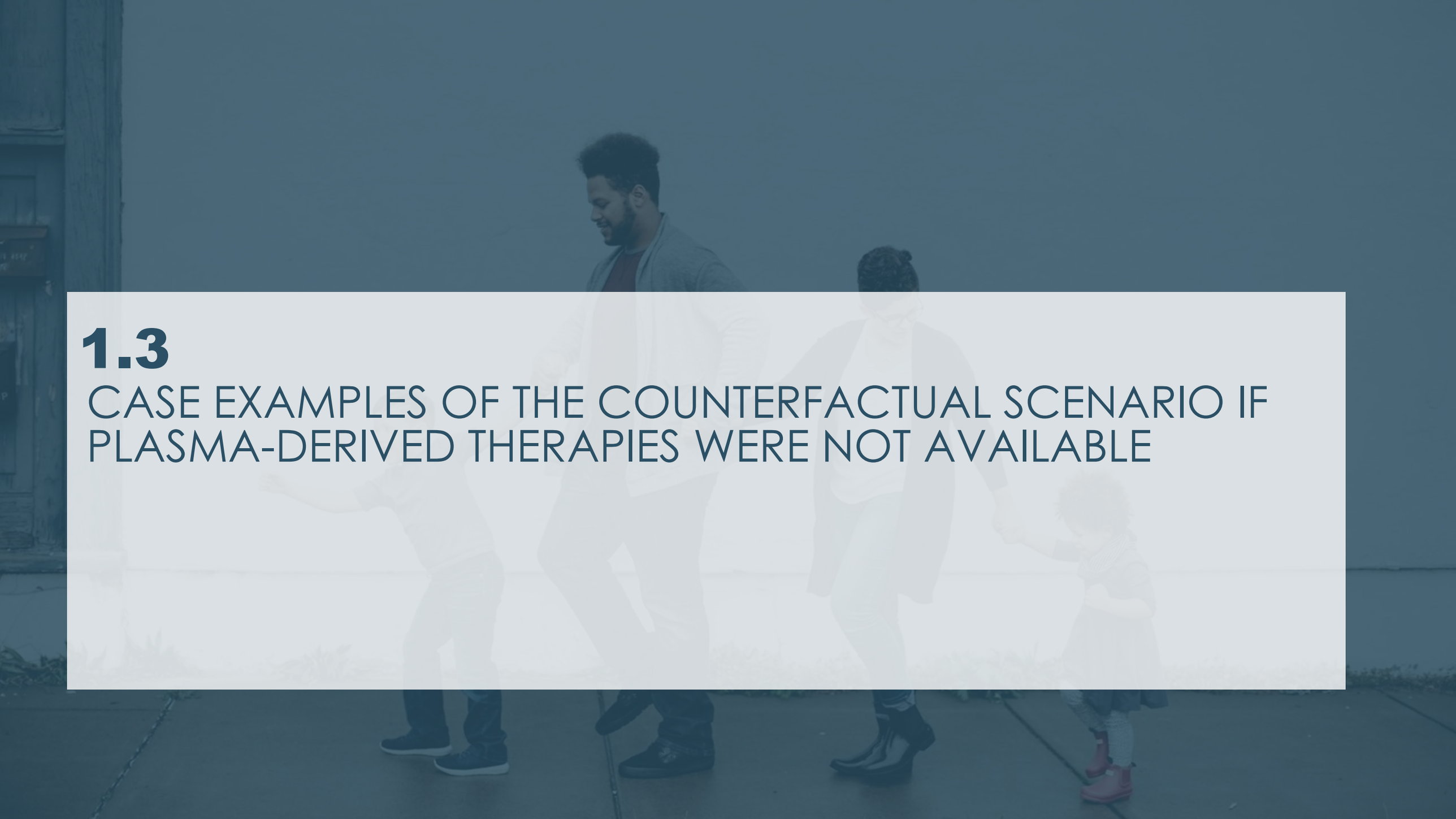
From 2018 through 2022, the number of clinical trials for rare diseases increased constantly, with over 16,000 studies performed globally.[1] These all rely on the willingness and goodwill of patients to participate.

Table 2. Estimate of European patients participating in clinical trials
Number of patients, 2015-2025

Condition	Number of clinical trials	Participants in the EEA, actual[1]	Participants worldwide, actual[1]	Participants in the EEA, extrapolated[2]	Participants worldwide, extrapolated[2]
Haemophilia A (factor VIII deficiency)	104	1,849	4,638	3,205	8,175
Haemophilia B (factor IX deficiency)					
von Willebrand disease	14	85	165	198	385
Other factor deficiencies (e.g., factor I, II, V, V+VIII, VII, X, XI, and XIII)	10	371	887	464	1,109
Antithrombin III deficiency	2	Na	Na	Na	Na
Alpha-1 antitrypsin deficiency	18	161	309	414	795
Hereditary angioedema, types 1 and 2	35	653	1,975	994	3,005
Primary immunodeficiency (PID)	12	298	1,013	1,116	2,026
Chronic inflammatory demyelinating polyneuropathy (CIDP)	20	558	1,013	1,082	2,660
Immune thrombocytopenic purpura	40	541	1,330	1,082	2,660
Multifocal motor neuropathy	4	56	74	112	148
Kawasaki disease	6	109	295	327	885
Total	**265**	**4,681**	**11,104**	**8,423**	**19,905**

Note: Number of clinical trials and participants relates to the period 1 January 2015 to 1 July 2025. / 1) Only including clinical trials where participant numbers are available / 2) Including all clinical trials. In the case of missing participant numbers, the condition-specific mean participant number is used.
Source: Copenhagen Economics based on the European Clinical Trial Register (ECTR).

Notes: 1) Novotech (2023).



1.3
CASE EXAMPLES OF THE COUNTERFACTUAL SCENARIO IF PLASMA-DERIVED THERAPIES WERE NOT AVAILABLE

Case: Patients with immunodeficiencies treated with IG have better health and quality of life

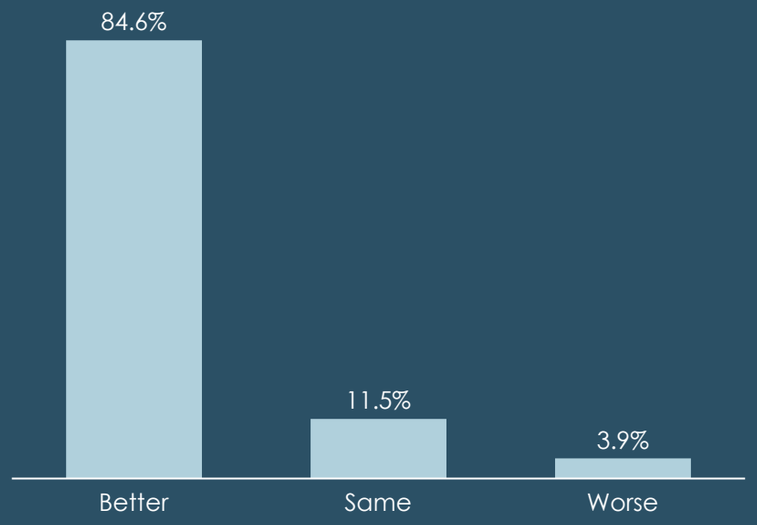
Treatment leads to improved health

Treatment with IG in patients with SID has been shown to reduce infection frequency, emergency room visits, and hospitalisations. Patients also report better self-assessed health after initiating IG treatment. An example is shown in Figure 5. It depicts results from a study that examined self-assessed health developments of patients after initiation of IG replacement therapy, where 84.6 percent perceived their health as better than before IG replacement therapy, while only 15.4 percent reported the same or worse health.

Treatment leads to higher quality of life

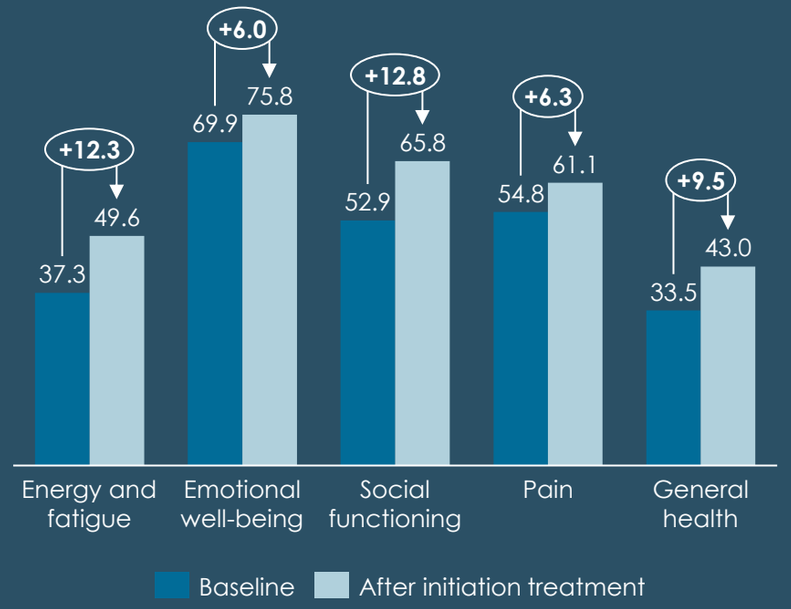
Patients with PID consistently report higher quality of life from treatment. Figure 6 shows an example of this using the Short Form Health Survey with 36 questions (SF-36). Across different domains, the quality of life of PID patients improves from 6.3 points for pain to 12.8 points for social functioning. These are substantial changes and will likely have large effects on patients.

Figure 5. Patient-reported health status among SID patients after IG treatment initiation
Share of patients



Note: SID patients were asked how they perceived their overall health status after initiation of IG replacement therapy: better, same or worse. N = 78. Source: Abadeh et al. (2023).

Figure 6. Quality of life by component among PID patients
Score on the SF-36



Note: The figure shows weighted averages of the SF-36 scores for SCIG (N= 93) and IVIG (N=11) to indicate the general improvement of initiating treatment. Source: Anterasian et al. (2019).

Notes: 1) Van Wilder et al (2021). / 2). Abadeh et al. (2023). / 3) Anterasian et al. (2019).

Case: Treatment with IG yields significant socioeconomic gains and reductions in healthcare expenditures – an illustration with research from the USA

Reductions in healthcare expenditures

Proper treatment of patients is associated with healthcare savings since well-treated patients are less likely to have co-morbidities and as such are less likely to require treatment for these. By way of illustration, Figure 7 shows how treating patients with PID with immunoglobulin G (IgG) reduces the expenditures to the treatment of co-morbidities with 28,021 USD per patient per year. In addition, reductions in the number of days a patient is hospitalised, the number of physician and ER visits, and the cost of other medicines (in particular antibiotics) yield a significant reduction as well. These amount to USD 81,009 per patient per year.

Socioeconomic gains

Well-treated patients are better able to participate in activities that benefit both themselves and society. Examples of such activities are increased labour market participation and productivity, reduced absence from school or work, and more. The socioeconomic gain from a well-treated patient is USD 4,875 per patient per year when only considering absence.

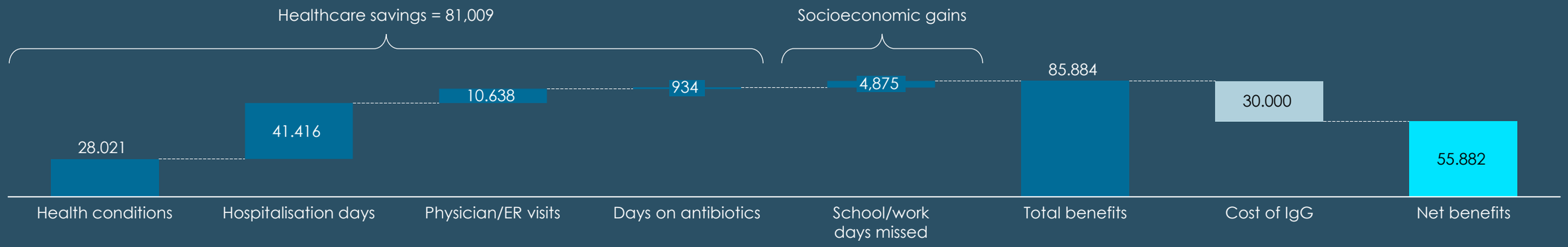
Net benefits

Adding up the total benefits yields USD 85,884 per patient per year and using a cost of IG of USD 30,000 per patient per year, the net benefits amount to USD 55,882 per patient per year. This is likely a lower bound for two reasons:

- A number of socioeconomic benefits are not included, e.g., labour market participation
- The patients' quality of life, see previous page, is not monetarised and included

While this builds on research conducted in the USA and serves as an illustration, there appears to be a need to undertake similar research in other areas (e.g. Europe) to broaden the evidence base further.

Figure 7. Benefits and cost of treating patients with PID with IgG compared to no treatment
Savings in USD per patient per year



Note: Data is from the US. Costs of procedures is based on hospital billings. The cost of IgG is similar to that found in Boyle and Scalchunes (2008). Health conditions include persistent otitis media, serious sinus and upper respiratory infections, viral infections, acute bronchitis, bacterial pneumonias, chronic obstructive pulmonary disease, and bronchiectasis.
Source: derived by Copenhagen Economics from results in Modell et al. (2017) on the costs of treating a patient with IG and the cost of not treating a patient.

Case: IG treatment has long been known to prevent infections in patients with SIDs and yet infections are still a common cause of death

Immunoglobulin can help prevent infections in patients with SID

SID often develops in patients with underlying conditions such as cancer. Chronic lymphocytic leukaemia is one example, where both the disease itself and its treatment weaken the immune system. This leaves patients more vulnerable to infections, which are often harder to treat and more dangerous for individuals who are already fighting cancer.

IG therapy can reduce both the frequency and severity of infections in patients with SID. This was for example shown in an US study on patients with chronic lymphocytic leukaemia. After initiation of IG replacement therapy, patients were 54 per cent less likely to get a severe infection, i.e., an infection leading to a hospitalisation or a treatment with any intravenous antibiotic, antiviral, or antifungal medication, see Figure 8. At the same time, the prevalence of hypogammaglobulinemia – a condition weakening the immune system characterised by low IG levels in the blood – declined, and patients were significantly less likely to experience any infections, i.e., both severe and non-severe infections.[1]

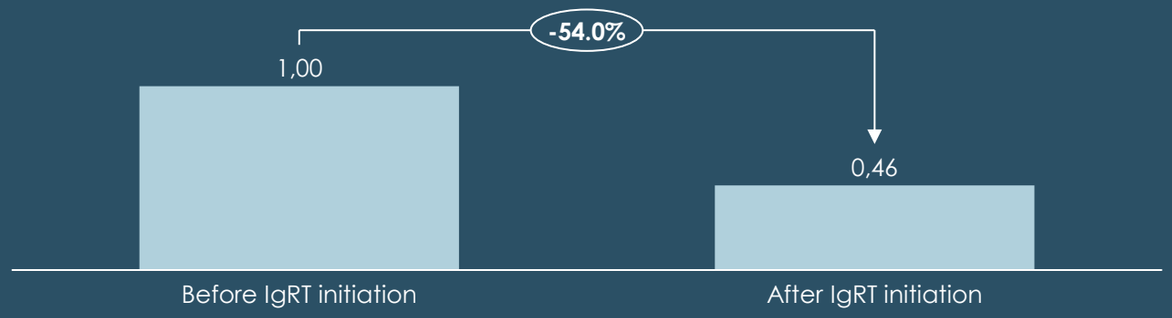
The efficacy of IG therapy in preventing infections for SID patients has been well documented for decades, with some results dating back to 1988.[2] However, despite this well-established and long-known efficacy, patients with SID remain undertreated. Evidence shows that only one in three high-risk SID patients receive IG therapy, and many of those treated receive it for shorter periods than recommended.[3]

Despite demonstrated efficacy of IG therapy, infections are still a major cause of death in patients with SID

Infections are the leading cause of death for patients with SID.[4] Evidence from the UK shows that up to 43 per cent of deaths among patients with chronic lymphocytic leukaemia are attributable to infections, see Figure 9. Of the 600 deaths that occurred over the study period of a CLL clinical trial in patients receiving their first course of treatment, 258 were attributed to fatal infections.[4]

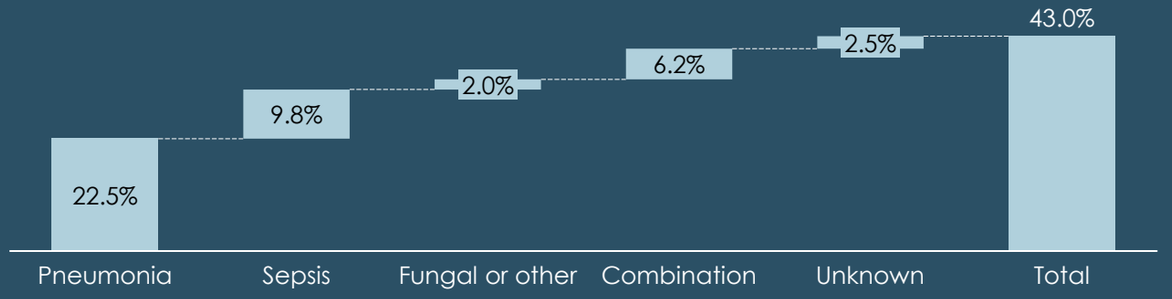
This highlights the central role of infection risk in SID patient mortality. It also underlines the need to improve treatment strategies for SID, where IG therapy is a proven treatment to reduce infections for these patients. However, while IG replacement therapy reduces infections, a direct mortality benefit in SID has not yet been established in the literature.

Figure 8. Efficacy of IG replacement therapy in preventing severe infections in patients with chronic lymphocytic leukaemia
Odds ratio of severe infections within 12 months follow-up time



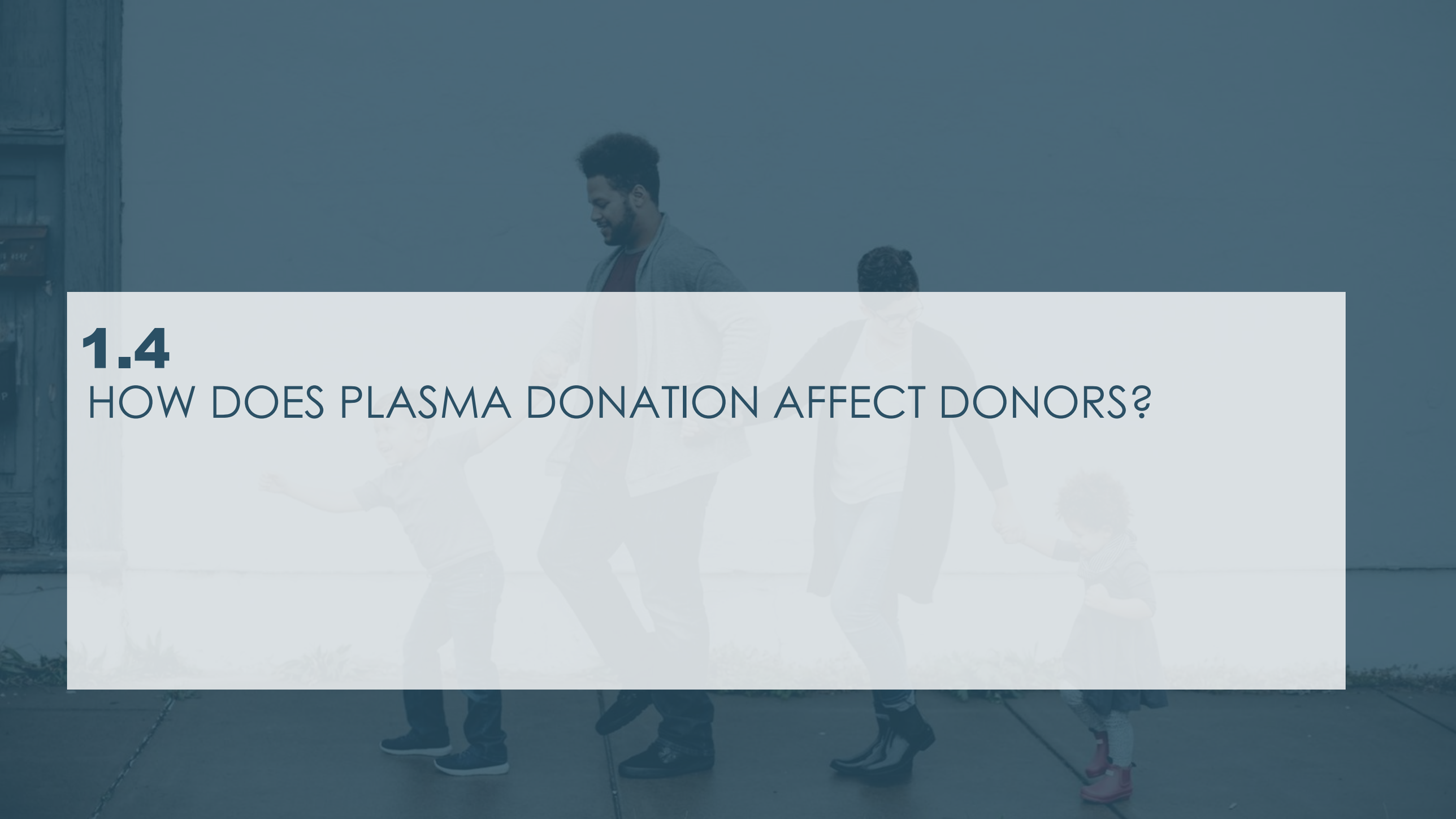
Note: The effect is based on a sample of 137 chronic lymphocytic leukaemia patients in the US who completed their 12-month follow-up after initiating treatment. The difference is statistically significant at the 0.001% significance level.
Source: Soumerai et al. (2024).

Figure 9. Cause of death due to infections in patients with chronic lymphocytic leukaemia
Share of deaths



Note: Numbers are based on a sample of 777 chronic lymphocytic leukaemia patients in the UK. 614 of these died before the end of the follow up.
Source: Else et al. (2021).

Notes: 1) Soumerai et al. (2024). / 2) See e.g. Gale et al. (1988). / 3) Ramakrishna et al. (2024). / 4) See e.g. Else et al. (2021).



1.4
HOW DOES PLASMA DONATION AFFECT DONORS?

No adverse effects from plasma donations have been shown based on available evidence

Plasma donors donate more often than whole-blood donors

Plasma donation is different from whole-blood donation as the same donor can donate plasma more frequently than whole-blood donors. In Europe, a maximum of 6 standard donations of whole blood per year are recommended from male donors and up to 4 per year from female donors with a minimum interval between standard donations of 8 weeks as it reduces haemoglobin and iron stores.[1] The minimum interval for plasmapheresis donations, on the other hand, is recommended to be at least 2 weeks, corresponding to 26 donations per year in the 22nd edition of the Blood Guide, published in March 2025.[1] As Europe needs more plasma this can thus be enabled by plasmapheresis donations.

National competent authorities can approve a plasma programme with a donation interval of less than two weeks given additional requirements that as a minimum include capturing and regularly monitoring adverse events, acting on donor health safety concerns, and measuring IgG levels at least every sixth donation.[2] If the national donation interval is less than 2 weeks, it is recommended that the donation interval should not be less than one week.[2] The possibility for plasma donors to donate more frequently than whole-blood donors is important because a single patient's treatment over one year can require plasma from many individual donations, see page 11.

Regulation on plasma donation varies between countries; in the US, donors can donate 625-800 ml of plasma twice weekly which translates to a maximum of 83 litres per year.[3] In Europe, a maximum of 880 ml per donation and a minimum interval of two weeks, as described above, is recommended.[1] European countries differ as well; the maximum amount is 15 litres in Spain[4], 39-51 in Germany[5], 32.5-42.5 in Austria,[6] and 25 (without anticoagulant) in the Czech Republic.[7]

More frequent plasma donations do not harm donors

There is no evidence that donating plasma in compliance with national regulations on donation intervals, frequency and volumes increases health risks. Instead, evidence shows that donors donating up to 60 times a year or 50 litres annually did not experience additional health risks compared with donors with lower donation frequency, if IgG levels were monitored and donation intervals adjusted.[8] Overall, the literature supports that frequent donations, when managed with appropriate safeguards, do not adversely affect donor health,[8] a conclusion consistent with decades of more or less frequent plasmapheresis in US and EU blood establishments, and data from Germany show that both donors and non-donors had protein levels above the reference value, see Figure 10.

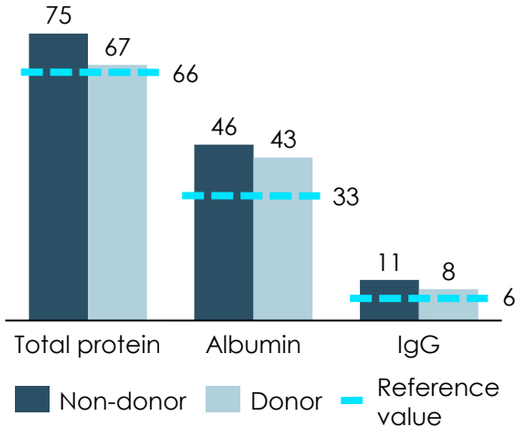
No conclusive evidence of adverse effects from plasma donation on donors

When anything is removed or extracted from a human body, there is always the question of how this affects the donor. With plasma, a healthy person will always produce more of it, and donation is not harmful. Reproducing the plasma requires usually less than 24 hours[4] and there has been a theoretical concern that intensive plasmapheresis can lead to plasma protein loss and increased risk of cardiovascular diseases[9]. However, these concerns have remained theoretical, as there is no conclusive evidence of adverse health effects from plasma donation, or even frequent donations.[10] There is thus a need for more scientific and evidence-based recommendations, see Box 3.

Plasma donors have non-harming protein levels

Available research shows plasma donors have lower protein levels than non-donors, but these levels are still above threshold values and thus not harmful to donors. This was found in a study comparing donors to non-donors on total serum protein, albumin, IgG, cellular immunity, red cell and iron levels, and cardiovascular risk. The protein levels were lower for donors than non-donors. However, the levels were still within reference values for 90-100 per cent of donors, depending on which protein was studied and the frequency of donation. Additionally, regular plasmapheresis was not found to have influence on cholesterol values or other risk factors for cardiovascular disease. Furthermore, both donors and non-donors had normal cellular immunity, which is an immune response unrelated to antibodies.[9]

Figure 10. Protein levels for donors and non-donors
Grams per litre



Note: Averages of all type of donors. Reference value represents the lowest point considered normal. Schulzki et al. (2006) find similar donor values (total protein and IgG).
Source: Tran-Mi et al. (2004).

Box 3. Evidence gap in guidelines

> Current recommendations [for donation of plasma] are made in the absence of conclusive studies of outcomes from different regimes of volumes and frequencies of plasmapheresis.

Source: European Directorate for the Quality of Medicines & HealthCare (EDQM) of the Council of Europe (2017).

Notes: 1) EDQM (2025). / 2) According to the EDQM (2025) guidelines, a donation interval between 1 and 2 weeks is allowed when the patient receives additional monitoring to determine the health impact of frequent donation / 3) Donation volume is weight dependent, see ABO Plasma (2025). / 4) Fundació Víctor Grífols i Lucas (2018). / 5) Bundesärztekammer (2023). / 6) Blutspendenverordnung (2025). / 7) Czech Ministry of Health (2024). / 8) Hoad et al. (2024). / 9) Tran-Mi et al. (2004). / 10) EDQM (2023).

1.5

WHAT THERAPY ALTERNATIVES EXIST AND TO WHAT EXTENT DO THEY MEET PATIENT NEEDS?

Rare diseases can be treated with different types of therapies, but for many patients, plasma-derived therapies are the only option

Plasma-derived therapies are not interchangeable and a one-size-fits-all but are biological treatments that differ in terms of concentration, tolerance, and more as well as mode of administration. A wide range of plasma-derived therapies thus enable patients and clinicians to use the best possible care specifically for that patient.

What are recombinant therapies?

A recombinant therapy functions in the same way as a plasma-derived alternative, as it consists of the same proteins. Instead of being based on human-plasma, these proteins are produced in a lab through inserting DNA into microorganisms, plant cell structures, insect and mammalian cell lines, or transgenic animals, and extracting and purifying the protein created. 60-70 per cent of recombinant protein therapies are produced in mammalian cells, primarily Chinese hamster ovaries.[1] Hence, a recombinant therapy does not only achieve the same treatment result as a plasma-derived therapy, but also achieves it in the same way. This is e.g. true for haemophilia A (factor VIII) deficiency for which there exists both plasma-derived and recombinant factor VIII.[2,3]

In addition to recombinant therapies, there are also other therapy alternatives to treat specific diseases. For example, the disease idiopathic thrombocytopenic purpura can also be treated through plasma exchange or plasmapheresis, which is a way to 'clean' the blood. Gene therapy, which modifies the patient's DNA, can also be used in some cases e.g. for some PIDs and SIDs.

Not all therapies have recombinant alternatives

However, recombinant therapies do not exist for all types of diseases. One example is PIDs, which is a group of diseases for which there are no recombinant alternatives. These patients have a reduced or absent function of their immune system. For these patients, plasma-derived IG is still the only treatment option.

Recombinant alternatives are not always available

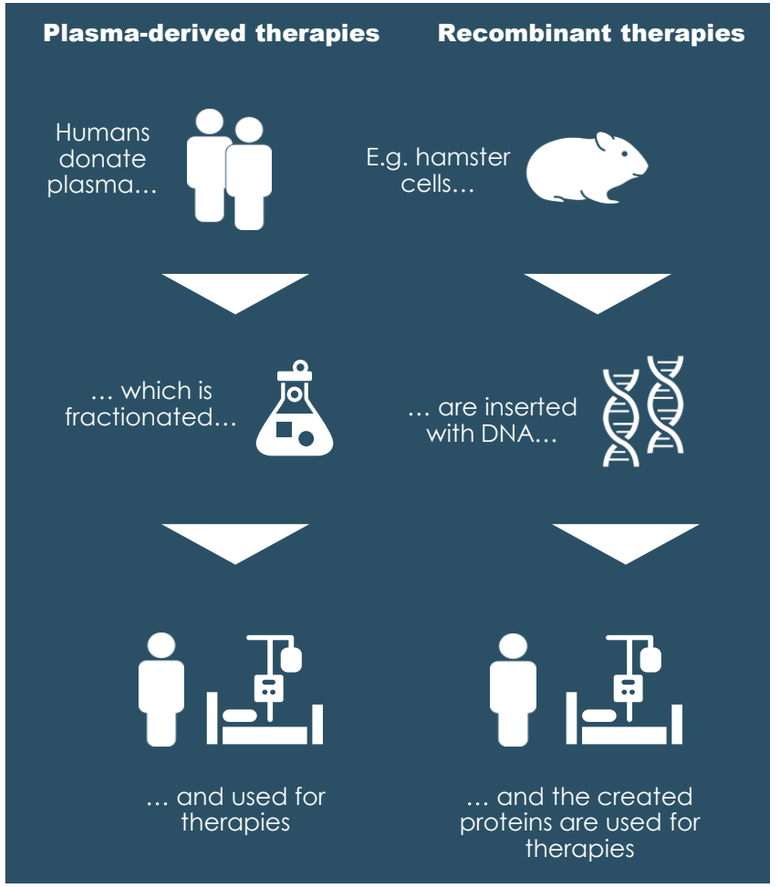
Even if a recombinant alternative exists for a specific condition, it does not mean it will be distributed in all markets or to all patients. Recombinant alternatives tend to be used more widely in developed countries with high quality of care, although plasma-derived therapies are used in these countries, too.

When both plasma-derived and recombinant therapies are available, patients with the same disease still use different treatments. E.g., in Germany, 22 per cent of patients with haemophilia use plasma-derived factor VIII and 78 per cent use a recombinant alternative.[3]

Patients require multiple treatment options

There are no one-size-fits-all therapies for orphan diseases, and the more therapy alternatives that are available, the better it is for the patients. Hence, the comparison between plasma-derived and recombinant alternatives becomes difficult, as patients react differently to the same therapy, and the same therapy from different manufacturers can provide different treatment experiences to patients.

Box 4. Plasma-derived therapies and recombinant therapies



Source: Copenhagen Economics.

Notes: 1) Grillberger et al. (2009). See also Jayapal et al. (2007). / 2) Please see the next page for a full overview. / 3) See page 27 for full map on plasma-derived factor VIII usage in Europe.

Which diseases have a recombinant treatment alternative?

Table 3. Diseases with recombinant treatment alternative

Disease or condition	Type of treatment	Does a recombinant therapy exist?	Medical need for plasma
Haemophilia A (factor VIII deficiency)	Coagulation factors and clotting factors	Yes	
Haemophilia B (factor IX deficiency)		Yes	
von Willebrand disease		Yes	
Other factor deficiencies (e.g., factor I, II, V, V+VIII, VII, X, XI, and XIII)		Yes, but not for all deficiencies and not a full-scale alternative[1]	
Protein C		No	
Antithrombin III deficiency	Antithrombin III	No[2]	
Alpha-1 antitrypsin deficiency	Alpha-1 antitrypsin or Alpha-1 Proteinase Inhibitor	No	
Hereditary angioedema , types 1 and 2	C1-esterase inhibitor	Yes	
Primary immunodeficiency (PID)	IGs	No	
Secondary immunodeficiency (SID)		No	
Chronic inflammatory demyelinating polyneuropathy (CIDP)		Yes[3]	
Immune thrombocytopenic purpura		Yes	
Kawasaki disease		Recombinant alternatives exist but are used only off-label because they are not approved in the EU; non-recombinant therapy alternatives exist	
Anti-D		No	
Multifocal motor neuropathy		No	
Other neuromuscular diseases		For most, recombinant alternatives do not exist; non-recombinant therapy alternatives exist	
Critical illnesses	Albumin	Therapy alternatives exist but they are not recombinant[4]	

Note: 1) There is a recombinant factor XIII and a recombinant factor VII alternative available. / 2) The only recombinant product, antithrombin alfa, had its EU marketing authorisation withdrawn in 2019 at the MAH's request. The molecule has undergone post-translational modification, with different binding properties to heparin, which is the primary substrate. / 3) Recombinant therapy exists (efgartigimod) but it was only approved in June 2025 and specifically "after prior treatment with corticosteroids or immunoglobulins," so it does not displace first-line IVIG. / 4) Crystalloids or colloids are used to replace blood volume loss. No alternatives for conditions causing low level of albumin (e.g., surgery, liver failure, pancreatitis).

The use of plasma-derived therapies is widespread throughout Europe – case example using haemophilia A

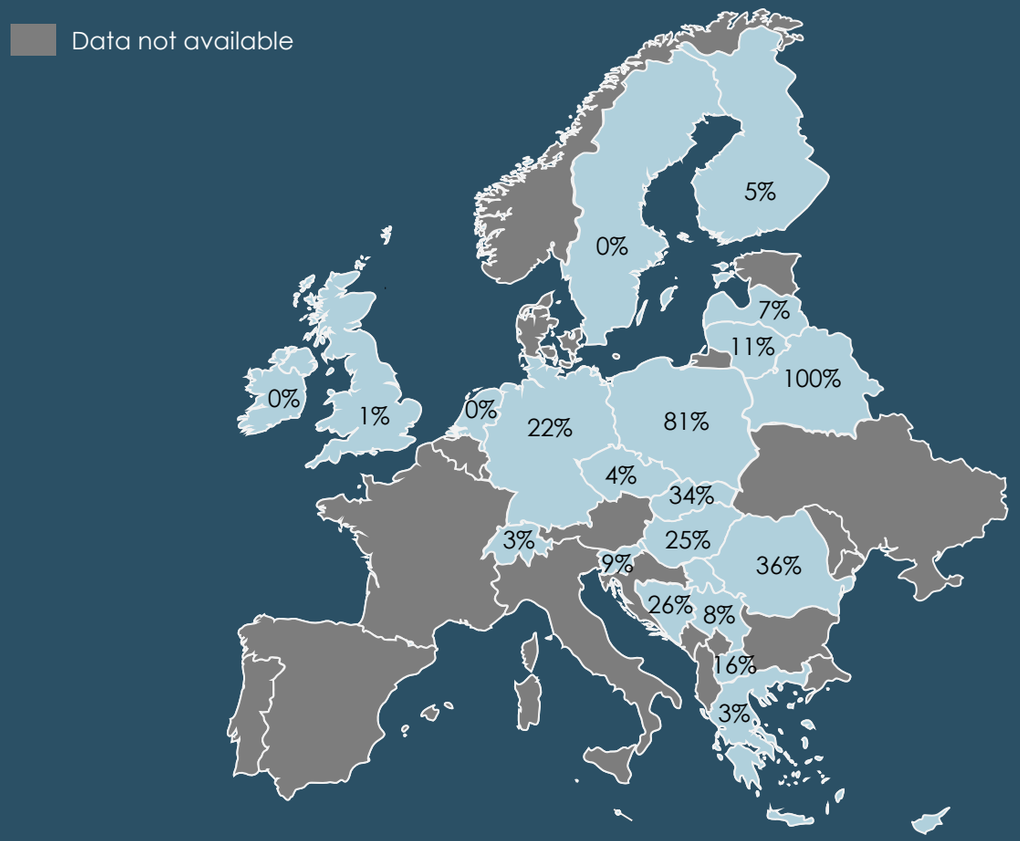
Plasma-derived therapies are used throughout Europe – also for conditions where recombinant alternatives exist

The use of plasma-derived therapies varies within Europe, but even for plasma-derived therapies where recombinant alternatives exist, plasma-derived therapies are still widely used. In the map to the right, we have depicted the share of plasma-derived factor VIII compared to recombinant factor VIII used to treat haemophilia by European country. The share of plasma-derived factor VIII ranges from 0 per cent (Sweden and Ireland) to 100 per cent (Belarus).

Plasma-derived therapies are used the most in Central and Eastern Europe. In particular, Poland and Belarus rely on plasma-derived factor VIII with shares of use above 80 per cent. Northern and Western Europe, use less plasma-derived therapies.[1]

Countries with higher standard of care tend to use more recombinant alternatives, even though plasma-derived therapies are not inferior to their recombinant counterparts. One reason for this is the poor reputation plasma-derived therapies acquired during the late 20th century when viruses like HIV spread – especially to patients with haemophilia. Thanks to diligent quality control, plasma-derived therapies are safe today, see pages 28 and 29. Another reason is the uncertainty of supply, which is the Achilles' heel of the plasma-derived therapies industry and a key reason to increased production of recombinant alternatives.

Figure 11. Use of plasma-derived factor VIII, 2023
Share of total use of factor VIII (IU)



Note: IU = International Units. 1 IU is defined as the concentration of coagulation factor in 1 ml of normal pooled plasma, see Fijnvandraat et al. (2012).
Source: Based on calculation from World Federation of Hemophilia (2023).

Notes: 1) Especially Norway, Sweden, Finland, the United Kingdom, the Netherlands, Switzerland and Ireland.

Quality control during every step of the process minimises the risk of pathogens being transmitted to patients

Page 1/2

Pathogen safety depends on safeguard measures, which ensure that only plasma from healthy donors is used in the manufacturing process. Further, the safety measures self-imposed by the industry often go beyond those required by regulation. With plasma-derived therapies, zero risk of pathogen transmission does not exist. However, the risk is practically limited to newly emerging diseases.

The plasma used for plasma-derived therapies is a substance of human origin and donated by human individuals. Humans carry infectious agents like viruses and bacteria, which means using any product with human protein will carry a risk of pathogen transmission. Plasma from individual donors is pooled into large donor pools, which are required to achieve sufficient volume for fractionation and to enable batch testing and validated safety controls. According to industry experts, each therapy could be made out of up to around 60,000 separate plasma donations from different human individuals, increasing the potential risks.

There have unfortunately been cases of disease transmission through plasma-derived therapies in the past. Especially patients with haemophilia were affected during the 1980s and 1990s with both human immunodeficiency virus and hepatitis C.[2] In the Mid 80s, large proportions of haemophilia patients in the US were infected by HIV and with hepatitis C.[1]

In 2009, a study found that since 1997, there have been no new cases of disease transmissions.[1] This is due to new industry protocols and guidelines as well as improved manufacturing processes. Today, plasma donations are safer than ever before.[3,4]

The quality control process is highly diligent

Today, the quality control process for plasma-derived therapies is diligent and highly regulated, e.g., by EU Guidelines on Good Manufacturing Practice (GMP).[6] It is noteworthy that the industry itself has imposed additional regulations and certifications in addition to those required by international and national authorities.[5] The best practice is summarised in three steps[7]:

1. Donors are screened and retained according to strict rules by health authorities. The rules relate to e.g. travel or specific behaviour that increases risk of carrying infectious agents.
2. The plasma from each donor is quarantined until it has been carefully tested for viruses such as human immunodeficiency virus and the hepatitis C virus. Any plasma even suspected of having traces of infectious agents is discarded.
3. The plasma components for medical use are purified and potential contaminants are inactivated or removed.

Due to strict regulation of the manufacturing and pathogen reduction processes, the risks have been minimised for all known diseases. A theoretical risk of transmission exists still today, but this is very small and is true for all biotechnology products and many recombinant therapy alternatives (something we will discuss in greater detail on the following page).[8]

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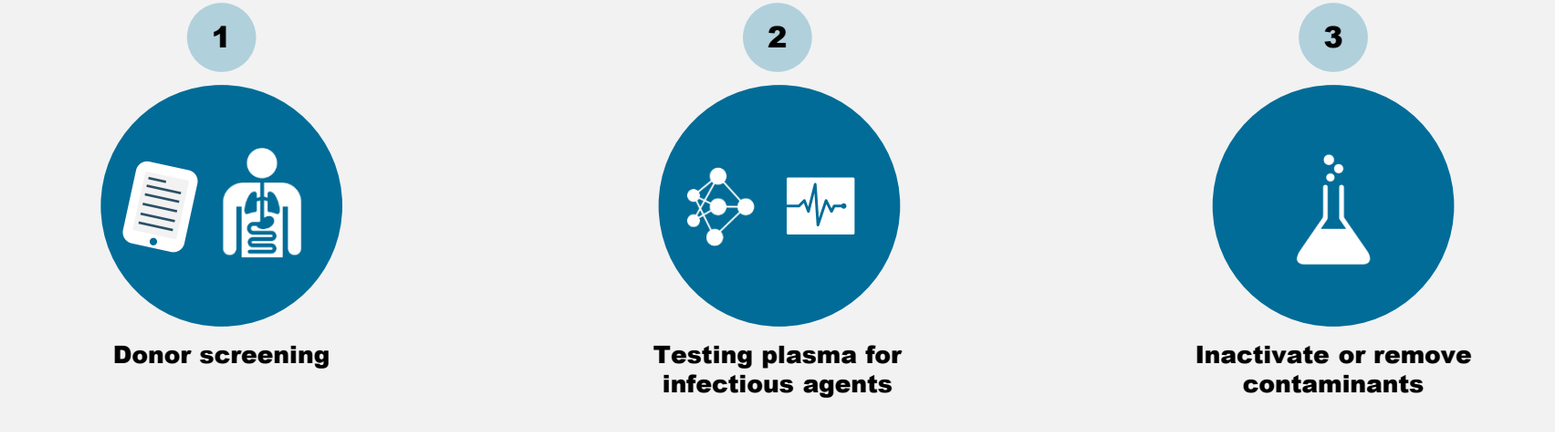
Figure 12. Quality control of plasma-derived therapies in three steps



Source: Copenhagen Economics.

Notes: 1) Grillberger et al. (2009). / 2) Rosendaal et al. (1991). / 3) The European Medicines Agency published in 1999 a document on testing and evaluating viral safety of biotechnology products derived from both human and animal origin, see European Medicines Agency (1999). / 4) U.S. Government Accountability Office (1997). / 5) See PPTAs IQPP certification program description (PPTA 2012) and PPTAs QSEAL voluntary standards program (PPTA 2020c). / 6) European Commission (2010). / 7) Immune Deficiency Foundation (2019). / 8) See also Barone et al. (2020).

Quality control during every step of the process minimises the risk of pathogens being transmitted to patients

Page 2/2

The risk is primarily for new, unknown diseases

The risk for transmitting pathogenic agents is practically limited to new, previously unknown disease agents, as tests do not yet exist for these diseases and current inactivation and removal techniques have not been tested to be effective against the new virus. Indeed, studies on pathogen inactivation and removal demonstrate effectiveness against a broad range of virus types. Likewise, new viruses – e.g. West Nile Virus, SARS virus – have not been transmitted through plasma derivatives in the past two decades.[1] Manufacturers cannot, however, be sure to remove or inactivate a virus they are unaware of. This was the case e.g. with HIV in the 1980s: little was known about the disease and how it was transmitted from person to person. Now the disease is understood, and new donor screening mechanisms as well as antibody tests, heat treatments, and solvent-detergent washing processes have been introduced to inactivate and remove human immunodeficiency virus as well as other pathogens.[2] For example, a study found that 100 per cent of plasma donations in Germany were screened for HIV1+2, hepatitis B and C, syphilis, Chagas disease, malaria, and Human T-cell Lymphotropic Virus type I and type II.[3]

Today, the quality control process is much more effective than in the 1980s and has provided protection even against some newly emerging diseases. This has been confirmed for several viral agents, also after emergence of Covid-19. It is concluded that Covid-19 is not a concern for the safety margins of plasma-derived therapies manufactured by PPTA member companies due to current procedures.[4]

Plasma is also safe when donors are compensated

The risk of pathogen transmission for plasma-derived therapies depends on the risk of donors carrying pathogenic agents. Hence, donor selection, retaining, and screening is of key importance to ensure patient safety.

Monetary compensation for plasma donations could potentially attract individuals at elevated risk of carrying a virus.[5] Through donor screening, high risk people like intravenous drug users are excluded from donating.[6] While there is some evidence in the literature to suggest that paid donors have a higher frequency of blood-borne infections than unpaid ones,[7] these studies are also criticised by others both for technical faults as well as being too narrow in their scope of what determines transmission safety.[8]

More importantly, even when pathogens cannot be detected, e.g., if the donors donate in a period when blood-borne viruses are not detectable by screening tests, "[…] *the preparation, purification and viral-inactivation procedures employed in the production of derivatives of pooled human plasma may render the difference between the safety of paid and unpaid donors for plasma products irrelevant.*" In addition, "*[…] industry regulations and standards protect the health of the donor, ensure the quality of plasma, and permit collection of sufficient plasma to meet the needs of patients*".[9]

Recombinant alternatives are also associated with a risk of pathogen transmission

Recombinant alternatives are also biological products, and hence have pathogen transmission risks just like plasma-derived therapies.[10] Both require diligent production chain supervision, which ensures high quality and safety of the product. Additionally, both can have risks from the raw material, which for plasma-derived therapies is plasma, and for recombinant alternatives the type of cells they are cultivated in.

The recombinant cells are created through cultivating and can be contaminated by bacteria and viruses during the process. The contamination risk depends on which cells the recombinant alternative is cultivated in. Especially, if the production process includes human plasma in some part of the process, the risks are the same as for plasma-derived therapies. There are recombinant alternatives produced without animal proteins, but 60-70 per cent are produced in mammalian cells, primarily Chinese hamster ovaries.[11] Only in recombinant alternatives that are produced without human or animal proteins can the pathogen risk be mostly eliminated.[12]

Box 5. Marginal benefits of recombinant therapies

> (…) the advantage of recombinant over plasma-derived clotting factors regarding risk of disease transmission is marginal, and should no longer be the basis for clinical decision making.

Source: Industry expert.

Notes: 1) Kreil et al. (2003), Barone et al. (2020), Kreil et al. (2007), Leydold et al (2012), Farcet et al. (2016), Farcet et al. (2017). / 2) US General Accountability Office (1997). / 3) World Health Organization (2017) / 4) PPTA (2020b) and ECDC (2020). / 5) High risk individuals, e.g. intravenous drug users or prostitutes. See GAO (1997). / 6) GAO (1997). / 7) Meta study by van der Poel et al. (2002) on 28 data sets. / 8) Bruers (2021). / 9) Weinstein (2018). / 10) Barone et al. (2020). / 11) Grillberger et al. (2009). See also Jayapal et al. (2007). / 12) Grillberger et al. (2009).

Plasma-derived therapies require a tailored approach

Unlike many traditional pharmaceutical products, plasma-derived therapies are usually not interchangeable for a given patient. A patient treated with a particular plasma-derived therapy does not necessarily tolerate or respond well to another therapy approved for the same condition. Additionally, some therapy alternatives are better tolerated and optimised for patient welfare than others and can improve the patient's treatment experience. Which qualities are appreciated differs from patient to patient, and the decision to change therapy should therefore be left to medical experts and patients.[1]

Here we take the example of IG therapy, which can be administered either intravenously or subcutaneously. The medical need for IG is high especially for patients with PID, as today there exist no alternative treatments. Patient groups still differ in what qualities they need from the therapy except for the essential IG. E.g. diabetics, elderly patients, and patients with heart disease require different features, see Table 4 directly adopted from Siegel (2005).

There are several features that affect which product is the right one for a specific patient, including sodium content, type and concentration of sugar, pH, volume load, and infusion rate.[1,2] The better a therapy can be fitted to a specific patient's needs, the fewer side effects they will experience and the higher their quality of life will be. Today, IVIG therapy alone has shown efficacy in over 100 disorders.[3]

Volume load of a therapy

The concentration of a product determines how much of it needs to be administered to achieve the desired effect. IVIG products differ in their concentration, ranging from 3-12 per cent. For example, a 70-kg patient would need 1400 ml to receive 2g of IG/kg if the concentration is 10 per cent, but 2800 ml if the concentration is 5 per cent. Some patients do not tolerate large volumes of fluid, e.g. patients with heart failure or small children and the elderly. Due to the concentration of other substances (like sodium) it can be risky to simply concentrate the product, as this can lead to other complications.[4]

Sugar content

Sugar acts as a stabiliser in IVIG products, and is added during the manufacturing process to some products.[5] This can be a problem for specific patient groups, especially diabetics. For a diabetic, it makes a big difference which type of sugar is used for the product, as glucose will require them to take more insulin while sucrose will not. The sugar level also affects which patient groups it is suited for, and especially patients predisposed to renal failure should have products that have lower sugar levels or are sugar-free.[6, 7]

Table 4. Features of IVIG that are concerns for patients with certain risk factors

	Sodium content	Sugar content	Concentration	Ph level	IG A	Volume load
Renal dysfunction	X	X	X			X
Heart disease	X		X			X
Diabetes mellitus, prediabetes		X				
Elderly	X	X	X			X
Neonatal, paediatric	X		X		X	X
Thromboembolic risk	X		X			X
IgA deficiency				X		

Source: Adopted directly from Siegel (2005), Table 5.

Notes: 1) Gonzalez et al. (2022). / 2) See Siegel (2005), p.81S for full list. / 3) Morse et al. (2025). / 4) Siegel (2005). / 5) See Abolhassani et al. (2015) for a list of sugar contents in selected commercial products. / 6) Siegel (2005). / 7) Guo et al. (2018).

Plasma-derived therapies provide different value to different patients

Convenience of therapy

The convenience of therapies is important for patients as well as healthcare personnel. This is especially true for the patients, as it relates to the time and the place they need to spend to receive their medication. Product concentration as well as infusion rate affect the perceived convenience of the patient and potential side effects. This implies that patients need to be able to make an informed decision in collaboration with their treating physician about which treatment to use as exemplified in Box 6.

The IG products come in various different package sizes, which means the product can be tailored to match the patients needs. Another convenience factor is that the product can come in, e.g., liquid form, which is directly usable but needs to be refrigerated.[1]

Additionally, IVIG and SCIG both have their own benefits and drawbacks, see Table 5. IVIG requires few administration sessions (half-life of 30-40 days) but leads to a peak in IG levels after infusion. With SCIG, we can distinguish between two different types: conventional SCIG (cSCIG) and facilitated SCIG (fSCIG). cSCIG is administered in lower volumes than IVIG, which eliminates peaks but also means it needs to be injected more often.[2] One patient might not be able to inject themselves or receive help from an informal caregiver or a healthcare professional and hence prefers IVIG, as it needs to be injected only every 3-4 weeks and with the help of a healthcare professional. Another patient might enjoy the flexibility and freedom of using cSCIG, as even if the treatment needs to be injected at least once a week, they can do it in the comfort of their own home.[3] fSCIG combines benefits of IVIG and cSCIG to some extent. It allows to infuse higher volumes of IG due to the additional enzyme, hyaluronidase, which implies fewer IG administrations than with cSCIG. At the same time, it allows for home administration, which creates additional flexibility and independence for the patient.[3]

SCIG methods are often preferred for children, as it is easier to self-administer either by the child or caregiver, which gives greater freedom and increases quality of life.[4]

IG, like any therapy, has side effects for some patients. The majority of side effects are mild, e.g. headache, fever, chills, or fatigue and pass quickly. However, some side effects are severe, including aseptic meningitis, renal impairment, thrombosis, and haematologic disorders. The severe side effects are very rare, affect less than 1 per cent of patients, and are associated with individual differences. Switching to cSCIG or fSCIG can help with side effects, both for patients who are currently experiencing side effects or for patients at high risk of developing them.[5] This can involve switching from IVIG to SCIG to avoid serious (systemic) side effects in favour of milder and local ones. There are several studies comparing side effects between the treatment types, but sample sizes are small. A meta-analysis on eight studies of in total 138 patients with chronic inflammatory demyelinating polyneuropathy (CIDP) showed that the risk of moderate and/or systemic adverse effects was 28 per cent lower in the cSCIG group compared to the IVIG group.[6]

Box 6. An informed patient decision

> While selection of IVIG or SCIG is ultimately a choice best left to the discretion of each patient and their treating physician, several factors warrant consideration so that patients can make informed decisions that best balance their needs, preferences, and lifestyles.

Source: Allen et al. (2020).

Table 5. Advantages and disadvantages for the patient of IVIG and SCIG

	IVIG	cSCIG	fSCIG
Advantages	• Monthly dosing due to higher volume (every 3-4 weeks) • Few administration sessions • Less involvement of the patient[1]	• Home-based therapy • Self-administration • Flexibility for e.g. travel or work • Low risk of systemic side effects • Suitable when poor venous access	• Home-based therapy • Self-administration • Monthly dosing and few administration • Flexibility for e.g. travel or work • Low risk of side effects • Suitable when poor venous access
Disadvan-tages	• Requires trained personnel • Greater use of hospital resources • Time-intensive travels • Severe side-effects (less frequent with new highly purified IVIG)	• Frequent dosing (min. 1 per week) • Requires patient involvement, reliability, training, and compliance • Local side effects (swelling, local inflammation, itch)	• Two-step process of hyaluronidase and Ig infusion which requires training • Requires patient involvement, reliability, training, and compliance • Higher volume

Notes: 1) Also possibility of home-based IVIG treatment in some countries.
Sources: Moore and Quinn (2008); Krivan et al. (2017); Rubinstein et al (2024); Li et al. (2024).

Notes: 1) Siegel (2005). / 2) Krivan et al. (2017). / 3) There is also the possibility of home-based IVIG treatment in some countries. / 4) Kobayashi et al. (2019). / 5) Guo et al. (2018). / 6) Guo et al. (2018), based on Racosta et al. (2017).

Home treatment and self-administration enabled by plasma-derived therapies can add value for patients, healthcare systems, and society

There is a general pressure on European healthcare systems with shortages of skilled personnel, a decreasing number of hospital beds, and long-term increase in future healthcare spending.[1] As part of a strategy to alleviate this pressure, multiple European countries have explicit goals to increase the option of home treatment and outpatient care. They have taken measures and are working actively to explore how both healthcare systems and patients can benefit from moving treatment to the patient's own home. Home care is appealing to many as it provides an additional option increasing patient choice and helps manage the growing demands for healthcare services and the resulting pressure on healthcare systems.[2] For European healthcare systems, expanding home treatment is a strategic opportunity to increase capacity and resilience.

Some plasma-derived therapies enable home treatment and self-administration for a range of diseases. For example, patients suffering from PID, SID, and CIDP can receive treatment with IG therapy. Such IG therapy can be administered either intravenously or subcutaneously. IVIG requires medical supervision and is therefore mostly administered at the hospital, whereas SCIG can more easily be administered at home often by the patient themselves.[3] While healthcare systems should provide the opportunity for treatment at home, the choice between IVIG and SCIG is ultimately a patient decision that should be made in agreement and under the advice of their clinician.

Healthcare treatment at home enabled by plasma-derived therapies can create value for society

Home administration of plasma-derived therapies can create value in three different ways:

- Improving quality of life for patients, see Figure 13
- Reducing costs for the healthcare system, see Figure 13, or freeing up scarce healthcare resources for other therapeutic areas and building resilient healthcare systems when patients self-administer their treatment
- Reducing lost work hours for patients and caregivers, see Figure 13, thereby benefiting society

By lowering the need for medical staff and hospital facilities, home treatment in combination with self-administration can free up capacity for other patients and help control healthcare expenditures. For appropriate patients, it also allows to integrate treatment into their daily life without travelling to a hospital, which can improve quality of life and reduce disruption at work, education, and other commitments, as well as the associated travel time and costs.[4] It can also reduce the need for caregiver support, freeing up their time, too.

Moving people from the hospital to healthcare treatment at home can create sizable health economic savings

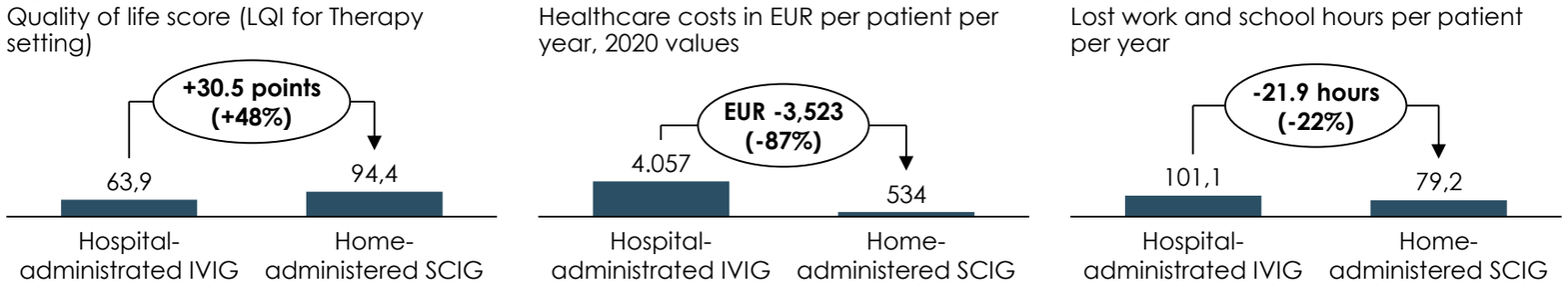
Data from Canada show that moving patients suffering from PID or SID from the hospital to home-based treatment can generate health economic savings. For patients treated with IG, the average administration cost per patient per year was EUR 3,523 lower for home-based and self-administered SCIG compared to hospital-administered IVIG, see Figure 13. The study concludes that self-administered SCIG is less costly for the health care payer, while also reducing nursing burden and freeing up clinic capacity for other patients.[4]

The results are in line with model-based evaluations of the effects of home administration of SCIG in Spain (savings of EUR 4,266 per patient per year, including costs of IG),[5] but smaller than findings from a Swiss study (savings of EUR 20,300 per patient per year)[6]. The Spanish study also finds productivity gains, for example, that patients lose 21.9 fewer hours of work or school per year when using SCIG instead of IVIG, see Figure 13.

Country-specific assessments are needed

The examples above show that plasma-derived therapies can generate economic value when self-administered at home by patients. At the same time, they also incur costs such as training of patients and the cost of the medicine. Therefore, it is important to assess their added value individually in every country by accounting for their cost, HCP resources needed, and suitability for the market's unique healthcare system.

Figure 13. Implications of hospital-based and home-based administration of IG therapy



Sources: Kan et al. (2022); Ritchie et al. (2022); Alsina et al. (2022).

Notes: 1) OECD (2024). / 2) See e.g., Healthcare Denmark (2025) or NHS (2025a). / 3) Blau (2016). / 4) Ritchie et al. (2022). The values reported here were converted from Canadian Dollars to Euros using the average 2020 exchange rate of 1 CAD = 0.65 EUR. / 5) Alsina et al. (2022). Monetary savings are measured in 2018 values. / 6) Perraudin et al. (2020). Savings are expressed in 2020 CHF values, which is converted to 2020 EUR using an CHF/EUR exchange rate of 0.93 suggested in the paper.

Patients value treatment choice and many prefer plasma-derived therapies that enable home and self-administration

Choice of treatments supports personalised care for patients

Home treatment and self-administration not only create societal value by freeing up time for appropriate patients, caregivers, and healthcare personnel, but they also create value by offering increased treatment choice.

Multiple treatment options are often highlighted as positive for patients as they can help accommodate diverse patient needs.[1] For PID patients, for example, access to a broad range of IG therapy options enables personalised care, as patients differ in their medical requirements, lifestyle preferences, and product tolerability.[2] Increased treatment choice allows patients to select the treatment that best balances clinical effectiveness, convenience, and quality of life in close collaboration with their clinician.[3]

A study from Portugal finds that 97.6 per cent of PID patients prefer SCIG (facilitated SCIG (fSCIG) or conventional SCIG (cSCIG)), while only the remaining 2.4 per cent prefer IVIG, see Figure 14.[4] A key difference between SCIG and IVIG treatments is that in Portugal and many other countries, SCIGs provide the flexibility of home and self-administration. In addition, SCIGs offers greater flexibility in administration – via infusion pump or manual rapid-push – and are supplied as vials, prefilled syringes, and other ready-to-use presentations. While both cSCIG and fSCIG enable home treatment and self-administration, it is possible to infuse larger amounts of IG with fSCIG than with cSCIG, and as a result, fSCIG require less frequent administration.[4]

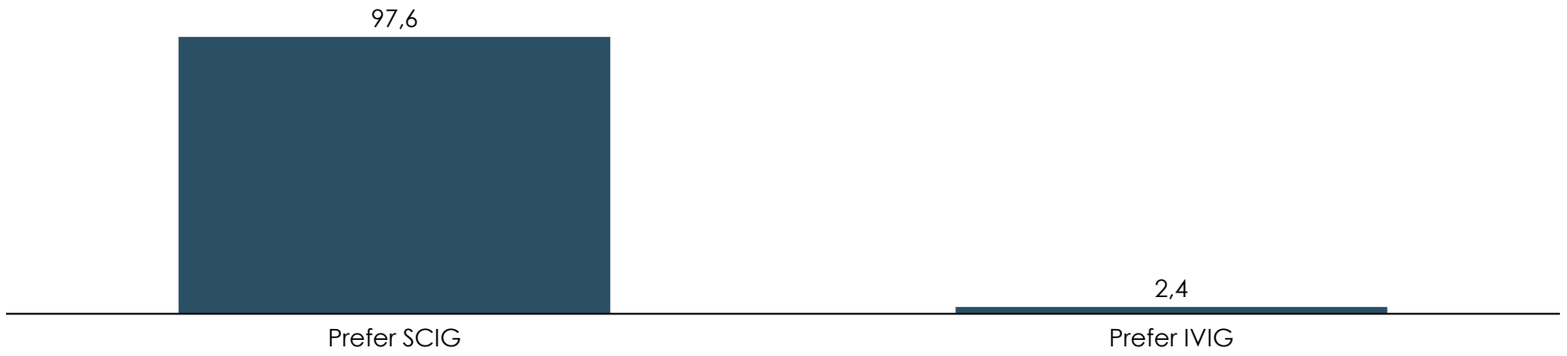
The Portuguese results are supported by findings in other countries:

- A Canadian study found that switching from hospital-based to home treatment offered patient choice for treatment and facilitated greater involvement of patients and caregivers.[5]
- Danish data show that 89 per cent of immunodeficiency patients who have experience with home treatment would choose treatment at home over treatment at the hospital.[6,7]

Enabling home-based IG requires the right ecosystem

To make patient choice between treatment options safe and sustainable, services should follow the European Nursing Guidelines for Immunoglobulin Administration with clear suitability checks, structured teaching before the first infusion, and competency-based sign-off led by specialist nurses.[8] Devices used at home should meet the requirements of the EU Medical Device Regulation and patients who engage in self-administration should know how to receive quick professional support (e.g., through a helpline) if needed.[9] Moreover, medicines supply should follow the EU Good Distribution Practice rules, so they are maintained to the point of home delivery.[10] Simple digital tools, such as teleconsultations or connected home-monitoring devices can help patients, carers and clinical teams detect changes early, act in time, and keep treatment on track.[11] Finally, patients should know how to report suspected side effects through the official EU system EudraVigilance.[12]

Figure 14. Example: PID patients prefer the flexibility of SCIG over IVIG treatment
Per cent of PID patients



Note: The figure shows the share of PID patients in Portugal who prefer SCIG (fSCIG and cSCIG) and IVIG. Preferences is based on survey responses.
Source: Copenhagen Economics based on Lemos et al. (2024).

Notes: 1) See e.g. Tadros et al. (2023) or Gonzalez et al. (2022). / 2) Jolles et al. (2015). / 3) Tadros et al. (2023). / 4) Blau et al. (2016). / 5) Streu (2016). / 6) Johansen et al. (2024), Patients who would "definitely" or "probably" ("helt sikkert" and "sandsynligvist" in Danish) choose home treatment. / 7) Similar results are also found in Australia, where 95.2 per cent of patients who have tried SCIG and IVIG believe that SCIG is the better treatment option, see Health Consult (2023). / 8) International Nursing Group for Immunoglobulin Administration (2021). / 9) Medical Device Regulation. / 10) European Commission (2013) / 11) MedTech Europe (2022) / 12) European Medicine Agency (2025).

CHAPTER 2
VALUE OF THE PLASMA-DERIVED THERAPIES INDUSTRY

Chapter 2 – Main conclusions

Increasing patient need for plasma-derived therapies

Patient need for plasma-derived therapies is increasing, which drives an increase in the demand for plasma for fractionation. This is the case despite the existence of recombinant and other alternatives. Not all conditions have alternatives to plasma-derived therapies and patients differ in their need for treatment. This explains the co-existence of plasma-derived and other therapies.

Patient need for plasma is driven by therapy in highest demand

The protein which requires the largest amount of plasma based on the patient needs and how much of this protein plasma contains, is the key in determining the demand for plasma. Today, the protein with the highest demand is IG. Hence, IG has to bear a large share of raw material costs.

Production process of plasma-derived therapies is longer and more expensive

The production process of plasma-derived therapies is much longer and more expensive than production of traditional pharmaceuticals. Production of plasma-derived therapies can require 7-12 months from donation to delivery of the therapy to patients, compared with around 2-3 months for traditional pharmaceuticals. Furthermore, raw material costs are the primary cost component for plasma-derived therapies, while for traditional pharmaceuticals the largest cost component is sales and marketing.

Risks for supply if tenders are not carefully designed

The large share of the total costs from raw materials lowers the flexibility for developers and manufacturers of plasma-derived therapies in setting prices. This is especially true for IG, which has to bear a large share of the raw material costs. Hence, tender specifications and pricing can have large effects on ability to supply. There are examples of tendering practices leading to therapy shortages (e.g. Spain and Romania).

The plasma-derived therapies industry supports the European economy

The plasma-derived therapies industry supports the European economy through direct, indirect, and induced effects. The direct economic effects relate to production within the plasma-derived therapies industry. The indirect effects estimate the value created by sub-contractors to the plasma-derived therapies industry, e.g. at plasma collection centres, cleaning companies, or IT solution providers. The induced effects represent the value created when employees, both in the industry and its sub-contractors, spend their income. Our indicative analysis suggests that the order of magnitude of these types of impact could be ~~9.7~~ around 14 billion EUR.

Donor compensation to increase plasma supply also supports the economy and employment

The spending of donor compensation supports an estimated 151 million EUR per year of the induced effect and 2,260 full-time equivalent jobs from compensations to plasma donors in Germany, Austria, the Czech Republic, and Hungary. As Europe's priorities evolve, for example through increased defence spending, it remains important to continue investing in health. This includes the plasma-derived therapies ecosystem, safeguarding the above contributions and ensuring that capacity keeps pace with patient needs.

Plasma collection centres have positive effects on the local community

Plasma collection centres can themselves have positive effects on the local community through a number of different channels such as employing staff, using local contractors, employees spending their income, and collaborative partnerships.

Box 7. Plasma supply and impact at a glance

Plasma-derived therapies:

- are increasing in demand
- are at risk of shortages due to the scarce availability of European donated plasma
- support the European economy directly from the industry through indirect and induced effects
- 151 million EUR and the indirect effect are supported by donor compensation, which also supports 2,260 jobs

Source: Copenhagen Economics.

2.1

PLASMA ECONOMICS, THE MARKET FOR PLASMA-DERIVED THERAPIES, AND IMPLICATIONS FOR THE PLASMA MARKET

How patient need is driven by the plasma-derived therapy with the highest demand

The plasma-derived therapies industry exhibits certain features that make it different from many other pharmaceuticals and have implications for how plasma-derived therapies are produced and procured. We start by explaining how plasma demand is derived and what this could mean for healthcare systems. We then review the key determinants of plasma production costs and examine how manufacturers are trying to keep production costs down. Finally, drawing on examples and experiences of industry experts, we explain what challenges the cost characteristic means for national players procuring plasma-derived therapies.

'Plasma Economics' explains the importance of last litre products

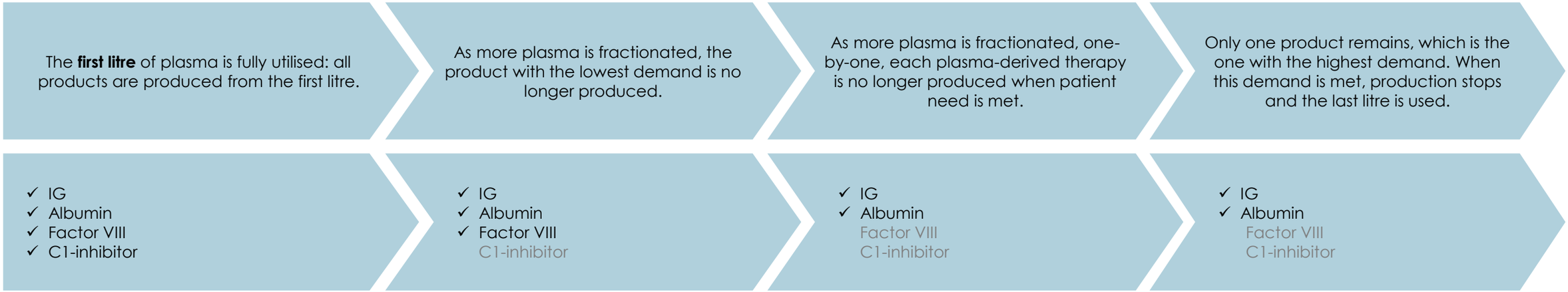
The protein, which requires the largest amount of plasma based on the patient needs and how much of this protein plasma contains, is the key in determining the demand for plasma. The MRB and industry experts refer to this as "*plasma economics*", as illustrated below.

The first litre of plasma is fully utilised since all the plasma proteins are processed and sold by the company. Hence, the first litre of plasma implies zero 'waste' of unprocessed plasma proteins.

As more plasma is fractionated, the products with low patient need due to smaller patient populations (such as factor IX, antithrombin III, etc.) are no longer produced. The high demand for other products with large patient populations, e.g. factor VIII, implies that additional plasma will be required to meet this demand.

In the end, only the products with the highest patient need – requiring the highest volume of fractionated plasma – remains. When demand for the final protein product is met, production stops, and the last litre is used.[1] The last litre products for plasma manufacturing today are IG and albumin.

Figure 15. Patient need for plasma illustrated



Note: IG, albumin, Factor VIII, and C1-inhibitor are used as the universe of all plasma-derived therapies for illustration purpose. The demand for each of the four therapies is illustrated as being highest for IG followed by albumin, Factor VIII, and C1-inhibitor, respectively.

Source: Copenhagen Economics inspired by the MRB and interviews with industry experts.

Notes: 1) Framework inspired by MRB and interviews with industry experts.

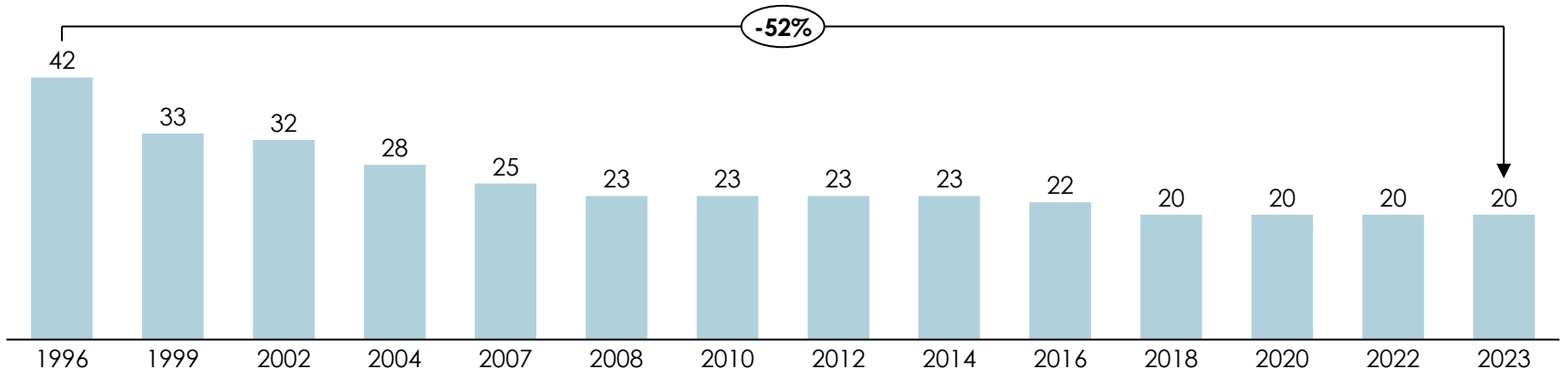
The plasma-derived therapy industry has sought to minimise the cost of their production process

The industry has minimised costs to a large extent, which enables them to deliver plasma-derived therapies at a lower cost than would otherwise be possible. A firm operating in a competitive market will seek to minimise the costs of its production process conditional on product quality and a number of other key aspects. The consolidation in the late 1990s and early 2000s is a concrete example of how this has been manifested in the plasma-derived therapies industry. In 1996 there were 42 fractionation plants in Europe. In 2007, that number had decreased to 25 fractionation plants and remained largely unchanged until 2016 (22 fractionation plants). By 2018, the number of fractionation plants had dropped by 52 per cent to 20 plants, where it has remained until 2023, see Figure 16.

Average plant capacity has increased 632 per cent in the same period from 287,000 litres per year in 1996 to 2.1 million litres in 2023, see Figure 17. A likely explanation for this consolidation is **economies of scale**. Given the complexity of the production process of plasma-derived therapies, including the rigid quality control needed, manufacturing requires large investments. It will be much cheaper to produce an additional unit of output for a company which has already done this investment than for a company that has not.

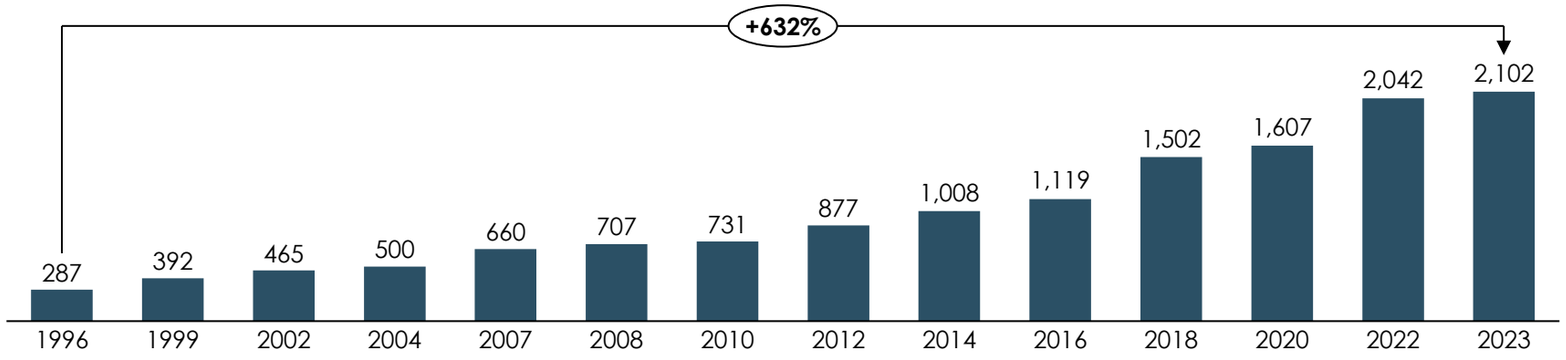
In addition, the industry may have been able to minimise costs by exploiting **economies of scope** as a consequence of using the same raw material to produce multiple products. If a given manufacturer is producing a therapy using IG, the added cost of also producing albumin will be lower as, due to the composition of plasma, the manufacturer already has the required raw material.

Figure 16. Number of fractionation plants in Europe
Number of fractionation plants



Source: MRB (2024b).

Figure 17. Average plant capacity for fractionation plants in Europe
1,000 litres of plasma



Source: MRB (2024b).

Immunoglobulin and albumin are market drivers and the two biggest components of plasma

As shown in Figure 18, the patient need for plasma-derived therapies is centred around IG and albumin. The most essential determinant of plasma need is the patient need for plasma-derived therapies.

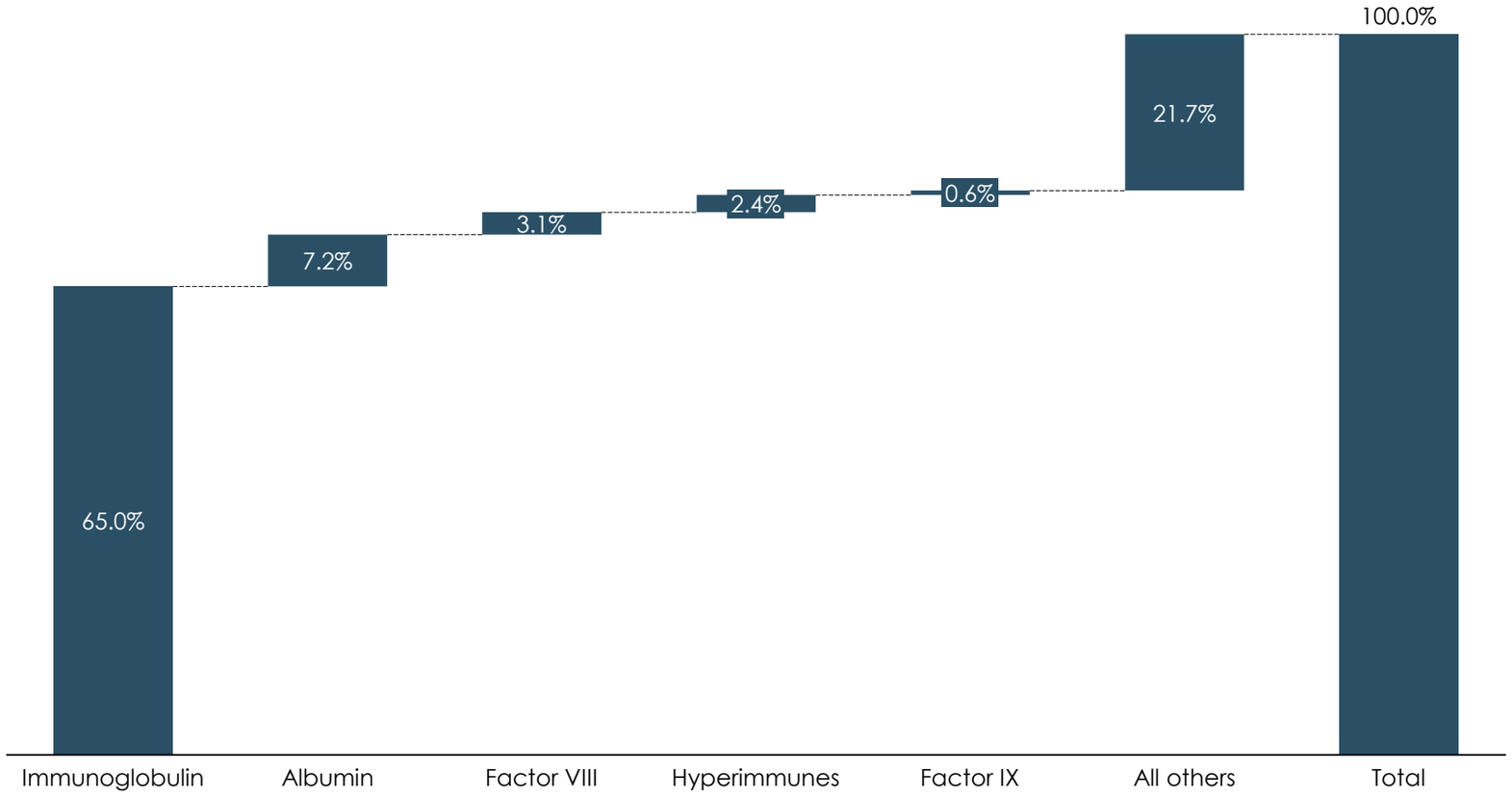
Plasma consists mainly of albumin and IG

The largest component of plasma is albumin, which constitutes 64.25 per cent of plasma, followed by IG, which constitutes 20.29 per cent, see page 11 for an overview. At the opposite end of the scale is factor VIII, which is less than 0.01 per cent of plasma. Between 18 – 20 products can be fractionated from a single litre of plasma, depending on the facility and plasma source.[1]

The composition of plasma affects demand for plasma

The composition of plasma implies that obtaining, say, 1,000,000 litres of plasma may be sufficient to meet the patient need for albumin in a country or region, but this does not necessarily mean that the amount of plasma is sufficient to meet the need for C1-inhibitor. This is because a litre of plasma consists of a higher share of albumin (64.25 per cent) than C1-inhibitor (0.29 per cent), see page 11. Self-sufficiency is therefore largely determined on the basis of plasma-derived therapies, i.e., does a country or region have sufficient plasma to meet the patient demand for albumin, IgG, alpha-1 antitrypsin, etc. Self-sufficiency is defined by the collection of sufficient domestic plasma for fractionation to meet national needs for PDTs, whether undertaken locally or internationally by public or private fractionators.

Figure 18. The market for plasma-derived therapies in Europe
Per cent of total market, 2023



Note: The market shares only include plasma-derived therapies.
Source: MRB (2024c).

Notes: 1) MRB (2024c).

The manufacturing process makes plasma-derived therapies more costly to manufacture than traditional pharmaceutical products

Manufacturing plasma-derived therapies is complex and time-consuming

Manufacturing of plasma-derived therapies can require 7-12 months from donation to delivery of the therapy to patients, compared with around 2-3 months for traditional pharmaceuticals.[1] This necessarily makes the manufacturing of plasma-derived therapies more costly than traditional pharmaceuticals.

The manufacturing of traditional pharmaceuticals requires few steps: compound mixing and capsule filling/tableting[2], after which the product is ready for packaging and distribution.

The manufacturing of plasma-derived therapies requires plasma collection from human donors, testing, fractionation, purification, and filling before the therapy is ready for packaging and distribution. A similar process is undertaken for many other biological pharmaceuticals.

The differences in the manufacturing processes are due to the use of human plasma as a raw material. The use of plasma requires manufacturers to follow protocols diligently and also a withdrawal period between collection and fractionation. In addition, the use of human plasma requires a number of testing procedures and purification to avoid the transmission of pathogens, see pages 28 and 29, which further increases the length of the production process.

Figure 19. Duration of delivering plasma-derived therapies versus traditional pharmaceuticals to patients

Source: Pharmaceutical Commerce (2016).

Notes: 1) Whittal et al. (2024). / 2) Traditional pharmaceuticals can in some cases require more complicated modes of administration than tablets/capsules, e.g., intravenous or subcutaneous administration.

More effective utilisation of the raw material to meet unmet patient needs can reduce unit costs of plasma-derived therapies

Plasma is underutilised

As some protein fractions and plasma-derived therapies are in higher demand than others, the plasma collected for fractionation today is underutilised. This is because of the features of 'plasma economics' described on page 37.[1]

Demand for plasma-derived therapies could be higher

There is production capacity available, as there is raw material, but there is no demand from payers (hospitals, health procurement bodies) for all the proteins derived from plasma today.[2] The lower demand stems largely from limited patient needs for many of the 'first litre' therapies. However, there could be unmet needs and further patients that could benefit from these therapies.

First, some patients with rare diseases never receive the correct diagnosis.[3] Other patients experience diagnosis delay, and the average delay is around 5 years or longer from symptom onset to an accurate diagnosis of a rare disease.[4] This can have severe consequences for patients.

A higher utilisation will imply a lower cost per unit

The economies of scale and scope that characterise the plasma-derived therapies industry (as outlined above) mean that higher utilisation of the raw material comes with lower unit costs. More specifically, the manufacturing cost of the therapies in highest demand, i.e., the last-litre products IG and albumin[5], will be lower if the use of first-litre products increases. Cost savings can enable a wider use of plasma derived therapies – especially in countries that rely on plasma-derived last litre products, such as albumin.

Further research appears necessary

While this conceptual framework makes economic sense, we have not found empirical evidence to substantiate it. Hence, further research appears necessary to establish the causal effect from a more effective utilisation of plasma to unit costs and eventually prices and utilisation.

The more effectively plasma is utilised for wider sets of treatments where there are unmet needs…

…the lower the unit cost of all therapies given the economies of scale and scope…

…and the greater the number of patients that can benefit from treatments.

Source: Copenhagen Economics.

Notes: 1) Framework inspired by MRB and interviews with industry experts. / 2) Based on interviews with industry experts. / 3) See, e.g., de Serres (2003) for an example with Alpha-1 antitrypsin deficiency. / 4) Global Commission to End the Diagnostic Odyssey for Children with a Rare Disease (2025). / 5) Demand is centred around, see page 39.

An end-to-end value chain is key to ensuring supply and price stability of plasma-derived therapies

The Covid-19 pandemic exposed vulnerabilities in the plasma supply chain

Since plasma is the key raw material in the manufacturing of plasma-derived therapies, shortage of plasma can reduce the supply of plasma-derived therapies. During the Covid-19 pandemic, plasma collection fell by 9.4 per cent in Europe.[1] In France, the plasma shortage resulted in a drop in IG production and subsequently an 11 per cent drop in IG supply to hospitals in 2021. This was followed by growing competition between EU Member States for IG supply.[2] These experiences highlight how quickly plasma sourcing disruptions ("economic shocks") can lead to shortages of plasma-derived therapies, especially, when countries receive most of their plasma from a single supplier country, such as the United States.

In addition, economic shocks can occur due to:

1. Supply changes when global dependence on plasma sources is high (e.g., when production timelines from suppliers are prolonged)
2. Increases in patient need for plasma-derived therapies
3. Other disruptions in the supply chain (e.g., when costs of fractionation factories or collection centres increase)

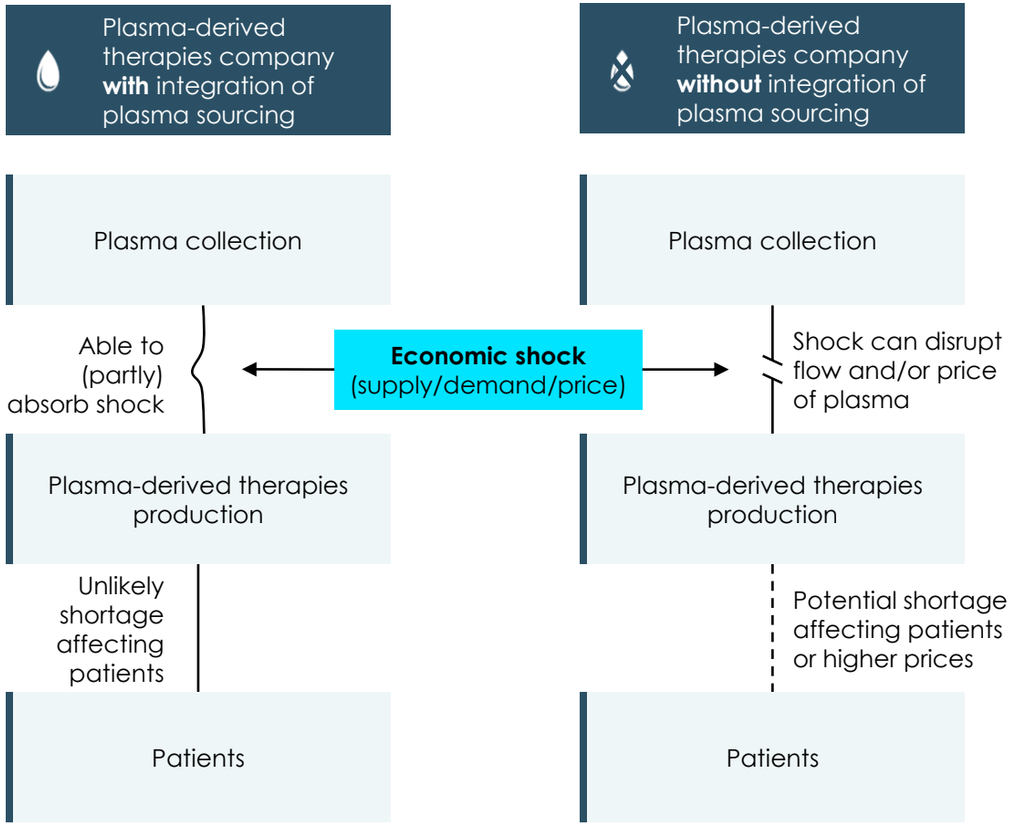
An end-to-end value chain stability can help alleviate supply risks due to economic shocks and support stable prices

Evidence from other sectors shows that stronger integrations of supply chains can reduce the risk of supply shortages when key production inputs are scarce in the case of a shock to the key input product. One example is how an electric automobile company was not affected by a global shortage of microchips in 2021 because they could design their own or update other less advanced chips that were available. Meanwhile other producers of electric vehicles were reliant on outside suppliers for microchips and technical expertise, which led to supply shortages for these manufacturers.[3]

Greater integration of plasma collection into the value chain thus strengthens the resilience to economic shocks to plasma collection and helps ensure stable supply, see Figure 20 for an illustration. In plasma-derived therapies, this would entail that therapy developers and manufacturers of plasma-derived therapies have plasma collection integrated into their supply chain, which we refer as an "end-to-end value chain".

57 per cent of the cost of plasma-derived therapies is manufacturing and raw material, which is significantly higher than the 14 per cent in the pharmaceutical industry, see page 45. This implies that sudden changes ("shocks") in the price of plasma will impact the price of plasma-derived therapies. An end-to-end value chain can alleviate such shocks, which enables manufacturers to ensure stable prices of plasma-derived therapies. The reason is that manufacturers can increase the collection of plasma for fractionation given that they have adequate tools to do so. Such tools likely include a sufficient donor pool, adequate capacity of plasma collection centres, and measures available to reimburse plasma donors for their time and inconvenience.

Figure 20. An end-to-end value chain strengthens the control of raw materials and increases resilience to disruptions



Source: Copenhagen Economics.

Notes: 1) Domanovic et al. (2023). / 2) Domanovic et al. (2023). / 3) Ewing (2022). See e.g., Bakshi et al. (2025) for a more general point.

Plasma-derived therapies are not suitable for stockpiling

Focus on supply chain resilience in medicines has increased in recent years

The COVID-19 pandemic exposed vulnerabilities in the EU's supply chains for medical products, increasing focus on security of supply. To achieve this, the EU has introduced initiatives including establishing strategic reserves of medicines, often referred to as stockpiling.[1]

Plasma-derived therapies are not suitable for stockpiling

The importance of plasma-derived therapies is widely recognised with at least 10 to 15 of these products included in the EU Union List of Critical Medicines, qualifying them for strategic reserves and supply chain monitoring.[2] However, plasma-derived therapies are not suitable for stockpiling, see overview in Box 8.[3] If used for stockpiling, the stockpiling requirements could worsen supply challenges of plasma-derived therapies, undermining the goals of ensuring access to critical medicines.[3] In practice, however, several countries still impose stockpiling obligations for plasma-derived therapies, including the Netherlands, France, Greece, Finland and the UK. This shows that policies supporting stockpiling persist even though PDTs are not suitable for stockpiling.[4]

The OECD has outlined that stockpiling has limited effectiveness in long-term disruptions such as those that are present in the manufacturing of plasma-derived therapies due to the unique features of the supply chain that depends on plasma collection.[5] The OECD further outlines that the proliferation of national stockpiling policies can potentially worsen supply gaps.[5] Instead, policy action should focus on addressing the root causes of shortages, to mitigate (or reduce exposure to) risks of shortages[6], which in the case of plasma-derived therapies is limited supply of plasma for fractionation.

To avoid stockpiling of plasma-derived therapies, the industry has urged EU policymakers to strengthen the supply chain, increase plasma collection, and streamline the regulatory framework for plasma-derived therapies. This could help meet the continuously increasing patient need for plasma by addressing the underlying issues affecting the supply chain.[3]

Box 8: Challenges related to stockpiling plasma-derived therapies

Plasma is limited: Plasma-derived therapies rely on human plasma which is a scarce and finite resource. Unlike synthetic medicines, which can be produced quickly and from an abundant source of input material, the plasma collection and manufacturing of plasma-derived therapies are lengthy and cannot be sped up. This long process exceeds typical timelines for stockpiling strategies and, additionally, stockpiling in one country can reduce supply in neighbouring countries, undermining the principle of solidarity and exacerbating access risks in smaller countries. The supply chain - from donor to patient - must be planned months ahead of time to ensure medicine availability.[3]

Short shelf life: Plasma-derived therapies have a shorter shelf life, usually ranging from 24 to 36 months,[3] than other types of medicines with shelf life up to 60 months.[5] If large quantities are stockpiled, there is a risk that some doses expire before they can be used.[3]

Increased cost: Manufacturing plasma-derived therapies is more expensive than traditional medicines.[6] If producers are required to stockpile large amounts, production costs will rise even more, especially since these medicines often need cold storage and careful distribution.[3]

Source: Copenhagen Economics based on PPTA (2025b) and CPME (2015).

Notes: 1) European Commission (2025a). / 2) PPTA (2025a). / 3) PPTA (2025b). / 4) PPTA (2025c) / 5) CPME (2015). / 6) See e.g., Grifols S.A (2024).

Artificial intelligence tools are increasingly utilised in supply chain processes for plasma-derived therapies and to enhance the patient experience

The industry has continuously optimised the plasma-derived therapies supply chain

Over the past decades, the plasma-derived therapy industry has focused on optimising supply chains for plasma-derived therapies. Improvements include increasing the number and accessibility of plasma collection centres as well as improving production efficiency.[1]

Artificial intelligence tools are increasingly utilised to optimise supply chain processes

More recently, artificial intelligence (AI) is increasingly utilised across the plasma-derived therapy value chain. A recent market report highlights that AI algorithms are being employed to optimise a range of different processes such as donor recruitment and scheduling, predictive demand modelling and the development of innovative biopharmaceutical treatments.[2]

These systems enhance supply chain operations by forecasting donor availability, improving donor retention, and reducing idle time during plasma collection.[2] There are different examples of how pharmaceutical companies utilise these tools to increase efficiency and production processes, see Box 9 for a few examples.

To better meet patients' needs, AI is also used across the process from collection to manufacturing. This includes using AI modelling to reduce waiting times for donors, forecasting supply, and using AI-driven microscopes to improve pathogen safety testing.[3] AI is integrated into plasmapheresis devices to optimise collection parameters in real time, improving plasma yield and reducing procedure variability.[4] It is further applied in donor management systems that personalise screening and streamline donor scheduling, thereby enhancing efficiency at collection centres.[5] Also, it is used to automate and standardise plasma pooling (i.e., combining plasma from multiple donors) in IG manufacturing.[6]

AI tools generate a positive patient experience through enhanced healthcare treatment at home

AI-enabled tools in healthcare treatments at home can enhance the patient experience by making support more convenient, proactive, and tailored to individual needs. Integrating AI into healthcare treatments at home enables providers to use predictive analytics and personalised treatment plans to identify potential health risks early and tailor interventions to each patient.[7] Together with telehealth and remote monitoring, these tools expand access to care, strengthen patient engagement, and make personalised treatment plans easier to deliver at home. This improves convenience and outcomes for patients.[8]

Box 9: Examples on the use of AI from the industry

The use of data and AI to increase efficiency

A global pharmaceutical company has increased its reliance on data, AI, and advanced analytics to boost efficiency. This includes enhancing the donation experience, increasing plasma volumes, and optimising operations across the supply chain.

Key initiatives include:

- Predictive forecasting using AI to accurately anticipate demand.
- Simulation and mathematical modelling to optimise plasma centre labour capacity.
- Digital Twin technology to drive data-driven decisions and create efficiencies in manufacturing.

These measures have contributed to a 27 per cent reduction in IG lead time – the amount of time it takes from the start of production to final product – in 2022 compared with 2019. In parallel, the IG yield per litre of plasma has increased, reflecting the efficiency gains achieved.[9]

Increased reliance on AI to improve production processes

Over the past two years, another global pharmaceutical company has made significant strides to become data-driven and digitally empowered. A key initiative at its production sites is the deployment of AI to drive operational excellence, optimise production flows, as well as to improve yields.

The implementation of Advanced Analytics has already delivered notable early successes - with measurable yield enhancements observed for intravenous human normal IG at two production sites.[7]

Source: Copenhagen Economics.

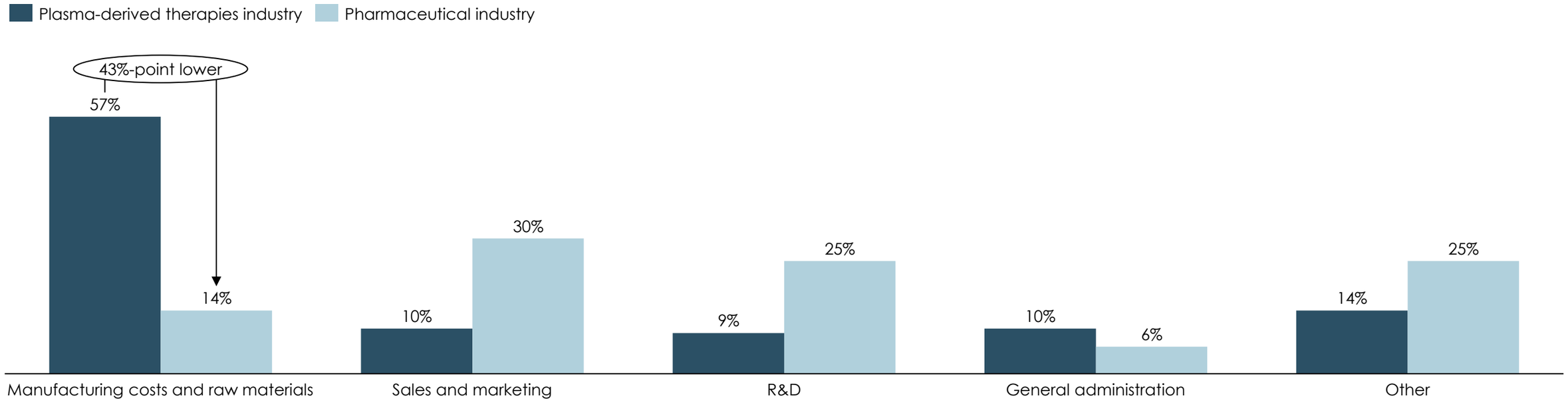
Notes: 1) Bolcato and Jommi (2024). / 2) BioSpace (2025). / 3) Takeda (2024). / 4) Fresenius Kabi (2025). / 5) Haemonetics Corporation (2023). / 6) ADMA Biologics (2024). / 7) Octapharma (2025). / 8) The Insight Partners (2025). / 9) Takeda (2023).

Unlike the traditional pharmaceutical industry, the majority of costs in the plasma-derived therapies industry are driven by manufacturing and raw materials

The majority of the costs associated with plasma-derived therapies consist of manufacturing and raw materials. Figure 21 shows that **57 per cent of the total cost** of producing plasma-derived therapies is from manufacturing costs and raw materials. This is in contrast to the traditional pharmaceutical industry where this number is estimate to be 14 per cent, i.e., 43 percentage points lower than in the plasma-derived therapies industry. The most important input factor – plasma – is thus a key component in both production of the final product and in terms of the share of costs.

A more recent source indicates that manufacturing costs and raw material account for as much as **69 per cent of the total cost** on average.[1] This is based on US data on cost of goods and services (COGS) from five plasma companies or plasma divisions of companies.

Figure 21. Cost structure of producing plasma-derived therapies and traditional pharmaceutical products
Per cent of total costs



Note: The pharmaceutical industry is based on chemical-based pharmaceuticals.
Source: Grabowski and Manning (2018).

Notes: 1) MRB (2022).

High costs for raw materials and plasma economics provide risks for supply if tenders are not carefully specified

Limited production capacities mean manufacturers need to prioritise supply

The supply of plasma-derived therapies is limited due to limited production capabilities in the short term, the long manufacturing process[1] and, critically, the limited supply of the raw material. Due to limited production capacity manufacturers have to prioritise supply. This is necessary to keep supply stable in countries with contracts in place. Unfortunately, currently, it also means not all patients can have access to all therapies.

Effects of pricing and tenders on supply

The large share of the total costs from raw materials[2] lowers the flexibility for developers and manufacturers of plasma-derived therapies in setting prices. This is especially true for IG, which, as it is a last litre product,[3] has to bear a large share of the raw material costs. Hence, tender specifications and pricing can have a major impact on ability to supply. In the worst case, tendering practices can lead to therapy shortages, as has been the case in, e.g., Spain and Romania, see examples in Box 10.

The problems can arise if 1) prices are driven so low in tendering processes that no manufacturers are able to supply, or 2) if patient need is higher or supply is lower than anticipated.

To avoid such problems, tenders can be strategically designed to ensure sufficient supply of plasma-derived therapies, see example from the UK in Box 10.

Box 10: Challenges in plasma supply and pricing

High costs of raw material are problematic if

There is an imbalance between patient need and supply
The supplier may not be able to meet demand if the price is set lower in one country than in other countries, or if prices of plasma has increased due to e.g. lower supply.

Prices are driven too low
Lower prices mean savings for payers and therefore benefits to patients and taxpayers. Payers, however, need to ensure that manufacturers can recover their costs and have an incentive to maximise the effectiveness of plasma-derived therapies.

Example: Therapy shortages due to imbalances between supply and patient need
Global demand for IG has risen steadily, while limited supply has led to intermittent shortages. This imbalance has led to what has been described as "the product follows the price", where countries with lower reimbursement levels, such as Spain, face difficulties in securing supply. The problem became acute during the COVID-19 pandemic, when donations fell and patient need rose, further straining the Spanish health system.[4]

Example: Rethink pricing environments to improve patient access
Romania has changed its pricing environment to enhance access to plasma-derived therapies. After patients experienced shortages, marketing authorisation holders no longer owe the quarterly contribution for the centralized consumption of medicines derived from human blood or human plasma reimbursed from the National Health Insurance Fund and Ministry of Health budget, often referred to as clawback tax.[5] This illustrates how a sustainable pricing environment is critical for uninterrupted patient access to plasma-derived medicines.

Example: Securing supply with strategic tendering
The UK has recently strengthened supply security for plasma-derived therapies through two tendering processes. In 2023, a plasma-derived therapy company won a tender to fractionate all domestically sourced plasma, ensuring that UK-collected plasma is fed back into the National Health Service (NHS). This reduces reliance on imports and enhances resilience in times of global shortages.[6] In parallel, the NHS operates a broader IG framework agreement, running from 2025 to 2027, which secures access to a range of plasma-derived therapies from multiple suppliers, thereby lowering the risk of supply gaps and enabling more individualised treatment to patient needs.[7] Together, these tenders combine domestic capacity with diversified international sourcing to safeguard patient access.

Source: Copenhagen Economics.

Notes: 1) See page 40. / 2) See page 45. / 3) 1) Framework inspired by MRB and interviews with industry experts. / 4) Solís-Díez et al., (2022). / 5) Government of Romania (in Romanian) / 6) Octapharma (2025). / 7) Immunodeficiency UK (2025).

Many European countries have adjusted their policies for plasma-derived therapies due to their unique characteristics

Unique policy approaches for plasma-derived therapies

Multiple European countries have adopted different types of measures to cater to the specific character of plasma-derived therapies, see Box 11. Examples of such measures include:

- Exemptions from standard cost containment policies, such as clawbacks, which means that companies selling plasma-derived therapies in these countries do not have to pay back as much of their revenues to the public health system as companies selling traditional medicines, if revenues exceed a given threshold.
- Lower tax rates on plasma-derived therapies than on other medicines.
- Less strict reference pricing, which allows more flexible pricing of plasma-derived therapies compared to other medicines. In practice, this means that countries with higher prices can be included when calculating the reference price. This leads to a higher reference price and gives manufacturers better possibilities to cover high production costs.
- Exemptions from price freezes, allowing more flexible pricing of plasma-derived therapies compared to other medicines. A price freeze means that medicine prices cannot increase beyond a certain level. When plasma-derived therapies are exempt from such freezes, their prices can be adjusted over time to reflect e.g. rising production costs.
- Specific tender frameworks that allow for inflation-adjusted prices

These measures highlight that plasma-derived therapies are treated differently due to their unique characteristics, such as reliance on human plasma, long and complex production cycles, and the high production costs associated with these therapies.

Box 11: Examples of special policy approaches for plasma-derived therapies

The UK, Belgium, Greece, Ireland, and Romania all allow for **clawback exemptions** for all or certain plasma-derived therapies.

Portugal applies a **lower tax rate** for plasma-derived therapies of 2.5 per cent compared to14.3 per cent for other medicines.

Estonia, Greece, Romania and Spain use **less strict reference pricing** for plasma-derived therapies than for other medicines.

Germany has a price freeze in place for many reimbursable medicines (including plasma-derived therapies), maintaining 2009 price levels, but IGs authorised in 2019 or later are **exempt from the price freeze**.

Denmark and the UK employ **tender frameworks** that allow for inflation-adjusted prices

Source: PPTA (2025c), Irish Pharmaceutical Healthcare Association & Health Service Executive (2021), *La Ley 7/2025 (2025), NHS (2025b).*

2.2

WHAT IS THE ECONOMIC VALUE OF THE PLASMA-DERIVED THERAPIES INDUSTRY?

The plasma-derived therapies industry has a wide geographic footprint and creates value throughout the European economy

A specialised industry that creates value to the European economy

The largest contribution of the plasma-derived therapies industry is the health and quality of life benefits it brings to patients. The societal contribution of the industry is not, however, limited to patient benefits but extends to economic impacts. We sought to examine the types of economic contributions the plasma industry can have on the wider economy.

The economic footprint of an industry or company is calculated through looking at the direct, indirect, and induced (or wage) effects, as depicted in the chart. The plasma-derived therapies industry has a geographically wide footprint, contributing to the economy not only in the European countries where fractionation centres are located, but also around those countries. Collection centres, for example, are spread out to attract as many donors as possible. The economic compensations that are used in the Czech Republic, Austria, Germany, and Hungary also add to the local footprints. Finally, the products are spread all over the world.

A complete economic footprint analysis requires large amounts of sensitive data

A fully-fledged footprint analysis requires large amounts of sensitive company-specific data. It has not been possible to obtain such information from all manufacturers of plasma-derived therapies in Europe. Since we do not have the detailed data to undertake a traditional footprint analysis, we have used available evidence to assess the order of magnitude of the economic footprint of the plasma industry. The approach is outlined below.

Direct effects
Jobs created and purchases of inputs needed for production

Indirect effects
Jobs created and purchases of input needed for production at suppliers

Induced effects
Wage effect as employees spend their income

Therapy developers & manufacturers

The therapy developers & manufacturers create direct economic value through employment and purchase of production materials needed for research & development, fractionation, quality control, and distribution of plasma-derived therapies. Direct effects also arise from plasma collection centres owned by the therapy developers & manufacturers.

Suppliers

For production, the therapy developers & manufacturers also need many products and services they do not provide themselves. These are bought from suppliers that need to employ workers and purchase inputs to run their services. This includes, e.g., IT services, security, cleaning, and transportation services. Additionally, 3rd party plasma sourcing also falls under this category.

Wages

All the employees at the therapy developers & manufacturers as well as their suppliers receive wages from their employers. When these wages are spent on groceries, clothes, housing etc., this creates additional economic activity. Furthermore, in countries where plasma donations are monetarily compensated, this additional wage also creates an effect when donors spend their income.

Source: Copenhagen Economics.

Methodology description: our approach to obtain an indicative estimate of the economic contribution of the industry

We use the inter-country Input-Output table from the OECD

As with a standard economic footprint analysis, we estimate the effects of the plasma-derived therapies industry in Europe by using so-called *multipliers*. These multipliers express the effects that investments by the plasma-derived therapies industry have on other parts of the European economy, in line with the capacity expansion described on page 38.

We calculate our multipliers from the inter-country Input-Output (IO) tables from Organisation for Economic Co-operation and Development (OECD).[1] This database covers 81 countries and 50 sectors.[2] These tables represent the supply and use relationships in USD millions between the 50 sectors and 81 countries for the year 2022. As we are interested in the European-wide effects, we used an aggregate table of the EU27 countries. From this table we are able to calculate direct, indirect, and induced (consumer spending) multipliers for the gross domestic product (GDP) including industry and donor centres and employment (donor centres only) effects.

The effects supported by the plasma-derived therapies industry

The data we used are based on the total global sales made in the plasma industry in 2023 of USD 32.5 billion.[3] Of the total global sales, we allocate 42.5 per cent to Europe.[4] We expect that this number does not correspond precisely to the countries included in the IO EU27 aggregation, although it should be highly correlated. Furthermore, we assume that the peripheral European countries would be unlikely to differ substantially in supply and use structure to the EU27. Nonetheless, this is reason to interpret the approximation with care.

Given an approximation of the total sales attributed to Europe, we used the multipliers for industry classification '*C21 - Manufacture of basic pharmaceutical products and pharmaceutical preparations*'. This classification corresponds to the International Standard Industrial Classification of All Economic Activities revision 4 sector C. 2100, which includes the processing of blood, amongst other processes.[5] As this is a broad sector, however, the multipliers should only be seen as a rough approximation for the plasma-derived therapies industry. This is because the structure of the plasma-derived therapies industry itself varies considerably with the average EU sector classification. Due to this variation in sectoral structure caution should be exercised when interpreting our approximation.

The multipliers are then multiplied by the share of the total sales produced in Europe to give the economic effect. As a final note, we translate the economic impacts on GDP from USD to EUR using the average 2023 exchange rate from the European Central Bank.[6]

The effects supported by donor compensation

In addition to the aggregated EU27 IO table, we use three primary sources of data to estimate the economic impact of collection centres.

1. Total plasma collected in 2023 by country (in litres)[7]
2. The average volume per donation by country[8]
3. Compensation per donor by country[9]

We collect this data for the four countries in the EU where compensation to donors is possible (Germany, Austria, the Czech Republic, and Hungary). Using these three data sources, we can estimate the total compensation given in each of the four countries individually. We use the following calculation for each country, c, to do so:

$$Total\ Compensation_c = \left(\frac{Total\ plasma\ collected_c}{Volume/donation_c}\right) \times Comp./donor_c$$

We use the sum of the results to arrive at a total of compensations of just under **178 million EUR.**

As this is pure compensation, we calculate induced effects alone. This effect describes how the compensation is spent in the wider economy. To do this, we calculate the multipliers for 'households'. This is done in the same way as it would be for any other sector. The result is an induced multiplier that describes the spending of money by households.

As we calculate individual country multipliers, the induced GDP and employment effect only captures the domestic consumption. As a result, spending in other countries and on imports is not captured in our estimates. Therefore, our estimations should be interpreted as a conservative approximation.

Furthermore, as we are considering compensation alone, our estimation is unlikely to capture all the economic dynamics. This is because the compensation offered is unlikely to cover the full economic cost incurred in travelling and donating plasma.[10] This is further reason to interpret out estimation with care.

Notes: 1) See OECD's inter-country input-output tables, OECD (2025). OECD does not include salaries and employment, so we collect this data from various data sources such as Eurostat. / 2) Based on the International Standard Industrial Classification rev. 4, see United Nations (2008), revision 4. / 3) MRB (2024c). / 4) MRB (2024b). / 5) United Nations (2008), revision 4. / 6) European Central Bank (2025). / 7) MRB (2025a). / 8) Estimated based on EDQM (2019), day 2. / 9) European Commission (2016). We adjust this to 2023 level using country level consumer price index (CPI) from Eurostat (2025). / 10) See, e.g., Platz et al. (2019).

The plasma-derived therapies industry makes a substantial contribution to the European economy

The plasma-derived therapies industry supports the European economy

Based on existing evidence, we obtain an indicative estimate that the plasma-derived therapies industry supports approximately 14.2 billion EUR throughout Europe (per annum).

These estimates indicate the gross value added by the plasma-derived therapies through three different effects (as shown in Box 12 and explained in detail on page 50).

1. Around 6.6 billion EUR of the total value is supported directly from the value added by the industry through employment and purchase of production materials needed for research and development, fractionation, quality control, and distribution of plasma-derived therapies.
2. Around 4.8 billion EUR of the total value is supported through the supply chain to those industries supplying the plasma-derived therapies industry. This includes everyone from the IT professionals to the construction industry, and all medical appliances and supplies in between.
3. Around 2.9 billion EUR of the total value is supported via spending of wages, i.e. induced effects in the plasma-derived therapies industry and supporting sectors. This spending effect supports, among others, the retail, hospitality, and utilities sectors.

The estimation is based on a number of assumptions and should be interpreted with care

As mentioned on page 50, we do not have the detailed data to undertake a traditional footprint analysis. Instead, we have used existing evidence to assess the order of magnitude.

The estimates are derived from a total market value of plasma-derived therapies worldwide of around 30 billion EUR in 2023 [1] and an estimated share produced in Europe of 42.5 per cent based on the share of plasma fractionated in Europe.[2]

Our estimation is based on the assumption that the plasma-derived therapies industry is similar in production structure to the industry 'C21 – Manufacture of basic pharmaceutical products and pharmaceutical preparations'. This is a strong assumption, see, e.g., page 45 for an illustration on the difference in cost structure.

As explained on page 51, the estimates should be interpreted with care, as they are indicative estimates of the value supported by the plasma-derived therapies industry.

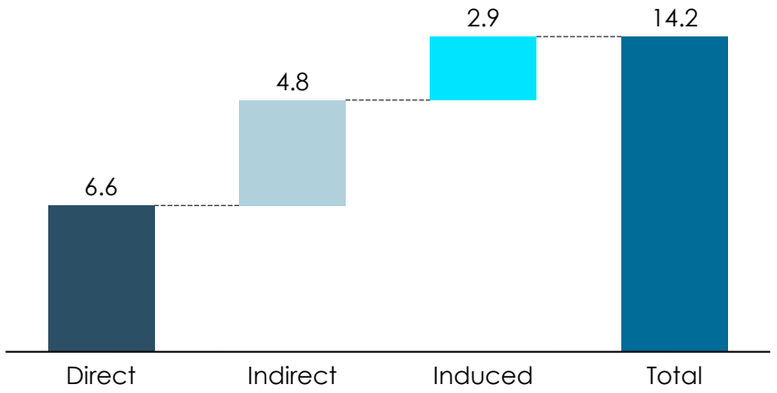
Box 12: Components of value added

The estimates of the value supported by the entire industry indicate the gross value added calculated as the sum of

- Direct effects = jobs supported and purchases of inputs needed for production
- Indirect effects = jobs supported and purchases of input needed for production at suppliers
- Induced effects = wage effect as employees spend their income

Source: Copenhagen Economics.

Figure 24. GDP supported by the plasma-derived therapies industry in Europe – indicative estimates
Billion EUR, per annum, 2023



Note: Based on data from 2023 and 2022. Source: Copenhagen Economics based on IO data from OECD (2025), market value of plasma-derived therapies in 2023 from MRB (2024c), and production share in Europe from MRB (2024b).

Notes: 1) 32.5 billion USD in 2023 from MRB (2024c) and an average exchange rate in 2023 of 1.0824 USD per EUR from the European Central Bank (2025). The market value does not include recombinant products. / 2) Share from MRB (2024b). We use this share as a proxy for the share of the total market value that is produced in Europe.

Spending in the wider economy of compensations to plasma donors supports an estimated 151 million EUR per year and 2,260 full-time equivalent jobs

Donor compensation in four European countries supports 151 million EUR in GDP

The spending effect supported by donor compensation results in an estimated 151 million EUR of GDP throughout Germany, Hungary, the Czech Republic, and Austria in 2023, see Box 14.

As the donor receives compensation for expenses spent in the economy, it will have an effect on GDP through an induced effect.[1] An estimated 168 million EUR was given in donor compensation to the four countries in 2023. The 151 million EUR estimate is lower than the total compensation, as the induced effect does not take into account imports and spending in other countries. It therefore represents an indicative estimate of the compensation value in Europe.

Donor compensation supports around 2,260 jobs

We estimate that through this spending, around 2,260 full-time equivalent[2] jobs are supported.

The estimations are based on plasma donation volumes in Germany, Austria, the Czech Republic, and Hungary in 2023.[3] We use a volume per donation of 850 ml. in all four countries to estimate the number of donations.[4] This approach yields conservative estimates of the GDP and employment supported. Compensations per donation is based on country-specific donation rates.[5]

Plasma collection centres themselves contribute to the local community

Besides these effects, plasma collection centres can have positive effects on the local community through a number of additional channels:

- Employing staff to operate the collection centre (direct effect), which may be as many as 7,865 individuals in 2023, see Box 15. This number will increase with the number of collection centres.
- Using local contractors for different tasks (indirect effect)
- Collaborative partnerships with local stakeholders, e.g., universities

Box 13. Induced effects from donor spending

The estimate of the value supported by the plasma collection centres indicates the gross value added calculated from

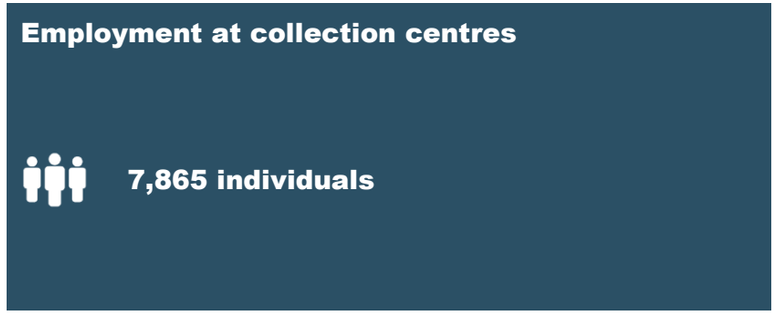
- Induced effects = monetary compensation effect as plasma donors in Germany, Austria, the Czech Republic, and Hungary use the compensation they have received

Source: Copenhagen Economics.

Box 14. GDP and employment supported by monetary compensations to donors in 2023 – indicative estimates

Note: From contributions made by donor compensation in Germany, Austria, the Czech Republic, and Hungary. Employment rounded to nearest 10.
Source: Copenhagen Economics based on donation volumes from MRB (2024b), average country-specific donor compensation from European Commission (2016), and average donation volume from European Plasma Alliance, see EDQM (2019), day 2.

Box 15. Number of individuals employed in commercial plasma collection centres in 2023 – indicative estimate



Note: Estimated number of individuals employed at 242 commercial collection centres in 2023. Note that the number of centres has increased since 2023.
Source: Copenhagen Economics based on number of commercial collection centres from MRB (2024a) and average number of employees from Haema. The average of 32.5 employees per centre is based on 1,300 employees across 40 centres.

Notes: 1) In practice, much of the economic supported activity happens before the donation – hence the money is 'compensation' for the cost incurred. / 2) Full-Time Equivalent jobs is defined as 40 hours per week per year. Hence, two part-time employees working 20 hours per week each would be considered as 1 full-time equivalent employee. This estimate is rounded down to the nearest 100. / 3) MRB (2024b). / 4) See, e.g., Pant et al. (2021) for an overview. Donation volumes are normally weight dependent with 850 ml. per donation only applying to individuals of a certain weight, e.g., above 80 kg. in Germany. / 5) European Commission (2016). We adjust this to 2023 level using country level CPI from Eurostat (2025) (link). / 6) The TS093 project, see EDQM (2019).

The plasma-derived therapies industry also creates value through other channels which are not estimated here

Figure 25. Value creation through the plasma-derived therapies industry

Source: Copenhagen Economics.

In addition to the economic footprint based on direct, indirect, and induced effects, the plasma-derived therapies industry also creates economic value through several other channels throughout the value chain. We do not quantify these here, which makes our estimation conservative.

Better care extends life-expectancy and increases participation

When patients get better care, they live longer and healthier lives. Proper care increases labour market participation and the income of the state, as we showed in chapter 1.3. An example of increased life expectancy are patients with haemophilia who had a life expectancy of 13 years in the early 20th century.[1] In 2018, life expectancy had approached normal and was only 5 years lower than that of an average person.[2]

Better health for patients

Plasma-derived therapies increase the quality of life for patients with rare diseases. For some, they are the only treatments option. This extends their life-expectancy and allows them to lead a fuller life with less focus on thinking about their disease. Quantifying the value of this is difficult, but the example with life-expectancy for haemophilia patients provides an idea. European males with haemophilia would have an additional 59 years to live, which would translate to over 4.6 million EUR if we assume an added year is worth EUR 168,357.[3]

Investments in healthcare through education and clinical trials

The plasma-derived therapies industry invests in the standard of the healthcare system through educating personnel as well as developing and testing new drugs in clinical trials. The clinical trials are also a way in which the patients support the development of new therapies. Clinical trials increase the productivity and standard of the healthcare system, which benefits society as a whole. Our study on the economic impact of clinical trials by pharmaceutical companies in Denmark found that one clinical trial improved GDP by DKK 902,000, or around EUR 120,800.[4] This is likely an upper bound for the value of rare disease clinical trials, as the number of participants and people involved are fewer than in other clinical trials.

Investments in new, better products can decrease health care spending

New and better products are created to optimise production, e.g. maximise plasma utilisation and increase patient welfare. Additionally, new products can save health care costs. An example is moving to SCIG from IVIG. SCIG can be self-administered, which saves both hospital and physician costs. A study from the US found that hospital costs decreased from USD 4,187 to USD 1,836 when moving to SCIG, and physician costs from USD 744 to USD 84.[5] Hence, moving to SCIG could both lower healthcare costs and improve care capacity.

Technology spillovers to other industries

The plasma-derived therapies industry continues to conduct research to improve both manufacturing equipment and therapy delivery devices for the benefit of patients using the therapies. Furthermore, the research can also benefit patients on other therapies and the healthcare industry at large through technology spillovers. One example is BAXJECT®, which allows haemophilia patients to prepare their medication without using sharp needles and is safer, faster, and easier than previously existing application methods. This method can also be used for other types of treatments.[6] Another example is the Flexbumin GALAXY® container, which is a container that has been developed for albumin but is used extensively by pharmaceutical products. The container is safe from contamination thanks to a four-layer system and is also free of harmful plastic substances.[7]

Notes: 1) National Bleeding Disorders Foundation (n.d). / 2) My Hemophilia Team (2023). Average life expectancy for men in Europe in 2023 is 78 years. / 3) Average life expectancy for men in Europe in 2023 is 78 years, so patients with haemophilia can expect 72 years (75 78 minus 10 5 years lower life expectancy). The estimates on the value of a statistical life year vary significantly. We have decided to use Schlander et. al (2023) reporting a value of EUR 168,367 for Europe. As a euro tomorrow is not as much as one today, we have discounted future payments with 3 per cent discount rate. / 4) Copenhagen Economics (2017). The exchange is EUR 1 = DKK 7,46. / 5) Fu et al. (2018). / 6) EurekAlert (2002) Baxter introduces Baxject needleless transfer device at International Haemophilia Congress. / 7) Flexbumin, Medical Device Development (2011).

CHAPTER 3
OUTLOOK FOR THE PLASMA-DERIVED THERAPIES INDUSTRY AND SCENARIOS GOING FORWARD

Chapter 3 – Main conclusions

There is an increasing patient need for plasma overall. There is an increase in the use of especially IG, but a decrease in use of products with recombinant alternatives. Today, Europe is reliant on plasma imports from the US from where it receives around 40% of its plasma. So far, the US has been able to supply sufficient amounts to meet European patient need.

Risks with the 'As-is' scenario

If the industry continues in an As-Is scenario, there are a number of potential threats to the supply of plasma.

IG needs to bear almost the full cost of plasma collection and fractionation, which may not be sustainable for the industry as a whole.

The European supply of plasma-derived depends to large extent on the plasma supply from the US.-Europe's exposure to the US supply of plasma is exacerbated due to the increasing patient need for plasma-derived therapies. Moreover, the US' own fraction throughput grows faster than its plasma collection,[1,2] which implies that the US might be not be able to export as much in the future as it did in the past.

Relying on plasma obtained from monetarily compensated donors in the US, while not allowing monetary compensation of donors in all but four European countries, appears contradictory.

There are concerns over 'Commoditisation'

Based on interviews with experts in the plasma-derived therapies industry, there is a risk of over commoditisation in the industry, i.e., a situation where products that are distinguishable and differ in terms of product characterisation end up being viewed as a simple commodity.

There are several means of compensating donors

There are two broad classes of donor compensation available: monetary and non-monetary. These compensations both seek to mitigate the disincentives associated with the donation, as they do not exceed the loss incurred. Monetary compensation and reimbursement include reimbursement of travel costs and compensation using discounts and tax reliefs. Non-monetary compensation includes small gifts, health checks, or time off work. If any transfer to donors exceeds the loss incurred from the donation and thus provides an incentive to donate for those who would otherwise not have chosen to do so, it is a payment or a reward. These are both illegal in the EU, ethically problematic, and are not considered relevant.

Monetary compensation is in line with voluntary and unpaid donations

Firstly, a reimbursement of incurred expenses such as travel costs is not providing an incentive to donate for those who are not already inclined to do so. It is therefore ethically acceptable to reimburse incurred expenses since doing so abides with the principle of voluntary and unpaid donations and is in line with European legislation.

A further monetary compensation is consistent with voluntary and unpaid donations insofar as it does not exceed the loss incurred.[1] These are, however, viewed as controversial by many, likely due to the difficulty in defining when a monetary transfer is a payment and when it constitutes compensation.

Non-monetary compensation is also consistent with an altruistic focus given that it does not exceed the loss incurred.[3] There is, for example, research to suggest that non-monetary compensation can be used to attract donors leading to a 15-20 per cent increase in donations.[4]

A paradigm shift is required

A paradigm shift in the compensation of plasma in Europe that includes a small monetary or non-monetary compensation will be ethically acceptable, significantly increase donations, make the European supply of plasma-derived therapies more resilient to shocks in the supply of plasma, and ensure that plasma used for fractionation in Europe comes from voluntary and unpaid donors. In addition, the ethical considerations should take on the patient perspective as well as the donor perspective and ask, if it is ethically acceptable to limit the treatment options for patients suffering from rare diseases.

Box 16. Donor incentive levers

Availability of plasma can and should be increased by mitigating disincentives to donate using:

- reimbursements
- monetary compensation
- non-monetary compensation

Source: Copenhagen Economics.

Notes: 1) MRB (2024b). / 2) European Commission (2025c). / 3) Nuffield Council on Bioethics (2011) and Platz et al. (2019). / 4) Lacetera and Macis. (2012).

3.1
THE CURRENT TRENDS SHAPING THE PLASMA-DERIVED THERAPIES INDUSTRY

Industry investments across collection, fractionation, and distribution support a sustainable supply of plasma-derived therapies

Plasma suppliers are making substantial investments across the end-to-end value chain covering collection, fractionation and distribution to strengthen the sustainability of supply of plasma-derived therapies in Europe and globally, see Figure 26. We screened annual reports and press releases from CSL, Grifols, Kedrion Biopharma, and Takeda between 2021–2025, as well as key news outlets, to exemplify a few investments made by the industry.

Suppliers continue to expand and diversify plasma collection networks in Europe and globally

CSL is scaling collection capacity through technology upgrades, introducing new plasmapheresis collection equipment (Rika Plasma Donation System and iNomi™) over FY2025.[1] Grifols is expanding its physical collection through acquisitions, investing USD 265 million in 2024 to acquire 14 plasma centres and committing USD 79 million in 2025 and USD 62 million in 2026 for additional centre purchases.[2] Kedrion Biopharma is investing USD 260 m in over 40 new collection centres in the U.S,[3] and Takeda has expanded its plasma donation network by 110% since 2018 and opened ca. one new centre every two weeks in 2023[4].

Suppliers invest in fractionation and manufacturing expansions

In Marburg, Germany, CSL opened its USD 470 million base-fractionation facility,[5] while Grifols is doubling its plasma fractionation capacity in Europe by opening a new plant in Spain.[6] Kedrion Biopharma is investing EUR 150 million to a new factory in Bologna, Italy,[7] and Takeda has invested EUR 350 million to a new production plant in Rieti, Italy[7],

Suppliers invest in infrastructure and logistics hubs to improve reliability and reduce delivery lead times

CSL invested CHF 250 million to expand its Bern manufacturing site and logistics hub (Protinus), connected to its logistics and service centre.[9] Grifols is investing as part of a joint EUR 280 million program to build a plasma logistics hub in Egypt to improve supply reliability and shorten delivery lead times to hospitals.[10] Kedrion Biopharma is investing USD 80 million in IT infrastructure,[12] and Takeda opened a new automated warehouse in Belgium spanning 6,700 m² to reduce delivery lead times and improve supply operations.[11]

Figure 26. Industry investments across collection, fractionation, and distribution

CSL	**84** plasma centres equipped with new plasmapheresis collection equipment[1]	**USD 470 m** investment in base-fractionation facility in Germany[5]	**CHF 250 m** investment into Bern, Switzerland manufacturing site and logistics hub[9]
Grifols	**USD 265 m** investment into 14 new plasma centres in 2024[2]	**EUR 160 m** investment into new manufacturing site in Spain[6]	**EUR 280 m** investment to build a plasma ecosystem in Egypt[10]
Kedrion Biopharma	**USD 260 m** investment in developing over 40 new collection centres in U.S.[3]	**EUR 150 m** investment into new factory in Bologna, Italy[7]	**USD 80 m** investment in IT infrastructure[11]
Takeda	**110%** increase in plasma donation centres between 2018 and 2024[4]	**EUR 350 m** investment into production plant in Rieti, Italy[8]	**6,700 m²** automated warehouse opened in Belgium[12]

Sources: See footnote.

Notes: 1) CSL (2024) / 2) Grifols (2025) / 3) Kedrion Biopharma (2025) / 4) Takeda (2024) / 5) CSL (2023) / 6) Grifols (2025) / 7) Il quotidiano Economico Toscano (2025) / 8) Takeda (2024) / 9) CSL (2019) / 10) Grifols (2025) / 11) Kedrion Biopharma (2025) / 12) Takeda (2024)

Patient need for last litre plasma-derived therapies is increasing, which leads to an increase in the demand for plasma

Europe imports plasma from the US as EU countries are not self-sufficient, i.e. do not collect enough plasma for fractionation domestically to cover the domestic need for plasma-derived therapies.[1]

Donated plasma is a scarce resource

Adequate supply of plasma-derived therapies in the future is uncertain, as the availability of donated plasma for fractionation remains uncertain. As shown in Figure 27, demand for IG, the biggest driver of plasma demand, is increasing and is expected to grow by additional 37 per cent until 2028 relative to 2022. A key factor behind this growth is the increased use of IG to treat SID among cancer patients.[2] To respond to this growing need for IG, manufacturers are scaling up their production, see Figure 28.

There is a scarce amount of donated plasma available, not only in Europe but also worldwide. This is due to the limited availability of donors who are able or willing to donate. The increasing demand for plasma-derived therapies requires a focus on where the plasma used to manufacture these products should come from going forward.

Demand is increasing, but only for some products

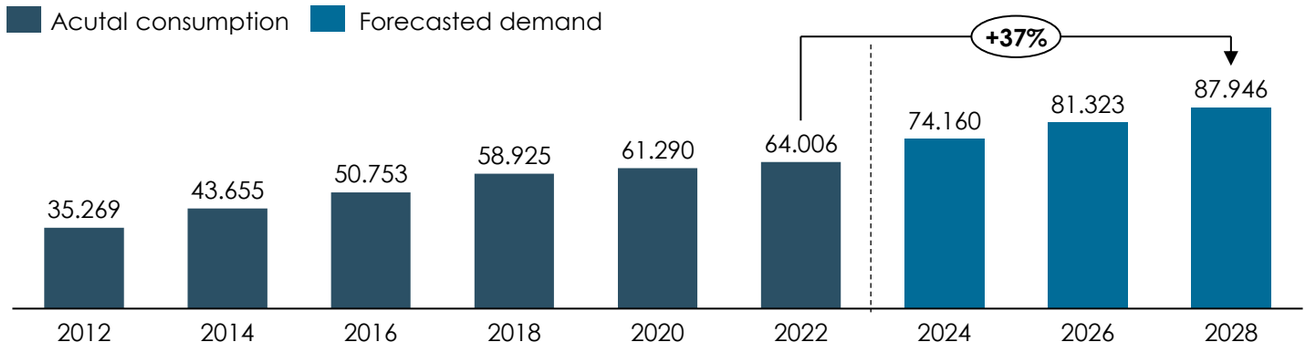
A combination of plasma economics,[3] plasma components, and patient needs determine the demand for plasma. Currently, there is an increase in the use of last litre products, e.g. IG, but a decrease in use of products with recombinant alternatives. This is a threat to the industry as a whole, as IG needs to bear almost the full cost of plasma collection and fractionation.

Box 17. High IG consumption among CIDP patients adds to growing demand

CIDP patients typically require high volumes of IG, oftentimes higher than those on replacement therapy for immunodeficiency.[4,5] As a result, CIDP accounts for about 22-27% of total IG use in Western European countries.[6] Moreover, as prevalence rises with age and updated diagnostic criteria identify more patients, more people will need IG to treat CIDP in the future.[7] Together, higher volumes per patient and more diagnosed patients create pressure on IG consumption and further increase the demand for IG at a time when donated plasma is scarce and Europe relies on imports.

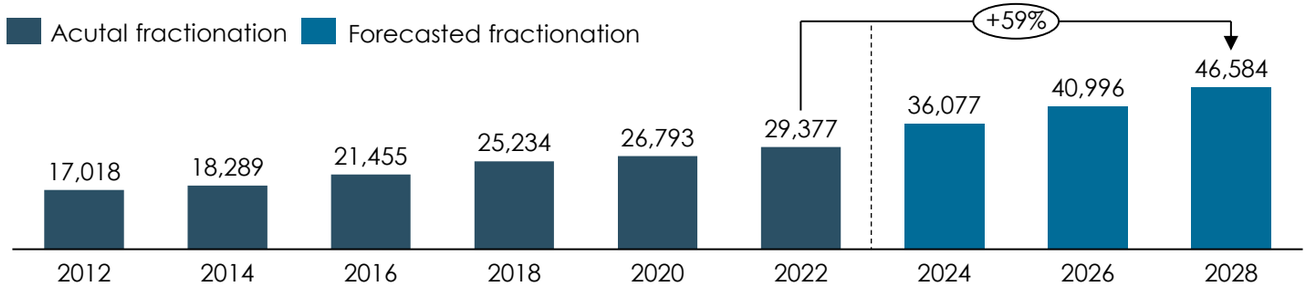
Source: Copenhagen Economics.

Figure 27. IG consumption in Europe from 2012-2022 and forecast from 2024 – 2028
Kilograms



Source: MRB (2023) and MRB (2024a).

Figure 28. Fractionation throughput in Europe from 2012 – 2022 and forecast from 2024 – 2028
1,000 litres



Note: Forecast is based on expected growth rates in plasma collection MRB (2024b).
Source: MRB (2024b).

Notes: 1) Domanovic et al. (2023). / 2) de Albornoz et al (2024) / 3) See page 37, framework inspired by MRB, and interviews with industry experts. / 4) European Medicines Agency (2021). / 5) European Medicines Agency (2024). / 6) MRB (2024a) / 7) Muley and Beydoun (2023).

Europe’s plasma fractionation throughput exceeds Europe’s plasma collection

The plasma-derived therapies industry in Europe is highly dependent on fractionated plasma, which is not adequately supported by Europe’s own plasma supply.

Europe’s plasma fractionation throughout has increased by 6.6 per cent per year since 2008

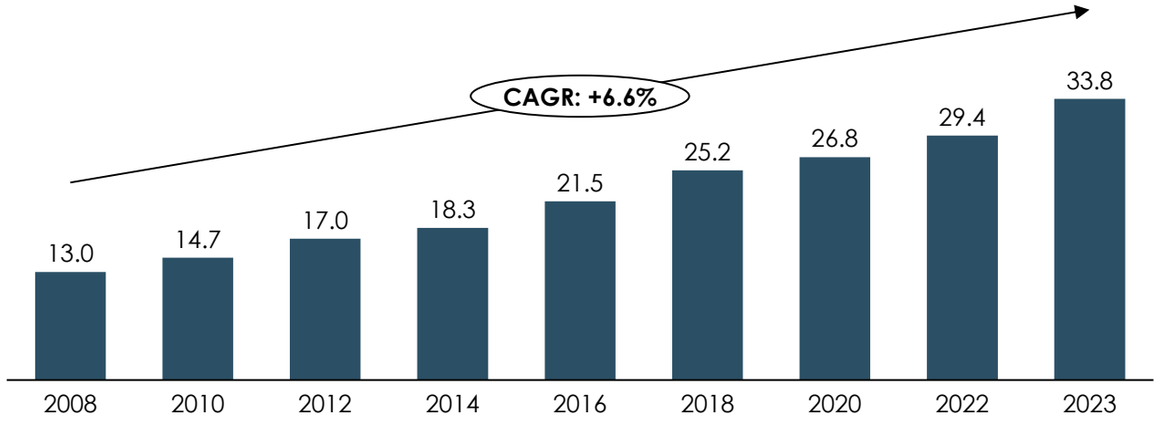
Europe’s plasma fractionation throughput is constantly increasing. It increased from 13 million litres in 2008 to 33.8 million litres in 2023, see Figure 29. This constitutes an average yearly increase of 6.6 per cent.[1] It comprises both sourced and recovered plasma from commercial and non-commercial collections. However, note that the fractionated plasma in Europe does not only cover the demand in Europe. Some of the fractionated plasma is also exported to other continents.

Europe faces a substantial undersupply of plasma

In 2023, Europe collected only 10 million litres of plasma for fractionation, see Figure 30 This reflects 11,76% of the total collected plasma worldwide[2] and falls short of Europe’s own fractionation capacity. Figure 30 also shows that the annual growth of plasma collection Europe (4.3%) is smaller than the annual growth of the fractionation throughput (6.6%). 50% per cent of the plasma is collected in private plasma collection centres in Germany, Austria, the Czech Republic and Hungary.[3]

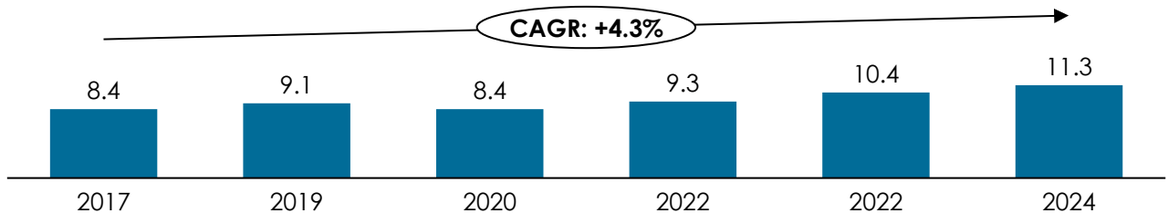
The largest share of plasma that is used for fractionation is collected in North America with 57 million litres in 2023. This is almost 6 times as much as in Europe although the fractionation throughput in North America in 2023 was only 29.4 million litres and thus lower than in Europe.[1]

Figure 29. Plasma fractionation throughput in Europe
1,000,000 Litres



Note: Compounded average growth rate (CAGR) of 6.6 per cent from 2008 to 2023.
Source: MRB (2024b).

Figure 30. Plasma collected for fractionation in Europe
1,000,000 Litres



Source: MRB (2025b).

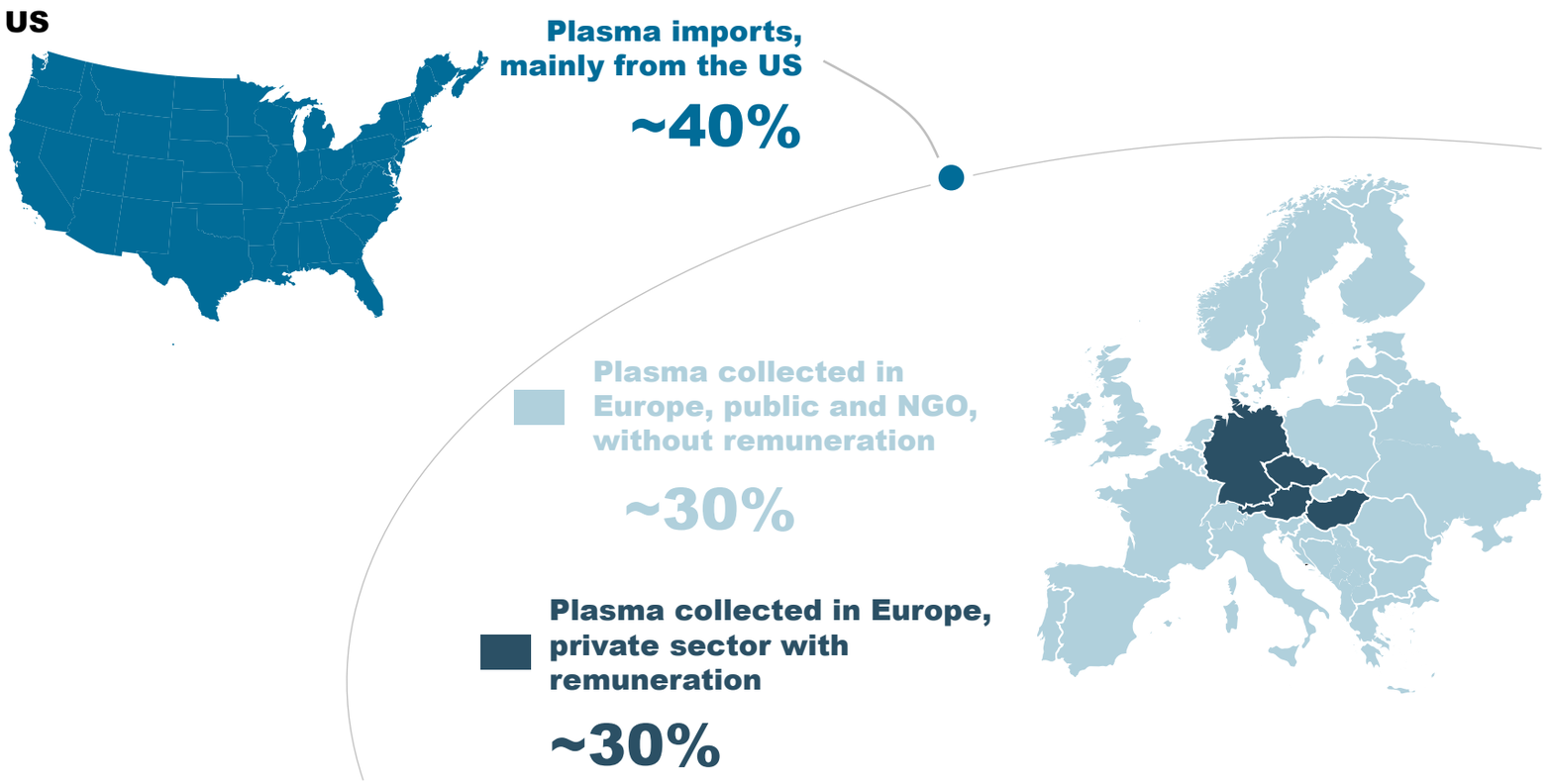
Notes: 1) MRB (2024b). / 2) European Commission (2025d). / 3) Pijuan (2025)

Europe relies heavily on US supply of plasma to meet patient needs

Around 40 per cent of the total plasma needed in Europe is imported from the US

Europe imported around 40 per cent of its total plasma in 2023 and is heavily reliant on plasma from the US, see Figure 31. However, total plasma imports include plasma for all purposes (e.g., also fresh frozen plasma), not only plasma for fractionation. European public and NGO blood collection services collected 30 per cent of plasma need, and the European private sector, which is allowed to remunerate donors, collected the remaining 30 per cent from only four countries (Austria, Czech Republic, Germany, and Hungary).[3]

Figure 31. Imports of plasma to Europe in 2023
Share of total plasma need



Note: The figure shows plasma for all purposes (e.g., also fresh frozen plasma), not only plasma for fractionation.
Source: Multiple sources report that Europe imports around 40 per cent of its plasma, see Ockenfels and Roth (2023), Merz (2023) or Simonetti and Smith (2024). MRB data shows that 50 per cent of the plasma collected in Europe stem from commercial sources and the other 50 per cent were from non-commercial sources in 2023, see European Commission (2025c).

Notes: 1) Ockenfels and Roth (2023). / 2) Merz (2024). / 3) European Commission (2025c).

Europe’s reliance on US plasma exports poses a risk for its fractionation industry

The US is currently able to support a substantial share of its plasma to Europe and other countries since it exceeds their domestic patient needs by 105.8%, see Figure 32. However, relying on US plasma to meet the plasma need of Europeans creates a dependency and poses a risk.

Europe’s reliance on US plasma exports could jeopardise the European fractionation industry

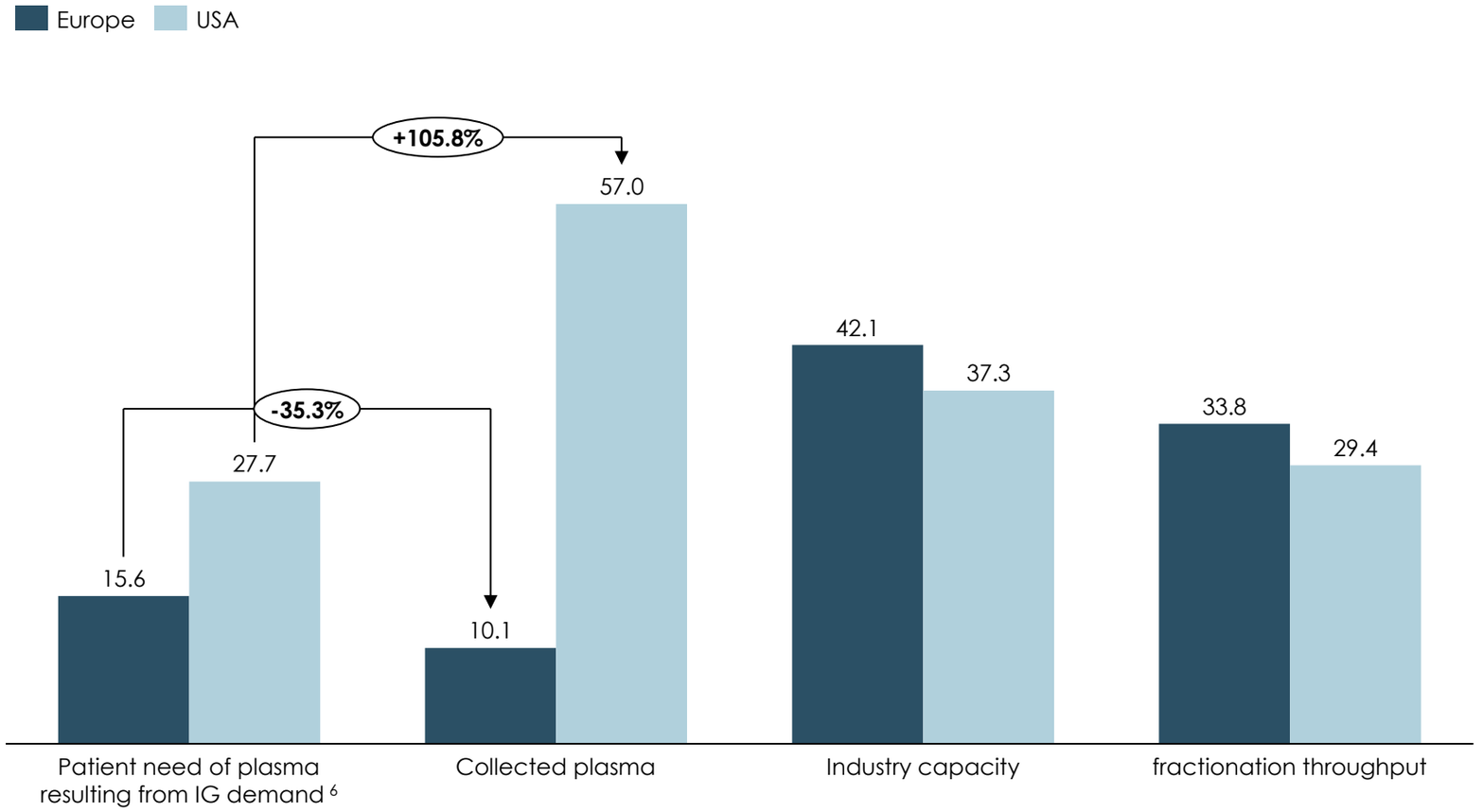
Europe has built the largest fractionation industry in the world with a capacity of 42.1 million litres,[1] which exceed the 15.6 million litres[2] of plasma needed by European patients, see Figure 32. However, Europe collects only 10.1 million litres of plasma,[3] which is insufficient to meet the needs of European patients.

Today, Europe addresses that problem by importing a sizable share of plasma from the US, which allows Europe to fractionate 33.8 million litres of plasma[4], see Figure 32. This is sufficiently much to meet its own IG demand and even export plasma derived-medicines, but is below the amount needed to run its fractionation capacity at full load of 41.2 million litres.

However, the annual growth rates of plasma fractionation (Europe: 6.6 per cent, see page 58; North America: 8.4 per cent[1]) exceed the growth rates of plasma collection (Europe: 4.3 per cent, see page 59; North America; 7.0 per cent[5]) both in North America and in Europe. Therefore, in the future, the US could end up exporting less raw plasma but more finished plasma-derived medicines. his could pose a risk for Europe's plasma-derived therapies industry in the form of insufficient amounts of plasma for fractionation.

Figure 32. Plasma demands and supplies in Europe and the US

Million litres of plasma in 2023



Source: Copenhagen Economics based on MRB (2024a, b, c, d).

Notes: 1) MRB (2024b). / 2) MRB (2024a). / 3) MRB (2024c). / 4) MRB (2024b). / 5) European Commission (2025c). / 6) 4.5 g of IG can be gained from one litre of plasma (EC 2025c).

There are risks of commoditising plasma-derived therapies that have intrinsic value in being heterogeneous

Commoditisation of products can have unintended consequences

The design of reimbursements policies and pharmaceutical tenders is very important for the delivery of plasma-derived therapies, and ultimately for patient health. Viewing heterogeneous products as a single commodity will not match heterogeneous patient needs.

Commoditisation is an industry change which is characterised by increase in product homogeneity. When products are standardised, the customer cost of switching from one product to another is lowered. This makes customers more price sensitive and tends to drive down consumer prices.[1] An example of a therapy where patients have benefitted from commoditisation is factor VIII. Even if the plasma-derived and recombinant products are not identical, they have similar properties. When recombinant alternatives entered the market, prices were driven down. Now all factor VIII therapies are cheaper, which is beneficial for patients and healthcare systems. Even so, the market does not function perfectly for all patients. The prices for the plasma-derived VIII have to be low to remain competitive with the recombinant alternatives. This leaves other plasma-derived therapies to carry a higher share of the cost of plasma, placing the interests of one patient group against the interests of another.

Commoditisation of an industry is characterised by

- increasing homogeneity of products
- higher price sensitivity among customers
- lower switching costs
- greater industry stability[4]

Commoditisation can, however, have unwanted side effects for some product groups, especially if there is an intrinsic value in a product being heterogeneous. Examples of products that can be problematic to treat as commodities include high-risk medical procedures, complex diagnostics, and specialty pharmaceuticals[2], where plasma-derived therapies belong to the latter category.

IG therapies are a useful example of the value heterogeneity of products can bring to patients, as we have explained in detail in chapter 1, as different patient groups need therapies with different concentration, sugar content, or pH level.

There are risks of over commoditisation for plasma-derived therapies

There can be risks of commoditisation for plasma-derived therapies today, which can stem from reimbursement approaches together with the finite budgets available for healthcare systems.

For example, reimbursement policies vary depending on IG therapy and in some countries only one product is reimbursed.[3] Treatment with both IVIG and SCIG is covered by the national healthcare system in most European countries, but both are not consistently available in lower- or mid-income regions of the world even though the treatments are not always substitutes for an individual patient. This can lead to patients using a suboptimal therapy for their specific medical need, even if more optimal ones would be available in the same price range.

Similarly, tender practices can also lead to the risk of commoditisation. If tendering is based solely on price, there is a risk of missing other valuable qualities therapies have, e.g. providing different quality of life to patients. In the worst case, pushing down prices in tenders can even lead to supply shortages, see example from Romania on page 46.

Box 18. Personalised treatment matters

> The importance of personalised treatment is all the more relevant given that many different Ig therapies are available, differing in terms of their ingredients and production, and individuals can respond differently to each of them.

Source: Bousfiha et al. (2017).

Notes: 1) Reimann et al. (2010). / 2) BCG (2015). / 3) Bousfiha et al. (2017).

3.2
THE MEANS USED TO INCREASE PLASMA DONATION RATES TODAY

A long list of initiatives to increase plasma donations is available

Numerous means of compensating and incentivising donors

To increase donation rates a wide range of compensations and incentives have been proposed in the academic literature and/or implemented in real life, see Box 19.

The use of money to compensate donors for the disutility associated with their donation is often proposed. Others favour vouchers, discounts, and tax reliefs as means of compensating donors without having to rely on a monetary transfer. Some researchers propose donating an amount to a charity organisation (possibly of the donor's choice) instead of transferring the amount directly to the donor.[1]

According to Article 54 of the EU SoHO Regulation, compensation may take the form of fixed allowances or non-financial compensation, with an upper limit that guarantees financial neutrality. Such compensation is considered compatible with the principle of voluntary and unpaid donations.[2]

Some researchers advocate for an unregulated market for donations where the price is determined by demand and supply. This is not considered relevant in the present report since it is in direct violation with the view of voluntary and unpaid donations – also referred to as voluntary and non-remunerated donations – by the European Union. It is thus not considered policy relevant.

All Member States follow the principle of voluntary and unpaid donations, but the view on what constitutes an unpaid donation varies, see page 65 for an overview by European Member State. Reimbursement of incurred costs associated with the donation is proposed by many and used in several European Member States. Small gifts and tickets to movies, concerts, and more have also been proposed and is used in several European Member States. Some propose health checks, time off work, and reciprocity as means of compensating donors. Article 53 requires SoHO entities to register donors in entity-level, national or international registries to track donation frequency and prevent donors from donating more often than permitted. [2]

Awareness and information are prerequisites, but more evidence is needed on the effectiveness of donor information campaigns

The need for adequate information of the benefits of donating is often stressed. Campaigns with that goal have been carried out in numerous countries in Europe. There is limited evidence on the effectiveness of campaigning. One example is a field experiment from Argentina, where potential donors were provided with information on donations.[3,4] This did not increase donation rates compared to the control group (where people were only asked to participate). The EU SoHo Regulation states that references to compensation schemes should not be included in advertising, promotional, or publicity activities related to donor recruitment.[2]

In all, the evidence is scant and it is not possible to draw firm conclusions about the effectiveness of raising awareness and 'nudging' people to donate through information sharing. Further research would therefore seem important.

Digital channels and contextualised advertising are new and promising ways

Digital platforms like social media provide a direct link between recipients of plasma-derived therapies, collection centres, and donors. This can and should be utilised to narrow the distance between donor and recipient with stories about how donations help. For example, one study encouraged newly registered blood donors, after their registration but before their first donation, to follow the blood bank's Facebook page. The treatment group was 32 per cent more likely to make a first donation and made 17 per cent more donations in total compared to the control group which was not encouraged to follow the Facebook page.[5] The links between recipients and donors are often provided on collection centres' webpages, but there may be prospects in further exploring this path. Contextualised advertising provides means to target marketing to relevant customers. This, too, is a path worth exploring in more detail.

Box 19: Examples of compensations and incentives

- Monetary compensation
- Cash payment
- Travel cost reimbursement
- Charity donation
- Vouchers
- Discounts
- Tax relief
- Gifts: T-shirts, key rings, pens, bags, sweatbands, blankets, mugs, jackets, coolers, umbrellas, hats
- Tickets: Concert, movie, lottery/raffle ticket or ticket to donor-exclusive event
- Health check: Blood pressure, blood test for cholesterol, laboratory test for human immunodeficiency virus
- Donor appreciation: Certificate, plaque, badge/pins, stickers, award ceremony, media recognition
- Time off: Time of work/school
- Reciprocity: Community service credit, blood credit

Notes: This extensive list is not linked to the EU SoHo Regulation and some compensations and incentives in the list are prohibited in certain countries.
Source: Based on list in Chell et al. (2018) using the terminology from page 69.

Notes: 1) Mellström and Johannesson (2008). / 2) Regulation (EU) 2024/1938 of the European Parliament and of the Council (2024). / 3) Iajya et al. (2013). / 4) An alternative group were provided with 'social recognition', in terms of being mentioned in a newspaper article. This did not increase donation rates either. / 5) Ramondt et al. (2025).

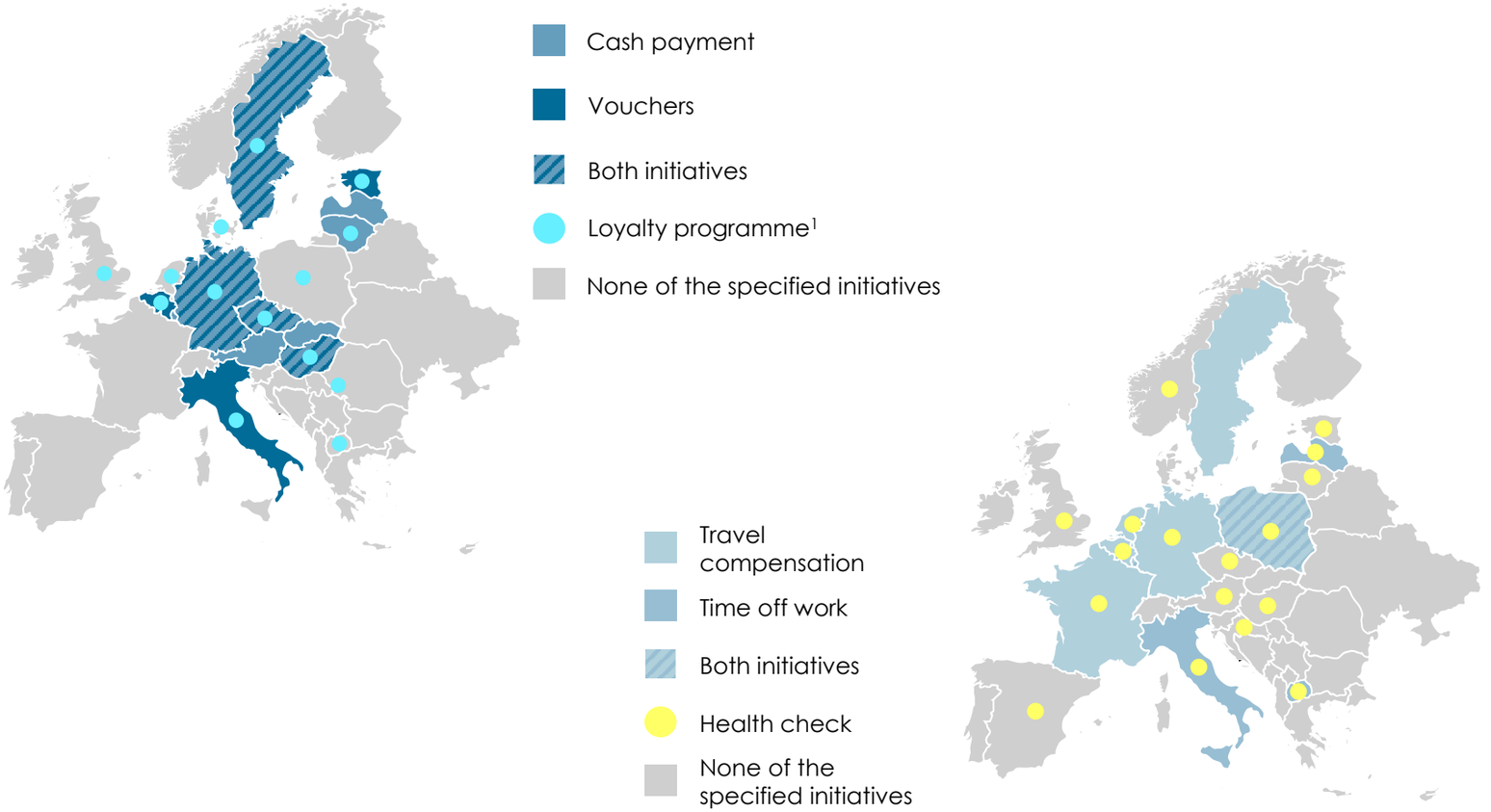
What constitutes an unpaid donation varies from one Member State to another

The EU SoHO Regulation outlines that compensation for plasma donations may take the form of fixed allowances or non-financial compensation in alignment with a voluntary and unpaid donation, but it leaves the details of compensation to national legislation. As a result, the practical interpretation of what counts as 'unpaid' differs across Member States. Some allow fixed allowances or non-financial benefits, while others only permit reimbursement of direct expenses. This has led to a variety of compensation models across the EU.

To give an overview of differences within the EU, we have mapped out different initiatives available for donors in Figure 33. In addition to these initiatives, some countries also offer gifts, taking part in a lottery and entertainment during the donation. Most countries offer snacks.[1]

In seven countries, donors receive a fixed monetary sum per donation, typically ranging from EUR 10 to 45. In Latvia and North Macedonia, donors are granted additional paid time off work, while in Lithuania and Poland, the time taken for donation does not need to be made up. Four countries offer time off from work. [2]

Figure 33. Monetary and non-monetary incentive programmes in the EU



Note: 1) Koch et al. (2024) define loyalty programmes as schemes that grant extra benefits such as vouchers or gifts, additional health checks, recognition items, or long-term perks to repeat or high-frequency plasma donors to encourage continued donation.
Source: Koch et al. (2024).

Box 20. Different interpretation of compensations

> Member States have taken different approaches to interpreting what voluntary and unpaid donation means. […] [A] measure is considered a "compensation" in one country and is viewed as an "incentive" in another.

Source: European Commission working document of 10 October 2019.

Notes: 1) All countries but Lithuania offer snacks. / 2) Koch et al. (2024); Italy, Latvia, Poland, North Macedonia. / 3)

3.3
FRAMEWORK FOR ETHICALLY ACCEPTABLE WAYS TO INCREASE DONATION RATES

Ethical viewpoints affect which initiatives are likely to considered appropriate

The literature on which initiatives best motivate donors is inconsistent and the results vary across studies, both across and within countries. As is stated in one meta study, "*the philosophical and ethical disagreement on the appropriateness of incentives has constrained research*".[1]

Hence, to review which means to increase donation rates can be implemented and what effect they would have, it is important to first lay out an ethical framework. Collectively, we call the different means *initiatives*. We have chosen to evaluate the ethical controversy of the different initiatives by relying on the Nuffield Council of Bioethics' Intervention Ladder. Further, we will discuss why we could apply different initiatives to plasma and blood donations.

The principle of voluntary and unpaid donations

The regulation on compensating donors in the EU relies on the principle of voluntary and unpaid donations. This is stated as a matter of principle in the EU directive on setting standards for human blood and blood components.[2] The ethical reasoning behind this is to avoid exploitation of the poor and to make sure no human is allowed to risk their health for money.[3]

Some view monetary compensation as a payment, others as a compensation

Providing donors with a fixed amount of cash after donation can be considered in two ways:

- A monetary payment that more than offsets the disincentives with the donation and thus creates incentives to donate, or;
- A monetary transfer for inconvenience (including foregone earnings), pain, etc. that offsets the non-monetary losses and disutility associated with the donation and thus is a compensation.

If monetary compensation is viewed as a payment, it is viewed as unethical and opposed in several directives.[2] If it is viewed as a compensation, it is in line with the European legislation and should not give rise to ethical concerns since it is altruistic focused. Opponents of monetary compensation view them as the former, whereas advocates likely view them as the latter.

Box 21. Voluntary vs. unpaid payments

> A donation is considered voluntary and non-remunerated if the person gives blood, plasma, or cellular components of his/her own free will and receives no payment for it, either in the form of cash or in kind which could be considered a substitute for money.

Source: Council of Europe recommendation of 29 June 1998, L203/18, 9 d).

Box 22. EU distinction: compensation vs. incentive

> Compensation means reparation strictly limited to making good the expenses and inconveniences related to the donation (…)
> Incentive means inducement/stimulus for donation with a view to seeking financial gain or comparable advantage;

Source: European Commission (2016).

Notes: 1) Chell et al. (2018). / 2) For example European Union Directive 2001/83/EC and Directive 2002/98/EC. / 3) Nuffield Council of Bioethics (2011).

The more altruistic focused, the more likely initiatives are to be implemented

In order to evaluate the controversy of proposed compensations and incentives, we build on the Nuffield Council of Bioethics' Intervention Ladder as illustrated in Figure 34. What we have chosen to call initiatives, the Council calls interventions. The ladder helps classify different initiatives (ranging from informing about the need for donations to financial incentives) as altruist or non-altruist focused.[1]

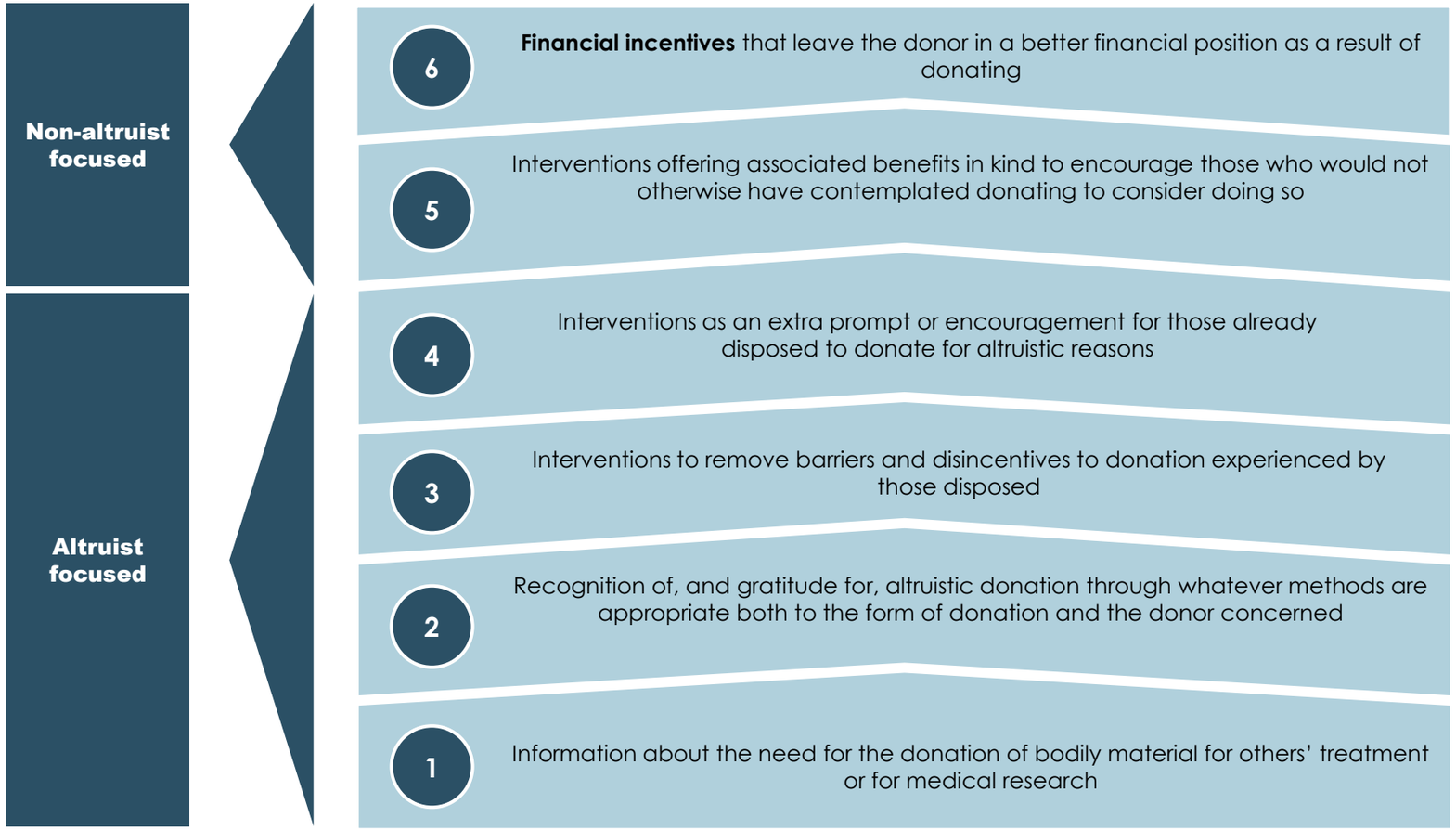
The Nuffield Council of Bioethics is an independent body that examines ethical issues within biology and medicine.[2] We use their intervention ladder, as it is widely cited and recognised within health ethics research. The ladder is for all types of donations and is not restricted only to plasma or blood donations.

Rungs 1-4 of the ladder differ in terms of organizational involvement as well as in potential costs. However, all strive to stimulate the donors selfless concern for others (also labelled his/her altruistic motives) and do not differ on ethical grounds. Interventions in these categories are ethically unproblematic, as they are considered voluntary and unpaid. Rungs 5-6 are, on the other hand, non-altruist focused and require ethical scrutiny on a case by case basis. In general these interventions are inconsistent with the voluntary and unpaid donation principle.[3]

Box 23. Why non-altruist interventions need closer scrutiny

> Non-altruist-focused interventions are not necessarily unethical but may need to be subject to closer scrutiny because of the threat they may pose to wider communal values.

Figure 34. The intervention ladder with increasingly controversial suggestions for compensating donors



Source: Nuffield Council of Bioethics (2019).

Source: Nuffield Council on Bioethics (2011).

Notes: 1) See Nuffield Council of Bioethics (2011), chapter 6. / 2) Nuffield Council on Bioethics (n.d.).

It is important to distinguish between initiatives incentivizing or removing disincentives to donate plasma

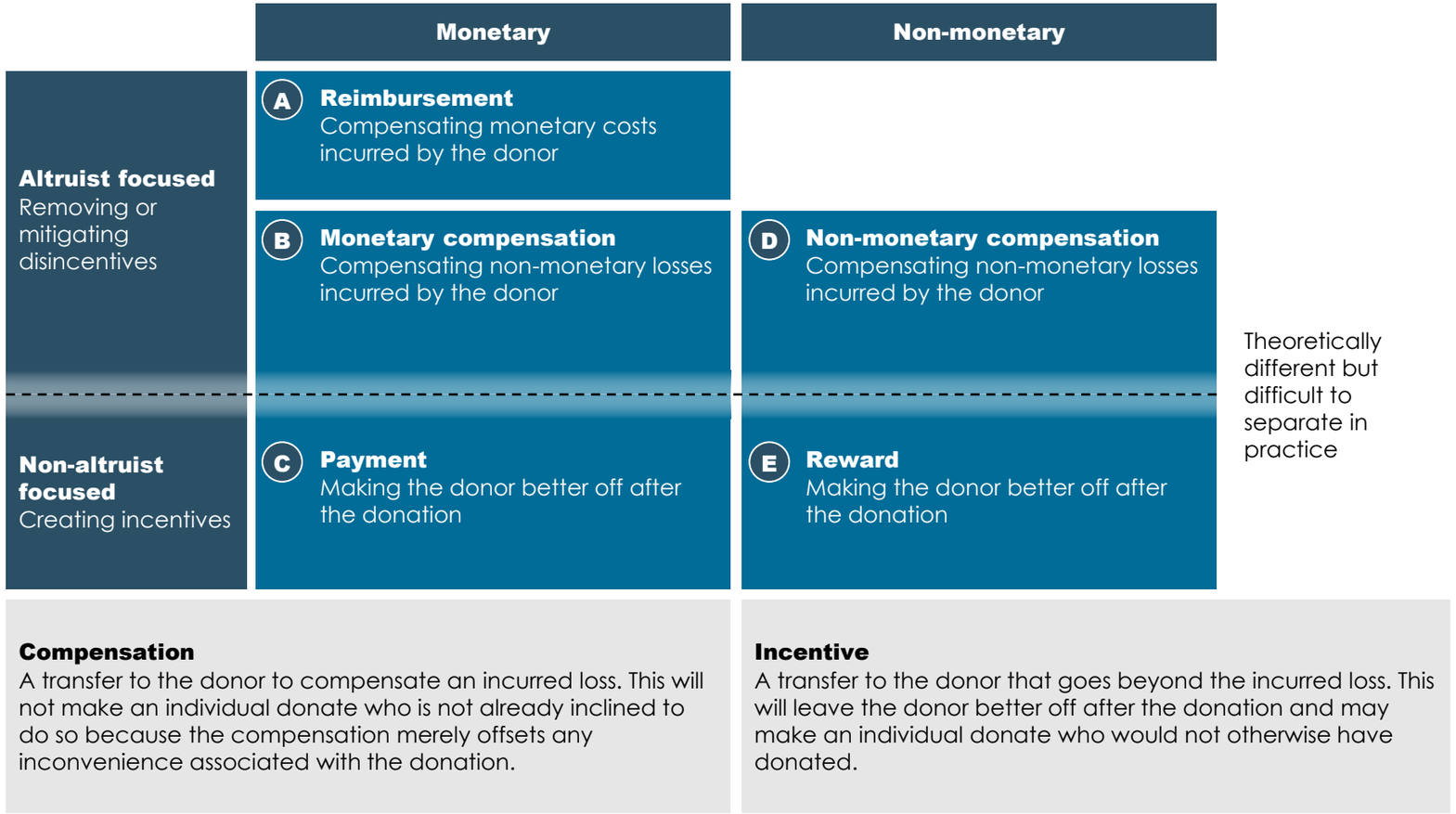
It is important to distinguish between initiatives that **create incentives** and can make someone donate who would otherwise not have donated, and those that merely **mitigate the disincentives** associated with the donation. [1] The first is a payment or reward and is labelled non-altruistic focused, while the second is only a compensation for ,e.g., time spent and is altruist focused. Compensations will not make an individual donate in the absence of altruism or selfless concern for the wellbeing of others if the level of compensation does not exceed the loss incurred from the donation.[2]

Five categories of initiatives

We distinguish between five categories of initiatives as illustrated in Figure 35. If a monetary transfer is made to offset a monetary cost incurred by the donor, it is labelled a **reimbursement (A).** If a monetary transfer is made to offset a non-monetary loss associated with the donation, it is labelled a **monetary compensation (B).** Non-monetary losses includes pain, inconvenience, and more. If the monetary transfer is larger than monetary costs and non-monetary losses incurred, it is a **payment (C).** If a non-monetary transfer is offered to a donor to offset a non-monetary loss associated with the donation, this is labelled a **non-monetary compensation (D).** If the non-monetary transfer is larger than the non-monetary losses incurred, it is a **reward (E).**

In section 3.4, we discuss potential compensation schemes in light of this framework. We refer to the appendix for a more detailed analysis of each category.

Figure 35. Framework for initiatives



Note: The letters to the left are used on the four pages in the appendix where each of the initiatives is described in further detail, see pages 81-84.
Source: Builds on Platz et al. (2019).

Notes: 1) Framework by Platz et al. (2019). The authors use the framework to explain why many existing proposals (including monetary compensation) to raise donation rates are seen as controversial, and conclude that compensation beyond the reimbursement of incurred monetary costs should itself be non-monetary for living donations viewed as a whole, i.e., including, for example, kidney donations. This is based on potential concerns about overlapping spheres when combining living donations (i.e., health) and monetary compensations. / 2) Unless these have an economic value, there is a market for them and they are transferable, which would make them a substitute for money, see, e.g., Council Recommendation of 29 June 1998.

Applying different compensation schemes for plasma and blood donors seems reasonable

No adverse effects on blood donation rates

There is a general concern that monetary compensation to plasma donors will crowd out blood donations that are uncompensated since the compensation will make plasma collection centres 'steal' blood donors. Actually, blood donations are also compensated in Europe. Today, most European countries allow the same or similar initiatives for both whole blood and plasma donations.[1]

There is evidence that monetary transfers to plasma donors do not decrease blood donation rates. Using the opening of 10 plasma collection centres in the Czech Republic between 2007 and 2010 as a natural experiment it was found that:[2]

- Blood collection numbers and rates have remained relatively stable over the past 10 years with neither sharp upticks nor declines.
- This stability in blood collection has persisted despite the opening of 10 plasma collection centres between 2007 and 2010.
- This same stability in blood collection has persisted despite a dramatic increase in predominantly compensated source plasma collection during the same time frame, moving from 6.8/1,000 donations per person in 2006 to 63.4/1,000 donations per person in 2010.

Plasma donations and blood donations differ in frequency and time used

Arguments on compensations that apply to blood donations are not necessarily applicable to plasma donations in developed countries.

An average whole-blood donor donates 1.9 times a year, while an average plasmapheresis donor donates 11.9 times a year.[3]

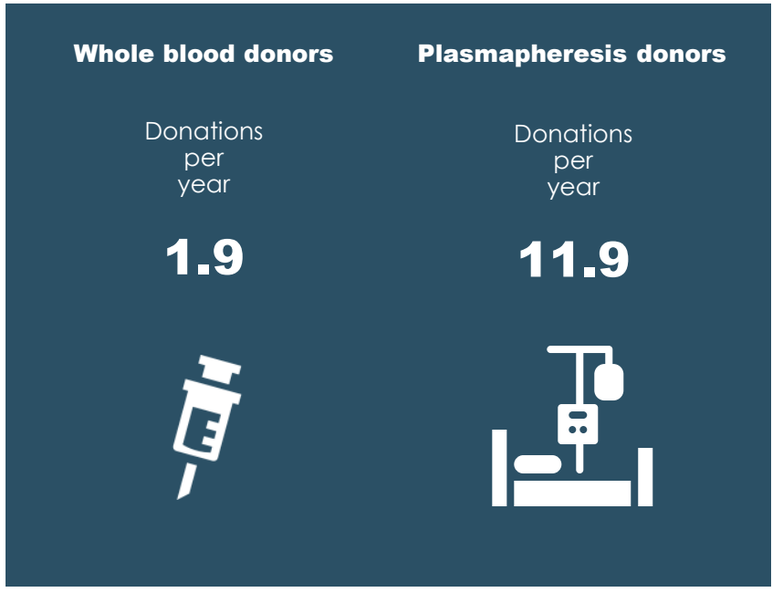
These estimates are based on German data, so we note that plasmapheresis is monetarily compensated in Germany. There is a big difference between doing something every month and doing it biannually. Note that in Europe the regulations for the maximum amount of blood and plasma donations differ as well. While the average European country allows a maximum of four whole blood donations per year, 33 plasma donations per year are permitted, on average.[4] Advocates of monetary compensation argue that it is important to:

- recognise the intrinsic difference between whole blood/blood components for transfusion and plasma for fractionation, and to implement targeted policies to encourage plasma collection and raise awareness on the importance of donating plasma for fractionation;
- differentiate within the European legislation between whole blood/labile blood components intended for transfusion and the collection of plasma intended for fractionation;
- take into consideration patients' perspective, as any reform will have an impact on patient access to care;
- clearly recognise the compensation of source plasma donors for their time and inconvenience compatible with voluntary unpaid donation.[5]

The differences between plasma donations and blood donations as outlined above makes a strong case for applying different compensation schemes for the two types of donations.

We note that the Nuffield Council of Bioethics concludes regarding plasma in the UK "*given the importance of the need for plasma [...] and the highly regulated nature of the donor recruitment and quality systems, it would seem likely […] that reward for donors in these circumstances would constitute an ethically vindicated rung 6 of our Intervention Ladder*."[6]

Box 24: Average yearly number of donations per donor



Note: Based on German data. Plasmapheresis donations are monetarily compensated in Germany.
Source: Ritter et al. (2008).

Notes: 1) Creative Ceutical (2015) and European Commission (2016). / 2) PPTA (2020a) based on Lacetera and Macis. / 3) Ritter et al. (2008). / 4) European Commission (2023). / 4) Ritter et al. (2008). / 5) PPTA (2022a, 2022b). / 6) Nuffield Council on Bioethics (2011).

3.4

WHAT ARE THE MOST PROMISING MEANS TO INCREASE PLASMA DONATION RATES?

Compensation of donors will likely increase the total number of donations without increasing the risk of pathogen transmission

There is research to suggest that compensation (monetary or non-monetary) of plasma donors is likely to increase the total number of donations, and unlikely to increase pathogen transmissions and crowd out blood donations.

Risks associated with compensation of donors

In one of the most seminal papers on blood donation by Titmuss proposed the theoretical idea that introducing monetary transfers for blood donations would 'crowd out' altruistic donations, potentially lowering the total number of donations.[1] In addition, he proposed that it would lead to increased risk of pathogen transmission since less healthy individuals would donate. Even though his thoughts were centred around blood donations, the concerns apply to plasma donations as well.[2]

No clear evidence on a crowding out effect from monetary compensation

The idea of a crowding out effect when monetary transfers are made has been partially supported by works in blood donations.[3] However, the authors find no evidence of a crowding out effect when the monetary transfer is instead made to a charitable organization or given in the form of vouchers. Another author suggests that there might be a threshold level, such that smaller payments relative to costs are considered compensation (and a recognition of one's sacrifice) that may positively affect the supply, whereas payments that are too large and that fully or even excessively compensate for costs and losses could reduce the supply, since the altruistic utility from the action is reduced.[4]

A study found that introducing compensations were considered mildly to moderately encouraging for donation (range, 9.7-65.5 per cent of different donor segments were encouraged by different compensations). Fewer donors reported compensations as discouraging (range, 0.7-12.2 per cent). The overall net benefit was positive, implying that introducing compensation will likely lead to increases in the number of donations.[5] Similarly, three studies using natural experiments on non-monetary blood donor compensation find that the use of compensation increases the total amount of donations.[6]

Another study looked at whether respondents are willing to accept initiatives (both monetary and non-monetary such as paid leave, blood screening or small gift) in exchange for donating blood. The study was done in both the US and Germany, and a major part responded positively to the initiatives.[7]

Mixed evidence of less healthy individuals donating plasma

The use of an 'expense allowance' for plasma donations in Germany has not shown any indication of an effect on prevalence and incidence data relating to the groups of donors.[8] There is some evidence, dated back in 1990s though, that test-positive rates for commercial plasma donors are substantially higher than those of volunteer whole blood donors, ranging from about 2 to 20 times higher on the different tests.[9] Three studies using natural experiments on non-monetary blood donor compensation find that the use of compensation and the economic value of the compensation do not increase the share of ineligible subjects or the share of unusable donations.[6]

The quality control process when producing plasma-derived therapies is very comprehensive, see pages 28 and 29. If a person infected by, say, human immunodeficiency virus tries to donate plasma, current donor screening processes are likely to flag the donor as unfit to donate. If this should fail – if the donor is untruthful about his/her medical state, for example, the testing of pathogens will flag the donated plasma as unfit to process. As such, though it is theoretically problematic to have less healthy donors, the quality control makes it less of an issue in practice.

Box 25. Ensuring quality regardless of incentive

> However, we note here that this [that altruistic donations ensure quality of supply] does not appear to be an especially compelling consideration: even to the extent that it is correct, the remedy surely lies in an effective system of monitoring and quality control to be required whatever the regime of donation in order to ensure that only materials of an appropriate quality are made available to recipients.

Source: Nuffield Council of Bioethics (2011), chapter 5, p. 142.

Notes: 1) Titmuss (1970). / 2) From centering around whole blood donations, these considerations have been considered for all types of donations. E.g., see discussion in Nuffield Council of Bioethics (2011). / 3) Mellström and Johannesson (2008) and Lacetera and Macis (2012). / 4) Le Grand (2003). / 5) Chell et al. (2018) based on Glynn et al. (2003) and Sanchez et al. (2001). / 6) Lacetera and Macis. (2012), Goette and Stutzer (2019), and Iajya et al. (2013). / 7) Sadler et al. (2018). / 8) European Commission (2006). / 9) U.S. Government Accountability Office (1997).

Non-monetary compensation can be an alternative to monetary compensation, but it is less effective and difficult to administer

Monetary compensation may not be feasible

The effectiveness and ease of administration in monetary compensation makes it a first best solution, as reviewed on the previous page. However, the current legislation and the resistance to monetary compensation throughout Europe makes it unclear whether a system with monetary compensation of plasma-donors can be implemented.

Non-monetary compensation may be viewed as more ethical

There is also some degree of aversion to monetary compensation in the general population; a study found that respondents were more reluctant to receive pure cash than vouchers for blood donations.[1] A theoretical study explains in the framework of political philosophy why non-monetary compensation is likely to be viewed as more ethical than monetary compensation.[2]

Non-monetary compensation will likely affect donation rates

The donor demotivation from monetary compensation can potentially lead to a so-called crowding out effect from monetary rewards on blood or plasma supply, as the altruistic individual does not favour cash.[3] This is examined in Costa et al. for blood donations in 15 European countries which finds a crowding out effect for monetary compensation but not for non-monetary compensation.[4] Hence, using non-monetary rewards would still leave the altruistic donor with the feeling of doing something for the common good, and not crowd out these donors.

However, in systems where cash payment incentives have been introduced, a majority of donors see this as a key motivator to donate and, hence, indicate they would stop donating if the incentive were removed.[5]

Offering a cash payment within a voluntary and unpaid donation system can potentially demotivate donors, as some current donors in a voluntary and unpaid donation system might stop donating if cash incentives are introduced, and new paid donors may stop donating when the incentive is removed. Hence, "*the middle ground of noncash incentives must be considered to cut across the dichotomy of altruistic donation versus paid donation*".[6]

A study from the US among blood donors using a natural experiment among 14,000 American Red Cross blood drives and 500,000 blood donations shows that donations increased by 15-20 per cent on average when compensation was offered.[7] The effect increased with the economic value of the compensation, but a substantial proportion of the increase in donations is explained by donors leaving neighbouring drives without compensation to attend drives with compensation. This displacement also increases with the economic value of the incentive.

Larger administrative burden

Relying on non-monetary compensation rather than monetary compensation would imply a larger administrative burden for collection centres. This will make the total cost of using such non-monetary compensations greater than the cost of the compensation itself. This – together with possible concerns about the effectiveness of such donations in increasing donation rates – reduces the cost effectiveness of non-monetary compensations. Notwithstanding the administrative burden, non-monetary compensations may be viewed as more appropriate from an ethical and (therefore) political perspective.

Box 27. Nudging altruism with non-monetary incentives

> (…) altruistic behaviour could be motivated by non-monetary means and thus nudge individuals to act in a manner that provides collective benefit

Source: Costa et al. (2013).

Box 28. Non-monetary compensation as an ethical solution

> (…) an ethically acceptable solution to the problem of donor compensation could be to provide donors with non-monetary compensation for the non-monetary disutilities associated with living donations,

Source: Platz et al. (2019).

Notes: 1) Lacetera and Macis (2010b). / 2) Platz et al. (2019). / 3) Titmuss (1970). / 4) Costa-Font et al. (2013). The authors use the term 'rewards', which has been changed to 'compensation' for consistency with the framework on page 69. / 5) Lacetera and Macis (2010b.) / 6) Chell et al. (2018). / 7) Lacetera et al. (2012).

Monetary compensation is ethically justifiable, effective, easy to administer, and can significantly increase donation rates

Real-world evidence shows a clear pattern

On the face of it, monetary compensations appear to be often associated with higher donation recruitment. The implementation of such compensations mostly shows a significant. [1] One study used the introduction of monetary compensation in the Czech Republic and shows an increase in donation rates from 6.8/1,000 to 63.4/1,000 between 2006 and 2010, i.e., almost a ten-fold increase.[2] In general, donation rates of plasma in the four European countries where monetary compensation is implemented are far greater than in other European Member States. For example, plasmapheresis donation rates were 30.4/1,000 and 58.8 in 2012 in Germany and the Czech Republic, respectively. For comparison, the highest donation rates in the same year in countries without monetary compensation were 19.2/1,000 in the Netherlands, 9.4/1,000 in Belgium, and 7.5/1,000 in France. In the low end, donation rates were 0.6/1,000 in Denmark, 0.5/1,000 in Spain, and 0.2/1,000 in Greece.[3]

EU framework update allows of compensation

The new EU SoHO Regulation replaces the former Blood and Tissues & Cells Directives. Under Article 54(2), while donation remains voluntary and unpaid, Member States may allow compensation, including fixed allowances or non-financial forms, on transparent criteria, with the conditions set in national law.[4] The EU SoHo Regulation states that references to compensation schemes should not be included in advertising, promotional, or publicity activities related to donor recruitment.[4]

There is a stigma for monetary compensation of all body parts

There is a strong stigma on exchanging any human body parts, including plasma, for money. This makes monetary compensation politically problematic, even when framed as compensation rather than incentive.[5]

Given the difficulties in Europe to achieve a sufficient amount of plasma without monetary compensations, it appears reasonable to nevertheless consider the different variants of monetary compensations in line with Article 54(2) of the SoHO Regulation.

A monetary compensation is not a payment

A monetary transfer is not equivalent to a payment if it does not constitute a financial gain or comparative advantage. Importantly, the 2004 Directive notes that donors may receive compensation, given that it "*(…) is strictly limited to making good the expenses and inconvenience related to the donation*".[6] In Germany, an expense allowance between EUR 17 and 39 is given to plasma donors.[7] For comparison, the minimum wage in Germany in 2025 is EUR 12.82 per hour.[8]

Some policies are in place with a value far greater than a small monetary compensation

An interesting example is time off work in relation to a plasmapheresis donation. A total of 16 (57 per cent) European Member States provide time off work for employees in the public sector. The corresponding number for employees in the private sector is 13 (48 per cent).[9] As an example, Italy introduced one full day off work for blood and plasma donors in 1967, which is still in place today.[10] In fact, 10 of the 16 countries that provide time off work (public sector) give at least one full day off work.[9] Italy does not have a national minimum wage that can be used as a proxy for the minimum value of a day off. Moreover, compensating time off from work is also considered over-compensation if it exceeds "*other than that reasonably needed for the donation and travel*".[11] Given that a donation takes approximately one and a half hours plus travel time, a full day off may be an overcompensation. The acceptance of such policies (i.e., incentives) while still opposing monetary compensations with lesser monetary value seems contradictory.

Box 26. Policy inconsistency on donor compensation

> The policy of some countries is to meet identified patient need for PDMPs [plasma-derived medicinal products] by importing PDMPs produced from compensated donations while at the same time advocating a seemingly contradictory policy of prohibiting donor compensation within their own borders.

Source: Skinner et al. (2016), p. 2892.

Notes: 1) Chell et al. (2018). / 2) PPTA (2020a) based on Lacetera and Macis. / / 3) Creative Ceutical (2015) / 4) Regulation (EU) 2024/1938 of the European Parliament and of the Council (2024) / 5) See discussion in White (2015) regarding payment for plasma donations in Canada. / 6) European Parliament and the Council (2004), European Commission (2016). / 7) Koch et al. (2024). / 8) WSI Mindestlohndatenbank (2019 2025). / 9) European Commission (2016). Per cent based on 27 Member States. / 10) Lacetera et al. (2012), and AVIS (2019). / 11) European Commission (2016).

Reimbursement of incurred monetary costs associated with the donation should always be done to remove disincentives

Reimbursement is legal and abides with the principles of donation

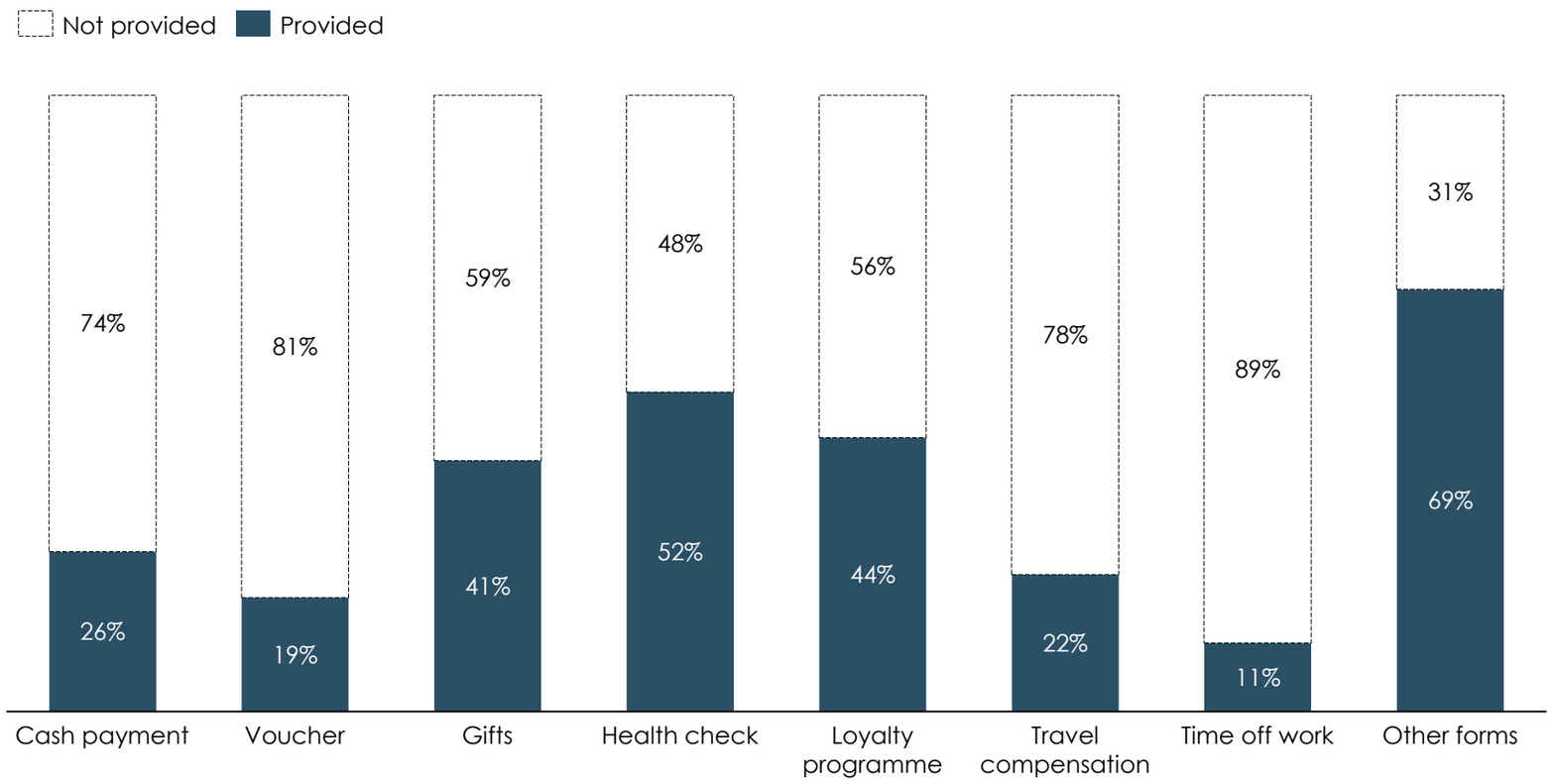
Reimbursements are compatible with European legislation (the EU SoHO regulation), the principle of voluntary and unpaid donations, and the principle of an altruistic focus. Besides the administrative burden, there is nothing that precludes reimbursements from being made and no immediate ethical concerns should arise.

There appears to be a need for an increased focus on sufficient reimbursement

Reimbursement of travel costs is a straightforward example of a reimbursement that appears justified under any circumstances. If such a reimbursement is not used, it may hinder a donation if the out-of-pocket transportation expense incurred by the donor is greater than the altruistic gain from the donation.

Nevertheless, reimbursements are often not made in various EU countries, which creates disincentives to donate. An illustration of the number of Member States that provide specific reimbursements, based on a study from 2024, is provided in Figure 36. For example, travel costs to donors are only reimbursed in 6 (22 per cent) European Member States.[1] Only three Member States (14 per cent) allow time off work to donate, e.g. Latvia or Italy. Fourteen Member States (52 per cent) have mandatory health checks in connection to plasma donation, and e.g. Austria and Estonia offer additional health information if requested.[1]

Figure 36. EU Member States offering different plasmapheresis reimbursement types
Share of EU Member States



Note: Other forms include lottery, snacks, entertainment, and recognition. Health checks are mandatory health checks pre-donation.
Source: Koch et al. (2024).

Notes: 1) Koch et al. (2024). Per cent based on 27 Member States.

APPENDIX AND REFERENCES

APPENDIX

Appendix: Additional conditions that can be treated with plasma-derived therapies

Table 6. Additional conditions

Condition	Plasma-derived therapy
Burns	Albumin
Cardiopulmonary bypass	
Cirrhosis complications	
Major surgery	
Shock	
Trauma	
Plasma exchange treatments	
Acute Respiratory Distress Syndrome	
Bleeding/trauma	Coagulation factors
Liver disease	
Anticoagulant overdose	
Acute Inflammatory Demyelinating Polyneuropathy (Guillain–Barre)	Immunoglobulins
B-Cell Chronic Lymphocytic Leukaemia	
Multiple Myeloma	
Cytomegalovirus	
Hepatitis A, B	
Organ and bone-marrow transplants	
Paediatric human immunodeficiency virus	
Rabies	
Rh disease	
Tetanus	
Varicella	
Alpha-1 antitrypsin deficiency	Protease inhibitors

Source: Grabowski and Manning (2018).

Appendix: Notes to table on diseases that are treated with plasma-derived therapies

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All prevalence estimates are gender neutral and per 50,000 individuals. All estimates are based on a European population of 600 million individuals except for Kawasaki Disease, which is based on 21 million children in Europe under the age of 5.

1. Source: European Medicines Agency. (2021, May 27). *EU/3/20/2380 – orphan designation for treatment*. European Medicines Agency. Available here. The source mentions an approximate prevalence rate in the EU of 0.7 in10.000 in 2022. The gender distribution in Europe is assumed to be 50/50.
2. Source: Iorio, A., Stonebraker, J. S., Chambost, H., Makris, M., Coffin, D., Herr, C., ... & Data and Demographics Committee of the World Federation of Hemophilia. (2019). Establishing the prevalence and prevalence at birth of hemophilia in males: a meta-analytic approach using national registries. Annals of internal medicine, 171(8), 540-546. Available here. The study estimates a prevalence of Hemophilia B of all severities of 3.8 per 100 000 males (range: 3.2–4.4) in six high-income countries.
3. Source: Du, P., Bergamasco, A., Moride, Y., Truong Berthoz, F., Özen, G., & Tzivelekis, S. (2023). Von Willebrand disease epidemiology, burden of illness and management: a systematic review. Journal of Blood Medicine, 189-208. Available here. Systematic Literature review which reports three different estimates from three European countries (France, Italy and the UK). We use the median prevalence rate from Italy indicated as 5.4 per 100,000.
4. Source: World Federation of Hemophilia (2018). *Report on the Annual Global Survey 2017*, table 16. Available here. Data from 24 European countries (not all countries report on all factor deficiencies). Does not include Bosnia and Herzegovina, Bulgaria, Croatia, Germany, Iceland, Kosovo, Macedonia, Switzerland, Spain, the Netherlands, Austria, and Finland.
5. Source: MedlinePlus Genetics. (2013). *Hereditary antithrombin deficiency*. U.S. National Library of Medicine. Available here. from The report mentions a prevalence range from 1 in 3000 to 1 in 2,000, which is scaled to an interval of 16,67 in 50,000 to 25 in 50,000 We use the midpoint to determine the number of patients.
6. Source: Greulich, T., Nell, C. Hohmann, D. (2017). The prevalence of diagnosed a1-antitrypsin deficiency and its comorbidities: results from a large population-based database. European Respiratory Journal, 49(1). Available here. The study reports a prevalence rate of 23.7 in 100,000.
7. Source: Yong, P. F., Coulter, T., El-Shanawany, T., Garcez, T., Hackett, S., Jain, R., ... & Worth, A. (2023). A national survey of hereditary angioedema and acquired C1 inhibitor deficiency in the United Kingdom. *The Journal of Allergy and Clinical Immunology: In Practice*, *11*(8), 2476-2483. Available here. The study reports a prevalence range from 1:100,000 to 1:150,000 for hereditary angioedema (HAE) types I and II combined for Europe. We use the midpoint of 0.63 in 50,000 (range: 0.5–0.75 in 50,000).
8. Source: Boyle, J. M., & Buckley, R. H. (2007). Population prevalence of diagnosed primary immunodeficiency diseases in the United States. Journal of clinical immunology, 27(5), 497-502. Available here. Lower bound estimate (95 per cent confidence interval), point estimate, and upper bound estimate amount to 151,769, 256,588, and 361,408 individuals out of the US population (297,386,040). While several papers use prevalence estimates based on registries, these are generally seen as being underestimates of the true patient population since only diagnosed cases are included in such registries. Based on community prevalence estimate from Boyle & Buckley (2007), which includes diagnosed and undiagnosed cases; no comparable population-wide European estimate is available as of 2025. Registry-based figures (e.g., ESID) are substantially lower and reflect only diagnosed case, see, e.g., Gathmann, B., Grimbacher, B., Beauté, J., Dudoit, Y., Mahlaoui, N., Fischer, A., ... & Kindle, G. (2009). The European internet-based patient and research database for primary immunodeficiencies: results 2006–2008. Clinical & Experimental Immunology, 157, 3-11 and Modell, V., Knaus, M., Modell, F., Roifman, C., Orange, J., & Notarangelo, L. D. (2014). Global overview of primary immunodeficiencies: a report from Jeffrey Modell Centers worldwide focused on diagnosis, treatment, and discovery. Immunologic research, 60(1), 132-144.
9. Source: Broers, M. C., Bunschoten, C., Nieboer, D., Lingsma, H. F., & Jacobs, B. C. (2019). Incidence and prevalence of chronic inflammatory demyelinating polyradiculoneuropathy: a systematic review and meta-analysis. Neuroepidemiology, 52(3-4), 161-172. Available here. The study reports a pooled prevalence rate of 2.8 er 100,000.
10. Source: Liu, X. G., Hou, Y., & Hou, M. (2023). How we treat primary immune thrombocytopenia in adults. *Journal of Hematology & Oncology*, *16*(1), 4. Available here. The study reports a prevalence range of 9 to 20 in 100,000 for immune thrombocytopenic purpura (ITP) in Europe. We use the midpoint.

Appendix: Notes to table on diseases that are treated with plasma-derived therapies

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11. Source: GBS Organisation Europe. (n.d.) MMN. Available here. The page reports a prevalence rate of 0.6 per 100,000 CIDP patients.
12. Source: The incidence rate for Kawasaki Diseases stems from: Odingo, M., Rutter, M., Bowley, J., Peach, E. J., Lanyon, P. C., Grainge, M. J., ... & Pearce, F. A. (2023). The incidence of Kawasaki disease using hospital admissions data for England 2006–2021. Rheumatology, 62(9), 3117-3125. and Gradoux, E., Di Bernardo, S., Bressieux-Degueldre, S., Mivelaz, Y., Ksontini, T. B., Prsa, M., & Sekarski, N. (2022). Epidemiology of Kawasaki Disease in children in Switzerland: a national prospective cohort study. Swiss Medical Weekly, 152(2122), w30171-w3017. Available here.
    The study reports an incidence rate between 10 and 15 per 100,000 children under 5 years. To determine the prevalence, we multiply the incidence rate by 8/52 to account for the fact that Kawasaki disease usually lasts 8 weeks, see Cirndle et al (2017). This provides a prevalence range of 1.5 to 2.3 per 100,000 children below the age of 5. To estimate the number of children in Europe currently affected by Kawasaki disease, we multiply the prevalence rate by the number of children under the age of 5 in Europe. The UN estimates that ca. 21.5 million children under the age of five live in Europe (not including Russia and Turkey), see UN (2024) retrieved here. This results in an estimate of 516 patients.

European countries include the following countries in 2025[1]:

Albania, Austria, Belarus (2020), Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Kosovo (2022), Latvia, Lichtenstein, Lithuania, Luxembourg, Macedonia, Malta, Moldova, Monaco, Montenegro, the Netherlands, Norway, Poland, Portugal, Romania, Switzerland, Serbia, Slovakia, Slovenia, Spain, Sweden, Ukraine (2022), and the United Kingdom[2].

42 countries in total with a total population of approximately 600 million individuals.

Notes: 1) Data from Eurostat 2025 if not 2025 newest year available was stated in brackets. / 2) Office for National Statistics / 3) UNICEF supplemented with approximations using demographic data.

Appendix: A) There is a strong case for monetary reimbursement of incurred costs

What are the effects?

Reimbursement is largely uncontroversial since it is easy to ensure that no donor is in a better financial position after the donation compared to before. A donor who is required to, say, take the bus to a collection centre at a price of EUR 2 and is reimbursed exactly EUR 2 is not financially better or worse off compared to if (s)he did not donate.

This will only have an effect on the marginal donor, those who are close to donating but face out-of-pocket expenses high enough to offset the altruistic utility they receive from the donation. As the donor receives no extra benefits, the reimbursement does not attract a person to donate who would not otherwise have considered doing so.

European legislation

Reimbursement of monetary costs associated with plasma donations is in line with the European legislation. Monetary costs could include travel costs, forgone earnings, and medical care. The terms of reimbursement are, however, left to the European Member States:

Box 29. Reimbursements for travel costs

> (…) reimbursements of direct travel costs are compatible with voluntary non-remunerated donations.

Source: Council recommendation of 29 June 1998, L203/18.

Nuffield council on bioethics

A reimbursement is consistent with rung 3 on the Nuffield Council on Bioethics' Intervention Ladder since it is an "*Intervention[s] to remove barriers and disincentives to donation experienced by those disposed*". The focus is thus altruistic and donations are driven by donors' intrinsic motivation to donate even if reimbursements for incurred costs are given.

Checklist:

- In line with the European legislation ☑
- Voluntary ☑
- Unpaid ☑
- Altruistic focused ☑
- Corresponds to rung 3

Controversy of monetary reimbursement

Source: Copenhagen Economics.

Appendix: B) Monetary compensation can be effective as a means of decreasing disincentives associated with the donation

What are the effects?

A ~~recent~~ study found that perceived blood transfusion safety and personal motivations may play a larger role in willingness to donate than receiving certain compensations and incentives. Specifically, potential willingness to donate was neither related nor negatively related to positive attitudes toward receiving cash.[1] The study is based on data received from 27,868 participants from 28 EU countries. Interviews, from which the data are gathered, are related to blood donation and took place in 2014. Interviews sought to catch participants' willingness to donate and identify willingness motivators, and were conducted as face-to-face interviews. The study uses logistical multilevel regression. There are two drawbacks of the study:

- It relies on hypothetical scenarios of donating rather than actual donors.
- Something considered a moral or ethical issue is asked in a face-to-face interview.

In a field experiment in Argentina, individuals received flyers with an invitation to donate blood. Each group received a different initiative, ranging from information on the importance of donations to supermarket vouchers. There were three different groups receiving vouchers: the first received USD 20 (approximately equal to the wage of 1.5 hours), the second USD 60 (4.5 hours) and the third USD 100 (1 day). Of these, at least the first category can be seen as a monetary compensation of the time spent donating. In this case, the lowest level of compensation did not increase donations compared to only providing information or giving a complementary T-shirt.[2]

However, several other studies have found positive effects from monetary compensation. One study used the introduction of monetary compensation in the Czech Republic and shows an increase in donation rates from 6.8/1,000 to 63.4/1,000 between 2006 and 2010, i.e., almost a ten-fold increase.[3] In general, donation rates of plasma in the four European countries where monetary compensation is implemented are far greater than in other European Member States. For example, plasmapheresis donation rates where 30.4/1,000 and 58.8 in 2012 in Germany and the Czech Republic, respectively. For comparison, the highest donation rates in the same year in countries without monetary compensation were 19.2/1,000 in the Netherlands, 9.4/1,000 in Belgium, and 7.5/1,000 in France. In the low end, donation rates were 0.6/1,000 in Denmark, 0.5/1,000 in Spain, and 0.2/1,000 in Greece.[4]

European legislation.

Monetary compensation for inconvenience associated with the donation is in line with European legislation. However, monetary compensation is only considered legal when: 1) the amount of money compensates the inconvenience associated with the donation, but without 2) over-compensating so as to create an incentive to donate. Compensating time off from work is also considered over-compensation if it exceeds "*other than that reasonably needed for the donation and travel*".[5]

Nuffield council on bioethics.

A monetary compensation is, just like a reimbursement, consistent with rung 3 on the Nuffield Council on Bioethics' Intervention Ladder since it is an "*Intervention[s] to remove barriers and disincentives to donation experienced by those disposed*". The focus is thus altruistic and donations are driven by donors' intrinsic motivation to donate even if monetary compensation of inconvenience associated with the donation is given.

Checklist:

- In line with the European legislation
- Voluntary
- Unpaid
- Altruistic focused
- Corresponds to rung 3

Controversy of monetary compensation to offset losses

Source: Copenhagen Economics.

Notes: 1) Huis In 't Veld et al. (2019). / 2) Iajya et al (2013). In fact, all forms of initiatives except for $60 and $100 coupons attracted zero donors. / 3) PPTA (2020a) based on Lacetera and Macis. / 4) Creative Ceutical (2015). / 5) Council Recommendation of 29 June 1998.

Appendix: C) and E) Monetary compensation does not seem advisable when viewed as a payment that creates incentives for donors who would otherwise not donate

What are the effects?

According to the literature, monetary payments and rewards increase donation rates. E.g., in the Argentinian field experiment mentioned previously, a USD 60 voucher increase turnout from 0 per cent to 0.43 per cent, and a USD 100 voucher further to 0.83 per cent. Furthermore, offering USD 100 instead of USD 60 more than doubled the number of usable donations.[1] Additionally, both initiatives also affected people who had not been contacted, with total turnout increasing to 0.5 per cent and 1.1 per cent if these donors are included.[2] As these initiatives compensate more than the time needed for donation, we categorise them either as a payment or reward, depending on whether the coupon could be sold and exchanged directly for cash.

However, there is some evidence for a crowding out effect on altruistically motivated donors when monetary compensation is introduced. This idea was first introduced by Titmuss.[3] The crowding out would potentially reduce the amount of donations following an introduction of a payment or reward.

European legislation

The European legislation has a principle to encourage voluntary and unpaid donations of both blood and plasma.

Hence, the EU does not consider any type of payment or reward for donated human components to be legal or ethically acceptable. Small tokens, refreshments, and reimbursements of travel costs are the only compatible initiatives.

Nuffield council on bioethics

A reward is consistent with rung 5 on the Nuffield Council on Bioethics' Intervention Ladder since it offers a benefit to the donor and tries to encourage people to donate who would not otherwise have done so. Similarly, a payment is consistent with rung 6, as it equates to: "*Financial incentives that leave the donor in a better financial position as a result of donating*".

Hence, both these initiatives are non-altruistic and require ethical scrutiny according to the Council. To determine if a non-altruistic initiative can be justified, the following factors should be examined:

- The welfare of the donor;
- The welfare of other closely concerned individuals;
- The potential threat to the common good;
- The professional responsibilities of the health professionals involved; and
- The strength of the evidence on all these factors.

The Nuffield Council on Bioethics states that plasma may constitute an ethically justifiable rung 6 of the intervention ladder due to the importance of plasma.[3,4]

Checklist:

- In line with the European legislation ☐
- Voluntary ☐
- Unpaid ☐
- Altruistic focused ☐
- Corresponds to rung (payment) 6
- Corresponds to rung (reward) 5

Controversy of monetary compensation as an incentive

Source: Copenhagen Economics.

Notes: 1) Iajya et al (2013). All the results presented in the text are statistically significant. / 2) Only the increase in the £100 group is statistically significant. / 3) Titmuss (1970). / 4) Nuffield Council on Bioethics (2011). This is in a UK context, but likely applicable to the rest of Europe.

Appendix: D) Non-monetary compensations viewed as a means of reducing disincentives associated with the donation

What are the effects?

Non-monetary compensation can be any type of object like a T-shirt, cap, or umbrella. Additionally, it can be a voucher to redeem an object given that this voucher cannot be exchanged for cash. If it can be exchanged for cash, it becomes a monetary compensation.

In the above-mentioned Argentinian field experiment, one group was promised a T-shirt if they turned up to donate within three weeks. Interestingly, this did not attract any more people than just providing information on the usefulness of donations.[1] In fact, both groups had 0 donors when over 2,000 flyers were distributed.

A meta study finds that "*certain incentives*[2]*, specifically discounts and tickets (that are non-transferable/redeemable for cash), gifts, and paid time off work have the strongest evidence base for potential use within a* voluntary and non-remunerated *system*". These types of initiatives are likely to attract young and/or first-time donors and will be more successful in retaining new and infrequent donors. On the other hand, older donors to a larger extent claim not to be interested in initiatives. This exemplifies the conclusion in the study that there are no initiatives that would be favoured by all donors and nondonors alike.[3]

The effect of non-monetary compensations on donations is mixed in the literature, but with strong indications of an effect.[4] Overall, this appears to be the best way forward within a voluntary and unpaid system – sometimes referred to as voluntary and non-remunerated – like the one recognised in all European Member States and mandatory or encouraged in 25 Member States.[5]

European legislation

Non-monetary compensation for inconvenience associated with the donation is in line with European legislation, just as monetary compensation described earlier. Here, too, it is important not to over-compensate so as not to give a reward to the donor and incentives for him/her to donate.

Nuffield council on bioethics

A non-monetary compensation is, just like a monetary compensation and a reimbursement, consistent with rung 3 on the Nuffield Council on Bioethics' Intervention Ladder since it is an "*Intervention[s] to remove barriers and disincentives to donation experienced by those disposed*". The focus is thus altruistic and donations are driven by donors' intrinsic motivation to donate even if non-monetary compensation of inconvenience associated with the donation is given.

Box 28. Nudging altruistic behaviour

> (…) altruistic behaviour could be motivated by non-monetary means and thus nudge individuals to act in a manner that provides collective benefit

Source: Costa et al. (2013).

Checklist:

- In line with the European legislation
- Voluntary
- Unpaid
- Altruistic focused
- Corresponds to rung 3

Controversy of non-monetary compensation

Source: Copenhagen Economics.

Notes: 1) Iajya et al (2013). / 2) Here, we would use the word 'initiative' instead, as all the mentioned initiatives are what we would call compensations. / 3) Chell et al. (2018). / 4) Lacetera et al. (2013) / 5) European Commission (2016).

REFERENCES

References

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Abadeh, A., Shehadeh, S., Betschel, S., Waserman, S., Cameron, D. W., & Cowan, J. (2023). Clinical outcomes of immunoglobulin treatment for patients with secondary antibody deficiency: Data from the Ontario immunoglobulin treatment case registry. Plos one, 18(11), e0294408.

Abdou, N. I., Greenwell, C. A., Mehta, R., Narra, M., Hester, J. D., & Halsey, J. F. (2009). Efficacy of intravenous gammaglobulin for immunoglobulin G subclass and/or antibody deficiency in adults. International archives of allergy and immunology, 149(3), 267-274.

Abolhassani, H., Asgardoon, M. H., Rezaei, N., Hammarstrom, L., & Aghamohammadi, A. (2015). Different brands of intravenous immunoglobulin for primary immunodeficiencies: how to choose the best option for the patient? *Expert Review of Clinical Immunology*, *11*(11), 1229–1243. https://doi.org/10.1586/1744666X.2015.1079485.

ADMA Biologics. (2024). ADMA Biologics successfully implements innovative AI program. ADMA Biologics. Available here.

Aledort, L. (2016). The evolution of comprehensive haemophilia care in the United States, perspectives from the frontline. Haemophilia, 22(2), 676-683.

Allen, J. A., Gelinas, D. F., Freimer, M., Runken, M. C., & Wolfe, G. I. (2020). Immunoglobulin administration for the treatment of CIDP: IVIG or SCIG?. Journal of the neurological sciences, 408, 116497.

Alsina, L., Montoro, J. B., Moral, P. M., Neth, O., Pica, M. O., Sánchez-Ramón, S., ... & González-Granado, L. I. (2022). Cost-minimization analysis of immunoglobulin treatment of primary immunodeficiency diseases in Spain. The European Journal of Health Economics, 23(3), 551-558.

Anterasian, C., Duong, R., Gruenemeier, P., Ernst, C., Kitsen, J., & Geng, B. (2019). Quality of life differences for primary immunodeficiency patients on home SCIG versus IVIG. Journal of Clinical Immunology, 39(8), 814-822.

ABO Plasma. (2025). How Often and How Much Plasma Can You Really Donate. Available here.

AVIS. (2019). Association of Voluntary Italian Blood Donors (Italian: Associazione Volontari Italiani Sangue, AVIS). Available here.

Bakshi, N., Swinney, R., & Tuna, A. K. (2025). Building supply chain resilience through vertical control. University of Utah, Duke University, and Tilburg University. https://doi.org/10.48550/arXiv.2307.12345.

Barone, P.W., Wiebe, M.E., Leung, J.C. et al. (2020). Viral contamination in biologic manufacture and implications for emerging therapies. Nature Biotechnology, 38. 563–572.

BCG (2015). Escaping the doghouse: Winning in commoditized markets. Boston Consulting Group. Available here.

Benbrahim, O., Viallard, J. F., Choquet, S., Royer, B., Bauduer, F., Decaux, O., ... & Lévy, V. (2019). The use of octagam and gammanorm in immunodeficiency associated with hematological malignancies: a prospective study from 21 French hematology departments. Hematology, 24(1), 173-182.

BioSpace. (2025). Blood plasma market to reach US$ 79.5 million by 2032, driven by rising plasma-derived therapies demand and growing geriatric population. Available here.

Biopharma (2025) Biopharma Plasma: a key player in reforming the blood system in Ukraine. Available here.

Blau, I.-W., Conlon, N., Petermann, R., Nikolov, N., & Plesner, T. (2016). Facilitated subcutaneous immunoglobulin administration (fSCIg): A new treatment option for patients with secondary immune deficiencies. Expert Review of Clinical Immunology, 12(7), 705–711. https://doi.org/10.1080/1744666X.2016.1183482.

Blutspenderverordnung (BSV), Federal Law Gazette II No. 100/1999, last amended by Federal Law Gazette II No. 30/2025, § 8. (2025). Austrian Legal Information System (RIS). Available here.

Bolcato, M., & Jommi, C. (2024). Shortage of plasma-derived medicinal products: What is next? Narrative literature review on its causes and counteracting policies in Italy. Frontiers in Pharmacology, 15, 1375891. https://doi.org/10.3389/fphar.2024.1375891.

Bousfiha, A. A., Duff, C., & Hsieh, E. (2017). Ensuring access to immunoglobulin therapies for people with primary immunodeficiency: a need to improve individuals' quality of life and the sustainability of health-care systems. Frontiers in Immunology, 8, 1165.

Boyle, J. M., & Buckley, R. H. (2007). Population prevalence of diagnosed primary immunodeficiency diseases in the United States. Journal of clinical immunology, 27(5), 497-502. Available here.

Boyle, M. L., & Scalchunes, C. (2008). Impact of intervenous immunoglobulin (IVIG) treatment among patients with Primary Immunodeficiency diseases. Pharmaceuticals Policy and Law, 10(1-4), 133-146.

Broers, M. C., Bunschoten, C., Nieboer, D., Lingsma, H. F., & Jacobs, B. C. (2019). Incidence and prevalence of chronic inflammatory demyelinating polyradiculoneuropathy: a systematic review and meta-analysis. Neuroepidemiology, 52(3-4), 161-172. Available here.

References

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Bruers, S. (2022). Blood Donation and Monetary Incentives: A Meta-Analysis of Cost-Effectiveness. Transfusion Medicine Reviews, 36(1), 48–57

Bundesärztekammer. (2023).Guideline on the collection of blood and blood components and the use of blood products (Haemotherapy Guideline): 2023 comprehensive revision. Available here

Burnouf, T. (2008). Current status of fractionated plasma products. *Hématologie*, *14*(1), 36-47. Available here.

Chell, K., Davison, T. E., Masser, B., & Jensen, K. (2018). A systematic review of incentives in blood donation. Transfusion, 58(1), 242-254.

Copenhagen Economics. (2017). The value of clinical trials in Denmark (Danish title: Værdien af kliniske forsøg i Danmark).

Costa-Font, J., Jofre-Bonet, M., & Yen, S. T. (2013). Not all incentives wash out the warm glow. Kyklos, 66(4), 529–551. https://doi.org/10.1111/kykl.12034.

CPME. (2015). CPME position paper on rules regarding expiration dates of pharmaceuticals (CPME 2014/074 Final). Available here.

Creative Ceutical. (2015). An EU-wide overview of the market of blood, blood components and plasma derivatives focusing on their availability for patients. Creative Ceutical Report, revised by the Commission to include stakeholders' comments. Available here.

Czech Ministry of Health. (2024). *Decree No. 143/2008 Coll., on detailed requirements to ensure the quality and safety of human blood and its components (Blood Decree), as amended* [Annex 3, Part A, Sec. 2.3]. Available here.

de Serres, F. J. (2003). Alpha-1 antitrypsin deficiency is not a rare disease but a disease that is rarely diagnosed. Environmental health perspectives, 111(16), 1851-1854.

Carrillo de Albornoz, S., Higgins, A. M., Petrie, D., Irving, A., Fanning, L., Weinkove, R., Crispin, P., Dendle, C., Gilbertson, M., Johnston, A., Keegan, A., Pepperell, D., Pullon, H., Reynolds, J., van Tonder, T., Trotman, J., Waters, N., Wellard, C., Weston, H., … & McQuilten, Z. K. (2024). Economic evaluation: immunoglobulin vs prophylactic antibiotics in hypogammaglobulinemia and hematological malignancies. *Blood advances*. Available here

Domanović, D., von Bonsdorff, L., Tiberghien, P., Strengers, P., Hotchko, M., O'Leary, P., Thibert, J.-B., Magnussen, K., Erikstrup, C., Spekman, M., Chesneau, S., Jones, J., Møller, B. K., Verheggen, P., Gogarty, G., Elzaabi, M., de Angelis, V., Candura, F., Mali, P., … Thijssen-Timmer, D. (2023). Plasma collection and supply in Europe: Proceedings of an International Plasma and Fractionation Association and European Blood Alliance symposium. Vox Sanguinis, 118(1), 1–9. https://doi.org/10.1111/vox.13491.

Du, P., Bergamasco, A., Moride, Y., Truong Berthoz, F., Özen, G., & Tzivelekis, S. (2023). Von Willebrand disease epidemiology, burden of illness and management: a systematic review. Journal of Blood Medicine, 189-208. Available here.

ECDC. (2020). European Centre for Disease Prevention and Control. Coronavirus disease 2019 (COVID-19) and supply of substances of human origin in the EU/EEA. Available here.

EDQM. (2019). Comparison of immunity in the general population versus blood donors. Day 2.

EDQM (2025). European Directorate for the Quality of Medicines & HealthCare. Guide to the preparation, use and quality assurance of blood components. 22th Edition.

Elmadani, M., Mokaya, P. O., Omer, A. A. A., Kiptulon, E. K., Klara, S., & Orsolya, M. (2025). Cancer burden in Europe: a systematic analysis of the GLOBOCAN database (2022). BMC cancer, 25(1), 447. https://doi.org/10.1186/s12885-025-13862-1.

Else, M., Blakemore, S. J., Strefford, J. C., & Catovsky, D. (2021). The association between deaths from infection and mutations of the BRAF, FBXW7, NRAS and XPO1 genes: a report from the LRF CLL4 trial. Leukemia, 35(9), 2563–2569. https://doi.org/10.1038/s41375-021-01165-w.

Erin Streu, R. N. (2016). Subcutaneous immunoglobulin in oncology clinical practice. Clinical Journal of Oncology Nursing, 20(4), 437.

EurekAlert. (2002). Baxter introduces Baxject needleless transfer device at international Haemophilia Congress. Available here.

Europa Donna. (n.d.). Breast cancer facts. Available here.

European Blood Alliance (2016). EBA fact sheet on European self-sufficiency for blood components and plasma for fractionation. Available here.

European Blood Alliance and International Plasma and Fractionation Association (2020). Plasma-Derived Medicinal Products (PDMPs) and Plasma Supply into the Future. Available here.

European Central Bank. (2025). Euro foreign exchange reference rates. European Central Bank. Available here.

References

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European Commission. (2000). Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products. Official Journal of the European Communities, L 18, 1–5. Available here.

European Commission (2006). Report from the commission to the Council and the European Parliament. Report on the promotion by Member States of voluntary unpaid blood donations. Brussels, 17.5.2006. COM(2006) 217 final.

European Commission (2010). EudraLex. The Rules Governing Medicinal Products in the European Union, Volume 4. EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use. Annex 14: Manufacture of Medicinal Products Derived from Human Blood or Plasma. Brussels, SANCO/C8/AM/an D(2010) 380358. Available here.

European Commission. (2016). Commission Staff Working Document on the implementation of the principle of voluntary and unpaid donation for human blood and blood components as foreseen in Directive 2002/98/EC on setting standards of quality and safety for the collection, testing, processing, storage, and distribution of human blood and blood components and amending Directive 2001/83/EC (SWD(2016) 130 final). Brussels, 21 April 2016. Available here.

European Commission. (2023). Blood Donation in the EU: Exploring behavioural insights for innovative interventions - A literature review and an overview of the blood donation landscape in the EU Editors, Publications Office of the European Union, Luxembourg, 2023, doi:10.2760/226289, JRC134207.

European Commission. (2025a). Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions: Preparing the EU for the next health crisis: A Medical Countermeasures Strategy (COM(2025) 529 final). Available here.

European Commission. (2025b). Critical Medicines Act. Health and Food Safety. Available here.

European Commission. (2025c). EU SoHO regulation and plasma supply continuity [Conference presentation]. EDQM Stakeholder Event on Plasma Supply Continuity, Strasbourg, France. Available here.

European Commission. (2025d). Rare diseases and European Reference Networks. Directorate-General for Health and Food Safety. Available here.

European Commission. (2025e). SoHO Regulation. Health and Food Safety. Available here.

European Medicines Agency. (1999). Working Party on Herbal Medicinal Products: Comments on the European Commission guideline on dossier requirements for Type I variations (Notice to applicants, Vol. 2A). Available here.

European Medicines Agency. (2021). EU/3/20/2380 – orphan designation for treatment. European Medicines Agency. Available here.

European Medicines Agency. (2021). Guideline on core SmPC for human normal immunoglobulin for intravenous administration (IVIg). Available here.

European Medicines Agency. (2024). Hizentra: EPAR—product information. Available here.

European Medicines Agency. (n.d.). European clinical trials register (ECTR). Available here.

European Parliament and of the Council. (2001). Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use. Official Journal of the European Communities, L 311, 67–128. Available here.

European Parliament and of the Council. (2003). Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC. Official Journal of the European Union, L 33, 30–40. Available here.

European Parliament and the Council (2004), Directive 2004/23/EC. Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

European Rare Disease Organisation. (2025). European Parliament establishes new Intergroup on Cancer & Rare Diseases. Available here.

Eurostat. (2025). Harmonised index of consumer prices (HICP) – annual data. Eurostat. Available here.

Ewing, J. (2022). Why Tesla soared as other automakers struggled to make cars. The New York Times. Available here.

Farcet, M. R., & Kreil, T. R. (2017). Zika virus is not thermostable: very effective virus inactivation during heat treatment (pasteurization) of human serum albumin. Transfusion, 57(3pt2), 797-801.

Farcet, M. R., Lackner, C., Antoine, G., Rabel, P. O., Wieser, A., Flicker, A., Unger, U., Modrof, J., & Kreil, T. R. (2016). Hepatitis E virus and the safety of plasma products: Investigations into the reduction capacity of manufacturing processes. Transfusion, 56(2), 383–391.

References

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Fresenius Kabi. (2025). Fresenius Kabi receives FDA 510(k) clearance for adaptive nomogram enhancing plasma collection efficiency on Aurora Xi Plasmapheresis System. Fresenius Kabi. Available here.

Fu, L.W., Song, S., Isaranuwatchai, W., & Betschel, S. (2018). Home-based subcutaneous immunoglobulin therapy vs hospital-based intravenous immunoglobulin therapy: A prospective economic analysis. Annals of Allergy, Asthma & Immunology, 120(2), 195-199.

Fundació Víctor Grífols i Lucas. (2018). Ethics and plasma donation: An overview (Monographs of the Víctor Grífols i Lucas Foundation, No. 47). Fundació Víctor Grífols i Lucas.

Gale, R. P., Chapel, H. M., Bunch, C., Rai, K. R., Foon, K., Courter, S. G., & Tait, D. (1988). Intravenous immunoglobulin for the prevention of infection in chronic lymphocytic leukemia. A randomized, controlled clinical trial. The New England journal of medicine, 319(14), 902-907.

García-Pérez, L., Linertová, R., Valcárcel-Nazco, C. et al. Cost-of-illness studies in rare diseases: a scoping review. Orphanet J Rare Dis 16, 178 (2021). https://doi.org/10.1186/s13023-021-01815-3.

GBS Organisation Europe. (n.d). MMN. Available here.

Global Commission to End the Diagnostic Odyssey for Children with a Rare Disease. (2025, February). From idea to action: Accelerating rare disease diagnosis — 2024 end-of-year report. Available here.

Glynn, S. A., Williams, A. E., Nass, C. C., Bethel, J., Kessler, D., Scott, E. P., ... & Retrovirus Epidemiology Donor Study. (2003). Attitudes toward blood donation incentives in the United States: implications for donor recruitment. Transfusion, 43(1), 7-16.

Godier, A., Greinacher, A., Faraoni, D., Levy, J. H., & Samama, C. M. (2018). Use of factor concentrates for the management of perioperative bleeding: guidance from the SSC of the ISTH. Journal of Thrombosis and Haemostasis, 16(1), 170-174.

Goette, L., & Stutzer, A. (2020). Blood donations and incentives: Evidence from a field experiment. Journal of Economic Behavior & Organization, 170, 52–74.

Gonzalez, J. M., Ballow, M., Fairchild, A., & Runken, M. C. (2022). Primary immune deficiency: Patients' preferences for replacement immunoglobulin therapy. Frontiers in Immunology, 13, 827305. https://doi.org/10.3389/fimmu.2022.827305.

Grabowski, H. G., & Manning, R. L. (2018). Key economic and value considerations in the U.S. market for plasma protein therapies (Technical report). Bates White Economic Consulting.

Gradoux, E., Di Bernardo, S., Bressieux-Degueldre, S., Mivelaz, Y., Ksontini, T. B., Prsa, M., & Sekarski, N. (2022). Epidemiology of Kawasaki Disease in children in Switzerland: a national prospective cohort study. Swiss Medical Weekly, 152(2122), w30171-w3017. Available here.

Greulich, T., Nell, C. Hohmann, D. (2017). The prevalence of diagnosed a1-antitrypsin deficiency and its comorbidities: results from a large population-based database. European Respiratory Journal, 49(1). Available here.

Grifols S.A. (2024). The differential value of plasma-derived medicinal products (PDMPs). Available here.

Grifols. (n.d.). Flexbumin. Available here.

Guo, Y., Tian, X., Wang, X., & Xiao, Z. (2018). Adverse Effects of Immunoglobulin Therapy. Frontiers in immunology, 9, 1299.

Haemonetics Corporation. (2023). Haemonetics receives FDA clearance for enhancements to NexSys PCS® plasmapheresis system. Haemonetics. Available here.

Health Consult (2023) Evaluate and Develop Options to Improve Access to Subcutaneous Immunoglobulin (SCIg).

Healthcare Denmark. (2025). Innovative hospital services in Denmark. Available here.

Hoad, V. C., Castrén, J., Norda, R., & Pink, J. (2024). A donor safety evidence literature review of the short-and long-term effects of plasmapheresis. Vox Sanguinis, 119(2), Huis In 't Veld, E. M. J., de Kort, W. L. A. M., & Merz, E. M. (2019). Determinants of blood donation willingness in the European Union: a cross-country perspective on perceived transfusion safety, concerns, and incentives. Transfusion, 59(4), 1273–1282. https://doi.org/10.1111/trf.15209.

Iajya, V., Lacetera, N., Macis, M., & Slonim, R. (2013). The effects of information, social and financial incentives on voluntary undirected blood donations: Evidence from a field experiment in Argentina. Social Science & Medicine, 98, 214-223.

Immune Deficiency Foundation. (2019). Immunoglobulin replacement therapy. Available here.

Immunodeficiency UK (2025) Changes in Immunoglobulin Product Supply in 2025. Available here.

International Nursing Group for Immunoglobulin Administration (2021) European Nursing Guidelines for Immunoglobolin Administration. Available here.

International patient organization for primary immunodeficiencies (2018) Romania – Immunoglobulin shortage affects PID patients. Available here.

References

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Iorio, A., Stonebraker, J. S., Chambost, H., Makris, M., Coffin, D., Herr, C., ... & Data and Demographics Committee of the World Federation of Hemophilia. (2019). Establishing the prevalence and prevalence at birth of hemophilia in males: a meta-analytic approach using national registries. Annals of internal medicine, 171(8), 540-546. Available here.

Irish Pharmaceutical Healthcare Association (IPHA) & Health Service Executive (HSE) (2021). Framework agreement in the supply and pricing of generic, biosimilar, and hybrid medicines. Available here.

Jayapal K. P., Wlaschin K. F., Hu W. S. & Yap M. G. S. (2007). Recombinant protein therapeutics from Cho Cells - 20 years and counting. CHO Consortium: SBE Special Edition 40–47.

Johansen, M. B., Kass, E. D., Hauge, A. M., Risbjerg, A. W., & Christensen, J. (2024). Når behandlingen rykker hjem: En undersøgelse af fagprofessionelles og patienters erfaringer med subkutan hjemmebehandling. VIVE – Det Nationale Forsknings- og Analysecenter for Velfærd (in Danish). Available here.

Jolles, S., Orange, J. S., Gardulf, A., Stein, M. R., Shapiro, R., Borte, M., & Berger, M. (2015). Current treatment options with immunoglobulin G for the individualization of care in patients with primary immunodeficiency disease. Clinical and Experimental Immunology, 179(2), 146–160. https://doi.org/10.1111/cei.12485.

Joshi, A. Y., Iyer, V. N., Hagan, J. B., Sauver, J. L. S., & Boyce, T. G. (2009). Incidence and temporal trends of primary immunodeficiency: a population-based cohort study. In Mayo Clinic Proceedings (Vol. 84, No. 1, pp. 16-22). Elsevier.

Kan, A. K. C., Leung, G. M. K., Chiang, V., Au, E. Y. L., Lau, C. S., & Li, P. H. (2022). Ten-year population trends of immunoglobulin use, burden of adult antibody deficiency and feasibility of subcutaneous immunoglobulin (SCIg) replacement in Hong Kong Chinese. Frontiers in Immunology, 13, 984110.

Kindle, G., Alligon, M., Albert, M. H., Buckland, M., Edgar, J. D., Gathmann, B., ... & Seidel, M. G. (2025). Inborn errors of immunity: Manifestation, treatment, and outcome—an ESID registry 1994–2024 report on 30,628 patients. Journal of human immunity, 1(3), e20250007.

Koch, E., Leiße, A., Veseli, B., Jensen, J., Spekman, M., Merz, E. M., ... & Clement, M. (2024). Incentives for plasma donation. Vox Sanguinis, 119(8), 775-784.

Kobayashi, R. H., Gupta, S., Melamed, I., Mandujano, J. F., Kobayashi, A. L., Ritchie, B., … Litzman, J. (2019). Clinical Efficacy, Safety and Tolerability of a New Subcutaneous Immunoglobulin 16.5% (Octanorm [Cutaquig®]) in the Treatment of Patients With Primary Immunodeficiencies.

Kreil, T.R., Berting, A., Kistner, O., Kindermann, J. (2003). West Nile virus and the safety of plasma derivatives: verification of high safety margins, and the validity of predictions based on model virus data. Transfusion, 43 (8), 1023-1028.

Krivan, G., Jolles, S., Granados, E. L., Paolantonacci, P., Ouaja, R., Cissé, O. A., & Bernatowska, E. (2017). New insights in the use of immunoglobulins for the management of immune deficiency (PID) patients. American journal of clinical and experimental immunology, 6(5), 76–83.

Kreil, T.R., Unger, U., Orth, S.M., Petutschnig, G,. Kistner, O., Poelsler, G., Berting A. (2007). H5N1 influenza virus and the safety of plasma products. Transfusion, 47 (3), 452-459.

La Ley 7/2025, de 28 de julio, por la que se crea la Agencia Estatal de Salud Pública y se modifica la Ley 33/2011, de 4 de octubre, General de Salud Pública. Boletín Oficial del Estado, núm. 181, 101405–101429. Available here.

Lacetera, N., & Macis, M. (2010a). Social image concerns and prosocial behavior: Field evidence from a nonlinear incentive scheme. Journal of Economic Behavior & Organization, 76(2), 225-237.

Lacetera, N., & Macis, M. (2010b). Do all material incentives for pro-social activities backfire? The response to cash and non-cash incentives for blood donations. Journal of Economic Psychology, 31(4), 738-748.

Lacetera, N., & Macis, M. (2012). Time for blood: the effect of paid leave legislation on altruistic behavior. The Journal of Law, Economics, & Organization, 29(6), 1384-1420.

Lacetera, N., Macis, M., & Slonim, R. (2012). Will there be blood? Incentives and displacement effects in pro-social behavior. American Economic Journal: Economic Policy, 4(1), 186-223.

Lacetera, N., Macis, M., & Slonim, R. (2013). Economic rewards to motivate blood donations. Science, 340(6135), 927-928.

Le Grand, J. (2003). Motivation, agency, and public policy: Of knights and knaves, pawns and queens. Oxford University Press. https://doi.org/10.1093/0199266999.001.0001.

Lemos, M. S., Cruz, J. P., & Faria, M. (2024). An integral approach to assess the 3 human normal immunoglobulin formulations for primary immunodeficiency in Portugal: Combining costs, patients' preferences, and HCP choices. ISPOR Europe 2024, Barcelona, Spain.

References

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Leydold, S.M., Farcet, M.R., Kindermann, J., Modrof, J., Pölsler, G., Berting, A., Howard, M.K., Barrett, P.N., Kreil, T.R. (2012). Chikungunya virus and the safety of plasma products. Transfusion, 52 (10), 2122-2130.

Li, Z., Nagy, A., Lindner, D. et al. Tolerability and Safety of Large-Volume Hyaluronidase-Facilitated Subcutaneous Immunoglobulin 10% Administered with or without Dose Ramp-Up: A Phase 1 Study in Healthy Participants. J Clin Immunol 44, 148 (2024). https://doi.org/10.1007/s10875-024-01742-5

Liu, X. G., Hou, Y., & Hou, M. (2023). How we treat primary immune thrombocytopenia in adults. Journal of Hematology & Oncology, 16(1), 4. Available here.

Medical Device Development (2011) Top ten green medical devices. Available here.

MedlinePlus Genetics. (2013). Hereditary antithrombin deficiency. U.S. National Library of Medicine. Available here.

MedTech Europe. (2022). Remote Patient Monitoring – now or never: Unlocking the full potential of remote patient care. Available here.

Mellström, C., & Johannesson, M. (2008). Crowding out in blood donation: was Titmuss right?. Journal of the European Economic Association, 6(4), 845-863.

Mendez, C. M., McClain, C. J., & Marsano, L. S. (2005). Albumin therapy in clinical practice. Nutrition in clinical practice, 20(3), 314-320.

Merz, E. (2024). The availability of plasma donors and plasma: A sociologist's perspective. Vox Sanguinis, 119(2), 131–133. https://doi.org/10.1111/vox.13588.

Meyts, I., Bousfiha, A., Cunningham-Rust, R., Marcos, A., Torgerson, T., Lee, Y. N., … & Kwan, S. Y. (2020). Primary immunodeficiencies: A decade of progress and a promising future. Frontiers in Immunology, 11. https://doi.org/10.3389/fimmu.2020.625753.

Modell, V., Quinn, J., Ginsberg, G., Gladue, R., Orange, J., & Modell, F. (2017). Modeling strategy to identify patients with primary immunodeficiency utilizing risk management and outcome measurement. Immunologic research, 65(3), 713-720.

Moore, M. L., & Quinn, J. M. (2008). Subcutaneous immunoglobulin replacement therapy for primary antibody deficiency: advancements into the 21st century. Annals of Allergy, Asthma & Immunology, 101(2), 114-121.

Morse, B. A., Motovilov, K., Brode, W. M., Tee, F. M., & Melamed, E. (2025). A review of intravenous immunoglobulin in the treatment of neuroimmune conditions, acute COVID-19 infection, and post-acute sequelae of COVID-19 Syndrome. Brain, Behavior, and Immunity, 123, 725-738.

MRB (2022). The plasma proteins market in the United States 2022.

MRB. (2023). Data & Analysis of Immunoglobulin Supply and Plasma Requirements in Europe 2010–2021.

MRB. (2024a). Global usage and forecast of the immunoglobulin (IG) market by country 2023 -2030.

MRB. (2024b). The global plasma fractionation landscape through 2032.

MRB. (2024c). The plasma proteins market in Europe.

MRB. (2025a). European commercial source plasma collection: Ecosystem analysis, cost benchmarking & forecast by country to 2033.

MRB. (2025b). Global Blood & plasma collections and use 2023/2024.

MRB. (n.d.). Introduction to the plasma industry. Available here.

Muley, S., & Beydoun, S. R. (2023). Impact of the updated chronic inflammatory demyelinating polyneuropathy guideline on everyday practice. Frontiers in Neurology, 14, 1196261. https://doi.org/10.3389/fneur.2023.1196261.

My Hemophilia Team (2023), Hemophilia A Prognosis: What Is the Life Expectancy?. Available here.

National Bleeding Disorders Foundation (n.d) History from AD to the present. Available here.

NHS (2025a). Guidance to integrated care boards and providers on developing outpatient parenteral antimicrobial therapy (OPAT) services. Available here.

NHS (2025b). NHS framework agreement for human albumin & normal and anti-D immunoglobulin [Contract notice]. Contracts Finder. Available here.

Novotech. (2023). Rare disease – Global clinical trial landscape (2018-2022). Available here.

Nuffield Council on Bioethics (2011). Human Bodies: Donation for Medicine and Research.

Nuffield Council on Bioethics. (n.d.). Nuffield Council on Bioethics. Available here.

Ockenfels, A., & Roth, A. (2023). Consequences of unpaid blood plasma donations. VoxEU.org. Available here.

Octapharma. (2025). How Big Data is changing the game at Octapharma. Available here.

References

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Odingo, M., Rutter, M., Bowley, J., Peach, E. J., Lanyon, P. C., Grainge, M. J., ... & Pearce, F. A. (2023). The incidence of Kawasaki disease using hospital admissions data for England 2006–2021. Rheumatology, 62(9), 3117-3125

OECD. (2024). Health at a glance: Europe 2024: State of health in the EU cycle. OECD Publishing. https://doi.org/10.1787/b3704e14-en.

OECD. (2025). Inter-country input-output (ICIO) tables. OECD. Available here.

Pant, S., Bagha, R., & McGill, S. (2021). International plasma collection practices: project report. Canadian Journal of Health Technologies, 1(12).

Perraudin, C., Bourdin, A., Vicino, A., Kuntzer, T., Bugnon, O., & Berger, J. (2020). Home-based subcutaneous immunoglobulin for chronic inflammatory demyelinating polyneuropathy patients: A Swiss cost-minimization analysis. PLoS One, 15(11), e0242630.

Pijuan, S. (2025). *Pay in blood: The worrying EU dependency on US plasma*. EUobserver. Available here.

Platz, T. T., Siersbæk, N., & Østerdal, L. P. (2019). Ethically Acceptable Compensation for Living Donations of Organs, Tissues, and Cells: An Unexploited Potential?. Applied health economics and health policy, 17(1), 1-14.

Powell, J. S. (2009). Recombinant factor VIII in the management of hemophilia A: current use and future promise. Therapeutics and clinical risk management, 391-402.

PPTA. (2020a). Key economic and value considerations for plasma-derived medical products (PDMPS) in Europe. Available here.

PPTA. (2020b). New Coronavirus (Sars-Cov-2) and the safety margins of plasma protein therapies. Available here.

PPTA. (2022a). PPTA statement on the draft EU substances of human origin regulation. Available here.

PPTA. (2022b). Position paper on the EU blood, tissues and cells (BTC) regulation. Available here.

PPTA. (2023a). Plasma Protein Therapeutics Association. Plasma protein therapies – uniquely saving lives. Available here.

PPTA. (2025a). National and EU Stockpiling Requirements Do Not Ensure Equitable Access to Plasma-Derived Medicinal Products. Available here.

PPTA. (2025b). The problem with mandatory stockpiling of plasma-derived medicines in the European Union. Available here.

PPTA (2025c). PDMPs in National Drug or Healthcare Policy.

PPTA. (2025d). PPTA welcomes recognition of pharmaceutical supply chain diversity in EP rapporteur's draft report on the Critical Medicines Act. Available here.

PPTA. (n.d.). Plasma. Available here. Ramakrishna, B., Espinoza, G., Zhang, X., Ida, F., Yoon, L., Shen, J., ... & Ataher, Q. (2024). Real-World Insights into the Demographics, Infection Burden, and Use of Immunoglobulin Replacement in Patients with Chronic Lymphocytic Leukemia and Secondary Immune Deficiency. Blood, 144, 1863.

Ramondt, S., Kerkhof, P., & Merz, E.-M. (2025). Boosting blood donations through Facebook engagement: Randomized controlled field trial. Journal of Medical Internet Research, 27, Article e64740.

Regulation (EU) 2024/1938 of the European Parliament and of the Council of 13 June 2024 on standards of quality and safety for substances of human origin intended for human application. Official Journal of the European Union, L 1938, 17.7.2024. Available here

Reimann, M., Schilke, O., & Thomas, J. S. (2010). Toward an understanding of industry commoditization: Its nature and role in evolving marketing competition. International Journal of Research in Marketing, 27(2), 188-197.

Ritchie, B., Martins, K. J., Tran, D. T., Blain, H., Richer, L., & Klarenbach, S. W. (2022). Economic impact of self-administered subcutaneous versus clinic-administered intravenous immunoglobulin G therapy in Alberta, Canada: a population-based cohort study. Allergy, Asthma & Clinical Immunology, 18(1), 99.

Ritter, S., Willand, L., Reinhard, B., Offergeld, R., & Hamouda, O. (2008). Blutspenderpopulationen in Deutschland: Demographie und Spendeaktivität : Ergänzung zum Bericht des Robert Koch-Instituts zu den Meldungen nach section sign 22 Transfusionsgesetz [Demography and donation frequencies of blood and plasma donor populations in Germany]. Bundesgesundheitsblatt, Gesundheitsforschung, Gesundheitsschutz, 51(8), 915–925. https://doi.org/10.1007/s00103-008-0613-7.

Rosendaal, F. R., Smit, C., & Briet, E. (1991). Hemophilia treatment in historical perspective: a review of medical and social developments. Annals of hematology, 62(1), 5-15.

References

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Routes, J., Costa-Carvalho, B. T., Grimbacher, B., Paris, K., Ochs, H. D., Filipovich, A., ... & Ye, X. (2016). Health-related quality of life and health resource utilization in patients with primary immunodeficiency disease prior to and following 12 months of immunoglobulin G treatment. Journal of clinical immunology, 36(5), 450-461.

Rubinstein, A., Mabudian, M., McNeil, D. et al. Long-Term Safety of Facilitated Subcutaneous Immunoglobulin 10% Treatment in US Clinical Practice in Patients with Primary Immunodeficiency Diseases: Results from a Post-Authorization Safety Study. J Clin Immunol 44, 181 (2024). https://doi.org/10.1007/s10875-024-01769-8.

Sadler, A., Shi, L., Bethge, S., & Mühlbacher, A. (2018). Incentives for Blood Donation: A Discrete Choice Experiment to Analyze Extrinsic Motivation. Transfusion medicine and hemotherapy : offizielles Organ der Deutschen Gesellschaft fur Transfusionsmedizin und Immunhamatologie, 45(2), 116–124. https://doi.org/10.1159/000481142.

Sanchez, A. M., Ameti, D. I., Schreiber, G. B., Thomson, R. A., Lo, A., Bethel, J., ... & Retrovirus Epidemiology Donor Study. (2001). The potential impact of incentives on future blood donation behavior. Transfusion, 41(2), 172-178.

Schlander, M., Hernández, D., Schwarz, O., & Schaefer, R. (2023). What Is a Year of Life Worth? Empirical Findings from Worldwide Economic Studies on the Value of a Statistical Life [Poster session]. Poster presented at ISPOR Europe 2023, Copenhagen, Denmark. Available here.

Shah, N., Mustafa, S. S., & Vinh, D. C. (2023). Management of secondary immunodeficiency in hematological malignancies in the era of modern oncology. Critical Reviews in Oncology/Hematology, 181, 103896. Available here.

Siegel J. (2005). The product: All intravenous immunoglobulins are not equivalent. Pharmacotherapy, 25(11 Pt 2), 78S–84S. https://doi.org/10.1592/phco.2005.25.11part2.78S.

Simonetti, A., & Smit, C. (2024). Europe needs 2 million extra donors of blood and plasma: How to find them?. Vox Sanguinis, 119(2), https://doi.org/10.1111/vox.13540.

Skinner, M. W., Hedlund Hoppe, P. A., Grabowski, H. G., Manning, R., Tachdjian, R., Crone, J. F., & Youngner, S. J. (2016). Risk-based decision making and ethical considerations in donor compensation for plasma-derived medicinal products.

Solís-Díez, G., Turu-Pedrola, M., Roig-Izquierdo, M., Zara, C., Vallano, A., & Pontes, C. (2022). Dealing With Immunoglobulin Shortages: A Rationalization Plan From Evidence-Based and Data Collection. Frontiers in Public Health, 10, Article 893770. https://doi.org/10.3389/fpubh.2022.893770.

Soumerai, J. D., Yousif, Z., Gift, T., Desai, R., Huynh, L., Ye, M., Banatwala, A., Clear, L., Pinaire, M., Belsky, G., Hsieh, Y. G., Herrick, C., Darnell, E. P., Duh, M. S., Sanchirico, M., & Murphy, S. N. (2024). IgG testing, immunoglobulin replacement therapy, and infection outcomes in patients with CLL or NHL: real-world evidence. Blood Advances, 8(16), 4239–4249. https://doi.org/10.1182/bloodadvances.2024013073.

Tadros, S., Prévot, J., Meyts, I., Sánchez-Ramón, S., Erwa, N. H., Fischer, A., Lefevre, G., Hotchko, M., Jaworski, P. M., Leavis, H., Boersma, C., Drabwell, J., van Hagen, M., Van Coillie, S., Pergent, M., Burns, S. O., & Mahlaoui, N. (2023). The PID Odyssey 2030: Outlooks, unmet needs, hurdles, and opportunities—Proceedings from the IPOPI global multi-stakeholders' summit (June 2022). Frontiers in Immunology, 14, 1245718. https://doi.org/10.3389/fimmu.2023.1245718.

Takeda. (2023). Leading sustainable growth through end-to-end innovation [Conference presentation]. Investor Presentation. Available here.

Takeda. (2024). Harnessing the power of technology to better meet patient needs. Fast Company. Available here.

The Insight Partners. (2025). Global & United Kingdom home healthcare market to 2031. The Insight Partners. Available here.

Titmuss, R. (1970). The right to give. In The Gift Relationship (Reissue): From Human Blood to Social Policy (pp. 202–210). Chapter, Bristol University Press.

Tran-Mi, B., Storch, H., Seidel, K., Schulzki, T., Haubelt, H., Anders, C., ... & Hellstern, P. (2004). The impact of different intensities of regular donor plasmapheresis on humoral and cellular immunity, red cell and iron metabolism, and cardiovascular risk markers. Vox sanguinis, 86(3), 189-197.

U.S. Government Accountability Office. (1997, June). Blood safety: Enhancing safeguards would strengthen the nation's blood supply (GAO/HEHS-97-143). U.S. Government Printing Office.

United Nations. (2008). International Standard Industrial Classification of All Economic Activities Revision 4. United Nations Statistics Division. Available here.

van Der Poel, C. L., Seifried, E., & Schaasberg, W. P. (2002). Paying for blood donations: still a risk? Vox Sanguinis, 83(4), 285–293. https://doi.org/10.1046/j.1423-0410.2002.00239.

References

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van Wilder, P., Odnoletkova, I., Mouline, M., & de Vries, E. (2021). Immunoglobulin Replacement Therapy is critical and cost-effective in increasing life expectancy and quality of life in patients suffering from Common Variable Immunodeficiency Disorders (CVID): A health-economic assessment. PLoS One, 16(3), e0247941.

Weinstein, M. (2018). Regulation of plasma for fractionation in the United States. Annals of Blood, 3(1).

White, L. (2015). Does Remuneration for Plasma Compromise Autonomy? HEC Forum, 27(4), 387–400.

Whittal, A., Albiero, A., Belmonte, M., & Patris, J. (2024). EPH127 drivers and consequences of plasma-derived medicinal product shortages [Poster abstract]. Value in Health, 27(12, Suppl.), S2.

World Federation of Hemophilia (2018). Report on the Annual Global Survey 2017, table 16. Available here.

World Federation of Hemophilia. (2024). Report on the Annual Global Survey 2023. Available here.

World Health Organization. (2017). The 2016 global status report on blood safety and availability. Available here.

WSI Mindestlohndatenbank (2025). Institute of Economic and Social Research, Hans-Böckler-Foundation (German: Wirtschafts- und Sozialwissenschaftliche Institut, WSI, der Hans-Böckler-Stiftung). Available here.

Yong, P. F., Coulter, T., El-Shanawany, T., Garcez, T., Hackett, S., Jain, R., ... & Worth, A. (2023). A national survey of hereditary angioedema and acquired C1 inhibitor deficiency in the United Kingdom. The Journal of Allergy and Clinical Immunology: In Practice, 11(8), 2476-2483. Available here.

THE IMPACT OF PLASMA-DERIVED THERAPIES IN EUROPE

The health and economic case for ensuring sustainable supply

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