Supplementary information

Qualitative analysis of the design and implementation of benefit-sharing programs for biologics across Europe

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Supplementary Table 1. Comparative overview of design and implementation criteria for benefit-sharing programs implemented across Europe. The results presented in Supplementary Table 1 have been obtained by combining information from the literature with the expert input of interviewees regarding benefit-sharing programs.

ADOPTERS OF BENEFIT-SHARING STRATEGIES - Initiatives established at the national level

FRANCE [1-7] – Examples of benefit-sharing programs.
-Pilot/experimentation program: Expérimentation pour l'incitation à la prescription hospitalière de médicaments biologiques similaires délivrés en ville.
-General program: Programme d'efficience et pertinence de la prescription hospitalière de médicaments biologiques délivrés en ville.

Design conditions agreed for benefit-sharing programs	Outcomes from the implementation of benefit-sharing programs	Implementation facilitators (+) and barriers (-)
>Scope of the initiative: national initiative. -The general benefit-sharing program was based on the participation of hospitals that have signed specific contracts (CAQES)[1] with the ARS[2]. Other NHS hospitals have adhered to the pilot benefit-sharing initiative. -Benefit-sharing initiatives not necessarily coupled with managed-switch programs. **>Target molecules:** etanercept, adalimumab, insulin glargine. **>Setting:** molecules prescribed in the hospital and dispensed in the retail sector. **>Timeframe:** etanercept and insulin glargine (2018-2021); adalimumab (2019-2022) **>Participation in benefit-sharing and % distribution of savings:** -All the hospitals that have concluded a contract to improve the quality and efficiency of care (CAQES) with the ARS participate in the general benefit-sharing program. Additionally, 62 NHS hospitals and clinics voluntarily participated in the pilot program (etanercept: 40 hospitals/clinics; adalimumab: 40 hospitals/clinics; insulin glargine: 23 hospitals/clinics). -A 80% biosimilars uptake objective has been set for 2022. General program - For each unit of biosimilar product prescribed at the hospital and dispensed by a community pharmacy, 20% of the price difference between the reference product and its biosimilar goes to the hospital management/financial department. **Incentive payed directly to the hospital.** Pilot program /experimentation- For each unit of biosimilar product prescribed at the hospital and dispensed by a community pharmacy, 30% of the price difference between the reference product and its biosimilar goes to the clinical units that were involved in the generation of savings. The hospital administrations/financial departments receive the incentive and this is expected to go to the clinical care units. **>Savings reinvestment plan:** hospitals participating in the pilot programs were asked to provide a plan for the reinvestment of savings. To date, hospitals have not reported on the achieved outcomes. Outcomes will be analysed by 2022 when the programs finalize.	**>ETANERCEPT –** evaluation after 24 months of the implementation of the experimentation program. Analysis based on data from 40 hospitals. -The use of etanercept biosimilars increased by 23 points (44.2% uptake) in 24 months within the experimentation group *versus* a 16 points increase in the control group. For the achieved uptake levels, savings in the order of EUR 650K were expected. Similar etanercept biosimilar uptake levels extended to the totality of NHS hospitals would yield savings of approximately EUR 1.4M. -Remunerations provided to hospitals within the experimentation group (S1 2020); $\bar{x}$=EUR 20,402 (min.1,743 – máx.98,966) **>ADALIMUMAB -** evaluation after 22 months of the implementation of the experimentation program. Analysis based on data from 40 hospitals. -The use of adalimumab biosimilars increased from 4% to 33% (+29 points points increase was reported. -Projected savings by 2022: not specified. -Remunerations provided to hospitals within the experimentation group (S1 2020); $\bar{x}$=EUR 40,948 (min.4,002 – máx.424,107) **>INSULIN GLARGINE** – evaluation after 24 months of the implementation of the experimentation program. Analysis based on data from 23 hospitals. -The use of insulin glargine biosimilars increased from 15% to 31% (+16 points) by 24 months in the experimentation group. In the case of the control group, only a 11 points increase was reported. -Projected savings by 2022: not specified. -Remunerations provided to hospitals within the experimentation group (S1 2020): $\bar{x}$=EUR 2,343 (21-7,817)	(+) Efficient and fluent communication between the central government and the regional health authorities, and the regional health authorities and the hospitals management. (+) Setting-up incentives that go directly to clinical departments. (+) Establishing plans for the reinvestment of savings in advance. (-) The data publicly available do not allow to determine whether the payer's investment in benefit-sharing has led to short-term financial benefits for the payer. (-) The implementers do not monitor how savings are redistributed once they reached the hospitals. (-) Lack of transparency regarding the reinvestment of savings. Sometimes, the instructions clinical departments receive to claim their corresponding share of savings are unclear. (-) Communication barriers between the involved stakeholders. (-) It is unclear how hospitals/clinical departments have communicated with patients about the outcomes achieved after the implemntation of the benefit-sharing initiative.

IRELAND [8-12] – 'Best-value' biologics (BVB) initiative.
-Parties involved in the BVB initiative: Health Service Executive (HSE) Medicines Management Programme; HSE-Primary Care Reimbursement Service; Hospital management and clinical departments.

Design conditions agreed for benefit-sharing programs	Outcomes from the implementation of benefit-sharing programs	Implementation facilitators (+) and barriers (-)
>Scope of the initiative: national initiative implemented in the context of the BVB initiative. -Benefit-sharing initiatives coupled with managed-switch programmes. **>Target molecules**: TNFαi[3] in the 'High Tech' medicines programme (etanercept/ adalimumab). **>Setting:** molecules prescribed for the first time in the hospital and dispensed in the retail sector. **>Timeframe:** 2019-2021 **>Participation in benefit-sharing and % distribution of savings:** -The HSE set an 80% prescription target to be reached by 2021 for best-value etanercept (Benepali®) and adalimumab products (Imraldi®, Amgevita®, Hulio®, Idacio®). -Hospital clinical departments (rheumatology, gastroenterology, dermatology) receive EUR 500/patient initiated or switched to a BVB. **>Savings reinvestment plan:** each hospital clinical team must submit an application to request the corresponding share of the benefit-share program. Within this application, clinical teams indicate how savings are planned to be reinvested. The HSE-Primary Care Reimbursement Service reviews/administers these applications.	**>Evolution in the number of patients treated with a BVB:** 12 months after the start of the BVB initiative (May 2020), the number of patients treated with BVB was 20 times higher for adalimumab and 17 times higher for etanercept. **>Biosimilar uptake levels:** 12 months after the initiation of the BVB initiative, the penetration of BVB amounted to 50%. **>Cost-savings:** the initiation/switch of 11,627 patients yielded savings of EUR 22.7M. **>Savings reinvestment:** approximately 16% of the total savings (EUR 3.6M) were returned to the clinical departments that generated them. It is unclear how each hospital management team/ department leader has decided to reinvest savings. In some cases, savings have been used to develop online biologic registries and to increase the infusion rooms' capacity for IV formulations.	(+) Establishing criteria to identify BVB. Establishing clear prescribing guidelines for treatment-naïve/established patients. (+) Information sessions were organised for hospitals to explain the BVB initiative, including the benefit-share arrangement. Easily reachable implementation leaders have been designated to address doubts of HCPs. (+) Timely monitoring of uptake levels for BVB via the online prescription system and identification of sites that have experimented challenges reaching the prescription objectives. Follow up meetings have been organised to support these sites. (+) Since February 2020, Only BVB were reimbursed for naïve patients. (+) Transparency regarding the savings share going to clinical departments. (-) Limited information published in the literature on the strategies used by the different healthcare sites for savings' reinvestment. (-) Benefit-sharing may not be needed in the future if reimbursement restrictions for non-BVB are extended to established patients. (-) It is unclear how hospitals/clinical departments have communicated with patients about the outcomes of benefit-sharing.

PORTUGAL [13-15] – Contrato-Programa (Incentivos para os hospitais e centros hospitalares).
Parties involved in contract negotiations: ACSS[4] – Hospital managers; **Supporting role:** Infarmed[5`]

Design conditions agreed for benefit-sharing programs	Outcomes from the implementation of benefit-sharing programs	Implementation facilitators (+) and barriers (-)
>Scope of the initiative: national initiative involving all NHS hospitals. -Benefit-sharing initiatives not necessarily coupled with managed-switch programs. **>Target molecules:** all hospital-use molecules exposed to biosimilar competition (adalimumab, bevacizumab, enoxaparin sodium, epoetin, etanercept, filgrastim, follitropin alpha, infliximab, insulin glargine, pegfilgrastim, rituximab, somatropin, teriparatide, trastuzumab). **>Setting:** hospital. **>Timeframe:** 2016 – present. **>Participation in benefit-sharing and % distribution of savings:** -Participation was compulsory for NHS hospitals. They were required to reach a minimum of 20% biosimilar uptake within the first year of biosimilar market entry. -If compliant with the uptake objective, 15-25% of the savings are retained by the hospitals for reinvestment. Savings can remain at the level of the hospital administration or be distributed to clinical departments. If non-compliant with the uptake objective, a penalization is applied that corresponds to máx. 3% of the total financial amount for the health unit. **>Savings reinvestment plan:** -Each hospital can decide on the best options for reinvestment and they do not have to inform ACSS about it. Feasible options for savings reinvestment: service increases/improvements, additional staffing, counselling/information services for HCPs and patients. The priority in general has been to use savings to fund for innovative treatments.	**>Biosimilar uptake levels** (average for 2021 up to May; these are average uptake levels calculated for all NHS hospitals in Portugal) [16]: **Adalimumab**: 56%; **Enoxaparin sodium**: 67.6%; **Epoetin**:13.9%; **Etanercept**: 64.1%; **Filgrastim**: 100%; **Infliximab**: 86.6%; **Rituximab**: 75.5%; **Somatropin**: 28.4%; **Trastuzumab**: 48.4%; **>Cost- savings:** **Infliximab:** According to consumption data up to 2018, Infarmed has estimated that NHS hospitals would have spent extra EUR18.9M if infliximab biosimilars would have not reached the market [17]. **Adalimumab:** According to consumption data up to 2020, Infarmed has estimated that NHS hospitals would have spent extra EUR39M if adalimumab biosimilars would have not reached the market [18]. **>Savings reinvestment:** -It is unclear how each hospital management team has decided to reinvest savings. It is unclear what percentage of the savings retained within hospitals has reached specific clinical departments (e.g. rheumatology).	(+) Infarmed organised early multi-stakeholder information sessions about biosimilars. (+) Early engagement of key opinion leaders. (+) Benchmarking meetings for NHS hospitals, together with ACSS, SPMS[6] and Infarmed, to discuss the progress regarding biosimilar uptake. (+) Overall willingness of hospital management to initiate benefit-sharing. (+) Biosimilar prescription target (20%) set upon consensus. (+) Availability of scientific literature supporting the safety of switching. (+) Reopening of hospital tenders following the market entry of biosimilars. (+) Active pharmacovigilance system and open channels for HCPs to communicate safety concerns to government bodies. (-) Limited transparency regarding cost-savings and savings redistribution/reinvestment. It is unclear how the specific clinical departments benefit from the savings and what is the proportion allocated to each department. It is unclear how patients have directly benefitted from the use of biosimilars and whether patients have been informed about this. (-) Limited monitoring of the outcomes achieved via benefit-sharing. (-) Lack of a guidance on how to implement benefit-sharing initiatives and on how to create durable service improvements via savings reinvestment. (-) Limited capacity to expand benefit-sharing strategies to the retail sector.

ADOPTERS OF BENEFIT-SHARING STRATEGIES - Initiatives based on national guidelines and established at the regional/local level

ENGLAND [19-31]
Parties involved in contract negotiations: Local CCGs[7] - NHS Trusts - representatives of hospital clinical departments (*specific examples provided in the **Supplementary Table S2**)

Design conditions agreed for benefit-sharing programs	Outcomes from the implementation of benefit-sharing programs	Implementation facilitators (+) and barriers (-)
>Scope of the initiative: benefit-sharing programs can be designed according to general NHS guidelines, but the specific conditions are based on local agreements between providers and local clinical commissioning groups (CCGs). **>Target molecules:** benefit-sharing programs are applicable to high-cost biologics excluded from the National Tariff and funded separately by commissioners. Included molecules: TNFαi, rituximab. **>Setting**: hospital-use products and products delivered via home-care services. **>Timeframe:** 2015-present. Although uncommon, some benefit-sharing programs are still ongoing. Within each site and for a specific molecule, benefit-sharing programs usually have a short duration (~ 1-2 years). **>Conditions agreed for benefit-sharing and % distribution of savings:** -Treatment-naïve patients: BVB uptake objective set at 90% within 3 months of biosimilar market entry. -Established patients: BVB uptake objective set at 80% within 12 months of biosimilar market entry. -The most common approach for benefit-sharing has been to agree on a 50:50% split of savings between providers and commissioners (the calculation of the savings potential may be based on list prices or on contract prices). Sometimes, it has been agreed in advance what proportion of the 50% share of savings will go to the clinical departments.	**>Savings reinvestment plan:** generally established prior to the start of the managed-switch program. **>Biosimilar uptake levels:** the uptake levels generally achieved are in line with the set objectives. **>Cost-savings:** The NHS has estimated yearly savings of up to 300M due to biosimilars use. **>Savings reinvestment:** overall, savings have been used to (1) improve infrastructures and the catalogue of services; (2) hire HCPs able to support and improve monitoring for managed-switch processes; (3) establish online patient registries; (4) increase/facilitate access to biologics. See more detailed information within the **Supplementary Table S2.**	(+) Establishment of a Commissioning Framework for biologics that initially supported benefit-sharing initiatives. (+) Clear objectives for the prescription of BVB included in the NHS Commissioning Framework for Biologics. (+) Fluent communication between Trust management boards and hospital clinical departments. Generally clear communication with patients about the outcomes of benefit-sharing programs. (+) Capacity of the clinical departments within a hospital to present a robust business case (to CCGs) that justifies benefit-sharing. (-) Sometimes lengthy negotiations between CCGs and Trusts regarding the % split of savings. (-) Unclear conditions for the redistribution of savings between Trusts and hospital clinical departments**.** (-) Limited reporting of outcomes after benefit-sharing. Although most Trusts/CCGs have been involved in benefit-sharing, only examples corresponding to 11 Trust have been identified in the literature. (-) Reduction in the price gap between the originator and its respective biosimilars. (-) Changes in the regulatory environment and recommendations regarding the implementation of biosimilar policies. The NHS no longer incentivises the establishment of benefit-sharing schemes. (-) Urgent financial needs to be addressed within the healthcare system. This required using the savings generated by biosimilars outside of the clinical departments that generated them.

SCOTLAND [32, 33] – Examples of benefit-sharing programs.
-Lothian NHS Trust –Tertiary IBD[8] Centre in Edinburgh (Western General Hospital).
-Grampian NHS Trust – hospital rheumatology clinics in the Grampian area.

Design conditions agreed for benefit-sharing programs	Outcomes from the implementation of benefit-sharing programs	Implementation facilitators (+) and barriers (-)
>**Scope of the initiatives:** local initiatives involving specialized NHS rheumatology and IBD clinics. Benefit-sharing initiatives coupled with managed-switch programs. **Benefit-sharing in the Lothian region** >**Target molecules:** infliximab, adalimumab (IBD patients). >**Setting:** hospital. >**Timeframe: 2015 – 2017 (**~ 2 years, including a 12-months follow-up after switching**).** >**Conditions agreed for benefit-sharing and % distribution of savings:** -It was agreed to initiate all the new patients on biosimilar infliximab and to switch all eligible patients from originator infliximab to the biosimilar alternative. -The % split of savings between the Trust and the IBD department has not been specified. >**Savings reinvestment plan:** -Reinvestment plan established prior to signing the benefit-sharing contact. It was requested to fund for additional staffing and for the implementation of a therapeutic drug monitoring system. **Benefit-sharing in the Grampian region** >**Target molecules:** etanercept. >**Setting:** homecare. >**Timeframe: 2016 – present (**~ 2-year contracts**).** >**Conditions agreed for benefit-sharing and % distribution of savings:** the Trust agreed on making an investment prior to the switch. This was to fund for needs associated to the setting-up of managed-switch programs (invest-to-save concept). >**Savings reinvestment plan:** it was requested to fund for additional staffing.	**Benefit-sharing in the Lothian region** >**Biosimilar uptake levels:** the totality of eligible patients were switched from originator infliximab to biosimilar infliximab (N=110). >**Cost-savings:** the managed switch program generated a 46.6% reduction in cost savings. >**Savings reinvestment:** -The benefit-sharing program paid for the salary of a senior pharmacist and a clinical fellow. Additional staffing supported the managed-switch process. The continuity of the newly-hired staff members has been ensured after the switch. -Via benefit-sharing, it was possible to implement a therapeutic drug monitoring system. The implementation of this system has supported switches for other active principles (e.g. adalimumab). **Benefit-sharing in the Grampian region** Patients' satisfaction with the managed switch program was reported to be high. No additional information has been published about achieved outcomes in terms of biosimilar market shares and improvement in the quality of care.	(+) Capacity of the clinical departments within a hospital to present a robust business case (to the Trust) that justifies benefit-sharing. (+) To present a business case that includes a clear timeframe for benefit-sharing and that estimates the potential for savings for the established timeframe. (+) To present a plan for the reinvestment of savings that improves patients' care and the efficiency of the system. Proposals for reinvestment that ensure a positive and long-lasting impact are prioritized over actions with a short-lasting impact. (+) Fluent communication between Trusts Management Boards and hospital clinical departments. (-) Low receptiveness of NHS Trusts to agree on benefit-sharing schemes. (-) Urgent financial needs to be addressed within the healthcare system and that require using the savings generated by biosimilars outside of the clinical departments that generated them. (-) Limited transparency in the reporting of outcomes after benefit-sharing.

WALES [34] - Local benefit-sharing program organised at the hospital-level in Cardiff

Design conditions agreed for benefit-sharing programs	Outcomes from the implementation of benefit-sharing programs	Implementation facilitators (+) and barriers (-)
>**Scope of the initiative:** local initiative involving a hospital in Cardiff. - The oncology/hematology clinical departments have been the beneficiaries, as well as patients treated by specialists in these units. -The benefits of the initiative can be expanded in the future to other areas and patients relying on the intravenous administration of biologics (e.g. gastroenterology). >**Target molecules:** rituximab. >**Setting:** hospital. >**Timeframe:** unknown. >**Conditions agreed for benefit-sharing and % distribution of savings:** unknown.	>**Cost-savings:** intravenous rituximab biosimilars were predicted to save one hospital £300,000 -335,000/year over the subcutaneous reference biologic. The number of patients needed to be initiated/switched on a biosimilar to realize these cost-savings has not been specified. >**Savings reinvestment:** -In order to get chemotherapy, patients needed to travel through large urban areas. Savings have been used to develop infusion clinics closer to the homes of oncology/hematology patients. This has facilitated the clinical follow up/monitoring process. -Patients have reported their satisfaction with the shorter traveling times, the ease of parking and the improved follow up.	Not specified

ADOPTERS OF BENEFIT-SHARING STRATEGIES - Initiatives established at the regional/local level		
GERMANY [35-41] – Examples of selective contracts that incorporate benefit-sharing strategies. **-Vertrag über ein strukturiertes Arzneimittel-Management von Biologika und Biosimilars (BioLike) nach §84 Abs.1 Satz 5 SGB V.** Insurer groups (sickness funds) – KVs[9] – individual prescribers. **-Vertrag zur Besonderen Versorgung in der Rheumatologie gemäß nach §140a SGB V.** Insurer groups -BDRh (Professional Association of German Rheumatologists).		
Design conditions agreed for benefit-sharing programs	**Outcomes from the implementation of benefit-sharing programs**	**Implementation facilitators (+) and barriers (-)**
Benefit-sharing contracts implemented according to the article §84 Abs.1 Satz 5 of the Social Code Book V (SGB V). >Example: BioLike Initiative implemented by BARMER. >**Scope of the initiative:** this initiative started with a pilot program for the region Westphalia-Lippe. Over the years and after a successfull experience in the pilot region, the initiative has been extended to Bremen, Bavaria, Berlin, Brandenburg, Hamburg, Thüringen, North Rhine, Lower Saxony, Rhineland-Palatinate, Saarland, Saxony. -Benefit-sharing contracts have been established for the clinical areas of: rheumatology, gastroenterology and dermatology. Not for every region it has been possible to agree on contracts for these areas. The BioLike initiative was adressed to individual prescribers working in the ambulatory sector and affiliated to KVs. -Benefit-sharing initiative not necessarily coupled with managed-swtich programs. >**Target molecues:** TNFαi. >**Setting:** ambulatory sector. >**Timeframe:** 2015-present. >**Conditions agreed for benefit-sharing and % distribution of savings:** -Prescribers can participate voluntarily in the benefit-sharing initiative. If they decide to paticipate, they are asked to identify and engage eligible patients in the initiative. In the context of the BioLike initiative, several biosimilar prescription objectives have been set. These objectives may vary according to the specialty and the regions, and are different from the biosimilar prescription quotas agreed at the regional level. If compliant with the requirements of the benefit-sharing initiative: a) Prescribers received a symbolic financial remuneration. Details about the specific remunerations provided have not been made public. b) Prescribers were exempted from adhereing to budget caps concerning the prescription of biologics c) Prescribers received information about the benefits offered by biosimilars and about real price differences (after rebates/discounts) between the originator and its respective biosimilars. >**Savings reinvestment plan:** Not specified. By removing the budget caps for the prescription of biologics, patients' access to biologics should have increased. **Benefit-sharing contracts implemented according to the article § 140a of the Social Code Book V (SGB V).** >**Scope of the initiative:** benefit-sharing contracts have been established for the area of rheumatic diseases between insurer groups and the Professional Association of German Rheumatologists. >**Target molecules:** TNFαi for rheumatic diseases. >**Setting:** ambulatory sector. >**Timeframe:** 2017-present >**Conditions agreed for benefit-sharing and % distribution of savings:** not specified	>**Biosimilar uptake levels:** it is unclear how biosimilars uptake has varied as a result of benefit-sharing programs. -Using as an example the region where the pilot BioLike program was implemented (Westphalia Lippe), uptake (Q4 2018) for infliximab and etanercept biosimilars surpassed the 70%. - In other regions (e.g. Brandenburg, Berlin, Saxony, Saxony Anhalt, Baden-Württemberg) biosimilars uptake has been more modest (<60% for infliximab and etanercept, Q4 2018) [42]. >**Cost-savings:** detailed data associated to benefit-sharing initiatives have not been made public. -BARMER has published a report calculating estimated savings if originator molecules were to be completely replaced by biosimilars [36, 41]. More than EUR 43M would have been saved by 2018. (cost-savings estimated for adalimumab: ~ EUR 41.8M; etanercept: ~ EUR 8.5M; infliximab: ~ EUR 1.5M). This estimate has not been adjusted by real biosimilar uptake levels achieved. >**The evaluation of outcomes has been difficulted by:** **(1)** The establishment of different prescribing targets/quotas for biosimilars at the regional level and for biosimilars included in benefit-sharing contracts. **(2)** The differing conditions of the benefit-sharing contracts established for the regions (e.g. contracts may differ in the remunerations given to prescribers).	(+) Establishment of national-level recommendations for biosimilar prescribing targets. (+) Regional-level agreements on biosimilar quota and monitoring activities to control/report on biosimilar uptake levels. (+) Fluent communication between (1) Insurer groups and the KVs and between (2) KVs and their affiliated members (Statutory Health Insurance Accredited Physicians). (+) Transparency on real price differences between originators and biosimilars for the prescribers that participate in benefit-sharing initiatives. (+) Establishment of a pilot program that allows to evaluate outcomes prior to wider implementation efforts. (-) Changes in the regulatory environment for biosimilars. (-) Due to multiple biosimilar policies implemented simultaneously, it is unclear whether increases in biosimilar uptake are due to benefit-sharing. (-) Lack of transparency in the reporting of outcomes after benefit-sharing. It is unclear how patients have been informed about the outcomes achieved as a result of the benefit-sharing strategy. (-) Unclear indicators to measure the success of benefit-sharing initiatives in terms of quality of care.

ITALY [43-46] – Examples of benefit-sharing programs.
-Campania region - DRG n.66 (14.07.2016)/ '*Misuri de incentivazione dei farmaci a brevetto scaduto e dei biosimilari'.*
Parties involved in negotiations:Regional health agency – hospital management – clinical departments
-Local approaches towards benefit-sharing.
Parties involved in negotiations: Hospital managers/pharmacy – clinical departments

Design conditions agreed for benefit-sharing programs	Outcomes from the implementation of benefit-sharing programs	Implementation facilitators (+) and barriers (-)
Benefit-sharing in the Campania region: **>Scope of the initiative:** regional-level initiative involving NHS hospitals in Campania. Benefit-sharing initiative not necessarily coupled with managed-switch programs. **>Target molecules:** all hospital-use molecules exposed to biosimilar competition**.** **>Setting:** hospital. **>Timeframe:** 2016-present. **>Conditions agreed for benefit-sharing and % distribution of savings:** -50% of the savings generated via biosimilars use are kept by the hospital administration and are destined to fund for innovative treatments. From the savings kept at the hospital, 5% are destined to the clinical departments that were involved in the savings' generation. -The remaining 50% of the savings is kept within the pharmaceuticals budget of the regional administration. **>Savings reinvestment plan:** reinvestment to fund for innovative treatments. **Local initiatives involving NHS hospitals (e.g. Lombardy)** In other regions, the regional health agencies have considered that the biosimilar policies in place (e.g. purchasing framework agreements, biosimilar quotas) are sufficient to ensure cost-savings after biosimilar market entry. In these cases, benefit-sharing has not been supported at the regional-level. However, individual hospitals have been able to agree on the redistribution of savings among the clinical departments that generated them. The conditions for benefit-sharing in these cases have not been published in the literature.	**>Biosimilar uptake levels:** data up to December 2020 for Campania [47] Adalimumab: 44.8%; Bevacizumab: 30.1%; Low molecular weight heparin: 52.4%; Epoetin: 81.9%; Etanercept: 42.8%; Filgrastim: 99.3%; Follitropin alpha: 5.4%; Infliximab: 93.7%; Insulin glargine: 18.8%; Insulin lispro: 0%; Pegfilgrastim: 100%; Rituximab: 100%; Somatropin: 8.9%; Teriparatide: 0%; Trastuzumab: 84.2%. **>Cost-savings:** not specified**.** **>Savings reinvestment:** savings reinvested into funding innovative treatments and into increasing efficiencies within the system.	(+) Establishment of standardized framework agreements to purchase biologics. (+) The inclusion of multiple molecules within the benefit-sharing agreements allows the long-term continuity of these initiatives. (-) Lack of transparency in the reporting of data: achieved savings and the outcomes of the savings' reinvestment process. The impact of the reinvestment of savings has not been reported, and patients may not be aware of this aspect. (-) Lack of appropriate indicators to monitor improvements in quality of care after benefit-sharing.

SWEDEN [48, 49] – Benefit-sharing examples in Skåne.

Design conditions agreed for benefit-sharing programs	Outcomes from the implementation of benefit-sharing programs	Implementation facilitators (+) and barriers (-)
>Scope of initiative: To contain pharmaceutical expenditure, the region of Skåne has been active organizing managed-switch programs for biologics (infliximab) in the area of rheumatology. The generated savings have been redistributed locally to the hospitals via benefit-sharing and this has allowed to increase funding for innovative products (e.g. vedolizumab) across therapeutic areas. - At a more local level, the Skåne University Hospital organised a managed-switch programme for patients on originator recombinant human growth hormone (rhGH) in 2009. This program and the linked benefit-sharing strategy were organised in collaboration between the Department of Pediatrics and the hospital administration. The totality of the generated savings were kept by the hospital. It was not required to put part of the savings back into the regional healthcare budget. -Benefit-sharing initiatives have generally been coupled with managed switch programs. **>Target molecules:** somatropin, infliximab. **>Setting:** hospital/ examples identified in the region Skåne. **>Timeframe:** 2009 – present.	**The example of the Skåne University Hospital** >A full-switch of eligible patients was aimed. 98 out of 102 eligible patients accepted the switch. 6 patients switched back to the originator. **>Cost-savings:** the successful switch of 98 patients from originator rhGH to the biosimilar generated annual savings of EUR 650,000. The totality of savings was kept by the hospitals to increase efficiencies within the system and to cover for additional costs associated to thoroughly-monitored managed-switch programs.	(+) Timely monitoring of biosimilar uptake levels achieved by prescribers (evaluation at the county-level). (+) County-level recommendations for rheumatologists to prescribe infliximab biosimilars after the conclusion of the contract with the originator (2015). (+) Use of a Dialogue Teamwork Approach to support the managed-switch process. (+) Clarity in the information provided to HCPs and patients regarding the economic rationale behind switches. (-) Limited transparency regarding the savings redistribution/reinvestment. It is unclear how the specific clinical departments benefitted from the savings and what is the proportion allocated to each department. It is unclear how patients have directly benefitted from the use of biosimilars.

The Netherlands – Approaches towards benefit-sharing.
-Local agreements between insurer companies and hospital managers.
-Local agreements between hospital managers/pharmacy and hospital clinical departments.

Design conditions agreed for benefit-sharing programs	Outcomes from the implementation of benefit-sharing programs	Implementation facilitators (+) and barriers (-)
>**Scope of the initiatives:** -Benefit-sharing contracts have occasionally been agreed between insurers and hospital managers, and have been implemented when deemed necessary for a short duration (~1 year). In all other cases, the savings are expected to be returned to health insurance companies. In the Netherlands, these companies are non-profit cooperatives that either allocate savings to maintain reserves or return part of the savings to policyholders in the form of lower premiums. The objective of these initiatives has been to support HCPs in the switch to biosimilars when changes in injection devices are required (e.g. etanercept). In the case of agreements established between insurers and hospital managers, insurers have allowed hospitals to keep a bigger that usual proportion of the savings generated from cost-effective prescribing. -Benefit-sharing programs have also been established at a very local level between the hospital pharmacy/managers and the clinical departments that have been involved in the generation of the savings. In these cases, benefit-sharing can happen without involving health insurance companies. These programs are based on savings that are not claimed by insurers and that are generally kept by the hospital's administration. >**Setting:** hospital. >**Timeframe:** 2016-present. >**Savings reinvestment plan:** savings have been reinvested into covering additional costs/resource needs associated to managed-switch processes, and into improving patients' quality of care (e.g. online patient registries and remote patients monitoring systems).	Not specified.	(+) Fluent communication between insurers and hospital managers/pharmacists (+) Willingness of health insurance companies to cover for the extra time investments that managed-switch programs require. Health insurance companies are open to investigate and implement best practices for benefit-sharing. (-) Unclear objectives for benefit-sharing. Sometimes, savings have been shared after being generated, but a plan/business case for benefit-sharing has not been prepared in advance. (-) Lack of transparency in the reporting of outcomes. (-) Limited communication with patients regarding the cost-savings achieved as a result of managed-switch programs.

NON-ADOPTERS OF BENEFIT-SHARING STRATEGIES [15]	
Austria	We have not identified proposals to implement benefit-sharing in the future. Policies such as (1) the mandatory price cuts for biologics after biosimilar market entry and (2) the single-winner tendering system that favours the most cost-effective product, are considered sufficient to ensure cost-savings after biosimilars market entry. It is unclear whether these strategies help stakeholders (especially patients) realise the societal value offered by biosimilars.
Belgium [50]	Vandenplas, et al. have presented a proposal for a sustainable off-patent biologic and biosimilars market in Belgium. This proposal includes a catalogue of measures that could be implemented, including incentivizing prescribers via benefit-sharing strategies. It is still unknown whether it would be feasible to implement benefit-sharing strategies in the context of the Belgium healthcare system. Further discussions would be needed to determine the proper implementation setting (retail *vs*. hospital) and the scope of the initiative (national *vs*. local). Another aspect to be discussed should be whether the use of BVB (this may include originators) should be promoted instead of focusing only on biosimilars.
Finland [51]	We have not identified proposals to implement benefit-sharing in the future. In Finland, the use of biosimilars in ambulatory care has been modest in comparison to the hospital use of these products. Sarnola k, et al. have identified that once the specialist initiates a patient on an originator biologic, the choice tends to remain unchanged at the level of ambulatory care. In this context, it would be interesting to implement benefit-sharing strategies for molecules prescribed by specialists and normally dispensed/administered at the ambulatory care level. But, the option to implement benefit-sharing has not been formally discussed, partly because HCPs are supposed to prioritize cost-effective prescribing as part of their working routine, and also because real price differences between an originator product and its respective biosimilar alternatives can be modest. However, in the case of etanercept and adalimumab, price differences between the originator and the lowest cost biosimilar, have been estimated to be EUR 6,300 per patient in a year and EUR 1,200 per patient in a year, respectively. Other factors such as: (1) the multichannel financing system, (2) the lack of consistent guidelines for the use of expensive medicines and (3) the limited patient experience with biosimilars, may hinder the future implementation of benefit-sharing strategies.
Norway	We have not identified proposals to implement benefit-sharing in the future. Policies such as transferring high-cost medicines (biologics) from the general reimbursement scheme to the hospital tendering system have supported the rapid adoption of biosimilars. The hospital system in Norway is based on single winner tenders awarded on the basis of price, and so far, it has favoured the most-cost effective biologics. According to the outcomes of the tender, a ranking is made by the Norwegian Hospital Procurement Trust according to price differences. Physicians are prompted to favour the use of the cheapest product (usually a biosimilar). These measures are considered sufficient to ensure cost-savings after biosimilars market entry. It is unclear whether these strategies help stakeholders (especially patients) realise the societal value offered by biosimilars.
Poland	We have not identified proposals to implement benefit-sharing in the future. In Poland, it is legally allowed to prescribe biologics (including biosimilars) by INN. The National Health Fund (NHF) has decided to support INN prescribing in hospitals via financial incentives targeting prescribers. According to this initiative, if hospitals purchase biologics with the lowest prices, they would obtain a higher rate of settlement for non-drug health services. This measure, together with reimbursement restrictions for less cost-effective products, is considered sufficient to ensure cost-savings after biosimilar market entry. These measures may not be as efficient as benefit-sharing strategies in helping stakeholders (especially patients) realise the societal value offered by biosimilars. If benefit-sharing strategies are implemented in the future, the priority for savings' reinvestment would be to broaden and facilitate patients' access to biologics.

Romania	We have not identified concrete proposals to implement benefit-sharing in the future. No explicit mechanisms have been used so far to specifically encourage the contracting and prescribing of biosimilars. In this context, there is no legal framework to support the implementation of incentives targeting prescribers. This situation might change following recent updates in the therapeutic protocols (May 2021). The updated protocols officially recommend the switch of stable patients from an originator to biosimilars. This may prompt the establishment of local managed-switch programs that could, in principle, be supported by benefit-sharing strategies. Currently, a benefit-sharing component could be added to individual purchase contracts concluded between the National Health Insurance House and suppliers (art.221 lit. m) of Law no. 95/2006 [52]. Based on expected cost-savings, the National Health Insurance House may identify avenues for savings reinvestment with hospital managers and clinical departments or in ambulatory care, and formulate proposals for a legislation update. In the case of Romania, the priority for savings reinvestment would be to broaden and facilitate patients' access to biologics.
Slovenia	We have not identified proposals to implement benefit-sharing in the future.
Spain [45]	The Spanish Biosimilars Association (BioSim) has recently organised information sessions for HCPs and patients about European experiences with benefit-sharing programs and has commissioned a study (Riesgo, I et al.) on how to operationalise benefit-sharing programs [53]. The proposal for benefit-sharing of Riesgo and collaborators is based on the regional organization of health competencies in Spain and on the fact that biologics are mainly hospital-use products. According to this, the proposal advocates for hospital-based benefit-sharing programs implemented at a local level. Benefit-sharing programs would be linked to managed-switch programs that respect the patient's autonomy to decide whether or not to proceed to the switch. The following elements would be needed for a successful implementation: 1) an actively engaged multidisciplinary group of HCPs; 2) a comprehensive needs assessment plan for the switch process; 3) the establishment of clear inclusion/exclusion criteria for patients being switched; 4) an information system capable of monitoring efficacy and pharmacovigilance outcomes during/after the switch; 5) a patients' support program for switch-related aspects; 6) a clearly established formula to calculate the percent distribution of savings. It is not known whether this proposal would be implemented by Spanish regional authorities/hospitals in the future. But, this is a first step towards establishing clear benefit-sharing criteria. Based on insights from our study, this proposal would benefit from clarifying some additional elements: 1) the program duration; 2) the target molecules to be included 2) the methods for the prospective calculation of savings; 3) the expected distribution of savings (direct/indirect beneficiaries); 4) the methods for saving reallocation and reinvestment; 5) the selection of key performance indicators; 6) the appropriate mechanisms to involve patients/patients advocacy groups.

1. ARS: French Regional Health Agencies; 2. CAQES: Contrat d'Amélioration de la Qualité et de l'Efficience des Soins. Contracts to improve the quality and efficiency of care;3. TNFαi: Tumor necrosis alpha inhibitors; 4. ACSS: Administração Central do Sistema de Saúde. Central Administration of the Health System (Portugal); 5. Infarmed: Autoridade Nacional do Medicamento e Produtos de Saúde. Portuguese National Authority of Medicines and Health Products; 6. SPMS: Serviços Partilhados do Ministério da Saúde. Shared Services of Ministry of Health, Portugal; 7. CCGs: Clinical Commissioning Groups; 8.IBD: inflammatory bowel diseases; 9. KVs: Kassenärtzliche Vereinigungen. German Regional Associations of SHI Accredited Physicians.

Supplementary Table 2. Comparative overview of the design and implementation criteria for benefit-sharing programs implemented in England. The results presented in Supplementary Table 2 have been obtained by combining information from the literature with the expert input of interviewees regarding benefit-sharing programs.

ADOPTERS OF BENEFIT-SHARING STRATEGIES IN ENGLAND			
BERKSHIRE[22]			
Participating stakeholders	**Design conditions agreed for benefit-sharing programs**	**Outcomes from the implementation of benefit-sharing programs**	**Implementation facilitators (+) and barriers (-)**
Commissioners: NHS Berkshire West Clinical Commissioning Group (CCG). **Providers:** Royal Berkshire NHS Foundation Trust. > Clinical departments involved in the prescription of TNFαi. **Project overseen/coordinated by:** multidisciplinary biosimilar working group. >Medicines Optimization Network, Regional Procurement Pharmacists, Chief Pharmacists Group.	>**Timeframe**: 2015 – 2017. -Benefit-sharing program linked to a managed switch and agreed between commissioners and providers. >**Target molecules:** infliximab, etanercept, rituximab. **INFLIXIMAB** -**Timeframe**: 2015 – 2017. -Prescribed/administered in the hospital. **-50/50% split of savings.** Savings generated from BVB lower acquisition price (20-50% lower) against originator list price. **ETANERCEPT** -**Timeframe**: 2016 – 2017. -Prescribed in the hospital/ administered via home-care services. -Savings generated from a **fixed-price mechanism** (1-year duration). -The CCG agreed on a fixed recharge price for all biological brands £699,806. The fixed recharge price is 25% lower than the originator price and 6-10% higher than the procurement cost (£593,539) for the most-affordable biosimilar (Benepali®). -The Trust realizes the savings according to the 6-10% price gap. -The Commissioners can realize a 25% saving across the year (the CCG assumes the risk of price reductions for the originator). **ADALIMUMAB** -Cost-avoidance strategy by using BVB according to regional tender outcomes. **-Narrow price gap between products and limited savings potential** – benefit-sharing was not economically feasible.	**INFLIXIMAB** -Significant savings generated in the gastroenterology area after a **complete switch.** -The benefit-sharing program funded the **salary of a nurse to work in the infusion unit.** The nurse position has been maintained after switch completion. -They measured patients' satisfaction after the switch. **ETANERCEPT** -**Savings** generated after a complete switch (N=113 patients): **£95,017.** -The benefit-sharing program funded the salary of a **Band 7 locum pharmacist**. The pharmacist position has been maintained after switch completion. -The benefit-sharing program funded a medicines optimization program (improved monitoring during/after switch). - They measured patients' satisfaction after the switch. **ADALIMUMAB** - 80% target switches achieved within the first 2 months. -The pharmacists hired as a result of the benefit-sharing program for etanercept assisted the managed-switch process for adalimumab. -As a result of a general cost-avoidance strategy and the generation of savings within the NHS, the NICE threshold to initiative patients on biologics was expanded. -No savings reinvestment at the local level, but more patients across England get access to biologics.	(+) To establish, ahead of the availability of the biosimilar, a multistakeholder working group aimed at scanning opportunities for savings. >Being able to start negotiations with CCGs before biosimilar market entry. (+) Collaboration and fluent communication between Trusts and Commissioners. (+) Robust business plan for benefit-sharing. >Clear evaluation of the volume of patients eligible for a switch. >Clear evaluation of potential savings over time. >Capacity to propose avenues for savings reinvestment that can stay over time. (+) To run a patient-focused managed switch programme. (+) Implementation of a medicines optimization programme – exhaustive monitoring and frequent patients' visits. (+) Early and transparent communication with patients about the switch process, the potential for savings and the plans for savings reinvestment. (-) Narrow price gap between contract prices for originator and biosimilar brands. (-) Frequent price fluctuations. (-) NHS communication discouraging the further use of benefit-sharing schemes.
DERBYSHIRE [19, 25]			
Participating stakeholders	**Design conditions agreed for benefit-sharing programs**	**Outcomes from the implementation of benefit-sharing programs**	**Implementation facilitators (+) and barriers (-)**
>The Joint Area Prescribing Committee (JAPC) established principles for benefit-sharing directed to Derbyshire CCGs. >The establishment of local benefit-sharing programs is overseen by the Derbyshire High-cost Drugs Biosimilar Working Group.	>**Timeframe**: 2015 – present. -Benefit-sharing applicable to high-cost drugs excluded from the National Tariff. Not applicable to treatments commissioned by NHS England/ National Cancer Drugs Fund. -When economically feasible, a standard 50% benefit-share program (50:50 % split between Commissioners and Providers) is recommended. As the price of the originator drops, the 50:50% benefit-share is applicable to the new price. -Resource cost for initiation of switching processes will be covered with savings before apportioning the benefit-share. -The prescription targets for BVB established by the NHS will be used as a reference for local agreements. -The funds released via benefit-sharing may not necessarily be reinvested in the specialty/clinical area from which they were realized.	Not specified	Not specified

DORSET [20, 54]			
Participating stakeholders **Commissioner:** Dorset Clinical Commissioning Group. **Providers:** Dorset County Hospital, NHS Foundation Trust. The Dorset Area Prescribing Committee supported the initiative.	**Design conditions agreed for benefit-sharing programs** >**Timeframe:** April 2015 – 6 months duration for the switch. -Benefit-sharing program linked to a managed switch and agreed between commissioners and providers. >**Target molecule:** infliximab; IBD. >**50/50% split** of savings agreed between the commissioners and the Dorset Hospital NHS Foundation Trust. **>A managed-switch program for adalimumab not supported by benefit-sharing:** In the case of adalimumab, the cohort of patients was switched to biosimilar adalimumab when necessary. For this, a benefit-sharing program was not established. Therefore, the adalimumab managed-switch program was only supported by previous investments done to improve the IBD service and less resources were available to ensure an intensive monitoring process before, during and after the switch. In this context, the specific clinical departments that generated the savings did not directly benefit from them.	**Outcomes from the implementation of benefit-sharing programs** -After a complete switch of the patients' cohort, annual cost-savings of £220,000 were realized. The achieved cost savings permitted the increase of the IBD nursing staff to 2WTE and allowed the introduction of infliximab through antibody testing which has rationalized treatment decisions. -Additional staffing allowed for an IBD nurse to be present in the clinic during the switch and to update the patient management system on a regular basis. -Overall, benefit-sharing allowed to improve patients' monitoring alongside and after the switch. Tests of baseline clinical parameters before and after the switch were conducted and compared for the cohort of patients receiving biosimilar infliximab.	**Implementation facilitators (+) and barriers (-)** (+) Strong business plan for benefit-sharing presented prior to the negotiations with the commissioners. The plan already included information regarding resource needs for the switch and how to organize the reinvestment of savings. (+) Use of an online IBD registry (+ patient management system, + real time data collection tools). (+) Regular face-to-face visits with patients along the switch process. (-) Establishment of block payments for biologics based on use from the previous year. (-) Narrow price gap between contract prices for originator and biosimilar brands. (-) Frequent price fluctuations. (-) NHS communication discouraging the further use of benefit-sharing schemes. (-) Low receptiveness of commissioners to agree on benefit-sharing schemes. (-) Urgent financial needs to be addressed within the healthcare system and that require using the savings generated by biosimilars outside of the clinical departments that generated them.
EAST STAFFORDSHIRE [55]			
Participating stakeholders **Commissioners:** East Staffordshire CCG. **Providers:** Burton Hospitals NHS Foundation.	**Design conditions agreed for benefit-sharing programs** >**Scope of the initiative:** the Trust had been evaluated for compliance with commissioned NICE Technology Appraisals. Some improvements were introduced to increase compliance. Due to greater efficiencies and greater workers' engagement, the establishment of benefit-sharing contracts was facilitated. >**Timeframe:** the benefit-sharing initiatives were launched in 2017. >**Target molecules**: TNFαi prescribed in the field of rheumatology and dermatology. >**50/50% split** of savings agreed between the commissioners and the Burton Hospitals NHS Foundation.	**Outcomes from the implementation of benefit-sharing programs** -It was estimated that the potential for savings would correspond to £257K. Detailed information about the program outcomes has not been provided.	**Implementation facilitators (+) and barriers (-)** (+) Improved communication between the parties has allowed to agree on benefit-sharing conditions in the end. (-) Lengthy negotiations between commissioners and providers regarding the % split of savings for benefit-sharing. (-) NHS communication discouraging the further use of benefit-sharing schemes.
GLOUCESTERSHIRE [23]			
Participating stakeholders **Commissioners:** North Somerset and South Gloucestershire CCG. **Providers:** North Bristol NHS Trust.	**Design conditions agreed for benefit-sharing programs** >**Timeframe:** July 2015 – 3 months duration for the switch. >**Target molecules**: infliximab; IBD. >**50/50% split** of savings agreed between the commissioners and the North Bristol NHS Trust.	**Outcomes from the implementation of benefit-sharing programs** - 64/65 patients consented to the switch; 52 patients were switched to biosimilar infliximab. The switch of 52 patients over 3 months generated savings of £200,000. -It was decided to reinvest the savings into gastroenterology services. An additional pharmacist was funded to implement the switch using projected savings from the benefit-sharing program. This allowed for closer patients' monitoring and optimization of biologic treatments. -96% of the patients had the opportunity to speak to a pharmacist before the switch. Overall, 97% of the patients were satisfied with the changeover process.	**Implementation facilitators (+) and barriers (-)** (+) Multidisciplinary approach for the organization of the managed-switch program. (+) Educational sessions on biosimilars organised for the Medical Day Case Unit Nurses. (-) NHS communication discouraging the further use of benefit-sharing schemes.

GREATER LONDON [31, 56]			
Participating stakeholders	**Design conditions agreed for benefit-sharing programs**	**Outcomes from the implementation of benefit-sharing programs**	**Implementation facilitators (+) and barriers (-)**
North West London **Commissioners:** London North West London CCG. **Providers:** London North West University Healthcare NHS Trust. >Rheumatology unit: Northwick Park Hospital.	>**Timeframe**: 2017 – 6 months duration for the switch. -Benefit-sharing program linked to a managed switch and agreed between commissioners and providers. >**Target molecule:** etanercept; indications: rheumatoid arthritis. **>50/50% split of savings.** Savings generated from BVB lower acquisition price against originator list price. >Benefit-sharing funded a High-Intensity Switch Programme (HIP) – approximate cost: £20,000. The HIP included: >Education session by a local arthritis support charity. >Pre-switch appointment and enrolment into the British Society of Rheumatology Biologics Registry for Rheumatoid Arthritis (BSRBR-RA). >Setting-up a dedicated biosimilar switching clinic staffed by a rheumatology consultant, registrar and specialist pharmacist.	-The savings potential associated to the use of biosimilar etanercept has been calculated to be: £3,500 per patient in a year. This was expected to cover for the cost of a High-Intensity switch program (HIP). >Approximate cost of the HIP: £20,000 **>Outcomes of the HIP in comparison to standard switching procedures:** -Increased proportion of patients switched (95%, N=151) at 12 months compared to the standard switch program (75%) -Faster rate of switching and greater cost savings £500/patient compared to the standard switch program (£400/patient). -Overall cost savings expected for the total group of switched patients: £81,000	(+) Strong business case for benefit-sharing presented in advance. (+) Organization of information sessions for clinicals concerning the switch process – collaboration with communication experts (REAL group). (+) Establishing a dedicated biosimilar switching clinic. (-) NHS communication discouraging the further use of benefit-sharing schemes.
Participating stakeholders	**Design conditions agreed for benefit-sharing programs**	**Outcomes from the implementation of benefit-sharing programs**	**Implementation facilitators (+) and barriers (-)**
South East London **Commissioners:** South East London Clinical Commissioning Group. **Providers:** network of local NHS Trusts.	**>Scope of the initiative:** the establishment of benefit-sharing initiatives was facilitated in the context of the implementation of a SEL IBD pathway. -The IBD pathway was developed with the Area Prescribing Committee in partnership with expert patients, IBD clinicians, specialist nurses and pharmacists. This pathway involved the commissioning for (1) disease monitoring, (2) drug optimization, (3) funding of nursing and support staff, (4) cost predictions. >**Timeframe**: 2015 – 2017. -Benefit-sharing program linked to a managed switch and agreed between commissioners and providers. >**Target molecules:** treatments indicated for IBD.	**>Cost-savings:** the calculated savings per Trust would be £112,510K in a year. This calculation is not only based on cost-savings due to the prescription of BVB, but also due to reduced ED attendances, reduced hospital length of stay, optimization of treatment strategies, etc. >Benefit-sharing programs were organised to support ongoing service provision (e.g. telephone helpline, additional staffing, patients monitoring activities).	(+) Agreement on key performance indicators in advance. (+) Regular reporting of outcomes. (-) It is unclear how savings have been reinvested in each of the participating NHS Trusts. It is unclear which savings have been generated as a result of which measure. (-) NHS communication discouraging the further use of benefit-sharing schemes.
Participating stakeholders	**Design conditions agreed for benefit-sharing programs**	**Outcomes from the implementation of benefit-sharing programs**	**Implementation facilitators (+) and barriers (-)**
South East London **Commissioners:** South East London Clinical Commissioning Group. **Providers:** NHS Guy's and St Thomas' Foundation Trust.	>**Timeframe**: 2016- 6 months duration for the switch. -Benefit-sharing program linked to a managed switch and agreed between commissioners and providers. Involvement of the pharmacy team and nurses/clinicians within the rheumatology department. >**Target molecule:** etanercept. >**Setting:** biologic product administered via home-care services. -The percent split of savings has not been specified.	- 103/109 patients were switched to biosimilar etanercept. By the end of 2016, 78% of the patients had received biosimilar etanercept**.** - For the first 7 months of the financial year, the NHS had saved £112,410 as a result of the switch. -Via benefit-sharing, a face-to-face switching clinic with a specialist pharmacist and nurse was funded for patients forming part of the managed-switch program.	(+) Attending a face-to-face switching clinic with a specialist pharmacist and nurse. (+) The homecare delivery company offered training on the new device to patients (-) Unclear % split of savings between the parties and unclear procedures for savings redistribution. (-) NHS communication discouraging the further use of benefit-sharing schemes.

HAMPSHIRE [28, 29]			
Participating stakeholders **Commissioners:** 3 local CCGs, including the North Hampshire CCG. **Providers:** Hampshire Hospitals Foundation Trust.	**Design conditions agreed for benefit-sharing programs** >**Timeframe**: September 2015 – 6 months duration for the switch. -Benefit-sharing program linked to a managed switch and agreed between commissioners and providers. >**Target molecule:** infliximab; IBD. >**Setting**: hospital. >**50/50% split** of savings agreed between the commissioners and the NHS Trust.	**Outcomes from the implementation of benefit-sharing programs** - The switch of 88 patients over 6 months generated total cost savings of £ 232,575. Projected year savings: £540,000. - Cost-savings funded a new band 7 IBD biological nurse, a new band 7 IBD biological pharmacist and an IBD administrator. Staff costs totalled £90,000. -Patients' satisfaction with the switch was measured with the PROM scoring system. PROM data revealed very high satisfaction with the switch (mean score of 7.3; Range: 3-10) for overall disease control.	**Implementation facilitators (+) and barriers (-)** (+) Working party set up with a strong managerial support to deliver the managed-switch and the benefit-sharing project. (+) Engaged conversations between primary and secondary care facilitated the investment in the IBD service. (+) Due to the expected positive impact on patient care, patients were very supportive of the project. (-) NHS communication discouraging the further use of benefit-sharing schemes.
Participating stakeholders **Commissioners:** West Hampshire CCG/ other local CCGs. **Providers:** University Hospital Southampton NHS Foundation Trust.	**Design conditions agreed for benefit-sharing programs** **Previous experiences with benefit-sharing** In 2010, the Southampton University Hospital and the associated CCGs implemented benefit-sharing for biologics. This was prior to the initiation of managed-switch programs in 2015. Local CCGs invested £60,000 in order to implement an IBD biologcs nurse-led service. This service resulted in significant gains in care quality and costs. The savings achieved represented 15% of total yearly biologic costs. **Benefit-sharing program for infliximab** **Timeframe**: April. 2015 – March 2016. **-Target molecule:** infliximab; IBD. **-Setting**: hospital. **-50/50% split** of savings between commissioners and providers. -Following the NHS communication discouraging the use of benefit-sharing, this site has not been involved in further benefit-sharing programs (e.g. rituximab, adalimumab).	**Outcomes from the implementation of benefit-sharing programs** **Benefit-sharing program for infliximab** -Following the switch of 143 patients to biosimilar infliximab, drug acquisition costs decreased by £40,000 - £60,000 per month. Savings were achieved despite an ongoing increase in the number of vials of biologics dispensed. -The realised savings were used to invest in the capacity of the nurse-led IBD biologics service. Benefit-sharing funded the salary of a new band 7 specialist nurse, the 0.5 whole time equivalent for a WTE clerical post, a 0.2 WTE band 8 pharmacist and a 0.2 WTE band 6 dietitian. Staffing costs amounted to around 12% of the projected gross savings. -Patient's satisfaction with the switch was high (measured according to the PROM system). -The implementers consider that the reinvestment of savings has improved the clinical service, and also the quality of care for the whole IBD patient population of the area.	**Implementation facilitators (+) and barriers (-)** (+) Managed switch program designed with the input from multiple stakeholders: IBD patient panel, gastroenterologists, pharmacists and the IBD nursing team. (+) Risk management plan included within the managed-switch program. (+) Well-designed, continuous drug monitoring program. (+) Strong, trusting relationship between CCGs and the Trust. This was based on a previous successful experience with benefit-sharing. (+) Patient-focused approach. (-) Narrow price gap between contract prices for originator and biosimilar brands. (-) Frequent price fluctuations. (-) NHS communication discouraging the further use of benefit-sharing schemes.
NORTH WEST [24, 30]			
Participating stakeholders **Commissioners**: Bolton CCG, Bury CCG, Heywood, Middleton and Rochdale CCG, Oldham CCG, Salford CCG, Stockport CCG, Tameside and Glossop CCG, Trafford CCG, Wigan CCG. **Providers:** 8 Great Manchester Trusts. **Project coordinated/overseen by:** Greater Manchester Medicines Management Group – High Cost Drugs Subgroup.	**Design conditions agreed for benefit-sharing programs** -The Greater Manchester Medicines Management Group (High Cost Drugs Subgroup) has established the conditions for umbrella benefit-sharing contracts. More local arrangements outside of these conditions are allowed (e.g. individual negotiations with each Trust). -Benefit-sharing contracts can enter in effect after 3 months of the availability of biosimilars. It is recommended to base benefit-sharing on a 50/50 split of savings between Commissioners and Providers. -Recommended duration of benefit-sharing programs: 2 years with ongoing review. Resource implications required for implementation of benefit-sharing/ switch programs will be funded from the benefit-share payment over the 2-year period, either up-front or ongoing. >Based on these general conditions, benefit-sharing programs were established for **rituximab:** **-Timeframe:** 1st August 2017 – 1st August 2019. **-Setting:** Prescribed/ administered in the hospital. **-50/50% split** of savings. Savings generated from differences in contract prices. -Trusts could choose the best-value product to use (Truxima®, Rixathon®).	**Outcomes from the implementation of benefit-sharing programs** -The CCG-commissioned spend on rituximab across Greater Manchester was mainly attributed to the use of 500mg/50ml vials. Based on a 36.6% discount on the reference product price, switching 80% of the patients to rituximab best-value product was expected to generate savings of £427,600. These savings would be eligible for benefit-sharing across the Greater Manchester health economy.	**Implementation facilitators (+) and barriers (-)** (+) By establishing standard benefit-sharing principles for the Greater Manchester area, fewer negotiations are required. (+) Trusts and Commissioners working together to identify benefit-sharing opportunities. (-) The guidelines set for benefit-sharing at the Greater Manchester level do not provide detailed information on how clinical departments within Trusts would receive part of the savings and on how savings could be reinvested. (-) Lack of standard format for benefit-sharing prior to the document emitted by the Medicines Optimization Team in 2017. This has impeded fluent negotiations. (-) NHS communication discouraging the further use of benefit-sharing schemes.

YORKSHIRE [57]			
Participating stakeholders	**Design conditions agreed for benefit-sharing programs**	**Outcomes from the implementation of benefit-sharing programs**	**Implementation facilitators (+) and barriers (-)**
Commissioners: NHS Vale of York CCG, NHS Scarborough and Ryedale CCG. **Providers:** York and Scarborough Teaching Hospitals NHS Foundation Trust – The York Trust Rheumatology Service.	**-Timeframe:** 2016 – present. Each contract has had an average duration of 2 years. -Benefit-sharing program linked to a switch and agreed between commissioners and providers. **-Setting**: hospital/ products administered via home-care services. **-Target molecules**: etanercept, adalimumab, rituximab; rheumatology; gastroenterology and dermatology clinical departments. **-50/50% split** of savings. 50% benefit-share agreement against the originator cost price.	-A managed switch program for etanercept aiming for a 100% switch of the patient cohort (n=377) would lead to £1.64M savings. It has been reported that the savings objective was achieved and exceeded along the 2 years switch period. Approximately £1M were available to the Trusts for reinvestment in innovative drugs, staff/services development. -Clinical departments within a Trust received a limited share of the 50% savings available to the Trust. -In the case of adalimumab and rituximab, the savings potential was lower. The switch to adalimumab yielded savings in the order of hundreds of thousands of UK pounds. The savings potential was lower because originator brands reduced prices to be competitive with biosimilar versions.	(+) Identifying clinical and pharmacy champions to take the lead in implementing benefit-sharing programs. (+) Early identification of cost-savings opportunities. (+) Commissioners acknowledgement of the increased administrative workload associated to managed-switch programs. (+) Patients were informed about the potential for savings due to switching and about the options for savings reinvestment. Patients valued the opportunity for face-to-face discussions with HCPs. (-) Savings opportunity missed for infliximab. (-) NHS communication discouraging the further use of benefit-sharing schemes.

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