Navigating the Transition:
A Scoping Review of System-Level Factors in Biosimilar Integration for Immune-Mediated Inflammatory Diseases

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BioDrugs

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Search Strategy

Table 1. Concept table of key terms and phrases.

Keywords	**MeSH**	**Emtree**	**Free-Text**
Biosimilars	Biosimilar Pharmaceuticals Follow on Biologics	biosimilar agent	(followon or follow-on or subsequent entry) adj2 OR biologic* OR biosimilar*
Transition	Drug Substitution	drug substitution	switch* OR transition* OR change
System-level factors	Organization and Administration OR Logistics OR Coordination OR Patient Reported Outcome Measures OR Patient Satisfaction* OR Communication OR Patient Education OR Delivery of Health Care OR Decision Making OR Prior Authorization	"organization and management" OR organization OR OR patient-reported outcome OR patient satisfaction OR interpersonal communication OR patient education OR health care delivery OR decision making OR prior authorization	Implementation OR Authori*ation
Restrict search to: Publication year: 2006 to Current English language Exclude reviews			

Table 2. APA PsycInfo via Ovid Search Strategy (6th December, 2024)

#	Search Statement	Results
1	biosimilar pharmaceuticals.mp.	8
2	biosimilar*.mp	23
3	Follow on Biologics.mp.	5
4	or/1-3	25
5	Limit 4 to english language	24
6	limit 5 to yr="2006 – Current"	24
7	review*.mp.	643841
8	6 not 7	20

Table 3. PubMed (6th December, 2024)

#	Search Statement	Results
1	biosimilar pharmaceuticals	3998
2	biosimilar*	6475
3	"follow on biologics"	95
4	switch* or transition* or change* or drug substitution*	4,598,438
5	system	5,030,177
6	organisation or administration or authorisation or implement* or deliver*	7,539,933
7	"patient satisfaction" or "patient education"	229,806
8	"deliver* of health-care" or "deliver* of health care"	146,298
9	communication or "decision making"	1,149,656
10	or/1-3	6,500
11	or/5-9	11,847,832
12	4 and 10 and 11	1,002
13	limit 12 to english language	955
14	limit 13 to yr="2006 – Current"	954
15	Exclude Review[Publication Type]	722

Table 4. Embase via Ovid Search Strategy (6th December, 2024)

#	Search Statement	Results
1	biosimilar agent/	8086
2	biosimilar.mp.	12,669
3	(switch* or transition* or change* or drug substitution*).mp.	5,623,916
4	organi?ation and management.mp.	546,222
5	exp patient-reported outcome/	69,352
6	exp patient satisfaction/	183,673
7	exp patient education/	129,580
8	(deliver* of health-care or deliver* of health care).mp.	6709
9	(communication or decision making).mp.	1,243,879
10	1 or 2	12,669
11	or/4-9	2,043,217
12	3 and 10 and 11	433
13	limit 12 to english language	424
14	limit 13 to yr="2006 – Current"	424
15	exp "Systematic Review"/ or exp "Review"/	3,298,188
16	14 not 15	355

Table 5. Scopus (6th December, 2024)

#	Search Statement	Results
1	biosimilar*.ti,ab,kw.	9788
2	"follow on biologics"	1065
3	switch* or transition* or change* or drug substitution*	1,222,629
4	"patient reported outcomes"	192,496
5	system	41,921,724
6	organi?ation or administration or authori?ation or implement* or deliver*	22,237,932
7	"patient satisfaction"	321,574
8	"patient education"	331,783
9	"deliver* of health-care" or "deliver* of health care"	141,087
10	communication or "decision making"	19,841,929
11	or/1-2	10,235
12	or/4-10	55,843,490
13	3 and 11 and 12	1,050
14	limit 13 to english language	997
15	limit 14 to yr="2006 – Current"	996
16	Exclude review	740

Table 6. Web of Science (6th December, 2024)

#	Search Statement	Results
1	biosimilar (All fields)	6857
2	“follow on biologics” (All fields)	200
3	switch or transition or change or drug substitution (All fields)	10,466,323
4	system (All fields)	14,208,359
5	organi?ation or administration or authori?ation or implement* or deliver* (All fields)	7,509,055
6	“patient satisfaction” or “patient education” (All fields)	94,541
7	“deliver* of health-care” or “deliver* of health care” (All fields)	4,663
8	communication or “decision making” (All fields)	3,067,527
9	or/1-2	6,966
10	or/4-8	21,078,489
11	3 and 9 and 10	612
12	limit 11 to english language	595
13	limit 12 to yr="2006 – Current”	594
14	Exclude review	464

Table 7. Conference databases search strategy (3 December, 2024)

Conferences	Search term(s)	Results
United European Gastroenterology Week (UEG)	“biosimilar”	8 (2024)
European Crohn’s and Colitis Organisation (ECCO)	“biosimilar”	18 (2024)
Digestive Diseases Week (DDW)	“biosimilar”	28 (2024)
European League Against Rheumatism (EULAR)	“biosimilar”	36 (2024)
American College of Rheumatology (ACR)	“biosimilar”	18 (2024)
World Congress of Dermatology	“biosimilar”	6 (2023)
World Congress in Ophthalmology	“biosimilar”	2 (2024)

Table 8. Inclusion and exclusion criteria for studies.

	Inclusion Criteria	Exclusion Criteria
Population	Patients transitioning from any bio-originator to any biosimilar and receiving care in rheumatology, dermatology, gastroenterology, or ophthalmology Any healthcare providers or related stakeholders involved in a bio-originator to biosimilar brand change	● Patients/providers/stakeholders not involved in a biosimilar transition ● Patients receiving care in oncology or hematology
Intervention	Studies evaluating the process of a single transition from a bio-originator to a biosimilar	● Bio-originator to bio-originator transition ● Biosimilar to bio-originator transition ● Biosimilar to biosimilar transition
Comparators	No restrictions	No restrictions
Outcomes	Evaluation of the process of the brand change (e.g., in terms of system-level factors, such as the provision of information/communication/support or provider workload)	● No focus on evaluating the process of changing to biosimilars ● Focus is limited to safety, efficacy, or treatment persistence
Study Design	All studies, including real-world data, observational (prospective/retrospective), and experimental designs	● Editorial (commentary, letters to editor) ● Reviews and meta-analyses ● Guidelines
Language, Geographic Scope	● English ● Studies conducted globally	● Non-English languages
Time Period	● Conference abstracts from 2023 to 2024 ● 2006 until the present date	● Conference abstracts published before 2023

List of included studies

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Table 9. Overview of the included studies.

Author, Year	Type of Publication	Country reviewed	Population	Drug	Theme Facilitator/Barrier	Findings
Arnet et al. (2021) [1] [Journal article]	Cross-sectional	Belgium, Finland, Germany, Switzerland, Thailand	Pharmacists (N = 916)	NR	Theme 4. Communication & education Facilitator	Training on the topic of biologicals was obtained in the process of professional development, after initial professional education and licensure, by a mean of 35.4% of respondents (range: 13.2% in Thailand to 48.8% in Germany), but most respondents would be interested in receiving additional training on that topic (83.3% in Germany to 97% in Finland).
Awada et al. (2023) [2] [Journal article]	Cross-sectional	Lebanon	Pharmacists (N = 75)	NR	Theme 1. Regulatory and approval processes Barrier Theme 4. Communication & education Facilitator	Most pharmacists agreed to substitute generics if the brand was not available, while the prescriber's approval was essential for biosimilar switching. Over 50% received training/education on generics and biosimilars. Most reported that programs tackling generic sand biosimilars should be included in the curriculum of universities and the continuing education program of the order of pharmacists of Lebanon.
Baji et al. (2016) [3] [Journal article]	Cross-sectional (Discrete choice experiment)	Hungary	Physicians (N = 51)	NR	Theme 2. Healthcare care system policies, incentives Facilitator	77% of clinicians indicated concerns regarding the use of biosimilars in CD. However, 92% of them were willing to consider treatments with biosimilar, when certain benefits were offered with regards to the reimbursement conditions. Thus, clinicians are more willing to use biosimilars if their patients are the beneficiaries of the cost-savings, i.e. savings contribute to ensure continuous medicine supply, treat more patients, or patients in less severe conditions.

						We found that in the case of biological-naïve patients, the continuity of the medicine supply was the most important treatment attribute, followed by the severity of the disease and the frequency of efficacy check-ups (Wald chi^2 = 27.23, $p < 0.001$, Pseudo $R^2 = 0.20$). For patients already treated with biologicals, the type of the treatment was the most important determinant of choice, followed by the continuity of the medicine supply. Severity had positive but insignificant, and the frequency of checkups had negative but insignificant coefficients (Wald chi^2 = 21.99, $p < 0.001$, Pseudo $R^2 = 0.07$).

Barbier et al. (2022) [4] [Journal article]	Qualitative (Consensus-building study using the Nominal Group Technique)	Belgium	Physicians and hospital pharmacists (N = 13)	NR	Theme 1. Regulatory and approval processes Facilitator/Barrier Theme 2. Healthcare care system policies, incentives Facilitator/Barrier Theme 3. Infrastructure and Logistics Barrier Theme 4. Communication & education Facilitator/Barrier	Some participants requested clearer and more detailed guidance on conducting product switches, including specifying the measures to consider and clarifying terms like “necessary follow-up,” such as whether this refers to routine monitoring or additional monitoring. They also suggested the agency communicate aggregated data from clinical switch studies. Overall, participants emphasized the importance of more explicit guidance from regulators and professional associations, alongside the collection and utilization of multiple-switch or long-term follow-up data to better inform clinical decision-making. Participants identified issues with tender award criteria, noting a disconnect between criteria valued by healthcare professionals, such as rewarding longer market presence or requiring additional switch data, and their impact on maintaining a level playing field. Despite the FAMHP’s 2019 clarification that award criteria must relate to the tender’s subject matter, ambiguity persists. Hospital pharmacists also stressed the importance of timely information about biosimilar market entries to allow for the effective organization of tenders. In the hospital setting, lowering invoicing to 85% for biological medicines with available biosimilars, allowing hospitals to recoup savings from national tenders, was seen as a key driver for competitive tenders. Since tenders primarily influence in-hospital product decisions, the need for stakeholder incentives was less urgent than in the ambulatory setting. However, participants noted that tenders do not always lead to biosimilar uptake, as the reference product can also win based on competitive bids. Ensuring a

						level playing field in tenders was emphasized to maintain fair competition between reference products and biosimilars. Additionally, incentives based on a benefit-share model, where savings are reinvested to improve care processes, were considered valuable. Participants emphasized the need to revise the hospital financing system, as it currently incentivizes hospitals to choose high-priced products. Factors like brand loyalty and informal incentives from pharmaceutical companies were identified as potential decision-making drivers. To stimulate biosimilar use in ambulatory care, some participants suggested using market share quotas. The 2019 anti-TNF pilot project, which provided financial incentives to physicians for prescribing a certain percentage of biosimilars, was criticized. Participants raised ethical concerns about individual financial gains, deemed the compensation insufficient for the time spent on patient consultations, and found the administrative burden excessive. They advocated for incentives that would improve patient care, such as a benefit-share agreement funding additional staff, like nurses or pharmacy technicians, to assist with the switch process and changes in injection devices. Participating physicians noted that introducing a biosimilar, especially with a different injection device, would require additional consultation time. They also pointed out the lack of a support framework for switches in the ambulatory setting, such as staff capacity and informational materials. Participants highlighted the lack of practical, non-industry sponsored information and guiding

						principles for switch management. They emphasized the need for materials to assist with both switch management and patient communication. While education efforts have typically focused on specialist physicians and hospital pharmacists, there is a call to expand these efforts to include general practitioners and community pharmacists.

Barbier et al. (2021) [5] [Journal article]	Mixed methods (Survey and interviews)	NR	Hospital pharmacists and purchasers (N = 60) Purchasers and suppliers (N = 28)	NR	Theme 1. Regulatory and approval processes Facilitator/Barrier Theme 2. Healthcare care system policies, incentives Facilitator/Barrier	Participants emphasized the need for clarity on whether tenders should reopen with each new biosimilar entrant, as opening a tender when the first biosimilar enters can limit market opportunities for subsequent entrants. Dividing the market among multiple suppliers was widely recommended to ensure fair competition and sustainability in tender practices, though some hesitations were expressed due to increased complexity. Multiple winner tenders could reduce price pressure and provide more options for physicians, improving therapeutic freedom and helping mitigate supply chain issues. Delays in tender openings were criticized, with potential reasons including strategic contracts with originators to extend market exclusivity. Participants suggested that healthcare systems should anticipate biosimilar market entries and plan tenders accordingly. Contracts with originators should include clauses for reopening if biosimilars enter the market. Many interviewees believed current tender designs focused too much on short-term savings, leading to excessive price erosion. They cautioned against a "race to the bottom" and stressed the importance of rethinking tender practices for long-term societal and patient benefits. Additionally, involving physicians in the procurement process and educating healthcare professionals could increase adherence to tender outcomes. Financial stimulus can motivate hospitals to organize timely, competitive tenders, aligning hospital incentives with overall healthcare system savings. In Belgium, a 15% reduction in reimbursement for biologics where a biosimilar

						exists. A similar model exists in the Netherlands, where health insurers reimburse hospitals at list price but anticipate savings from negotiated discounts. Interviewees supported stakeholder incentives to increase motivation but cautioned against quotas or rewards for biosimilar uptake. Benefit-sharing models, where savings from tenders or biosimilars are shared between purchasing bodies or payers and the hospital were seen as an effective approach to incentivize stakeholders. Instead of offering positive benefit-share incentives, some approaches, like reducing reimbursement for biologicals with biosimilars in Belgium, have been used. Originator companies employ aggressive price drops to defend market share, limiting biosimilar market entry. Originators have more flexibility for deeper discounts due to recouped development costs, whereas biosimilar developers still need to recover their investments. It was also suggested that some originators lower prices so drastically that it forces other suppliers to exit the market.

Barbier et al. (2020) [6] [Journal article]	Qualitative (Semi-structured interviews)	NR	Physicians, hospital pharmacists, nurses, patients, and regulators (N = 44)	NR	Theme 2. Healthcare care system policies, incentives Facilitator/Barrier Theme 3. Infrastructure and Logistics Facilitator/Barrier Theme 4. Communication & education Facilitator/Barrier	Several pharmacists recommended a stepwise approach for switching to biosimilars, starting with a discussion among stakeholders and informing patients about the switch. The Dutch Association of Hospital Pharmacists' toolbox was cited as a useful guide. Most physicians and nurses and some regulators felt that tangible incentives would motivate stakeholders to invest time in the switch, particularly when it involved substantial effort. Incentives should align with the level of effort, such as larger rewards for more complex switches like subcutaneous products. Most participants felt individual financial incentives were inappropriate but considered reinvesting savings to improve patient care, like hiring additional staff or increasing monitoring, to be acceptable. In ambulatory care, defining incentives was challenging, especially in countries where these aren't part of the hospital budget. Some felt that tenders could reduce the need for additional incentives, while others highlighted that negative incentives, like lowering reimbursement levels (e.g., 80% of list price as in Belgium), effectively motivated hospitals to organize competitive tenders. A Dutch interviewee noted that lowering the patient's "own risk" insurance payment when agreeing to switch has been effective. The lower price of biosimilars was seen as the primary benefit, with some viewing it as the only one. However, some acknowledged that market competition could also reduce the price of reference products. Biosimilars should not automatically be favored, as reference product prices also typically decrease. Lower treatment prices were linked to improved patient outcomes,

						as more patients could be treated or treated earlier. Some saw biosimilar savings as a way to free up budget for innovative medicines and provide physicians more flexibility to prescribe new therapies. Practical barriers to automatic substitution include insufficient preparedness of pharmacists and systems, as most European countries don't mandate pharmacist substitution of biologics. Some physicians and regulators noted that biosimilars could improve care delivery through better administration devices or new routes not available with reference products. Availability of biosimilars can also secure supply during shortages. Factors beyond price, like supply reliability, value-added services, and user-friendly injection devices, were also considered when choosing products. Nurses highlighted the importance of assessing patient-friendliness, and pharmacists mentioned that packaging differences could reduce co-payments. Special attention should be given to patients self-administering therapy, who may need training on injection devices. Several interviewees attributed uncertainty about switching to misinformation from the pharmaceutical industry. They emphasized the need for a well-informed healthcare team to communicate confidently with patients. Unified messaging was seen as crucial, as verbal and non-verbal cues from HCPs can influence patient trust. Special consideration should be given to patients self-administering therapy, who may require injection device training. Pharmacists should also be trained to educate patients about potential changes in injection devices. Additionally, specialized pharmacies could

						handle substitution. Overall, there was consensus that the benefits of biosimilars should be communicated more clearly to promote sustainability in healthcare.

Barbier et al. (2020) [7] [Journal article]	Qualitative (Semi-structured interviews)	NR	Physicians, hospital pharmacists, nurses, patient(s) (representatives) and regulators across Europe (N = 44)	NR	Theme 1. Regulatory and approval processes Facilitator/Barrier Theme 3. Infrastructure and Logistics Barrier Theme 4. Communication & education Facilitator/Barrier	The FDA and EMA's conflicting messages on interchangeability create distrust. The FDA's framework suggests some biosimilars are more similar to biologics than others, leading to confusion. Impartial information from independent bodies like the EMA and NCAs is crucial. Regulators believe they are best placed to provide unbiased information. The EMA's biosimilar guidance documents are considered valuable by many interviewees. A more active collaboration between the EU and national regulatory authorities is needed to ensure consistent biosimilar messaging and targeted education. Collaborating among regulators, stakeholders, and medical societies to tailor information to specific needs was seen as essential for effective biosimilar implementation. Government support and local education events were also emphasized. Regulators warned that additional data-gathering expectations from healthcare providers could hinder biosimilar development. These extra clinical studies, required beyond licensing, can be costly for developers and delay timely product availability. Stakeholders across the healthcare sector emphasized the need for better education on biosimilars to overcome misconceptions and improve trust. Physicians, nurses, and pharmacists require more information on the biosimilar approval process, particularly regarding the reduced role of clinical trials in their development. Misinformation, often driven by biased messaging from the originator pharmaceutical industry, has led to confusion and

						resistance. Nurses and pharmacists also need specific training on biosimilar use and switching, while patients require clear, simple information tailored to their needs. Additionally, more active collaboration between regulators, healthcare providers, and stakeholders is essential to ensure consistent, evidence-based information and guidance. Independent, impartial information from regulatory bodies like the EMA and NCAs is crucial to dispelling myths and fostering trust in biosimilars.

Barbier et al. (2021) [8] [Journal article]	Cross-sectional	Belgium	Pharmacists and physicians (N = 207)	NR	Theme 1. Regulatory and approval processes Facilitator/Barrier Theme 2. Healthcare care system policies, incentives Facilitator/Barrier Theme 4. Communication & education Facilitator/Barrier	A survey of pharmacists revealed varied opinions on substituting biological medicines with biosimilars. Over half (58%) believed substitution should be allowed after consultation with the prescribing physician. A third (34%) felt automatic substitution could be appropriate in the future with more experience, while 26% supported automatic substitution depending on the product's complexity. However, only 10% supported immediate automatic substitution without restrictions. The majority (73%) agreed or fully agreed that substitution could occur after prescriber consultation, while 66% emphasized that the responsibility for switching between a reference product and its biosimilar should remain with the prescribing physician. Physicians cited cost savings (71%) as the primary reason for prescribing biosimilars, followed by confidence in EMA evaluations (42%), similarity to reference products (42%), and improved patient access to biological therapies (25%). Reasons against prescribing biosimilars included concerns about limited clinical testing (42%), patient uncertainty (33%), and insufficient knowledge about biosimilars (29%). Over half (55%) of physicians expressed the need for incentives to encourage biosimilar prescriptions in ambulatory settings. Preferred incentives included regulatory information about biosimilars, transparency on cost savings, and additional budgets for staff support. Similarly, 55% supported implementing an initiative like Belgium’s “Restart Biosimilar Medicines” program, which aimed to stimulate the use of

						biosimilars in the hospital, would be useful to stimulate the prescription of biosimilars in the ambulatory setting. Around 36% of pharmacists felt insufficiently trained to dispense and guide patients with biosimilars. Pharmacists reported feeling significantly less prepared to handle biosimilars compared to originators in general ($p = 0.023$). Only 22% felt sufficiently trained to lead patient discussions when dispensing originators, dropping to 13% for biosimilars. Many pharmacists found addressing patient questions about biosimilar similarity (47%), interchangeability (42%), and general information gaps (36%) particularly challenging. No significant differences were found in the self-assessed competency to dispense biologicals in general and biosimilars between pharmacists with more versus less than 20 years of experience as community pharmacist. Only when asked if they feel well trained and informed to dispense a biological, a statistically significant difference was found between groups ($p = 0.032$). 52% of physicians reported following training on biosimilars. However, 67% expressed the need for more information on both. National or regional professional physician associations were the preferred sources of guidance and education. For pharmacists, fewer had attended training, with 42% attending sessions on biologicals and 22% specifically on biosimilars. A significant majority expressed a need for more information (91% for biologicals, 96% for biosimilars), with 95% indicating interest in further training. National or regional professional organizations

						were also the most preferred source of information among pharmacists (51%).

Barbier et al. (2022) [9] [Journal article]	Qualitative (Semi-structured interviews)	NR	Healthcare professionals and pharmaceutical industry representatives (N = 14)	NR	Theme 4. Communication & education Facilitator/Barrier	Interviewees noted that the level of transparency in European Public Assessment Report (EPARs) varies, with newer versions being more detailed and structured than older ones. They suggested improving the depth of justifications provided for regulatory decisions to make them more understandable. While the EPAR is suitable for expert use, it was deemed too lengthy and complex for healthcare professionals, many of whom are unaware of its existence. To address this, a summarized version and more dynamic forms of information delivery, such as interactive platforms and videos, were proposed. Accessing relevant information from NCAs was reported to be challenging, particularly for non-experts. Healthcare professional organizations were identified as critical intermediaries to tailor regulatory information and build trust within their communities. These organizations could serve as active links between the EMA and healthcare providers, ensuring the effective translation of information. The EMA was praised for its leadership in biosimilar regulatory science and stakeholder outreach, particularly its guides for healthcare professionals and patients, which have helped foster trust. However, its website, although rich in resources, was criticized for being difficult to navigate. Some interviewees argued that promoting biosimilars lies outside the EMA's remit and should be driven by NCAs and professional organizations at the national level. Strengthening the collaboration between the EMA and NCAs was considered vital to ensure effective dissemination of information. National-level guidance by NCAs was believed to have a

						more direct impact on stakeholders.

Barbosa et al. (2021) [10] [Journal article]	Prospective observational	Spain	Patients (N = 134)	Etanercept	Theme 3. Infrastructure and Logistics	Most patients found administration easy with the biosimilar pen. Overall patient satisfaction was not improved with the switch from originator prefilled syringes to pens of biosimilar etanercept (23% extremely satisfied, 28% very satisfied, 23% satisfied, and 26% partly satisfied or not at all satisfied). No statistically significant difference was found between the study groups.
Beck et al. (2016) [11] [Journal article]	Cross-sectional	France	Physicians (N = 116)	Epoetin, filgrastim, somatropin or infliximab	Theme 1. Regulatory and approval processes Barrier Theme 2. Healthcare care system policies, incentives Facilitator Theme 4. Communication & education Facilitator	Majority of rheumatologists expressed a negative opinion about substitution by the pharmacist of a reference medicinal product with its biosimilar compound. Nine rheumatologists (out of ten) quoted ‘‘healthcare cost savings’’ as a positive element that might incentivize prescription of biosimilar medicines. A significant proportion of rheumatologists reported being informed through self-study and scientific publications [83.6% (95% CI 76.9–90.4)], pharmaceutical companies [75.9% (95% CI 68.1–83.6)], continuous training [72.4% (95% CI 64.3–80.5)] or colleagues [physician in 54.3% (95% CI 45.2–63.4) or pharmacist in 19.0% (95% CI 11.8–26.1) of cases]. Many also quoted seminar and conference attendance. Only 1 of 116 rheumatologists identified national health insurance as an information resource about biosimilar drugs.
Bergstra et al. (2024) [12] [Conference abstract]	Retrospective observational	France, Denmark, Czech Republic, Spain, Norway, Finland, Italy, Greece, Portugal, Canada, Romania, Korea, Switzerland, Argentina. Mexico, Colombia, Nigeria, South Africa	Patients (N = 18 countries)	Abatacept, adalimumab, etanercept, certolizumab, infliximab	Theme 2. Healthcare care system policies, incentives Barrier	Switching was reported to be mandatory in Italy, Canada and Denmark and recommended in Norway, Finland, Portugal, Romania, France, Spain and Sweden. In 2022, the proportion of biosimilar use ranged from 0% in Nigeria and South-Africa to 90% in Denmark and 100% in France.

				b, tocilizumab, rituximab and golimumab		Biosimilar use in lower middle- and upper middle-income countries was <10% during all years. Linear regression analyses showed a statistically significant negative association between GDP per capita and % biosimilar use from 2016 till 2022. In 2022, per 10.000 IntI$ increase in GDP per capita, the % biosimilar use in a country increased with 5.9 (95% CI 0.93; 11.0).
Carrillo S et al. (2024) [13] [Conference abstract]	Longitudinal cohort	Mexico	Patients (N = 73)	Adalimumab, rituximab and etanercept	Theme 3. Infrastructure and Logistics	9 patients (33%) had problems with the application of the biosimilar due to failure of the autoinjector device. This led to missed doses.
Chang et al. (2023) [14] [Journal article]	Retrospective observational	US	Patients (N = 30,530)	Infliximab	Theme 2. Healthcare care system policies, incentives Barrier/Facilitator	Authors used mixed logit regression controlling for patient, provider, and health plan characteristics as well as time-fixed effects. OOP costs per service date were $63.13 higher for infliximab originator compared with infliximab biosimilar among commercial enrollees and $19.76 higher among Medicare Advantage enrollees. Patients receiving treatment in an office setting were much less likely to switch to infliximab biosimilar compared with those receiving treatment in an outpatient hospital setting [OR: 0.178; *P*-value< 0.01; CI, (0.151, 0.209)]. There was no effect between switching to biosimilar and lagged OOP amount [OR: 0.935; *P*-value=0.202; CI (0.842, 1.037)]. Patients who had received 1 infliximab originator

						infusion were 63.7% more likely to switch to biosimilars than patients who had previously received 20 infliximab originator infusions [AME for 1 previous infliximab originator administration: 0.0063; CI (0.0048, 0.0078) versus AME for 20 previous infliximab originator administrations: 0.0023; CI [0.0020, 0.0025)]. There was no statistically significant difference in switching with higher lagged OOP amounts. A change in the administering provider was associated with a higher likelihood of switching to biosimilars [AME for switch in administering provider: 0.0028; CI (0.0023, 0.0034) versus AME for no switch in administering provider: 0.0012; CI (0.0010, 0.0015)]. Patients receiving treatment in physician offices were substantially less likely to switch to biosimilars than patients receiving treatment in the hospital outpatient department [AME for infusions in the outpatient department: 0.0048; CI (0.0040, 0.0056) versus AME for infusions in physician office: 0.0009; CI (0.0007, 0.0010)]. There was a higher likelihood of switching from originator to biosimilar associated with coverage changes that made the originator more expensive to the patient [AME change in preferred drug: 0.0021; CI (0.0015, 0.0025) vs. AME no change in preferred drug: 0.0012; CI (0.0009, 0.0014)]. The probability of switching to biosimilar was nearly identical across the different levels of the annual in-network deductible.
Chapman et al. (2017) [15]	Mixed methods	UK	Specialists (N = 234)	Infliximab and	Theme 2. Healthcare care system policies,	Cost saving was the dominant consideration when prescribing biosimilars. Cost saving to the

[Journal article]	(Cross-sectional survey and a retrospective drug utilization analysis)			insulin glargine	incentives Facilitator Theme 4. Communication & education Facilitator	respondents' organization influenced prescribing whether or not these savings were invested in the prescribers' department. Respondents weighted National Institute for Health and Care Excellence (NICE) guidance and robust pharmacovigilance studies on biosimilars equally likely to increase their use of biosimilars.
Cohen et al. (2016) [16] [Journal article]	Cross-sectional	US	Physicians (N = 1201)	NR	Theme 1. Regulatory and approval processes Facilitator Theme 4. Communication & education Facilitator	75% of physicians appear to trust FDA approval decisions: however, they will still want additional information when making treatment decisions. 13% of physicians, predominantly dermatologists and rheumatologists, will not solely trust the FDA's assessments and decision to approve the biosimilar and will seek more information. Presumably, these physicians will decide which medications to use based on their own assessments. Peer-reviewed literature is by far the most trusted and preferred information source for biosimilars among physicians (82%). The top trusted information sources include scientific journals (88%), FDA (73%), and physician peers (64%); however, dermatologists and rheumatologists indicated less trust in the FDA as an information source compared with other specialties at 64% and 58%, respectively. Physician trust in media was very low across all specialties. Journals, physician peers, and congresses/symposia are the primary trusted information sources for current information on biosimilars across specialties.
Costin et al. (2024) [17]	Retrospective observational	US	Pharmacy claims (N=6)	Bevacizumab, epoetin,	Theme 2. Healthcare care system policies, incentives	The authors use claims data from 2015 to 2019 and implement sequential regression models to assess the role of health plans on biosimilars

[Journal article]				filgrastim, infliximab, pegfilgrastim	Facilitator/Barrier	adoption. Health plan type plays a significant role in determining the likelihood of biosimilar uptake. Specifically, enrollment in a low-flexibility plan was associated with a higher probability of both switching to and initiating treatment with a biosimilar, while enrollment in a high-flexibility plan was associated with a lower probability of both switching to and initiating treatment with a biosimilar, compared with high-deductible plans. The probability of being a switcher was 1% higher ($p < 0.01$) for enrollees in a low-flexibility plan as compared with enrollees in high-deductible plans. The probability of being an initiator was 2% higher ($p < 0.01$) for enrollees in a low-flexibility plan as compared with enrollees in high-deductible plans. This effect size may seem small, but when considering that switchers comprise only 3% of the population, the magnitude of this effect is substantial, representing a 33% increase in the likelihood of switching to a biosimilar. In contrast, enrollment in a high-flexibility plan was associated with a lower probability of being a switcher (0.9% lower; $p < 0.01$) and a lower probability of being an initiator (1% lower; $p < 0.01$) when compared with high-deductible plans. These findings highlight the importance of health insurance plan design in promoting biosimilar uptake and suggest that low-flexibility plans may be more effective in encouraging biosimilar adoption.
Demirkan et al. (2022) [18]	Cross-sectional	22 countries including Turkey and US	Physicians (N = 114)	NR	Theme 4. Communication &	Concerning the diversity of information resources, the most common routes were

[Journal article]					education Facilitator	congresses, symposia, self-research, and scientific journals. A significant portion of the respondents stated that they wished to be informed about biosimilar medicines in the future through congresses/ symposia (, 75.4%) and webinars (61.4%). Two seniors noted that they had obtained information through anecdotal experiences or colleagues and two specialists quoted through a hospital pharmacy.
Druedahl et al. (2021) [19] [Journal article]	Qualitative (Semi-structured interviews)	NR	Multistakeholder (industry experts and European national medicines agency regulators) (N = 25)	NR	Theme 2. Healthcare care system policies, incentives Facilitator Theme 4. Communication & education Barrier	All biosimilar company participants predicted that biosimilar development costs would decrease if regulators waived or reduced the requirements for clinical trials for comparable efficacy. Biosimilar company participants described that lower development costs could incentivize further biosimilar development. Moreover, it could ease the current difficulties in obtaining return on investments for biosimilars. Further, a biosimilar participant specified that lower development costs would make more biologicals (and not only blockbusters) attractive for biosimilar development. A few participants (regulator and biosimilar company participants) also mentioned that originator companies previously spread what was termed as misinformation about biosimilars being inferior to the reference product. Further, it was stated this alleged spread of misinformation has caused skepticism amongst physicians regarding the safety and efficacy of biosimilars. A regulator stated that physicians' acceptance and trust will be a bigger challenge compared to the scientific questions related to reducing clinical comparability trial requirements. To facilitate physicians' trust, some regulators argued that there is a need for medicines agencies to clearly communicate and justify biosimilar approval

						requirements to physicians, if biosimilar clinical trials for comparable efficacy are to be waived or reduced.
Dylst et al. (2014) [20] [Journal article]	Qualitative (Semi-structured interviews)	Belgium	Multistakeholder (authorities, physicians, pharmacists, patients, academics and industry) (N = 19)	NR	Theme 1. Regulatory and approval processes Facilitator/Barrier Theme 2. Healthcare care system policies, incentives Barrier Theme 3. Infrastructure and Logistics Barrier Theme 4. Communication & education Barrier	Most interviewees expressed trust in the EMA and its registration procedures, though some physicians were skeptical, particularly regarding biosimilars. Product-specific biosimilar guidelines were widely regarded positively, but representatives of authorities suggested the need for clearer guidelines. Currently, national authorities in Europe handle biosimilar interchangeability and substitution, but one academic argued this should fall under the EMA's responsibility, given their oversight of the data. In addition to discounts, reference product manufacturers provide "fringe benefits" like sponsorships and services to hospitals, which may influence physicians' prescribing behaviors. Financial motives are a major barrier to biosimilar uptake in Belgium. Reference biopharmaceuticals have higher reimbursement limits than lower-priced biosimilars, and most are dispensed in hospitals, which rely on pharmacy profits. Manufacturers of originator products often offer discounts larger than the price difference with biosimilars, while biosimilar makers typically do not. As hospitals recover these discounts, dispensing reference products becomes financially attractive, though not for third-party payers. Hospitals also face additional logistics costs when stocking both reference products and biosimilars due to the short shelf life and cold-chain requirements of biopharmaceuticals.

						A significant barrier to biosimilar uptake is the lack of confidence from some stakeholders, particularly physicians and originator industry representatives, who question biosimilars' quality, safety, and interchangeability. This skepticism is partly due to an "information gap" where reference product manufacturers heavily market their products, but biosimilar makers do less. The biosimilar industry is working on addressing this gap. The representatives of the biosimilar industry pointed out the ambiguous and insufficient data provided on the website of the Belgian medicines agency (FAGG).
Edgar et al. (2021) [21] [Journal article]	Qualitative (Focus group)	US	Multistakeholder (managed care pharmacists and physician experts) (N = 8)	NR	Theme 2. Healthcare care system policies, incentives Facilitator Theme 3. Infrastructure and Logistics Facilitator	Favored strategies included "incentivizing providers by adjusting fee schedules for biosimilars" (62% of providers, 68% of managed care pharmacists) and "reducing cost sharing for patients using biosimilars" (79% of providers, 80% of managed care pharmacists). Focus group providers believed switching to biosimilars should be associated with tangible benefits to their practices and patients. Returns from these costs savings to health plans will increase provider reimbursement and can be ultimately reinvested by practices to hire pharmacy, nursing, or social worker staff. Another strategy that providers suggested was a pay-for-performance reward model that increases reimbursement. One of the providers' top strategies to overcome barriers of adoption was "expediting prior authorizations for biosimilars to simplify the process and enable immediate access" (80% providers survey, 69% managed care pharmacists).

Cohen et al. (2014) [22] [Journal article]	Qualitative (Survey)	US	Multistakeholder (payers and physicians) (N = 22)	NR	Theme 2. Healthcare care system policies, incentives Facilitator	All payers intended to promote use of biosimilars by differentiating between the originator biological and biosimilar through the use of co-payment or co-insurance tiering to steer patients and physicians towards biosimilars. Safety and efficacy were the most important factors when considering adoption of biosimilars on formularies. Cost-effectiveness and out-of-pocket costs to patients were the least important considerations.
Fisher et al. (2022) [23] [Journal article]	Cohort study (Prospective)	Canada	Patients (N = 7,358)	Etanercept	Theme 2. Healthcare care system policies, incentives Facilitator	By the end of the six-month transition period, 65.1% (1102) of the patients in the policy cohort had switched to a biosimilar version of etanercept, and 88.1% (1493) did so by the end of the one-year follow-up period.
Frantzen et al. (2019) [24] [Journal article]	Cross-sectional	France	Patients (N = 629)	NR	Theme 2. Healthcare care system policies, incentives Facilitator /Barrier Theme 4. Communication & education Facilitator /Barrier	(57%) of respondents thought the switching decision should continue to take place on medical prescription (57%), after a shared-decision-making process between the rheumatologist and the patient (69%). Scientific arguments acted as the best incentive to convert patients to biosimilar prescription, especially the existence of safety and efficacy data (47% of respondents) and the bio-similarity definition (33%). Another motivation was the prospect of savings to-come for the national health system (20%). 99% of respondents considered themselves sensitive to medication costs. 47% approved the principle of reducing-health-costs policies; but only 21% had no hesitation concerning the use of biosimilars because of the potential savings for the healthcare system. This ambivalence between the patients' concerns about medico-economical issues and their reluctance to be treated with

						biosimilars may be partially explained by a common preconception assuming that less expensive is lower quality (30%). Rheumatologists were considered the most influent source of information about biosimilars (78% of respondents) before the patient associations (64%) and health authorities (40%). The main sources of information about biosimilars were patient associations (50%), rheumatologists (39%), specialized magazines (30%) and the internet (20%). The two sources of information significantly associated with a sufficient information feeling were the rheumatologist (OR 2,31; IC 97.5% [1.35;4.00] ; $P < 0.05$) and the Therapeutic Education of Patient (TPE) sessions (OR 3.67; IC 97.5% [1.61-8.69]; $P < 0.05$). The most persuasive sources of information were rheumatologists (considered influent by 78% of respondents), the patient associations (64%) and the national health authorities (40%). According to respondents, the fear of less efficacy (61%) and safety (71%) comparatively to the originator biologic agent and poor trust in the pharmaceutical companies (40%) acted as the main deterring factors. Among the 21 converted patients (whose originator biologic had been switched for its biosimilar), 4 patients had not been informed that they were going to be treated with a biosimilar. Among the 17 informed patients, 4 patients had not been asked for their consent. According to most of the 629 responders, informing the patient is necessary (97%), useful in order to accept the

						treatment (91%) and it could improve compliance (88%). Fifteen percent thought the information given could enhance fears.
Gasteiger et al. (2022) [25] [Journal article]	Cross-sectional	NZ	Pharmacists (N = 142)	NR	Theme 4. Communication & education Facilitator	82% wanted written documents (e.g., brochures) to educate patients, with a focus on clear, jargon-free info, brand comparisons, and common questions. Other resources included websites (27%) and brief videos (10%) on drug administration. 4% wanted demo devices to show patients and to refer to Patient Support Programs from the manufacturer, while 3% sought pharmacist-specific training (e.g., webinars). 26% wanted information from reputable sources.
Gasteiger et al. (2023) [26] [Journal article]	Cross-sectional	NZ	Providers (N = 164)	Adalimumab	Theme 3. Infrastructure and Logistics Facilitator/Barrier Theme 4. Communication & education Facilitator	Providers were the least satisfied with training for the biosimilar device, information received from government agencies, and administrative workload during the transition. Participants were the most satisfied with the supply of the biosimilar, how early they were informed before the transition occurred, and their ability to receive information about the biosimilar. Satisfaction with the availability of alcohol wipes, sharps bins and the patient support program were also significantly lower after the transition period. Higher satisfaction with administrative workload ($P < 0.001$) and training for the biosimilar device ($P = 0.020$) predicted satisfaction following the transition ($F = 12.68$, $R^2 = 0.51$, $P < 0.001$). Satisfaction with sharps bins, alcohol wipes, patient support, and information from government agencies were not independent predictors. Participants were significantly less satisfied with the biosimilar than the bio-originator in terms of safety ($P < 0.001$), efficacy ($P < 0.001$), and quality of the device ($P < 0.001$) following the

						transition. Satisfaction with the availability of alcohol wipes ($P < 0.001$), sharps bins ($P < 0.001$), and the patient support program ($P < 0.001$) were also significantly lower after the transition period. Providers (n = 90) reported how their workload increased during the transition. Providers (46%) primarily reported the need to provide additional education and counseling, such as phone calls and appointments. Education attempts also included teaching patients to use the biosimilar device and addressing hesitancy from patients. The initial authorization process also increased workload (33%). For example, pharmacists often needed to double-check authorization numbers, and 25% of the pharmacists who responded also had to contact prescribers, such as to correct errors. Some providers (14%) also sourced their own resources and information. Providers (rheumatologists and nurses) primarily reported that the biosimilar device was easier to use, and the citrate-free buffer reduced pain when injecting, which helped with patient acceptance. The extended duration of the authorization process was also appreciated among all providers, along with patients automatically receiving new authorization numbers. Pharmacists reported the supply of the biosimilar to be helpful and the timing of the transition period, as they received plenty of notice. However, providers reported that the initial authorization process was complicated. This led to pharmacists experiencing dispensing errors, as the authority number was often attached to the wrong brand. Among all providers, participants reported that the biosimilar package (e.g., alcohol wipes and sharps bins), lack of a patient support

						program and resources, written information, or training complicated the transition. There appeared to be a lack of communication between specialist teams and primary care physicians. Pharmacists reported that general practitioners often did not discuss the brand change with patients, so they took on the role of educating patients. Providers also appreciated the written material and information they received about the biosimilar.
Gasteiger et al. (2024) [27] [Journal article]	Cross-sectional	NZ	Patients (N = 117)	Adalimumab	Theme 3. Infrastructure and Logistics Facilitator/Barrier Theme 4. Communication & education Facilitator	Participants were the least satisfied with the support and information received from patient support organizations, and training for the biosimilar device. Participants were the most satisfied with the ongoing supply of the biosimilar, the support they received from pharmacists during the transition period, and how early they were informed before the transition occurred. More satisfaction with the training for the biosimilar device ($p = .036$) was associated with higher satisfaction with the transition ($F = 4.63$, $R^2 = .33$, $p = .004$). Satisfaction with the patient support program, information and support received from patient support organizations, and alcohol wipes were not independent predictors. Compared with satisfaction before the transition period, participants were less satisfied with the provision of sharps bins ($p < .001$), alcohol wipes ($p < .001$), and the patient support program provided by the manufacturer ($p < .001$) after the transition period. Participants were also less satisfied with the quality of the biosimilar device ($p = .024$), safety ($p < .001$), and efficacy ($p < .001$). Satisfaction with obtaining prescriptions and authorization did not significantly differ

						between the two time periods. Over half reported that the biosimilar injection was less painful due to the citrate free buffer. Some participants also appreciated that the new device was easy to use and that the biosimilar controlled their disease just as well as the bio-originator. Participants also liked that the transition felt seamless, and the support from healthcare providers (especially specialists), and the information they received. However, the lack of alcohol wipes was a key problem as participants were often not aware of the lack of wipes before injecting and had to source their own supplies. The most common recommendation was to improve the communication before the transition occurs. All patients should be well informed before collecting their prescriptions and have the opportunity to discuss the change with their specialist team. Participants also requested more transparent and detailed information, such as the reason for the transition, cost of the biosimilar, and the supplies that would be provided. Other recommendations were to match 'like with like' and provide a comparable patient support program to that provided by the bio-originator manufacturer. It was also recommended to provide alcohol wipes, and the option to change back if necessary.
Giavatto et al. (2024) [28] [Journal article]	Cross-sectional	US	Multistakeholder (prescribers and pharmacists) (N= 75)	NR	Theme 3. Infrastructure and Logistics Facilitator/Barrier	Factors most important when selecting a biosimilar to substitute were patient support, including financial assistant programs (81.4%), out of pocket cost to patients (76.7%), and interchangeability designation (76.7%). Other factors included injection device (41.8%), supply chain (39.5%), citrate-free formulation

					Theme 4. Communication & education Facilitator/Barrier	availability (37.2%), real-world data (25.5%), product storage consideration (20.9%), latex free (18.6%), needle size (9.3%), and high dose concentration (9.3%). The top concerns about biosimilar substitution were administrative burden (65.9%), patient pushback (54.5%), lack of payor adoption (50.0%), and cost to patients (50.0%). Other concerns included efficacy of biosimilars (38.6%), safety of biosimilars (22.7%), additional inventory storage considerations (20.4%), evaluating when to recommend a biosimilar vs a reference product (38.6%), administrative burden (65.1%), providing additional patient education (15.9%), and prescriber pushback (38.6%) Main concerns about prescribing biosimilars were biosimilar efficacy (50.0%), safety (36.6%), disease progression after therapy switch (33.3%), patient buy-in (33.3%) and providing patient education (20.0%). Other concerns were evaluating when to prescribe a biosimilar vs a reference product (16.6%), overall biosimilar cost (16.6%), and manufacturing process (6.6%). Resources that would help increase understanding of biosimilars, include published data/real-world evidence of biosimilars (58.6%), the biosimilar landscape compared similarities and differences between approved biosimilars (55.1%), drug specific information about safety and efficacy (55.2%), and information about cost and reimbursement (41.4%). In addition to published data/real-world evidence of biosimilars (54.5%), the biosimilar landscape (75.0%), drug specific information about safety and efficacy (52.2%), and information about cost and reimbursement (70.4%), pharmacists also would like information about laws and regulations regarding interchangeability and substitution

						(72.7%), as well as background information of the biosimilars' approval process (40.1%). When pharmacists were asked what factors are most important when selecting a biosimilar to substitute (beyond payor designation), their top multi select choices were patient support, including financial assistant programs (81.4%), out of pocket cost to patients (76.7%), and interchangeability designation (76.7%).
Gibofsky et al. (2023) [29] [Journal article]	Cross-sectional	US	Patients (N = 500)	NR	Theme 1. Regulatory and approval processes Facilitator Theme 2. Healthcare care system policies, incentives Facilitator/Barrier	Most patients would be willing to accept pharmacist substitution of a biosimilar of its reference product, but the majority (51%) wanted the substitution communicated to themselves and their doctor, with 19% wanting to be informed themselves and 19% wanting their doctor to be informed. As of this writing, only 4 states have laws that prohibit a pharmacist substituting an interchangeable biologic without prior prescriber approval; however, the majority of states do require prescriber notification of such a substitution. 50% of current users said they received copay support. Among current biologic users who did not want to accept a switch, 42% were concerned about financial support. The present survey showed that among patients currently receiving and not currently receiving a biologic, biosimilar cost was considered part of the decision-making process for almost half of all respondents.
Greene et al. (2019) [30] [Journal article]	Mixed methods (Survey with qualitative components)	US	Pharmacy professionals (N = 300)	NR	Theme 1. Regulatory and approval processes Facilitator Theme 2. Healthcare	Based on pooled percentages for ratings of likely and extremely likely to overcome barriers to biosimilar adoption, the highest-rated strategies were for prescriber education about evidence from switching studies (91%) and FDA guidance on pharmacy-level substitution of reference biologics with biosimilars (90%). The lowest-

					care system policies, incentives Facilitator Theme 4. Communication & education Facilitator	rated strategies were for requiring therapeutic drug monitoring for patients who switch to biosimilars (39%) and using quotas to incentivize providers to prescribe biosimilars (40%). For 13 of the 16 strategies, the likelihood ratings did not differ significantly among respondents grouped by the 3 work organizations: managed care organizations (MCOs)/health plans, PBMs, and specialty pharmacies. For the strategy involving expedited prior authorizations for biosimilars, the pooled percentages of likely and extremely likely ratings were significantly lower for respondents in MCOs/health plans (55%) than in PBMs (73%) and specialty pharmacies (81%; $P < 0.001$). For incentivizing providers by adjusting fee schedules for biosimilars, the pooled percentages of likely and extremely likely ratings were significantly lower for respondents in specialty pharmacies (59%) than in MCOs/health plans (74%) and PBMs (75%; $P < 0.01$). For requiring therapeutic drug monitoring in patients who switch to biosimilars, the pooled percentages of likely and extremely likely ratings were significantly lower for respondents in MCOs/health plans (32%) than in PBMs (42%) and specialty pharmacies (45%; $P = 0.027$). For 4 of the 6 barriers, the difficulty ratings did not differ significantly among respondents grouped by the 3 work organizations. For the barrier involving concerns about the safety and efficacy of biosimilars among payers, the pooled percentages of difficult and extremely difficult ratings were significantly higher for respondents in specialty pharmacies (35%) than in MCOs/health plans (12%) and PBMs (19%; $P < 0.001$). For formulary management issues, the pooled percentages of difficult and extremely

						difficult ratings were significantly higher for respondents in specialty pharmacies (47%) than in MCOs/health plans (27%) and PBMs (28%; $P < 0.01$). For the qualitative analysis, the highest numbers of respondents' suggested strategies indicated primary implementation roles of biosimilar manufacturers (40%), the federal government (26%), and managed care organizations (15%). For example, continued efforts on the part of the FDA to remove barriers for getting biosimilars to market so that time between approval and market availability is significantly shortened and changing CMS payment formulas so that prescribing biosimilars is more profitable to provider.
Herndon et al. (2021) [31] [Journal article]	Cross-sectional	US	Multistakeholder (pharmacists, physicians and business leaders) (N = 76)	Filgrastim pegfilgrastim epoetin-alfa bevacizumab trastuzumab rituximab infliximab	Theme 2. Healthcare care system policies, incentives Barrier	Respondents rated rebate increases of reference biologics to payers as the most likely to prevent adoption (85%). This barrier rated the highest for respondents from health systems (79%), physician practices (38%), and pharmaceutical manufacturers (83%) individually. Pharmaceutical manufacturers responded that health-system formulary slow adoption was the second largest barrier.
Inotai et al. (2018) [32] [Journal article]	Cross-sectional	Bulgaria, Czech Republic, Hungary, Kazakhstan ,Latvia, Lithuania, Poland,	Policy experts (N = 20)	Infliximab, trastuzumab, and rituximab	Theme 1. Regulatory and approval processes Facilitator/Barrier Theme 2. Healthcare	According to this survey, in general, payers in CEE/CIS countries seem to have no concerns with extrapolation to indications. EMA registration is well accepted even if pivotal phase III data were to be extrapolated to other indications without additional phase III clinical trial evidence. In contrast, respondents in some

		Romania, Russia and Slovakia.			care system policies, incentives Barrier	countries—for example, in Bulgaria and in Slovakia—expected negligible or restricted use of biosimilars by clinicians in indications with only extrapolated data. This is especially true in the field of oncology, where respondents anticipated concerns from clinicians about extrapolating biosimilar access to other indications. In the "other" option, some respondents mentioned that even the price of original products may be reduced due to price erosion generated by internal price referencing. However, other respondents expressed their concern that the generated cost savings may be invested in other sectors of health care or even outside the health care sector and thus not improve patient access.
Jathanakodi et al. (2024) [33] [Journal article]	Mixed methods (Survey with some open-ended questions)	Canada	Patients (N = 120)	Adalimumab	Theme 3. Infrastructure and Logistics Facilitator/Barrier	Patients rated administration attributes, such as ability to use a pen independently, ease of performing self-injection, simplicity, ease of preparation, and ease of learning to use a pen, as most important. The SDZ-ADL pen was rated more highly than the ref-ADL pen for all attributes across the three areas evaluated: administration attributes, ease of learning to use, and pen characteristics. The greatest differences between the two autoinjectors related to the feedback mechanisms (visual and audible), for which the SDZ-ADL pen significantly outperformed the ref-ADL pen by more than 40% in the top two box score. Chi-squared tests showed that other statistically significant ($p \leq 0.05$) distinctions between the autoinjectors included the ease of performing self-injection, ease of preparation/setup, time to complete injection, process required to initiate

						the injection, simple/self-explanatory nature of the pen, convenient shape, ease of gripping the pen, and right size of the pen, all favoring the SDZ-ADL pen vs the ref-ADL pen. When asked to directly compare the performance of each autoinjector for each attribute, most patients reported a preference for the SDZ-ADL pen vs the ref-ADL pen for nearly all assessed attributes, except storage requirements. The difference was statistically significant ($p \leq 0.05$) for all attributes except needle concealment. Patients were asked to select which autoinjector they would prefer to use overall for their injections. 82% of patients preferred the SDZ-ADL pen over the ref-ADL pen. Among patients who preferred the SDZ-ADL pen over the ref-ADL pen, the main driving factors were less injection-site pain or lack of a burning sensation (n = 38; 32%) and buttonless activation (n = 38; 32%). Preference for the ref-ADL pen over the SDZ-ADL pen was mainly driven by its activation with a button (n = 12; 10%). When asked about the unique device features of the SDZ-ADL pen, respondents consistently perceived these features as “helpful”, with the proportion of respondents describing specific attributes as “helpful” as follows: color indicator, 90%; viewing window size, 88%; viewing window, 80%; buttonless activation, 75%. The proportion of patients describing these attributes as “helpful” was consistent between indications and between age groups. Regarding the device viewing windows, 88.3% of patients preferred the SDZ-ADL pen over the ref-ADL pen. Perceptions were that the large

						window of the SDZ-ADL pen was easier to see and confirm injection progress compared with that of the ref-ADL pen, and that the 360° visibility simplified viewing. Eight patients preferred the ref-ADL pen over SDZ-ADL pen in terms of the viewing window, noting that the viewing window is smaller, more discreet, and adequate to confirm the injection has been completed.
Kaneko et al. (2022) [34] [Journal article]	Cross-sectional	UK	Patients (N = 899)	Adalimumab	Theme 3. Infrastructure and Logistics Facilitator/Barrier Theme 4. Communication & education Barrier	21% highlighted the lack of training with the new injection device. After switching, the most commonly reported problem was 'worse pain' on injection with the biosimilar. The injection pain was said to be 'much worse' by 51% and 'slightly worse' by 23%. Ease of using the injection device was reported to be much worse by 22% of respondents. Respondents satisfied with the training for the new injection device reported fewer side effects (37% vs 60%), less pain when injecting (70% vs 83%,) and reduced difficulty in use of the injection device after the switching process (37% vs 66%). The training in use of the new injection device was associated with a significant reduction in reported pain on administering the new biosimilar, reporting of side effects and difficulty in using the device. Both satisfaction with written and verbal information about the switch to biosimilar provided by healthcare professionals was associated with fewer reported side effects. Provision of information perceived as being satisfactory significantly reduced participants' complaints regarding use of the new biosimilar injection device and in managing their self-reported disease activity. Sixteen per cent of participants were not at all satisfied with the written information about the

						switch to a biosimilar and 23% were dissatisfied with the verbal information received from their healthcare professionals. The proportion of participants with worse perception of the new biosimilar in term of side effects, ease of using the injection device and managing their symptoms was lower in the patients satisfied with the written (30% vs 63%, OR 0.15, 95% CI 0.06 to 0.40; 40% vs 62%, OR 0.35, 95% CI 0.21 to 0.58; 28% vs 69.1%, OR 0.11, 95% CI 0.02 to 0.49, respectively, all p values are less than 0.05) and verbal information (33% vs 59%, OR 0.15, 95% CI 0.06 to 0.40; 42% vs 60%, OR 0.45, 95% CI 0.28 to 0.72; 32% vs 63%, OR 0.20, 95% CI 0.05 to 0.74, respectively, all p values are less than 0.05). Respondents satisfied with the training for the new injection device reported fewer side effects (37% vs 60%, OR 0.15, 95% CI 0.06 to 0.41), less pain when injecting (70% vs 83%, OR 0.19, 95% CI 0.07 to 0.49) and reduced difficulty in use of the injection device after the switching process (37% vs 66%, OR 0.24, 95% CI 0.15 to 0.40) (all p values are less than 0.05). Training for the new device was associated with a significant reduction in reported pain on administering the new biosimilar (OR 0.20, 95% CI 0.07 to 0.55), reporting of side effects (OR 0.17, 95% CI 0.06 to 0.47) and difficulty in using the device (OR 0.25, 95% CI 0.15 to 0.41). Satisfaction with written and verbal information provided by healthcare professionals was associated with fewer reported side effects (OR 0.13, 95% CI 0.05 to 0.38) in respect of the written information and OR 0.15, 95% CI 0.05 to

						0.42 in respect of the verbal information). Provision of information perceived as being satisfactory significantly reduced participants' complaints regarding use of the new biosimilar injection device (OR 0.38, 95% CI 0.23 to 0.63 in respect of the written information and OR 0.45, 95% CI 0.27 to 0.73 in respect of the verbal information) as well as in managing their self-reported disease activity as compared with originator ADA (OR 0.05, 95% CI 0.004 to 0.57 and OR 0.15, 95% CI 0.03 to 0.84, respectively).
Lacosta et al. (2023) [35] [Journal article]	Mixed methods (Regional uptake data and semi-structured interviews)	Italy, Portugal, Spain	Hospital pharmacists, regulators, academics and industry representative (N = 10)	TNF-alpha inhibitor	Theme 1. Regulatory and approval processes Facilitator/Barrier Theme 2. Healthcare care system policies, incentives Facilitator/Barrier Theme 3. Infrastructure and Logistics Barrier Theme 4. Communication & education Barrier	Interviewees noted that incorporating biosimilar prescription objectives into regional guidelines and requiring prescribers to justify their therapy choices have supported cost rationalization in hospitals. However, this measure has faced opposition from stakeholders, including the originator industry and prescribers, with debates about whether it infringes on prescription freedom. Regional tribunals have generally ruled that justification requests do not violate this freedom, but varying levels of enforcement across regions have contributed to differences in biosimilar uptake, particularly for TNF-alpha inhibitors. Concerns were raised about hospital tenders with short time frames, which have necessitated parallel purchase procedures, leading to higher acquisition costs and limiting biosimilars' cost-saving potential. These tendering practices often focus solely on price and may not allow multiple winners, raising sustainability concerns due to excessive price pressures. The grouping of biosimilars and originator products in the same tender lot has also sparked legal disputes, delaying purchasing processes. Additionally,

						prescribers worry that these practices could disrupt therapeutic continuity for patients on originator biologics. Hospital pharmacists discussed whether differentiated purchase contracts should exist for biologic-naïve and biologic-experienced patients, given regulations prohibiting pharmacists from substituting biologic medicines. A national benchmarking system, similar to those in Italy and Portugal, was suggested to support biosimilar adoption. The AIFA considers originator biologics and biosimilars interchangeable, while emphasizing that treatment initiation and switching decisions remain with prescribers. Before the 2017 Budget Law and AIFA's endorsement of switching, policies largely focused on promoting biosimilar use among biologic-naïve patients. While these efforts were quickly implemented, they had limited impact on overall drug budget savings due to the smaller size of this patient group. The 2017 Budget Law encouraged biosimilar adoption while preserving therapeutic continuity. AIFA recognizes biosimilars and originator biologics as interchangeable, leaving initiation and switching decisions to prescribers. AIFA acknowledged regional health administrations and hospitals are allowed to implement policies promoting biosimilars if they align with cost-containment goals. Some regional administrations have adopted quotas and switching protocols to support biosimilar use even among biologic-experienced patients. In Portugal, the ACSS coordinates national health service financial resources and enforces biosimilar adoption through Contract-Programs

						with regional administrations. Hospitals achieving at least 20% uptake of new biosimilars within a year can reinvest 15–25% of the resulting savings, while failing to meet the quota may result in penalties. Although the 20% threshold is seen as achievable, it may not align with the ambitious switching goals recommended by the National Pharmacy and Therapeutics Committee. From a regulatory perspective, biosimilar policies have been effective in promoting biosimilars in acute care settings and overcoming initial resistance to switching. However, most hospital pharmacists interviewed have raised concerns regarding how to handle switches for patients receiving treatment with self-administered subcutaneous biologics (e.g., etanercept and adalimumab. Hospital pharmacists interviewed for this study are favorable to the existence of CNFT switching guidelines but pointed out two aspects that have affected early biosimilars adoption. First, the CNFT position statement on switching was only published in 2018 for infliximab and etanercept, and in 2021 for adalimumab. This implied a considerable time lag between biosimilars availability and switching guidance, and a missed opportunity to optimize cost-savings generation soon after biosimilars availability. Second, CNFT switching guidelines are to be viewed as recommended. According to the interviewed hospital pharmacists, resistance of clinical departments to switch patients receiving treatment with subcutaneous etanercept and adalimumab has been higher than for intravenous infliximab products. This is reflected in the observed gap between infliximab biosimilars uptake national average, and the national average

						for etanercept and adalimumab biosimilars.
Marín-Jiménez et al. (2021) [36] [Journal article]	Cross-sectional	Spain	Physicians and hospital pharmacists (N = 73)	NR	Theme 2. Healthcare care system policies, incentives Facilitator Theme 4. Communication & education Facilitator	Many participants agreed that there should be more than one brand for two main reasons: in order not to run out of stock, and, to stimulate competition in the biologicals medicine market. 28% of physicians were unaware of procedures and criteria behind the incorporation of biosimilars. A total of 23% of hospital pharmacists and 34% of physicians indicated their organizations have pre-defined criteria on the use of biosimilars. Some organizations follow regional objectives and criteria others have established some ("mandatory") criteria to start a biosimilar in biologic treatment-naïve patients or to switch all patients on infliximab. Others considered that specific or predefined criteria on the use of biosimilars are not needed. Almost 60% of participants reported that in their organizations, medical directors or other managers have proposed recommendations to prioritize biosimilars in biologic treatment-naïve patients, and to promote switches. The authors gathered some comments suggesting some kind of pressure to prescribe biosimilars especially in biologic treatment-naïve patients. The authors included a specific question for the hospital pharmacists about the importance of different activities related to biosimilars. They graded them from 1 (not important) to 10 (very important) as follows (means): Patients support programs 7.0 ± 2.7; Home-Delivery service 6.4 ± 2.8; Telepharmacy/telemedicine 7.2 ± 2.5; Hospital management educational support

						7.2 ± 2.4. Others considered that specific or pre-defined criteria on the use of biosimilars are not needed.
McClean et al. (2023) [37] [Journal article]	Quasi-experimental (Interrupted time series study)	Canada	Patients (N = 208,984)	Infliximab and etaner-cept	Theme 2. Healthcare care system policies, incentives Facilitator	The authors conducted an interrupted time series analysis to examine the change in proportion spent on and prescriptions dispensed of biosimilar infliximab and etanercept out of the total amount per agent after new start and biosimilar switching policies were implemented. New start policy: For etanercept, the authors detected a gradual monthly increase in the proportion of prescriptions dispensed that were biosimilar of 0.65% (95% confidence interval [95% CI] 0.44, 0.85), with no significant level change in use. No significant changes in use or spending were detected for biosimilar infliximab after the new start policy was introduced. Comparable results were quantified among disease-specific cohorts. Mandatory switching policy: In terms of total spending and number of prescriptions dispensed, proportional use of biosimilar infliximab increased from 21.6% to 74.6% and 33.7% to 78.9%, respectively, over the preintervention period. Similarly, biosimilar etanercept increased from 15.8% to 71.9% and 21.6% to 79.8% in terms of proportion of total spending and prescriptions dispensed, respectively. From the ITS, the authors observed significant level and trend changes among all study cohorts with respect to the proportion of biosimilar etanercept prescriptions dispensed and total spending after the switching policy was introduced. For example, there was a step change

						of 76.98% (95% CI 75.56, 78.41) in terms of the proportion of etanercept prescriptions dispensed post switch, in addition to a persistent gradual decrease of –0.95% per month (95% CI –1.04, –0.85), in the overall cohort in the post-switch period. There were significant level changes in the proportion of biosimilar infliximab prescriptions dispensed and total spending among all cohorts. Among the overall cohort, there was a step change of 58.43% (95% CI 52.11, 64.75), accompanied by a gradual decrease of –0.66% per month (95% CI –1.13, –0.20) in terms of the proportion of biosimilar infliximab prescriptions dispensed after the switch policy. With respect to the proportion of total spending on biosimilar infliximab, the authors observed nonsignificant monthly trend changes for all groups. When the proportion of biosimilar prescriptions dispensed were stratified by sex, the authors found similar associations across most groups. However, a significant level change was detected post new start among male subjects receiving etanercept (but not among female subjects or overall) in terms of the proportion of biosimilar prescriptions dispensed and total spending. The authors also identified unique associations in terms of biosimilar spending among female subjects receiving infliximab after the new start and switch policy: there was a significant positive trend in the post new start period and a significant downward trend post switch detected among female subjects and nonsignificant changes among male subjects. In general, the neighborhood income quintile–stratified analysis of the proportion of

						prescriptions dispensed of and total spending on biosimilar infliximab and etanercept demonstrated similar results to those from the overall cohort. Notable deviations in terms of the proportion of biosimilar prescriptions dispensed include a significant level change (3.83 [95% CI 0.08, 7.59]) post infliximab new start among the fourth highest neighborhood income quintile and a nonsignificant trend post switch among lower income quintiles. There was also a positive relationship between increasing neighborhood income quintile and the magnitude of level change post infliximab switch: the lowest income quintile demonstrated an immediate increase of 49.81% (95% CI 39.62, 59.99) compared to 66.38% (95% CI 56.76, 76.00) among the highest income quintile. In terms of proportion of total spending, the authors detected a negative trend post infliximab switch among the highest income quintile only (0.59 [95% CI –1.02, –0.16]). No deviations were detected with respect to etanercept. The authors conclude that mandatory switching policies were much more effective than new starting policies for increasing the use of biosimilar medications.
Messner et al. (2023) [38] [Journal article]	Cross-sectional	Germany and Switzerland	Pharmacists (N = 332)	NR	Theme 4. Communication & education Facilitator	In 2020 and 2022, four out of six attitudes of German and Swiss participants remained unchanged that were: being familiar with the term biosimilar, feeling sufficiently informed about biosimilars and sufficiently informed to dispense biosimilars, and being confident in handling patient queries regarding a therapy with a biological. In 2022, the confidence in handling patient queries regarding a therapy with a biosimilar

						differed significantly between Swiss and German participants (2020: DE: 42.9% vs CH: 40.3%, ns; 2022: DE: 26.7% vs CH: 41.6%; $p < 0.008$) as well as the confidence in substituting with a biosimilar with Swiss participants indicating a higher confidence than German participants (2020: DE: 15.5% vs CH: 30.6%, ns; 2022: DE: 17.3% vs CH: 32.7%, $p < 0.008$). A wide variety of information sources were named by the participants. The sources consulted once a week or more were primarily the Summary of Product Characteristics (SmPC)/Package leaflet (2020: DE: 40.5% vs CH: 35.5%, ns; 2022: DE: 40.0% vs CH: 35.6%, ns), followed by scientific publications (2020: DE: 26.2% vs CH: 21.0%, ns; 2022: DE: 24.0% vs CH: 13.9%, ns). In 2020 and 2022, a comparable percentage of participants had obtained training on biologicals (2020: DE: 48.8% vs CH: 41.9%, ns; 2022: DE: 44.0% vs CH: 48.5%, ns) and was highly interested in additional training on this topic (2020: DE: 83.3% vs CH: 88.7%, ns; 2022: DE: 81.3% vs CH: 89.1%, ns). In both years and countries, there was no significant difference in giving the correct answer for the biosimilar definition between participants who had received any training on the topic of biologicals and participants without any training (2020: DE with training: 48.8% vs without training 32.5%, ns; CH with training: 42.3% vs without training 55.9%, ns; 2022: DE with training: 63.6% vs without training 42.1%, ns; CH with training: 42.9% vs without training 42.0%, ns).

						In both years and independently of the country, knowing the substitution rules did not differ significantly between participants with and without training (2020: DE with training: 39.0% vs without training 25.0%, ns; CH with training: 23.1% vs without training 14.7%, ns; 2022: DE with training: 36.4% vs without training 39.5%, ns; CH with training: 44.9% vs without training 22.0%, ns).
Moorkens et al. (2019) [39] [Journal article]	Mixed methods (Analysis of market data) and semi-structured interviews)	Sweden	Multistakeholder (national pricing and reimbursement agency and experts) (N = 6)	Etanercept	Theme 3. Infrastructure and Logistics Barrier Theme 4. Communication & education Facilitator/Barrier	The additional workload associated with switching, due to having to call in patients to the hospital to see the prescribing physician for a new prescription, was acknowledged by the county of Stockholm. The attitude of key opinion leaders and clinic heads plays an important role in biosimilar uptake, as they are often members of a county council expert group and are believed to have an opinion based on review of the scientific literature. These opinions can both positively or negatively affect biosimilar uptake. Secondly, prescribing guidance to physicians is offered by the county councils in the form of recommendations. Follow-up on adherence by prescription monitoring further enforces this driver. Thirdly, financial streams and local gainsharing arrangements in counties lead to different levels of stakeholder incentivization.
Moorkens et al. (2017) [40] [Journal article]	Cross-sectional	24 countries	Experts (N = 24 countries, 20 EU Member States, plus Iceland, Norway, Russia,	Filgrastim, somatropin, erythropoietin alfa, insulin glargine,	Theme 1. Regulatory and approval processes Facilitator/Barrier Theme 2. Healthcare care system policies,	National tendering, tendering by INN, and a ‘product of the month’ system could be effective to achieve lower prices. HTA could assist in budget planning and help incentivize physicians. Pharmaceutical companies and national authorities should collaborate, on a national level as well as between countries, to support affordability through competitive price systems.

			and Serbia)	follitropin, infliximab and etanercep	incentives Facilitator/Barrier Theme 3. Infrastructure and Logistics Facilitator/Barrier Theme 4. Communication & education Facilitator	A hurdle that was identified by the country experts is that the EMA, which has all the data on the reference medicinal product, does not decide on biosimilar substitution and derogates this decision to the Member States. The question of interchangeability needs to be addressed at the European level as well. The development of a list for appropriate substitution would help. One of the experts offered mandatory use of the cheapest product, as decided by health authorities, as a measure to assist biosimilar uptake. Demand-side policies: Approximately half of the countries have incentives targeting physicians to prescribe biosimilars. In Germany, quotas exist for some biosimilars within the context of regionally negotiated economic targets. In addition, there can be incentives for physicians to prescribe economically, e.g., in Austria the physician is called upon to prescribe the most cost-effective product when several therapy options are available, providing an incentive for physicians to prescribe biosimilars. In Belgium, biosimilars are part of quotas for prescribing low-cost medicines. Most countries mention budgetary restrictions playing a role in prescribing a biosimilar. In the Netherlands, limitation of prescription of the originator medicinal product once the biosimilar has entered the market is sometimes enforced by insurance companies for reimbursement purposes. In some countries, physician incentives have been incorporated in pricing and reimbursement mechanisms with a view to stimulate biosimilar uptake. For instance, in Norway, all products paid by the hospitals (also some for-outpatient use) are subject to tendering. The physicians have to follow the ranking and

						use the cheapest product, which often is a biosimilar, except when there is a clinical reason not to use the cheapest product. With this system, biosimilar infliximab has reached a market share above 95%, and also the market share of biosimilar etanercept has been increasing to above 82%. Gain sharing, which is here defined as an incentive where part of the savings from using biosimilars goes to the hospital or prescribing physician, is also suggested as a meaningful solution. Quota: Furthermore, experts agreed that measures should be introduced to promote rational prescribing, and that adherence to these measures should be verified. For treatment-naïve patients it is generally accepted that they can safely be started on the biosimilar. Here, quota can help to increase uptake of biosimilars. The burden of switching now lies with the prescribing physician, and monitoring of patients on a biosimilar can be very resource intensive. Switching programs can for example be supported via insurance companies, but also pharmaceutical companies could provide supportive infrastructure (e.g., IT infrastructure), which supports pooling of data between different centers. In some countries, including Portugal and the Netherlands, scientific conferences are organized to educate stakeholders and stimulate the use of biosimilars. In Norway, several seminars for hospitals are arranged each year where results of the tenders are presented. In addition, lectures are organized of which several discuss the topic of biosimilars. Patients are mainly informed via

						patient organizations, leaflets or via letters when exposed to a switch. Information about biosimilars should come from an independent institution and should be precise and reliable. Lessons and training could be organized, for example in hospitals, where most biosimilars will be prescribed or at least the therapy is initiated. For patients, a questions and answers (Q&A) document could help to address frequently asked questions. The use of a common platform to share experiences and knowledge was suggested, and also ongoing publication of safety and efficacy data, so that evidence-based decisions can be made. Concerns related to switching and substitution possibilities, and the definition of a treatment-naïve patient should be addressed. Introduction of biosimilars in prescribing guidelines and clinical guidelines will be key to ensure increased uptake. A variety of educational policies are implemented across countries. In most countries, local initiatives exist among physicians in hospitals or ambulatory care. Also prescribing guidelines and clinical guidelines can inform physicians. Reported educational policies tend to target in the first instance physicians, whereas fewer policies were reported for patients.
Moorkens et al. (2021) [41] [Journal article]	Cross sectional	NR	Multistakeholder (experts) (N = 30)	Adalimumab	Theme 1. Regulatory and approval processes Facilitator Theme 2. Healthcare care system policies, incentives Facilitator/Barrier	A multi-winner tender for adalimumab was chosen to ensure sustainability of the market (sales are generated for companies and shortages are prevented). The implementation of the tender relies on a well-established system of guidelines for specific therapeutic areas. Competition is enhanced because companies know that physicians will prescribe the winning product. In Belgium, a pilot project (started in 2019) is testing a financial incentive that encourages

					Theme 3. Infrastructure and Logistics Facilitator/Barrier	physicians to prescribe a percentage of biosimilar adalimumab or etanercept in ambulatory care. The objective is to compensate for the time/effort of individual physicians to switch treatment, however, so far, the success has been minimal, with various stakeholders complaining that, on the one hand, they do not agree with financial incentives to support specific products and, on the other hand, that the amount paid is too small (personal communication). Other countries also use target agreements to stimulate physicians, e.g., in Germany (per region) and in Spain (for example for all hospitals in Catalonia that are financed by the public health system). In Lithuania, physicians are obliged by treatment guidelines, which are approved by order of the Ministry of Health, to prescribe new patients the least expensive TNF-α inhibitor. For some indications, this is biosimilar adalimumab. In Latvia, this economic incentive almost disappeared due to a confidential discount for originator adalimumab after which co-payment was lowered and is only minimal. In the Netherlands, some insurance companies support hospitals which have a less favorable biosimilar contract by giving a grant for the implementation of a biosimilar or providing higher reimbursement to the hospital, which would otherwise make a loss on dispensing biosimilars. In Germany and Austria, health insurance funds use rebate contracts and non-binding recommendations. In some countries, the internal reference price has decreased to the price level of the biosimilar (or even lower), resulting in an increased co-payment for patients on the originator product if the price of the originator product exceeds the reference price (Bulgaria, Latvia, and Romania). A large variation in list

						prices can be observed for originator adalimumab (40 mg syringe or pen) in the countries surveyed before loss of exclusivity. In most countries, additional (confidential) discounts and/or rebates existed before loss of exclusivity. Exceptions included Albania, Austria, Finland, Greece, Iceland and Romania. After loss of exclusivity, a larger variation in list prices can be observed for originator adalimumab in the countries surveyed than before loss of exclusivity. List prices ranged from €233.65 per unit in Austria to €955.47 in Germany (factor 4.1 difference). Overall, list prices of originator adalimumab (40 mg syringe or pen) decreased after loss of exclusivity rights in October 2018, and the entry of biosimilars to the market, from an average of €516 to €456 per unit (median of €430.11 per unit). In Romania, co-payment for originator adalimumab is covered via a Patient Access Scheme, but in order to receive a copayment waiver, patients need to go through an administrative process every 3 months. The biosimilar on the other hand is fully reimbursed without additional administrative hurdles. Sometimes a strategy was implemented even before loss of exclusivity, for example in Denmark and Scotland. In Denmark, preparations included statements to physicians on switching, letters to patients and ensuring the presence of additional nurses to support switching. It was noticed that the regions of North Glasgow and Clyde, which already had additional staffing for rheumatology for the etanercept switch, were able to quickly switch to the selected adalimumab biosimilar with high switching rates (near 100%). In South Glasgow, where staffing had not been approved, or for specialties where etanercept is not used (e.g., gastroenterology),

						much lower rates of uptake were observed.
Moura et al. (2024) [42] [Conference abstract]	Cross-sectional	Brazil	Physicians (N = 347)	NR	Theme 1. Regulatory and approval processes Barrier Theme 4. Communication & education Barrier	The specialists base their conduct on guidelines from SBR (49.0%), GEDIIB (36.8%), ANVISA (18.1%), FDA (19.0%) and EMA (16.3%). However, 57% are dissatisfied with the information received in scientific update channels and through manufacturers. Only 44 respondents (12.7%) are satisfied with the transparency in the production process of these drugs. Most respondents (84.3%) would prescribe a biosimilar. Among non-prescribers, the main reason given in both specialties was lack of confidence in these medications (67.2%), followed by lack of non-inferiority clinical studies (38.2%) and scarcity of information (36.4%).
Renton et al. (2019) [43] [Journal article]	Qualitative (Interviews)	UK	Patients (N = 9)	Adalimumab	Theme 2. Healthcare care system policies, incentives Facilitator Theme 3. Infrastructure and Logistics Barrier	Almost all respondents identified cost savings as a benefit of switching to a biosimilar (of note, this was mentioned in the pharmacy letter and prompting questions). Others identified benefits including greater accessibility to the drug. Increased access felt important for some who remember the challenges of getting biological medication for their child and the impact that doing so had on their lives. Some families highlighted that cost savings could mean that resources could be used elsewhere. Patients were anxious about having access to the same medication administration device (the bio-originator is available as either a prefilled syringe or prefilled auto-injecting pen) and the potential of having to use an unfamiliar device. Past versions of the adalimumab bio-originator

						contained a citrate preservative which contributed to stinging as the medication is injected. Several patients recall what this felt like and those that have never been on a stingy preparation were aware of its existence. Whether the new medication would sting was a prime concern, although some patients were able to balance a possible worse outcome on an individual level against a perceived benefit for society. The color of a biosimilar medication, administration device and its packaging was a major concern for most families. Some were concerned about the logistics of switching to a biosimilar and whether the home delivery process would be disrupted, especially given the need to store these medications in a refrigerator.
Roberts et al. (2024) [44] [Journal article]	Observational cohort (Retrospective)	US	Patients (N = 37650)	Infliximab	Theme 2. Healthcare care system policies, incentives Facilitator/Barrier	The authors used Poisson regressions and found that the strongest predictors of ever receiving biosimilar infliximab were insurance (Medicaid RR = 1.41, 95%CI 1.10–1.80; Private RR = 1.25, 95%CI 1.05–1.50 compared to Medicare) and the year of study entry (which increased from RR = 1.37, 95%CI 1.07–1.76 in 2017 to RR = 3.51, 95%CI 2.95–4.17 in 2022 compared to those entering in 2016). New users with Medicare were most likely to start on biosimilar infliximab from 2017 to 2019 compared to other insurance types, with 23% of new users in 2019 starting on a biosimilar. However, after 2019, the authors observed a flattening of the slope of uptake among Medicare beneficiaries, and only 37% of new infliximab starts for those with Medicare in 2022 were on a biosimilar. There was an increasing percentage of new users with Medicaid starting on a biosimilar over the whole study period ending with over half (55%) of users initiating a biosimilar by

						2022; biosimilar uptake was particularly steep between 2020 and 2021, nearly doubling during this time. Private insurance had the lowest uptake among new biosimilar starts through 2020 (less than 17% in 2020) but there was a threefold increase between 2020 and 2022 with just over half (51%) of new starts in 2022 being on a biosimilar. Interestingly, given the persistently low uptake among Medicare beneficiaries, there were four practices with a higher than average (and in some cases much higher) percent of Medicare beneficiaries with new starts on a biosimilar at all time points. Similarly, there were two practices that began adopting biosimilar infliximab among privately insured patients prior to the overall spike observed in 2021–2022. In the subgroup of patients who started on bio-originator infliximab, a greater percentage of patients with private insurance (16.9%) and Medicaid (14.2%) switched to a biosimilar compared to those with Medicare (9.7%). The majority (63.1%; n = 2499) of switches were completed in 2021 or 2022. Similar to the distribution of new starts on a biosimilar, the timing of switching is different by insurance with a higher proportion of the switches from bio-originator to biosimilar taking place in 2021–2022 for patients with private insurance (82.1%) and Medicaid (52.9%) compared to Medicare (37.6%). In the fully adjusted model, the rate of switching was significantly higher for patients with Medicaid (IRR = 1.96, 95%CI 1.38–2.77) or private insurance (IRR = 1.95, 95%CI 1.51–2.54)

						compared to Medicare. There was a slightly higher rate of switching for patients with PSA (IRR = 1.16, 95%CI 1.00–1.34) compared to RA, and patients in the West (IRR = 1.70, 95%CI 1.02–2.85) compared to the Midwest.
Roberts et al. (2024) [45] [Conference abstract]	Observational cohort (Retrospective)	US	Patients (N = 11,571)	Adalimumab	Theme 2. Healthcare care system policies, incentives Facilitator	In the first nine months of 2023, 2.2% of patients received a prescription for a biosimilar version of adalimumab. Those with private insurance (2.5%) or Medicaid (2.8%) were more likely to use a biosimilar than those with Medicare (1.2%) corresponding to a small difference by the authors (SMD = 0.3).
Rupert et al. (2022) [46] [Journal article]	Qualitative (Focus groups)	US	Physicians and pharmacists (N = 49)	NR	Theme 1. Regulatory and approval processes Barrier Theme 4. Communication & education Facilitator/Barrier	Most participants were familiar with the FDA's rigorous approval process for original biologics but had limited understanding of the biosimilar approval process. Some incorrectly believed the biosimilar process mirrored that of original biologics, requiring identical trials, while others correctly noted it was abbreviated but were unclear about the specifics. A third group mistakenly thought biosimilars faced stricter standards than original biologics, perceiving bio-similarity as an additional criterion. Physicians universally opposed pharmacists substituting interchangeable products without prescriber consent, citing concerns over patient safety and the difficulty of attributing side effects to the original or interchangeable product. Some pharmacists also expressed discomfort with unconsulted substitutions. Concerns about the abbreviated biosimilar approval pathway included perceptions that it might compromise patient safety due to reliance on assumptions rather than comprehensive empirical data. However, many acknowledged

						the necessity of this pathway to achieve cost savings. Participants were largely unfamiliar with interchangeable products and struggled to distinguish them from biosimilars. After learning the FDA's definition, many expressed concern that biosimilars are not held to interchangeability standards, and confusion about the distinction between biosimilars and interchangeables persisted. Participants expressed reluctance to prescribe or dispense biosimilar and interchangeable products without seeing detailed efficacy and safety data. Although pharmacists generally voiced more willingness to use biosimilars than physicians, both groups expressed a strong desire for more information—such as molecular structure, manufacturing processes, inactive ingredients, and safety and efficacy data. Physicians were especially vocal in their desire for more information about biosimilar safety and efficacy, including comparisons to the original biologics.
Stevenson et al. (2023) [47] [Journal article]	Cross-sectional	US	Pharmacists and pharmacy technicians (N = 507)	NR	Theme 4. Communication & education Barrier	Regarding FDA approval when asked if a pharmacist can substitute an interchangeable biosimilar without asking the prescriber, only 20% of respondents answered that this was true. Next, pharmacists were asked 6 true or false questions about the concept of interchangeability. In contrast to the previous question that asked broadly about an interchangeable biosimilar, this question asked more specifically if it "is appropriate for a pharmacist to dispense an interchangeable biosimilar in place of its reference product without authorization from the prescriber if consistent with state law." Overall, 53% respondents selected true; a numerically

						smaller proportion of community pharmacists understood this concept than the other groups (50% vs. 54%-61%). Overall, 81% of respondents correctly answered that approval of a biosimilar for all the indications of its reference product does not automatically make it interchangeable with the reference product. Notably, a smaller proportion of hospital or health system pharmacists (71%) understood this concept than those from other practice settings (81%-96%); this may be caused by the therapeutic equivalence concept that is frequently used within health system formularies. In the United States, licensing of biologic products as biosimilar to or interchangeable with a licensed reference biologic product is determined at the federal level by the FDA. However, state pharmacy laws regulate the substitution of inter-changeable biologic products. Most respondents (>75%) provided a correct answer to the series of questions pertaining to understanding of state pharmacy laws about interchangeability and substitution. Although laws regarding substitution of biosimilars vary among states, some elements are common to state regulations. Respondents were asked to indicate whether statements about common elements of state pharmacy practice laws regarding the substitution of biosimilar were true or false. Nearly all respondents understood key elements that are similar to generic substitution laws: 97% correctly answered that substitution can be prevented by the prescriber by indicating that the selected brand is medically necessary and 95% of records need to be maintained.
Tam et al. (2024) [48]	Observational (Retrospective)	NR	Quarterly IQVIA MIDAS	NR	Theme 1. Regulatory and approval processes	In three price-link policy comparisons, in which biosimilars were priced at -20% of their originator, two showed lesser reductions for the

[Conference abstract]			sales data (N = 13 countries)		Facilitator/Barrier Theme 2. Healthcare care system policies, incentives Barrier	comparator with the policy. Comparators with tendering policies generally showed greater expenditure reductions compared to those with absent tendering (four of six comparisons). Of these four, all were tenders in the retail setting. Conversely, tendering in the hospital setting did not achieve greater expenditure reductions. A greater concentration of tendering (regional vs local, or national vs regional) did not show greater reductions. There was only one pair for prescribing quotas (i.e., Belgium with quotas; France without quotas; hospital setting; infliximab), which showed the comparator with quotas had lesser expenditure reduction compared to the comparator without.
Tano et al. (2024) [49] [Journal article]	Observational (Retrospective)	France	Community pharmacies (N = 14,000)	Adalimumab	Theme 2. Healthcare care system policies, incentives Facilitator	Using adalimumab biosimilars will have saved €8.9 million in the experimental case hospitals and €7.5 million in the general case between January 2019 and October 2020, based on hospital prescriptions in the sample. The savings estimates for the NHI were €1.4 million higher in the experimental case, but the mean saved by box was lower for the experimental case than in the general case when compared to the volume of adalimumab dispensed in community pharmacies. Otherwise, the simulation with general case hospitals having the same monthly mean biosimilar rate as experimental case hospitals resulted in a €8.5 million savings, compared to €7.5 million with its proper mean biosimilar rate. General case hospitals had a significantly lower mean biosimilar uptake (16.7% vs 23.2%, *p* =

						0.029) than those included in the experimental case. Twenty-three of the 40 hospitals in the experimental case and ten out of the 91 hospitals studied in the general case had already taken part in the etanercept experiment. Biosimilar uptake was higher, but not statistically significant, for hospitals with prior experience in the adalimumab general case group (p = 0.086).
Teeple et al. (2019) [50] [Journal article]	Cross-sectional	US	Patients (N = 1,696)	NR	Theme 2. Healthcare care system policies, incentives Facilitator/Barrier Theme 4. Communication & education Facilitator/Barrier	More than half of patients were willing to pay at least $50 per administration/fill to avoid an NMS to a biosimilar. Given that most patients were paying $25 or less for their current biologic, this represents a willingness to pay a notable increase in OOP cost. Financial considerations were relevant among patients as well, with 71% of patients expressing concern that switching would cause them to lose the copay support or services they were receiving from the manufacturer of their current biologic. Although OOP cost was an influential factor for patients, most patients (62%) still indicated that they were willing to pay higher OOP cost to avoid an NMS to a biosimilar. While the specific dollar amount patients were willing to pay to avoid a switch varied, approximately half of all patients (52%) indicated they would pay at least $50 more per biologic administration/fill to avoid a switch to a biosimilar. Although the resulting increase in annual OOP cost would vary depending on the patient's biologic administration/fill schedule, it would equate to an annual increase of >$500 for many patients. Among those patients (19%) willing to pay $200 or more per administration/fill, the increase in annual OOP cost would exceed $2000 in many cases. Also of note, the OOP cost that patients were willing to pay to avoid a switch

						was significantly associated with the patient's OOP cost for their current biologic medication. However, despite this association, approximately half of patients were willing to pay at least $50 more per administration/fill, regardless of their current OOP cost. Willingness-to-pay was also significantly associated with the patients' level of satisfaction with current therapy. Of the 1696 patients included in the survey, 20% (n ¼ 337) reported they had previously received notification that the insurance coverage of their biologic was changing and they should consider switching to another originator biologic to avoid paying a higher cost. Most patients (79%) took at least one action to avoid the switch. Specifically, patient-reported actions to avoid a switch included asking the prescribing physician's office to appeal the switch (47% of patients), appealing to the insurance company to prevent the switch (33%), contacting a foundation or copay support program to seek financial assistance to stay on the current biologic (33%), and/or contacting employer's human resources manager to appeal the switch (7%). Among the 44% of patients (n = 150) who did switch, the majority (67%) did so to avoid paying a higher cost. More than half of patients (56%) went without therapy for administrative reasons during the period of transition from the previous biologic to the NMS treatment. In the present study, for example, 31% of patients reported paying $0 OOP cost for their current biologic. Thus, while an NMS to a biosimilar may yield cost-savings for another stakeholder (e.g. the health plan), it would not result in savings for patients. Although patients emphasized a need for

						information and evidence to support decision-making, our results indicate significant knowledge gaps regarding biosimilars among surveyed patients. Thus, patient education will be important moving forward to support informed decision-making among patients.
Teeple et al. (2019) [51] [Journal article]	Cross-sectional	US	Physicians (N = 297)	NR	Theme 2. Healthcare care system policies, incentives Barrier Theme 3. Infrastructure and Logistics Barrier Theme 4. Communication & education Facilitator/Barrier	Physicians familiar with biosimilars appeared more likely to be uncomfortable switching a stable patient due to insurance coverage than physicians with less familiarity. The key negative impacts of NMS were anticipated to be related to office management (60%), patient mental health (59%), treatment efficacy (57%) and patient safety (53%) (Figure 3). Among respondent physicians who infuse patients on-site, most indicated that it would create logistical (72%) and financial (67%) challenges to keep multiple infusible medications on-site if NMS between biologics and biosimilars were to become common practice. The clear majority of physicians did not want stable patients to undergo an NMS to a biosimilar. Various concerns appeared to fuel this opposition, including potential negative impacts on logistical and financial aspects of physician practice. These survey results suggest that physicians expect NMS between biologics and biosimilars to create greater physician practice burden. 54% of physicians were uncomfortable switching a stable patient to a biosimilar if insurance coverage was compelling the switch. This was significantly associated with the level of physician familiarity with biosimilars ($p = .003$). Physicians familiar with biosimilars appeared more likely to be uncomfortable switching a

						stable patient due to insurance coverage than physicians with less familiarity. Most physicians (75%) also reported that policies that compel stable patients to NMS to a biosimilar would disrupt the physician–patient relationship. The majority of physicians (63%) indicated there wasn't enough information or long-term data to make them comfortable prescribing biosimilars. Given these reported concerns, physicians understandably also expressed a desire for more guidance and data related to biosimilars. For example, 75% indicated that it would be helpful to have best practice recommendations for NMS incorporated into national disease treatment guidelines (e.g. from the American College of Rheumatology or the American College of Gastroenterology). At the time of this study, almost two-thirds of physicians (63%) did not believe they had enough information or long-term data to prescribe biosimilars. More than 80% of the physicians reported taking at least one action (or directing staff to do so) when a patient was faced with a potential switch due to insurance coverage changes, such as appealing the switch to the insurance company, coaching the patient on how to appeal the switch, or recommending that the patient take the alternative medication rather than appealing the switch.
Vogler et al. (2017) [52] [Journal article]	Cross-sectional	42 countries	Policymakers (N = 42 countries)	NR	Theme 1. Regulatory and approval processes Facilitator Theme 2. Healthcare	Demand-side measures to encourage biosimilar uptake: Prescribing by INN is a measure enforced by doctors that supports the uptake of generics as well as biosimilars. INN prescribing is in place in 35 European countries, Canada and South Africa, and is mandatory in 14 of the surveyed countries. It is only in Austria,

					care system policies, incentives Facilitator/Barrier	Denmark, Serbia and Sweden that prescription by INN is not permitted. Another key demand-side measure to enhance the uptake of off-patent medicines is to allow community pharmacists to substitute the originator medicine with an off-patent medicine. Several countries apply a pricing policy that sets the price of follower products in relation to the price of the originator medicine. For generics, this is called 'generic price link'. It is a commonly used practice that is applied in 30 of the 42 surveyed countries. Fifteen countries reported that they also apply such a strategy for biosimilar medicines. In most of the countries that apply a generic and biosimilar price link, the price difference between the originator medicine and the biosimilar is, sometimes considerably, lower than that between originator and generic medicine. This implies that biosimilar medicines tend to have higher prices.

Note. General = not specifically reported; NZ = New Zealand; NR = not reported