BioDrugs (2022) 36:217–229
https://doi.org/10.1007/s40259-022-00523-z

ORIGINAL RESEARCH ARTICLE

Qualitative Analysis of the Design and Implementation of Benefit-Sharing Programs for Biologics Across Europe

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Accepted: 22 February 2022 / Published online: 18 March 2022

Abstract

Background To encourage the rational prescribing of biologics, payers across Europe have experimented with the implementation of benefit-sharing programs. Benefit-sharing programs are incentive programs that promote the use of 'best-value' off-patent biologics and biosimilars by driving changes in prescribing practices. The aim of these programs is to generate savings that can be shared among stakeholders involved (e.g. health authorities/payers, health care professionals, hospital managers/administration) and are generally used to improve the quality of health care and to increase patients' access to innovative services and medicines. However, the scarcity of information concerning the design, implementation and outcomes of benefit-sharing programs limits the transfer of knowledge to institutions aiming to adopt these types of incentive schemes in the future.

Objective The aim of our study was to map benefit-sharing experiences across Europe, to compare their design and implementation characteristics and to assess the impact of the different benefit-sharing strategies on the use of 'best-value' biologics.

Method Our approach was based on a literature review and on semi-structured interviews with payers/insurers, regulators, health care professionals and industry representatives.

Results Our analysis revealed variable design characteristics for benefit-sharing programs, depending on the organization of the health care system, the specific timeframe, the care setting and the policy environment. All these aspects can influence the robustness of benefit-sharing initiatives and their potential to stay in effect over time. We also noted a generalized lack of transparency regarding the distribution of savings and how they are reinvested. This lack of transparency has raised questions on how to optimally implement benefit-sharing in the future.

Conclusions To realize the full potential of benefit-sharing programs, we identify the importance of (i) setting up and timely monitoring success indicators for these programs; (ii) including quality of care and access to care parameters as success indicators; (iii) establishing clear pathways for the transparent redistribution/reinvestment of savings and (iv) transparently communicating with patients about the outcomes of benefit-sharing programs.

1 Introduction

Biosimilars are biological medicines developed to be highly similar and therapeutically equivalent to originator biologics. Since 2005, the EMA (European Medicines Agency) has led the way in establishing regulatory pathways for the approval of biosimilars [1]. This has resulted in 71 biosimilar medicines authorized for marketing (up to January 2022) and used successfully in clinical practice [2–4]. Besides being effective and safe, biosimilars can induce competition when entering the market, generally contributing to lowered prices. As a result, biosimilars represent valuable opportunities for health care systems to generate cost savings and to increase patients' access to biologics [5, 6]. The introduction of biosimilars also broadens the offer of therapeutically equivalent medicines that can compete on the basis of multiple criteria besides price (e.g. product range including pack sizes and strengths available, administration devices, supply considerations, etc.). Ultimately, a wider

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Key Points

This study maps design characteristics of benefit-sharing programs implemented across Europe and identifies challenges that impede their implementation. This is with the final objective of generating evidence-based recommendations on how to operationalize benefit-sharing practices.

It is recommended to link the set-up of benefit-sharing initiatives with the establishment of indicators that focus on quality of care and access to care. These indicators are to be set by health care providers and patient advocacy groups, according to the needs of patients.

According to our research, the establishment of clear objectives and criteria to redistribute the savings is encouraged and should happen prior to agreeing on a benefit-sharing program.

It is recommended to increase transparency in the reporting of outcomes from benefit-sharing programs and to include patients in the communication strategy.

offer of products allows payers and providers to select the 'best value' or the most cost-effective options, while keeping or even improving quality of care standards. In Ireland, the HSE (Health Service Executive) Medicines Management Programme has established a list of criteria to select for 'best-value' biologics (BVB) [7, 8]. Also, in England, the NHS (National Health Service) has referred to selection criteria for BVB within its Commissioning Framework for Biological Medicines [9]. Other countries/health institutions have not explicitly published the criteria for the selection of the most cost-effective alternatives, but organize hospital tenders that consider other criteria in addition to price (e.g. Belgium, Finland, France, Portugal, Spain, Sweden) [10].

The intent to promote rational prescribing of biologics and to optimize cost savings has led payers and regulators to implement policies that support the use of BVB. In Germany, the establishment of biosimilar quotas and pharmaceutical spending caps has managed to keep a level playing field in the market. The success of biosimilar policies has been attributed to an already favorable environment and to the willingness of health insurance funds to set complementary benefit-sharing programs [11].These programs generate savings by supporting the use of BVB. The realized savings can be shared among stakeholders involved (e.g. health authorities/payers, health care professionals, hospital managers/administration) and are generally used to finance additional health services and innovative treatments, and to improve patients' quality of care. In the Netherlands, insurers have favored cost effective prescribing by applying reimbursement restrictions for originator products after biosimilar market entry [12, 13]. Also in Italy, clinicians' choice regarding the prescription of biologics with the same active compound has been restricted to the most cost-effective alternatives [14]. In France, the central government has implemented strategies for benefit-sharing for the molecules etanercept, adalimumab and insulin glargine [15]. These strategies were preceded by a convention (Rémunération sur objectifs de santé publique [ROSP]; 2016) providing prescribers with supplementary remunerations based on attaining public heath objectives, and that supported the prescription of insulin glargine biosimilars in ambulatory care.

To date, multiple countries have launched benefit-sharing initiatives for biologics. Institutions in Portugal, England, Italy and Germany pioneered these initiatives (2016), but there is no consensus on what their scope should be. Benefit-sharing (gainsharing) practices have been historically utilized in the industry as a way to actively engage employees in quality improvement processes and as a tool to align the objectives of employers and employees. However, the application of these types of practices to health care is more recent and required some adaptations [16]. In health care, benefit-sharing programs have been mostly used by payers/insurers/administrators to encourage health care professionals to make cost-effective choices. In the context of our research, most benefit-sharing initiatives have aimed to (i) set prescription objectives for BVB; (ii) engage prescribers in being compliant with the set objectives; (iii) generate and reinvest savings according to the needs of the stakeholders who produced them; and (iv) establish pathways for savings reinvestment that would fund additional health services and quality-of-care improvements. In Table 1, we provide a catalogue of terms used across Europe to refer to benefit-sharing programs that are consistent with the scope described above. Still, benefit-sharing programs with the same scope may differ in how they are designed and implemented, and in the achieved outcomes.

Little is known about the design and outcomes of benefit-sharing programs, about the elements that challenge/facilitate their implementation and about the reasons why some countries have not yet utilized benefit-sharing strategies. This study aims to fill this information gap by (i) categorizing the diversity of design characteristics for benefit-sharing programs implemented across Europe and (ii) identifying challenges regarding their implementation. The ultimate goal of this study is to generate evidence-based recommendations on how to operationalize benefit-sharing practices and on how to realize the full potential of these initiatives for all the stakeholder groups involved.

Table 1 Catalogue of terms that have been used across Europe to refer to benefit-sharing programs

Country of study	Terminology commonly used to refer to benefit-sharing programs
England	Gain-share/gainsharing/gain-sharing agreements (GSAs); agreements on how to share financial savings with local Clinical Commissioning Groups (CCGs) [17–30] The NHS commissioning framework for biologics refers to these programs as: *"Financial arrangements to incentivize the provider to implement processes that can maximize the early adoption and prescribing of biosimilars"* [9]
Scotland	Invest-to-save agreements/gainsharing programs [31, 32]
Wales	Gainsharing programs [33]
France	'*Expérimentation pour l'incitation à la prescription hospitalière de médicaments biologiques similaires délivrés en ville'* – Pilot program [34, 35] '*Programme d'efficience et pertinence de la prescription hospitalière de médicaments biologiques délivrés en ville'*– General program [36]
Germany	There is no consensus in the literature on how to refer to benefit-sharing strategies. The examples included below refer to selective contracts established between insurers and health care providers and that incorporate benefit-sharing strategies [37, 38]: *'Vertrag über ein strukturiertes Arzneimittel-Management von Biologika und Biosimilars (Biolike) nach §84 Abs. 5 Satz 1 SGB V'* [39] *'Vertrag zur Besonderen Versorgung in der Rheumatologie gemäß nach §140a SGB V'* [40]
Ireland	Gain-share arrangement [41, 42]
Italy	The term 'gainsharing' is generally used Benefit-sharing strategies are discussed in the context of initiatives aiming to incentivize the use of off-patent biologics and biosimilars: *'Misure di incentivazione dei farmaci a brevetto scaduto e del biosimilari'* [43]
The Netherlands	The term 'gainsharing' is generally used
Portugal	The conditions agreed for benefit-sharing are specified within contracts established between the Central Administration of the Health System (ACSS) and hospitals/hospital managers: *'Contrato-Programa Incentivos para os hospitais e centros hospitalares'* [44]
Spain	*'Programas de participación en las ganancias'* [45]
Sweden	Gain sharing programs/incentives for switch implementation [46, 47]
Other commonly used terms: benefit-sharing programs/programs to share benefits/shared saving strategies	

2 Methods

2.1 Literature Review

2.1.1 Search Strategy

Via a narrative literature review, we have identified publications about the design and implementation of incentive schemes that are based on benefit-sharing principles. We have restricted the search to incentive schemes that support the prescription of BVB (off-patent biologics and biosimilars) in Europe. The search strategy was based on the screening of scientific databases (PubMed/Medline; Embase; Google Scholar) and gray literature between August 2020 and February 2021.

To ensure completeness of the analysis, we used the following list of search terms: 'gainsharing', 'gainshare/gain share', 'saving sharing', 'benefit realization', 'benefit sharing', 'performance sharing', 'goal sharing', 'invest-to-save', 'shared savings' and 'savings'; combined with the terms 'biosimilars', 'biosimilar pharmaceuticals', 'best-value biologics', 'biologics'. These terms were adapted to the nomenclature of each specific database. When consulting gray literature repositories for country-specific information, we used the names that benefit-sharing programs receive in each country (see Table 1). We included full-text publications, conference abstracts, research posters, institutional documents written in English, French, German, Italian, Dutch, Portuguese and Spanish.

2.1.2 Data Analysis

We proceeded to a manual screening of the titles and abstracts. Once we discarded non-related records, we reviewed the publications based on their full text. Focusing on this selection of full-text records, we complemented the literature search by using a snowballing approach. The articles included in the final analysis were examined qualitatively according to the constructs of the Consolidated Framework for Implementation Research (CFIR) [48, 49]. This framework provides a selection of constructs that have been associated with effective implementation processes (see Sect. 2.2.2). In the context of our research, we used these constructs as a practical guide for the assessment and comparison of potential barriers and facilitators of benefit-sharing initiatives implemented across Europe [49]. It was

also considered of interest to explore the different reasons why some countries in Europe (Austria, Belgium, Finland, Norway, Poland, Romania, Slovenia, Spain) have not yet formally launched benefit-sharing initiatives.

2.2 Semi-Structured Interviews

Insights from experts across Europe regarding the design, implementation and outcomes of benefit-sharing programs were gathered via semi-structured interviews. The conduct of these interviews allowed us to complement the findings from the literature review and to investigate, in more detail, factors that affect the implementation and continuity of benefit-sharing programs.

2.2.1 Recruitment and Selection of Participants

The recruitment process was informed by the literature review phase of this study and by the networks of our research group. A selective sampling methodology was applied to achieve participation from diverse stakeholder groups and to ensure that all the participants have had an involvement in the design or implementation of benefit-sharing programs for biologics. Invited participants included health care professionals (prescribers, nurses, hospital pharmacists), representatives of the pharmaceutical industry, representatives of insurance companies, researchers and regulators.

2.2.2 Interview Guide and Interviews

The interview guide was developed based on the constructs and subconstructs of the CFIR framework [48, 49]. The guide consisted of questions about (i) the conditions agreed for benefit-sharing programs (e.g. target molecules, percent distribution of savings and savings reinvestment process); (ii) the stages and outcomes of the implementation process; (iii) the internal practices/policies affecting the implementation; (iv) the external practices/policies affecting the implementation; and (v) perceptions/learnings of stakeholders participating in benefit-sharing programs. The selection of questions was refined and validated by four experts from three European countries with a background in health sciences.

A total of 16 interviews were organized between February 2021 and June 2021 (see Table 2). These interviews were conducted with stakeholders from England, France, Germany, Ireland, Italy, the Netherlands, Poland, Portugal, Romania and Scotland. Experts from Austria, Finland, Slovenia, Spain and Sweden also contributed to our research by confirming/denying the presence of benefit-sharing initiatives for biologics in their respective countries. The interviews were carried out in English and via teleconferences. The participants received and signed an informed consent form informing them about the scope of the study and the conditions for data processing. If agreed by participants, the interviews were audio-recorded and transcribed verbatim. When the audio recording was not possible, the researcher took notes and wrote a summary report with the main conversation highlights. Interviews were carried out until saturation of the data. The transcripts of the interviews were pseudonymized and processed using the software QSS NVivo 12. The qualitative analysis and categorization of the data were based on the principles of the CFIR framework. To validate the accuracy of the analysis, the study results based on interview data have been shared with the participants prior to publication.

Table 2 List of interviews conducted and summary of the participants' background

Country of study	Number of interviews conducted	Interviewees' background
France	1	HCP
Ireland	1	Researcher/regulator
Portugal	2	Industry representative Researcher/regulator
England	4	HCP
Scotland	1	HCP
Germany	1	Insurer
Italy	2	Researcher Industry representative
The Netherlands	2	Insurer HCP
Poland	1	Industry representative
Romania	1	Researcher

HCP health care professionals

3 Results

The screening of articles from the literature allowed us to map countries in Europe where benefit-sharing programs have been implemented at some point in time (France, Germany, Ireland, Italy, Sweden, the UK). The conducted interviews confirmed the literature review findings and expanded our knowledge about benefit-sharing strategies implemented in the Netherlands and Portugal. For the countries of study, we have integrated the results of the literature review and the interviews, and we discuss separately (i) learnings from benefit-sharing experiences and (ii) the time evolution of benefit-sharing strategies.

3.1 Learnings from Benefit-Sharing Experiences

Benefit-sharing strategies have been implemented in health care systems across Europe that have different structural organizations. Countries such as Ireland, France and Portugal, where health care management at the central level is predominant, have established national-level initiatives [7, 8, 34, 42, 44, 50, 51]. In these cases, the involvement of the Health Services Executive (HSE) Medicines Management Programme (Ireland), the National Health Service Financial Division (DSS/SD1; France) and the Central Administration of the Health System (ACSS; Portugal) has been crucial to determine benefit-sharing conditions. In the UK, the National Health Services of the constituent countries have their own policies for the regulation of the use of biologics. For example, in England, the NHS has provided a common framework for the commissioning of biologics and has published some general guidance on benefit-sharing [9, 17, 18]. However, the establishment of benefit-sharing programs ultimately depends on the willingness of local Clinical Commissioning Groups and Trusts/clinical departments to start the negotiation process. Alternatively, in Scotland, the pertinent negotiations on benefit-sharing are established between the local Health Boards and the Trusts clinical departments [31, 32].

In countries such as Germany, Italy, the Netherlands and Sweden, where health care competences are highly decentralized, the organization of benefit-sharing initiatives has been local [39, 40, 43, 46, 47]. At the hospital level, the benefit-sharing initiative launched by the Campania region (Italy) constitutes the only example of a tri-party agreement among representatives of the regional government, hospital administrators and prescribers. In Sweden and the Netherlands, the organization of benefit-sharing initiatives has been generally prompted by individual hospitals. At the ambulatory care level in Germany, the launch of benefit-sharing programs has been attributed to not-for-profit membership-based health insurance institutions. These institutions are the standard of health insurance in Germany and currently provide coverage for more than 80% of the German population [52].

These examples show that benefit-sharing strategies can be implemented in systems with different health care organizational structures (centralized vs decentralized) and funding systems (tax-based vs based on social insurance contributions). In the following sections we include country-specific information about the design and implementation of benefit-sharing programs for biologics. This information is summarized in Supplementary Table 1 (see electronic supplementary material [ESM]).

3.1.1 National Initiatives

3.1.1.1 France The French National benefit-sharing program (2018–2022) targets molecules prescribed within the hospital, but dispensed by community pharmacies (etanercept, adalimumab, insulin glargine). For these molecules, an 80% biosimilars uptake objective has been set nationally to be achieved by 2022. This program incorporates two independent incentive schemes that differ in their design characteristics.

The more general scheme requires the compulsory participation of hospitals that have concluded a contract with the regional health agency (ARS) to improve the quality and efficiency of care (CAQES). For each unit prescribed, a remuneration corresponding to 20% of the price difference between the reference product and its biosimilar goes to the financial department of the hospital. Another incentive scheme was proposed for a limited number of hospitals (article 51; pilot program or experimentation); 62 hospitals have voluntarily adhered to this pilot program. A remuneration corresponding to 30% of the price difference between the reference product and its biosimilar is expected to go to the clinical departments that generated the savings. It has been reported that some clinical departments have experienced difficulties claiming their corresponding percentage of savings from the hospital management.

The launch of two independent incentive schemes with different characteristics offers a unique opportunity to compare relative implementation successes. Although the French benefit-sharing program is still ongoing, data after 2 years (October 2020) suggest that there is an 8.3-point difference in biosimilars uptake between the two initiatives and that biosimilar uptake levels are higher within the pilot program. This difference has been partly attributed to (i) the voluntary versus compulsory participation in the program; (ii) the greater percent remuneration for the pilot program; (iii) the greater capacity of the pilot program to allow for savings reinvestment at the level of the clinical departments; (iv) differences in the number of prescribers that participate in benefit-sharing. It has also been observed that the effectiveness in the communication with hospitals has had an impact on the implementation success of these initiatives. The principles of both incentive schemes have been communicated first by the central government to the regional health authorities, and subsequently, by the regional health authorities to the hospitals. In cases where some of the actors have not communicated effectively, this two-step approach has become an implementation barrier.

3.1.1.2 Ireland In Ireland, high-cost self-administered biologics such as TNFα inhibitors belong to the 'High Tech' medicines program. Patients are initiated on these molecules at the hospital and routinely get their medication via com-

munity pharmacies. It is a competency of the HSE Medicines Management Programme to implement policies that reduce spending within the 'High Tech' program. In this context, the market entry of biosimilars represents a cost-reduction opportunity. However, the penetration of TNFα inhibitor biosimilars in Ireland has been low. In 2018, the market share of infliximab biosimilars was only 25% [53]. In the case of etanercept, biosimilar market shares were still lower than 5% [42].

The HSE Medicines Management Team launched a BVB initiative (2019–2021) for adalimumab and etanercept products. The first step of this initiative was to establish criteria for identification of 'best-value' products. The application of these criteria resulted in the biosimilar versions (Imraldi®, Amgevita®, Hulio®, Idacio®, Benepali®) being selected as 'best-value'. Based on this selection, the HSE adapted the prescribing guidelines for treatment-naïve and established patients and set a BVB prescription target of 80% to be reached by 2021. To further incentivize the compliance of prescribers with the emitted guidelines, the HSE introduced a benefit-sharing initiative (June 2019). Via this initiative, the hospital clinical departments that initiate/switch patients to a BVB medicine are allocated €500 of the resultant savings per patient. Twelve months after the initiation of the BVB initiative, the penetration of best-value products amounted to 50%. The switch/initiation of 11,627 patients on BVB yielded savings of €22.7 million. Approximately 16% of the total savings (€3.6M) were returned to the clinical departments that generated them. In some cases, these savings have been reinvested into patient care via the development of online biologic registries or by increasing the capacity of infusion rooms for IV formulations.

Certain aspects have facilitated the implementation process for the Irish benefit-sharing initiative. One aspect has been the application, since February 2020, of reimbursement restrictions for non-'best-value products' in treatment-naïve patients. Another facilitating aspect has been the establishment and effective use of an online prescribing system for 'High Tech' drugs. This system allows tracking of prescribing activities and financial flows and addresses transparency issues that concerned Irish stakeholders when implementing benefit-sharing [54]. Finally, in order to address HCPs' doubts regarding the benefit-sharing initiative, easily reachable implementation leaders have been designated.

3.1.1.3 Portugal The Portuguese NHS has established policies to support biosimilars use at the hospital level, which is where high-cost biologics are mostly prescribed and administered. Communication about these policies started in 2013, when Infarmed (National Authority of Medicines and Health Products) organized various informative multi-stakeholder sessions. In 2016, a national benefit-sharing initiative was launched for all hospital-use biologics exposed to biosimilar competition. ACSS (Central Administration of the Health System) has been in charge of establishing contracts (Contratos-Programa) to agree with hospital managers on benefit-sharing conditions [44, 50]. These contracts are based on a clear principle: all the NHS hospitals are requested to participate in benefit-sharing and are asked to comply with a 20% biosimilars uptake objective within the first year of biosimilar market entry. This is applicable even if the price difference between the originator and the biosimilar is minimal. Hospitals compliant with this uptake objective get 15–25% of the generated savings back for reinvestment. Additionally, non-compliant hospitals can be penalized. So far, this is the only benefit-sharing example where a mechanism to penalize non-compliance is in place.

According to the participating interviewees, several aspects have facilitated the implementation of the Portuguese benefit-sharing strategy. One important aspect is the timely collection and publication of biosimilar uptake data from every NHS hospital [55]. Infarmed data suggest that biosimilar uptake has been high (> 50%) for almost every molecule [55]. This may be due to a combination of factors: (i) a benefit-sharing strategy that includes rewards and penalizations, (ii) a proactive communication strategy of the government bodies with HCPs and hospital administrations; (iii) the early engagement of key opinion leaders; (iv) legislations that support the reopening of hospital tenders following biosimilars market entry. However, although uptake data are monitored, the central government does not gather information about savings distribution and reinvestment. This is to be decided by each hospital, and to the best of the authors' knowledge, none of the involved hospitals has publicly reported on the outcomes of the savings reinvestment process. In this context, interviewees recommend establishing performance indicators to estimate the impact of the reinvestment of savings on the quality of care. This is expected to increase transparency regarding the financial flows.

3.1.2 Regional/Local Initiatives

3.1.2.1 The United Kingdom

England The NHS Commissioning Framework for biologics has supported the local establishment of benefit-sharing programs for high-cost biologics commissioned by Clinical Commissioning Groups (CCGs) and excluded from the National Tariff (e.g. infliximab, etanercept, rituximab). This framework specifies that benefit-sharing initiatives agreed among Commissioners and Trusts/providers are expected to have a short duration (~1–2 years) and to facilitate reaching the established uptake objectives for BVB (90% uptake for treatment-naïve patients within 3 months of biosimilar market entry; 80% uptake for established patients within 12

months of biosimilar market entry). In 2018 it was reported that out of the incentive schemes allowed for providers, benefit-sharing was used in 75% of the cases [56]. However, our literature search has identified benefit-sharing examples in only 11 NHS Trusts. This illustrates the need for Trusts to engage in more proactive reporting of outcomes after benefit-sharing. The main design characteristics and outcomes achieved for these benefit-sharing initiatives are presented in Supplementary Table S2 of the ESM.

The implementation of benefit-sharing programs in England has brought several challenges. Regarding the negotiations between Commissioners and Trusts, it has been reported that clinical departments have not always been formally included as recipients of the generated savings. In these cases, there was no straightforward path for the clinical departments to claim the corresponding savings. Also, although most benefit-sharing agreements relied on a 50:50 split of savings between Commissioners and Trusts, the negotiations required for consensus on the savings split have been time consuming. Regarding the continuity of benefit-sharing programs, this has been challenged by aggressive competition dynamics of originator manufacturers. In some cases, the price gap between originators and biosimilars was minimal and it was no longer economically feasible to use the traditional benefit-sharing schemes. In this context, Trusts have applied alternative benefit-sharing mechanisms based on fixed-price principles (see Sect. 3.2 and Supplementary Table S2 in the ESM). Finally, the recent use of emergency funding arrangements within the NHS (fixed budget set according to historical spending), has diminished the potential for the reinvestment of savings. In light of these challenges and in order to improve general efficiencies within the health care system, the NHS has recently disincentivized the use of benefit-sharing strategies. The rational use of biologics within the NHS and the reallocation of savings centrally has also led to important benefits for patients. This has been exemplified by the recent extension of NICE eligibility criteria to bDMARDs for patients diagnosed with rheumatoid arthritis. This modification of the treatment guidelines has been anticipated to have a positive effect on the quality of life of around 25,000 patients [57].

Scotland Following the increased utilization of high-cost medicines, NHS boards have been exploring avenues to make financial efficiencies. Regarding the optimization of biologics use, it was recommended to start treatment-naïve patients on the most affordable alternatives and to initiate switching processes for established patients. To address residual uncertainties regarding the safety of switching, the conduction of managed-switch programs has been supported. The implementation of managed-switch programs requires additional resources that have been funded by benefit-sharing schemes agreed with local Trusts.

In 2015, a tertiary IBD center in Edinburgh agreed with the local Trust (NHS Lothian) to initiate all Crohn's disease patients eligible for treatment with infliximab on the biosimilar, and to conduct a managed-switch for patients already receiving Remicade®. In total, 110 patients (all eligible patients) were switched to biosimilar infliximab without significant changes in efficacy or safety outcomes, and this generated a 46.6% reduction in costs. Via benefit-sharing, prospective savings were invested into hiring a senior pharmacist and a clinical fellow that implemented a therapeutic drug monitoring (TDM) system for patients diagnosed with inflammatory bowel diseases. This TDM system enabled patients' disease state to be evaluated before switching and minimized disease complications for patients due to inadequate treatment selection.

3.1.2.2 Germany In Germany, the payers and the providers are represented by health insurance companies (German: Krankenkassen) and the regional associations of Statutory Health Insurance Accredited Physicians (German: Kassenärztliche Vereinigungen; KVs), respectively. The market availability of biosimilars and the willingness of the system to optimize cost savings have triggered the establishment of policies to support biosimilars use. At the regional level, insurance companies and KVs agree on biosimilar quotas for the different specialties. To further optimize the savings potential offered by biosimilars, some health insurance companies have signed with the KVs benefit-sharing contracts for TNFα inhibitors. One example of a benefit-sharing initiative is the BioLike program implemented by the insurer company BARMER. This initiative is regulated according to §84 of the Social Code Book V (Vertrag über ein strukturiertes Arzneimittel-Management von Biologika un Biosimilars §84 Abs.1 Satz 5 SGB V) and was initiated in 2015 via a pilot project in the region of Westphalia-Lippe. The BioLike program aimed to engage individual prescribers working in the ambulatory sector and affiliated to KVs. Participating prescribers that engaged eligible patients in the initiative received financial and non-financial rewards. Following the pilot program in Westphalia-Lippe, similar benefit-sharing contracts were agreed between BARMER and different KVs (see Supplementary Table 1 in the ESM). The contracts for these regions can differ in the specific remunerations given to prescribers and have been established at different moments in time. This may explain why participating prescribers in some regions (e.g. Westphalia-Lippe) have engaged more actively with the initiative than prescribers in other regions.

In 2017, the Professional Association of German Rheumatologists (BDRh) and several health insurance companies established new benefit-sharing contracts. These contracts were regulated according to §140a of the Social Code Book V (SGB V) and aimed to engage multiple health insurance

companies and to support the involvement of all the regions in benefit-sharing. Although the outcomes of this benefit-sharing initiative have not been reported, it has been communicated that 12,000 patients with chronic inflammatory rheumatic diseases have already been involved, and that specific quality indicators to improve patient care have been established.

3.1.2.3 Italy In Italy, biologics for hospital use can be purchased on the basis of framework agreements when four or more competitors are marketed. Competition among products with the same active molecule is established on the basis of price, and the top three most affordable products are selected as winners. Prescribers are prompted to prescribe the most affordable products. However, the Italian regions have been reported to comply differently with this instruction, as there are ways for prescribers to overrule it (e.g. clinical arguments). Following the variable level of compliance with this prescribing guidance, the role of complementary affordability measures becomes relevant. Every region in Italy has implemented policy measures to support biosimilars use (e.g. prescribing targets). Campania is so far the only region where a benefit-sharing initiative has been formally adopted. The basis for the distribution of savings among the involved stakeholders has been legally established by the regional government (see ESM, Supplementary Table 1). Regarding the outcomes of the Campania benefit-sharing initiative, only achieved biosimilar uptake levels have been communicated. These achieved uptake levels cannot be evaluated in relation to baseline biosimilar uptake levels before the launch of the benefit-sharing initiative, as these data are not publicly known. However, available data up to December 2020 show that in the case of granulocyte-colony stimulating factors (GCSFs), rituximab and infliximab, this initiative has been successful, attaining higher uptake levels than the national average. However, for adalimumab, etanercept and somatropin, the attained uptake levels have been lower than the national average [58]. It is difficult to evaluate the reasons behind the partial success of the Campania initiative. This is due to the insufficiently transparent reporting of data. Although it is known that savings are reinvested into funding innovative treatments, it is not known what has been the impact of the reinvestment of savings.

Alternative local initiatives for benefit-sharing have been initiated by hospitals in other areas of Italy (e.g. Lombardy), where regional governments have not been interested in implementing benefit-sharing programs. In these regions, although there are enough mechanisms in place to optimize cost savings, these mechanisms do not ensure that the savings achieved are translated into tangible, direct benefits (e.g. improved monitoring, improved care and access to treatments) for the switched patients.

3.1.2.4 Sweden In Sweden, the procurement of biologics for hospital use is organized at the level of the county via tendering procedures. To contain pharmaceutical expenditure, the region of Skåne has been active in organizing managed-switch programs for biologics. In the case of infliximab, after the conclusion of the contract with the originator manufacturer (2015), all the rheumatologists in the county were recommended to initiate/switch patients to an infliximab biosimilar alternative. Although this was only a recommendation, the prescribing behavior of physicians was monitored and high uptake levels of biosimilar infliximab were achieved within a short time frame. The generated savings have been redistributed locally to the hospitals via benefit-sharing strategies. This has allowed increasing funding for innovative products (e.g. vedolizumab) across therapeutic areas. To the best of the authors' knowledge, the only benefit-sharing example reported in the literature in the region of Skåne dates back to 2009 (see Supplementary Table 1 in the ESM).

3.2 Factors Affecting the Continuity of Benefit-Sharing Strategies

The information presented in Sect. 3.1 indicates that there is no one-size-fits-all approach for benefit-sharing and that the design/implementation conditions for these programs need to adapt to the clinical, regulatory and political environment. However, it is possible to extract some common learnings (see Table 3).

The interviewed experts argue that the factors outlined in Table 3 are likely to challenge the continuity of benefit-sharing initiatives. It is of note that the establishment of short-duration benefit-sharing programs limited to one molecule (e.g. in England) minimizes risks related to the reduction of the savings potential over time. However, these types of initiatives generate benefits that are not likely to produce a long-term impact. For example, multiple institutions (e.g. England, Scotland) have reported that when reinvesting savings into hiring additional HCPs, it has not always been economically feasible to prolong the new contracts after the end of the managed-switch program. Therefore, the service improvements generated from a switch have not necessarily been able to support multiple future switches. Interviewees have also indicated that patients treated with a specific biologic may require a change to another biologic. In these cases, when the benefit-sharing strategy is only applied to the first biologic, the changes in the prescription volume towards the second biologic reduce the potential for savings over time.

Table 3 Factors identified by interviewees that have challenged the continuity of benefit-sharing programs

Factors that have challenged the continuity of benefit-sharing programs
Reduction in the *price gap* between the originator and its respective biosimilars
Reduction in the *volume of patients* eligible for a managed-switch program that is linked to a benefit-sharing strategy. Changes in prescription volumes for a molecule are common and are generally due to individual patient factors and to changes in prescribing guidelines/practices
Change in the *regulatory environment* and in the *conditions for reimbursement* of biologic medicines
Evolution of the *financial needs and constraints of health care systems*

3.2.1 The Experience of the Royal Berkshire Foundation Trust

As the price of the originator drug is reduced after the introduction of biosimilars, the margin for savings may be too small in order for a traditional benefit-sharing scheme to be economically feasible. To address this issue, the Royal Berkshire Foundation Trust in England has established, in collaboration with the local CCG, a benefit-sharing program based on a fixed-price mechanism [29]. This implies that, for a year, all the brands of a given biologic are recharged at a fixed price (75% of the originator price). This leaves a 6–10% gap between the fixed price and the price of the biosimilar brand. Trusts can realize 100% of this savings gap if the managed switch program is carried out efficiently. Using this model, CCGs can realize 25% of the generated savings, while ensuring higher uptake for biosimilars.

4 Discussion

To the best of the authors' knowledge, this is the first academic publication that conducted a detailed comparative analysis of design and implementation conditions for benefit-sharing programs implemented across Europe. Although some publications have comparatively described the characteristics of these programs, the limitations and challenges associated with their implementation have not yet been explored [10, 59]. It is also an added value of this study to include interviews with relevant stakeholders involved in the design/implementation of benefit-sharing strategies. Although we have managed to interview key actors for each of the European-level benefit-sharing programs reported in the literature, the number of included participants per country is low. We consider that the obtained information per country is representative of the country situation. However, we have not been able to describe the point of view of each of the stakeholder groups involved in benefit-sharing in each country, and we cannot ensure that the map of benefit-sharing strategies identified is complete. In countries where benefit-sharing strategies have not yet been implemented (e.g. Romania, Spain, Finland), we have aimed to identify some reasons behind unfavorable environments towards benefit-sharing. We acknowledge that the methods used for this analysis do not allow us to provide a comprehensive list of factors.

The analysis of design and implementation conditions for benefit-sharing programs has revealed variable characteristics. This is due to the necessity of these programs to adapt to the health care system organization, the regulatory environment and the specific care setting. In fact, our research provides examples of how the regulatory environment affects the implementation success of benefit-sharing programs. One example is the positive effect of the reopening of tender procedures after biosimilar market entry in Portugal. Also, in the case of the Irish benefit-sharing initiative, the application of reimbursement restrictions for non-BVB has been shown to facilitate compliance along with the initiative implementation. Most of the studied benefit-sharing initiatives have established uptake objectives for BVB, or more specifically, for biosimilars. Interviewed experts suggest that this approach has a positive motivation effect and that it encourages the unbiased and timely monitoring of outcomes achieved via benefit-sharing. In general, compliance with the set biosimilar uptake objectives has been reinforced via positive actions (reallocation of savings). Only the Portuguese example has incorporated a penalization element in case of non-compliance with uptake objectives. It is also still unclear whether offering voluntary versus compulsory participation in benefit-sharing strategies plays a role in implementation successes. According to the French experts interviewed, more evidence about this aspect should be available after the finalization of the French National benefit-sharing initiative.

Although there are multiple and variable approaches for benefit-sharing, there is an overall lack of clarity on the key benefits that can be offered by these initiatives. It has been generally supported by the literature that the implementation of benefit-sharing initiatives should improve value for money and generate efficiencies within the system. We discuss in this article how price gap reductions between originators and biosimilars may challenge the continuity of benefit-sharing initiatives. We encourage decision makers/institutions to consider this aspect in advance and to try to

anticipate the potential for savings generation over time. The duration of a benefit-sharing strategy should be adjusted in accordance with this estimation.

Our research also suggests that the capacity of benefit-sharing initiatives to align stakeholders' interests and to actively engage HCPs and patients in quality of care improvements has not been fully exploited. Most of the initiatives are unclear about how savings are distributed and reinvested locally. Also, certain initiatives (such as in England, France and Italy) have been successful in engaging health care providers at large, but not in involving the local health care actors. Further, the communication with patients regarding the generation and reinvestment of savings has been infrequent. In this context, four aspects are key for improvement: (i) ensuring clear pathways for participating clinical departments/HCPs to claim the corresponding savings, (ii) asking clinical departments/HCPs to provide in advance a proposal for savings reinvestment that considers patients' needs and that would have a long-term impact; (iii) improving the transparency of financial flows; (iv) establishing performance/success indicators able to evaluate quality of care improvements and that can be clearly monitored over time.

Table 4 summarizes key outcomes that the interviewed stakeholders consider should be achieved via benefit-sharing. In this table, we also outline recommendations aimed at achieving these outcomes. According to our analysis, these recommendations should be useful for multiple health care institutions across Europe.

Regarding the terminology used across Europe to refer to benefit-sharing/gain-sharing strategies, it has been suggested that the use of the word 'gain' may be only associated with monetary gains by some health care professionals and patients. However, the rational prescribing of biologics

Table 4 Proposal on how to unlock the potential of benefit-sharing programs for biologics

Potential outcomes to be achieved via the implementation of benefit-sharing strategies:

1. Improved value for money
2. Aligned interests for stakeholders in health care
3. Active engagement of HCPs and patients
4. Transparent redistribution and reinvestment of savings
5. Leveraged resources to: (1) address the needs of health care systems and societies at large and (2) improve patients' outcomes

The interviewed experts consider that benefit-sharing programs not able to achieve these outcomes are not designed/implemented to fulfil their potential. Below, we summarize recommendations on how to generate these benefits. These recommendations are based on the evaluation of already implemented benefit-sharing programs and on insights from stakeholders that have been directly involved in their design/implementation

Overview of recommendations

Pre-implementation phase—design

→ To present a strong benefit-sharing proposal/business case including:

A comprehensive estimation of the savings potential over the years. This estimation would depend on the evolution of prices and the number of eligible patients

A detailed analysis of resource needs to be covered by the benefit-sharing agreement

→ To establish a reasonable time frame for the agreement based on savings potential, resource needs and the future market availability of other molecules within the therapeutic area

→ To clearly define (in advance) the scope of the benefit-sharing program in terms of uptake and savings objectives, resources reinvestment and expected outcomes

→ To clearly specify (in advance) who would be the direct/indirect beneficiaries of the savings reinvestment process and to establish clear pathways for the redistribution of savings

Experts recommend that a proportion of savings flows back to the clinical departments that participated in the savings generation. These department should provide a proposal for the reinvestment of savings that is impactful for the clinical service and the patients

→ To establish mechanisms able to identify factors that may affect the continuity of benefit-sharing strategies

Implementation phase

→ To agree (at the health care site level) on performance indicators specific to quality of care improvements

Examples of quality of care parameters:

Earlier and/or increased access to biologics

Improved patient monitoring during a switch (frequency of follow-up visits, patient satisfaction regarding switch outcomes, online patient registries, therapeutic drug monitoring)

Reduction of disease-related complications due to improved pharmacologic disease management

Increased patients' trust in the use of biosimilar medicines

→ Compliance with the objectives of the benefit-sharing initiative should be monitored and reported regularly according to the established performance indicators

Communication strategy

→ To engage key opinion leaders in the pre-implementation phase

→ To facilitate discussions among all the stakeholders involved about conditions to be agreed for benefit-sharing

→ To report transparently on the outcomes of benefit-sharing programs (at the level of the patient, but also across institutions)

can lead to other types of benefits (earlier and increased patients' access to treatments, improved quality of care, etc.). To account for these benefits, we use in this manuscript the term 'benefit-sharing'. Our study findings suggest that a very characteristic potential value of benefit-sharing schemes is that they can align stakeholders' objectives/priorities around the rational use of biologics. We believe that the main drive to implement these types of schemes should be the aim to generate consensus around the broad societal value offered by BVB, rather than focusing only on financial gains or savings.

Finally, it is relevant to consider a proper timeframe/duration for benefit-sharing programs. Long-duration benefit-sharing strategies are subject to greater uncertainties regarding the stability of the potential for savings. However, short-duration initiatives established for a very limited selection of molecules may generate short-term benefits that are unlikely to have a stable impact on clinical practice. On the basis of these limitations, we would like to highlight the importance of having a holistic approach for the implementation of prescribing incentives for BVB. This implies setting up savings optimization strategies for every biologic in a therapeutic area. Thus, when patients are initiated on a different biologic within the therapeutic area, the potential for savings for the clinical department is not decreased. This approach should not only focus on molecules with biosimilar alternatives in the market, but on molecules likely to face biosimilar competition in the future.

4.1 Future Research

This study identifies implementation barriers and facilitators of benefit-sharing strategies using a qualitative analysis methodology. Our research shows that, in practice, benefit-sharing strategies have always been implemented in combination with other policies supporting the rational use of biologics. We refer on multiple occasions to the interaction among these policies. However, due to missing information on outcomes achieved after benefit-sharing, and because of the nature of this study design, we have not been able to establish merits associated with benefit-sharing strategies alone and in contrast to other biosimilar-promoting strategies. We consider that it would be of great interest for this field of research to conduct this analysis in the future.

Regarding the selection of 'most affordable' products and BVB for inclusion in benefit-sharing programs, it would be of interest for future research to describe the criteria used by each country for this selection. To explore this aspect, it would be interesting to interview experts involved in Health Technology Assessment evaluations in the countries of study. Although it was not possible during the study to conduct this analysis, we consider that this would be relevant for future research.

5 Conclusions

Benefit-sharing initiatives have the potential to align stakeholders' priorities regarding the cost-effective prescription and use of biologics. Although multiple examples across Europe report on how benefit-sharing has supported patients along managed-switch processes, the use of these practices has not always been translated into direct and long-term benefits for all the stakeholders involved. Our research suggests that, in order to realize the full potential of benefit-sharing initiatives, clear quality of care improvement objectives must be set and greater transparency around the reinvestment of savings must be encouraged.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40259-022-00523-z.

Acknowledgements The authors thank the participating interviewees for their contribution to this study and for their feedback on the manuscript. The authors would like to acknowledge the Research Consultation Service offered through the European Alliance of Associations for Rheumatology (EULAR) and would like to clarify that the content of the manuscript is the responsibility of the authors and does not necessarily represent the official views of EULAR. The authors would also like to thank Medicines for Europe for their insights on benefit-sharing initiatives, and would like to indicate as well that the content of the manuscript is the responsibility of the authors and does not necessarily represent the official views of Medicines for Europe. The authors would like to acknowledge the contribution of Dr Perter Lerk (Ziekenhuisapotheker, Gelre Ziekenhuizen), Dr Niels Boone (Ziekenhuisapotheker, Zuyderland Medisch Centrum), Caspar van Loosen (Beleidsadviseur NVZA), Apogen (The Portuguese Association of Generic and Biosimilar Medicines), Prof. Helder Mota-Filipe (Faculty of Pharmacy, University of Lisboa), Stemer Gunar (University Hospital Vienna, Pharmacy Department), Bernard Duggan (HSE-Medicines Management Programme), Dr Antoni Chan (PhD, FRCP; Consultant Rheumatologist and Physician Associate Medical Director at Royal Berkshire Foundation Trust), Pearl Avery (Patient Safety Practitioner at Dorset County Hospital Foundation Trust), Dr Sahar Barjesteh van Waalwijk van Doorn-Khosrovani (Department of Medical Advice and Innovation, CZ Health Insurance), Dr Bruno Fautrel (AP-HP), Mr Heikki Bothas (executive director of Finnish Generic Pharmaceutical Association), the Örebro University Hospital (Sweden) and the French Ministry of Health (Social Security Directorate).

Declarations

Funding This study was supported by KU Leuven and by the Fund on Market Analysis of Biologics and Biosimilars following Loss of Exclusivity (MABEL).

Conflict of interest SS, IH and AGV founded the KU Leuven Fund on Market Analysis of Biologics and Biosimilars following Loss of Exclusivity (MABEL). SS was involved in a stakeholder roundtable on biologics and biosimilars sponsored by Amgen, Pfizer and MSD; he has participated in advisory board meetings for Pfizer and Amgen; he has contributed to studies on biologics and biosimilars for Hospira (together with AGV and IH), Celltrion, Mundipharma and Pfizer, and he has had speaking engagements for Amgen and Sandoz. AGV is involved in consulting, advisory work and speaking engagements for a number of companies, a.o. AbbVie, Accord, Amgen, Biogen, Effik

Benelux, Fresenius Kabi, Medicines for Europe, Pfizer/Hospira, Mundipharma, Roche, Sandoz. TBL and ATS declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Availability of data and materials The data generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability Not applicable.

Ethics approval The interview guide and methodology for this study were approved by the Research Ethics Committee UZ /KU Leuven on the 28th of December 2021 (S64860).

Author contributions IH, SS, AGV, and TBL developed the idea for and were involved in the design of this study. ATS and TBL took part in data provision. TBL was involved in data collection and analysis. TBL drafted the initial version of the manuscript. IH, SS, AGV and ATS critically reviewed the manuscript. All authors read and approved the final manuscript.

Consent to publish Not applicable.

Consent to participate Informed consent was obtained from all individual participants included in the study.

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