



Real-World Evaluation of Biosimilar Substitution Practices in Ambulatory Pharmacy Care

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Abstract

Biosimilar substitution has moved from a theoretical regulatory category to a routine decision point in ambulatory pharmacy care, yet the pathway from biosimilarity to interchangeability to an actual pharmacy-counter substitution remains uneven and, in the United States, considerably more constrained than the accumulated clinical evidence would justify. This article synthesizes the real-world evidence and practice literature on biosimilar substitution in ambulatory pharmacy settings, tracing the regulatory logic that separates a biosimilar from an interchangeable biosimilar, the nocebo effect and communication factors that determine whether a clinically sound switch succeeds at the patient level, the accumulated randomized and real-world switching evidence across inflammatory disease, oncology, and endocrinology, the practice patterns and preparedness gaps documented among community and ambulatory pharmacists, and the policy and reimbursement levers that explain why biosimilar uptake varies so widely across countries with essentially the same underlying clinical evidence. Read together, the literature supports substitution as clinically sound and safety-neutral across the therapeutic areas studied at scale, while identifying pharmacist counseling structure, state-level substitution law clarity, and demand-side policy incentives, rather than any residual clinical uncertainty, as the binding constraints on realizing the full substitution opportunity in ambulatory practice.

Keywords: biosimilar substitution; interchangeability; ambulatory pharmacy; nocebo effect; biosimilar switching

1. Introduction

A biosimilar is not a generic. That distinction, obvious to the specialists who developed the regulatory pathway, is still routinely lost on the community and specialty pharmacists, prescribers, and patients who actually decide, day to day, whether a dispensed biologic changes from one manufacturer's product to another's. A small-molecule generic is chemically identical to its reference product; a biosimilar is a highly similar but not identical copy of a large, structurally complex protein produced in living cells, approved on the basis of analytical, pharmacokinetic, and, where needed, clinical data showing no clinically meaningful difference from the reference product in safety, purity, and potency. In the ambulatory setting — the retail and specialty pharmacy counter, the infusion suite, the endocrinology or rheumatology clinic where a patient picks up a refill — that distinction has become the practical crux of a rapidly expanding class of substitution decisions that pharmacists are now making, or helping patients and prescribers make, largely without the decades of settled practice norms that govern generic substitution.

The regulatory apparatus for this has matured substantially over the past decade. In the United States, the Biologics Price Competition and Innovation Act created a two-tier approval framework: a biosimilar is licensed on a demonstration of high similarity to its reference product, while an interchangeable biosimilar clears a materially higher evidentiary bar, including, where relevant, switching studies designed to show that alternating or switching between the reference product and the biosimilar produces no greater risk in terms of safety or diminished efficacy than remaining on the reference product alone. Only an interchangeable biosimilar may, under most state pharmacy laws, be substituted at the pharmacy counter without a new prescription from the treating clinician, in a manner that mirrors, but is legally and scientifically distinct from, generic substitution. Since the first interchangeable designation was granted to an insulin glargine biosimilar in 2021, uptake of that designation has been slow and uneven, and dispensing behavior at the pharmacy level has changed only gradually and with substantial state-to-state variation [1].

This article synthesizes what the literature — regulatory analyses, real-world switching studies, pharmacist and physician surveys, and health-system implementation

reports — has established about how biosimilar substitution actually functions in ambulatory pharmacy care, and where the open problems remain. We organize the discussion around five themes: the regulatory foundations that define biosimilarity and interchangeability and that set the legal boundary of what a pharmacist may do without prescriber sign-off; the nocebo effect and the psychological and communication barriers that shape whether a substitution succeeds or is reversed; the accumulated real-world evidence on switching outcomes across therapeutic areas, from inflammatory bowel disease to oncology to insulin; the practice patterns that ambulatory and community pharmacists have developed, or struggled to develop, around counseling, documentation, and multidisciplinary coordination; and the policy and reimbursement levers, largely European in origin but increasingly relevant in the United States, that determine how much of the theoretical substitution opportunity is actually realized. We close with an honest account of where the evidence base still falls short of what a pharmacy director or health system needs to build a fully confident substitution program.

It is worth being explicit about what this article is and is not. It is not a report of new clinical or operational data collected by the authors; it is a synthesis of the published real-world evidence and practice literature on biosimilar substitution, written with an ambulatory pharmacy audience in mind. Where we cite a specific number — a switching rate, an uptake percentage, an adverse-event count — it is a number reported in the cited source, not an estimate of our own. Where the literature is thin or contradictory, we say so rather than paper over the gap.

2. Regulatory Foundations of Biosimilarity and Interchangeability

The interchangeability designation is the single most consequential regulatory concept for ambulatory pharmacy practice, because it is the concept that converts a biosimilar from "a product the prescriber may choose to prescribe" into "a product the pharmacist may substitute at the counter." McKinnon and colleagues' systematic review of the biosimilarity and interchangeability evidence base lays out the underlying scientific logic plainly: biosimilarity is established through a stepwise "totality of evidence" approach, beginning with extensive analytical characterization of structure and function, followed by animal and clinical

pharmacology studies, and, where residual uncertainty remains, comparative clinical efficacy and safety studies — with interchangeability requiring, in addition, dedicated switching studies that isolate the effect of alternating between products from the effect of the underlying disease course [2]. Their review is candid that once analytical similarity is established, the marginal scientific value of large confirmatory clinical trials is limited, a conclusion echoed by subsequent regulatory science commentary, but that switching-specific data has nonetheless remained the practical and legal precondition for pharmacy-level substitution in most jurisdictions.

In practice, interchangeability has not translated quickly into pharmacy-level substitution behavior even where it has been granted. Ling and colleagues' 2025 survey of pharmacists and physicians treating immunological disorders found substantial gaps in real-world familiarity with both the federal interchangeability designation and the patchwork of state interchangeable-biosimilar substitution laws, which differ in whether they require prescriber notification, patient consent, or specific record-keeping at the point of substitution [1]. This state-level heterogeneity is not incidental friction; it is a first-order determinant of whether a community pharmacist in one state can substitute an interchangeable biosimilar with a simple entry in the dispensing record, while a pharmacist one state over must first place a notification call to the prescriber's office, a step that, in a busy ambulatory practice, is often enough to make the substitution not worth pursuing on that particular fill.

Professional consensus statements have tried to bridge the gap between what the regulatory pathway technically permits and what clinicians are comfortable acting on. Kay and colleagues' task-force recommendations on the use of biosimilars in rheumatological disease, produced under the auspices of a major international rheumatology body, explicitly endorse switching to a biosimilar under physician supervision as scientifically justified given the accumulated evidence, while also recommending that any switch be accompanied by patient education and, where feasible, monitoring for loss of efficacy or new adverse events — guidance that in practice places much of the counseling and monitoring burden on the ambulatory pharmacy and clinic staff who see the

patient between prescriber visits [3]. Barbier and Vulto's more recent commentary on "the final hurdles" to interchangeability argues that the scientific case for interchangeability is, for most approved biosimilars, essentially already made by the biosimilarity data itself, and that the additional switching-study requirement functions less as a genuine scientific necessity than as a regulatory and, in their reading, partly political reassurance mechanism — a view that, if it gains traction, would have direct implications for how quickly the interchangeable-biosimilar category expands and, with it, how much pharmacy-level substitution authority becomes available [4].

3. The Nocebo Effect and Psychological Barriers to Substitution

If the regulatory framework defines what substitution is legally permitted, the nocebo effect is the single most studied reason why a legally permitted substitution can still fail clinically. The term describes a negative outcome — new or worsened symptoms, perceived loss of efficacy, a decision to discontinue — that arises not from any pharmacological difference between the reference product and the biosimilar, but from the patient's (or, less often discussed, the clinician's) negative expectation about the switch itself. Colloca, Panaccione, and Murphy's review of the clinical implications of nocebo effects for biosimilar therapy situates this squarely within the broader placebo/nocebo psychobiology literature, arguing that expectation effects are not a soft or dismissible confound but a measurable driver of treatment discontinuation that mitigation strategies — balanced, non-alarming communication about the switch; framing that emphasizes similarity rather than difference; and shared decision-making rather than a unilateral pharmacy-level swap — can meaningfully reduce [5].

The empirical literature on how large this effect actually is has converged on a fairly specific and somewhat reassuring pattern: open-label switching studies, in which both patient and clinician know a switch has occurred, report discontinuation and perceived-flare rates that are consistently higher than those seen in blinded switching studies of the same molecules, a gap that is difficult to explain on pharmacological grounds alone and that points squarely at expectation as the driver. Kristensen and colleagues, examining this specific pattern across several biosimilar switching

programs, describe it explicitly as a placebo effect attributable to the switch being non-blinded rather than to any detectable difference in the product itself [6]. Braun and colleagues' review, written for a rheumatology audience with direct responsibility for managing switch programs, reaches a similar conclusion and places particular emphasis on the clinician's own communication style and confidence in the biosimilar as a variable that shapes the patient's response as much as any written patient information leaflet does [7].

The most recent and most comprehensive treatment of this literature, Car and colleagues' 2024 systematic review of placebo mitigation strategies, synthesizes the intervention studies specifically — not just the observational evidence that a placebo effect exists, but the trials of what actually reduces it — and finds that structured, proactive communication interventions (a dedicated conversation about the switch, rather than a passive mention at pickup; written materials that explain biosimilarity in plain terms; and, in several of the more resourced settings reviewed, a dedicated pharmacist- or nurse-led switch consultation) are associated with lower rates of both perceived adverse effects and treatment discontinuation relative to standard, minimally structured switch communication [8]. This finding matters directly for ambulatory pharmacy practice because it identifies the pharmacist's counseling encounter, not the regulatory approval itself, as the point in the care pathway where a placebo-driven failure is most plausibly prevented — and it is corroborated at the point of care by Levivien and colleagues' study of a dedicated clinical pharmacist consultation embedded in a multidisciplinary rheumatology switch program, which reported that patients who received the structured pharmacist consultation had markedly lower rates of switch-related discontinuation than historical or comparator patients switched without that dedicated encounter [9].

4. Real-World Switching Evidence Across Therapeutic Areas

The clinical trial evidence for switching is, by design, narrow: a single switch, under close monitoring, over a defined follow-up window. Real-world evidence has increasingly filled in the picture of what happens with repeated switching, longer follow-up, and the heterogeneous patient populations and adherence patterns of ordinary ambulatory care, and the pattern

that emerges is broadly reassuring on safety while still showing meaningful minority rates of switch-back.

Table 1: Representative real-world and randomized switching studies relevant to ambulatory biosimilar substitution, with the scope and headline safety/efficacy finding each cited source reports. [10,11,12,13,14].

Study	Scope	Design	Reported Finding
NOR-SWITCH [10]	482 patients, multiple inflammatory indications, single switch to CT-P13	Randomized, double-blind, non-inferiority	Biosimilar non-inferior to continued originator on composite disease-worsening endpoint
NOR-SWITCH extension [11]	Same cohort, 52-week open-label follow-up after delayed switch	Open-label extension	Efficacy sustained and no new safety signal after switching
Herndon et al. meta-analysis [12]	44 switch periods, 31 studies, 21 biosimilars; 5,252 switch vs 5,770 no-switch patients	Systematic review and meta-analysis	Risk differences for death, serious adverse events, and discontinuation each ~0, no excess risk from switching
Zheng et al. meta-analysis [13]	10,812 inflammatory bowel disease patients, including repeated switches	Systematic review and meta-analysis	Comparable immunogenicity, efficacy, and safety between switched and non-switched cohorts
Erçalışkan et al. [14]	Real-world IV rituximab switching cohort in hematology practice	Real-world switching study	Efficacy and safety after switch consistent with pre-switch treatment course

The clearest single trial-based anchor for this evidence base remains the NOR-SWITCH study, a randomized, double-blind, non-inferiority trial that assigned patients on stable originator infliximab therapy across several inflammatory disease indications to either continue the originator or switch to biosimilar CT-P13, and found the biosimilar arm non-inferior on the composite primary endpoint of disease worsening [10]. The trial's open-label extension, in which patients originally randomized to continue the originator were then switched to the biosimilar and followed for an additional year, found sustained efficacy and no new safety signal attributable to the (by then, second) switch, a result that speaks directly to the ambulatory-practice-relevant question of whether one switch materially changes the risk calculus for a subsequent switch [11]. Herndon and colleagues' 2023 meta-analysis, conducted by FDA scientists and pooling 44 switch treatment periods across 31 studies and 21 different biosimilars — 5,252

patients in switching arms against 5,770 in non-switching control arms — reported essentially indistinguishable rates of death, serious adverse events, and treatment discontinuation between the two groups, with risk differences for each outcome close to zero and confidence intervals that excluded any clinically meaningful excess risk from switching [12]. Zheng and colleagues' 2025 meta-analysis, focused specifically on inflammatory bowel disease and pooling data across 10,812 patients, reached a concordant conclusion for that indication specifically, finding comparable immunogenicity, efficacy, and safety outcomes between switched and non-switched cohorts even where switching occurred more than once [13].

Two other therapeutic areas illustrate how this pattern generalizes, and where it does not fully answer the practical ambulatory question. In hematology-oncology, Erçalışkan and colleagues' real-world study of switching intravenous rituximab therapy — an infusion-center rather than retail-pharmacy setting, but one with substantial ambulatory pharmacy involvement in preparation, scheduling, and patient counseling — reported efficacy and safety outcomes after the switch that were consistent with the pre-switch treatment course, adding to a growing body of oncology-specific switching evidence that has generally mirrored the inflammatory-disease findings [14]. In endocrinology, the picture is less about switching outcomes and more about substitution uptake itself: since insulin glargine became the first interchangeable biosimilar in 2021, dispensing-level studies have tracked how much of the theoretical substitution opportunity pharmacies have actually captured, a question that sits at the intersection of clinical evidence (which is reassuring) and operational and payer-driven factors (which, as the next two sections describe, have been the binding constraint far more often than clinical uncertainty).

It is also worth noting what these pooled figures do and do not tell an ambulatory prescriber or pharmacist about any single patient in front of them. A risk difference of essentially zero across thousands of pooled patients is a population-level statistic, built from studies that themselves varied in disease indication, switch frequency, and follow-up duration; it is reassuring evidence that switching is not, on average, hazardous, but it is not a guarantee that any individual patient's subjective response to a switch will track the average.

Ambulatory pharmacists reading these pooled results should take from them a defensible baseline expectation to set with a patient before a switch, not a promise that no patient will ever report a change in how they feel afterward.

Two caveats belong here alongside the reassuring headline numbers. First, essentially all of the large switching meta-analyses pool studies with a single or, at most, a small number of switches; genuinely long-run, multi-switch, multi-year ambulatory data — the pattern a patient on a chronic biologic might actually experience over a decade of formulary changes — remains comparatively sparse, a point Zheng and colleagues note explicitly as a limitation of even their relatively large pooled IBD cohort [13]. Second, "no significant difference in aggregate safety outcomes" is a population-level statement; it does not rule out that some individual patients experience genuine, clinically meaningful non-response or intolerance after a switch, and the aggregate reassurance from the meta-analyses is entirely compatible with ambulatory pharmacists and clinicians continuing to see, and needing to manage, individual switch-related complaints that do not show up as a signal in a pooled risk difference.

5. Pharmacist and Ambulatory Care Practice Patterns

The clinical evidence base on switching safety is, as the previous section shows, reasonably mature. The practice-level evidence on how ambulatory and community pharmacists actually operationalize substitution is considerably thinner, and what exists paints a picture of a workforce that is broadly supportive of biosimilars in principle but underprepared in specific, addressable ways.

Arnet and colleagues' multinational survey of community pharmacists' preparedness for substituting biologics and dispensing biosimilars, spanning several European countries plus comparator settings, found that while most surveyed pharmacists reported general familiarity with the concept of a biosimilar, a substantial share reported low confidence in explaining the difference between biosimilarity and interchangeability to a patient, and an even larger share reported that their pharmacy lacked a standardized counseling protocol or patient-information resource specific to biosimilar substitution, as opposed to the well-established generic-substitution counseling scripts most

pharmacies already had in place [15]. A country-specific instance of the same pattern is visible in Barbier and colleagues' survey of Belgian community pharmacists and physicians in ambulatory care, which found that self-reported knowledge of biosimilars correlated only weakly with confidence in actually counseling a patient through a substitution, and that physicians and pharmacists frequently disagreed about who was responsible for initiating that conversation in the first place — a coordination gap that, left unresolved, tends to mean the conversation happens late, incompletely, or not at all [16]. This gap between conceptual familiarity and practical readiness recurs across the survey literature: Ling and colleagues found a comparable pattern among United States pharmacists specifically around the interchangeability designation and state substitution law, with many respondents uncertain about their own state's notification requirements — a gap with direct legal, not merely educational, consequences, since a pharmacist who substitutes without following the applicable notification procedure may be out of compliance regardless of the clinical soundness of the substitution itself [1].

Where health systems have invested specifically in structured biosimilar-switch programs, the results have been more encouraging, suggesting the readiness gap is addressable rather than intrinsic to the pharmacy workforce. Bhardwaja and colleagues describe an integrated health system's experience implementing systematic biologic-to-biosimilar switching, in which a coordinated pharmacy-led program — encompassing prescriber notification, patient education materials, and structured follow-up — achieved high rates of successful, sustained switching across several therapeutic classes with a low rate of clinician-initiated switch-backs, a result the authors attribute directly to the structure of the program rather than to any property of the specific biosimilars involved [17]. Levivien and colleagues' rheumatology-specific pharmacist consultation model, discussed above in the nocebo context, is a narrower but methodologically cleaner version of the same finding: a dedicated pharmacist touchpoint, built specifically around the switch rather than folded into routine dispensing, measurably improved switch persistence [9]. Read together, these implementation studies suggest that the limiting factor in ambulatory substitution success is less often the biosimilar's clinical profile than the presence or absence

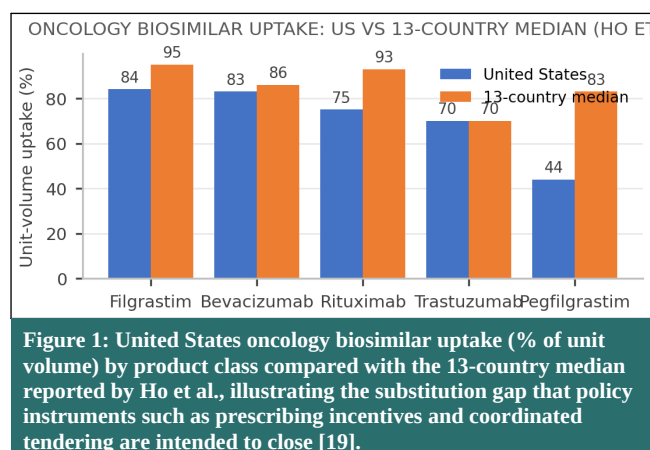
of a structured counseling and follow-up process around the switch — precisely the kind of process an individual retail pharmacy, absent system-level investment, may struggle to build on its own for every biosimilar-eligible product that reaches its shelves.

Sosulski's brief overview of biosimilars for a pharmacist audience captures the practical stakes of this gap concisely, framing biosimilar familiarity and counseling competence as a core professional-development priority for community pharmacy specifically, on the grounds that pharmacists, more than any other clinician in the ambulatory pathway, are positioned to have the substitution conversation at the exact moment — dispensing — when a patient's uncertainty about a changed product is most acute [18].

6. Policy Levers and Economic Drivers of Substitution

Clinical reassurance and workforce readiness are necessary but not sufficient conditions for substitution to occur at scale; reimbursement structure and formulary policy have, in the comparative literature, been shown to matter at least as much, and the cross-national variation in biosimilar uptake is large enough that it cannot be explained by clinical evidence differences, since the underlying clinical data is largely shared across jurisdictions.

Ho and colleagues' 2025 global analysis of oncology biosimilar uptake makes this variation concrete. Comparing thirteen countries, they found the United States ranked tenth in overall biosimilar uptake, at 75% of unit volume and only 58% of spending on biosimilar-eligible oncology biologics, against a median across the thirteen countries of 86% by units and 76% by spending; product-level uptake in the United States ranged from 84% for filgrastim down to just 44% for pegfilgrastim, against cross-country medians of 95% and 83% respectively for those same products, with Norway, Italy, and Sweden posting the highest uptake and New Zealand, Japan, and Belgium the lowest [19]. The authors estimate that the United States spent \$8.4 billion on these biologics during the study period, a figure that frames the uptake gap not as an abstract policy inefficiency but as a specific, quantifiable pool of unrealized savings.



The European policy literature offers the clearest account of what drives the high end of that range. Vogler and colleagues' review of policies to encourage biosimilar use across European countries catalogs the instruments in active use — demand-side measures such as prescribing quotas and gain-sharing arrangements that let prescribers or health systems retain part of the savings from biosimilar use, supply-side tendering that awards exclusive or preferred formulary status to the lowest-priced biosimilar in a therapeutic class, and, in several countries, pharmacy-level automatic substitution rules that function much closer to generic substitution than the more conservative American interchangeability framework — and finds that countries combining several of these levers simultaneously achieve the highest uptake [20]. Machado and colleagues' more recent systematic review of European biosimilar policy instruments reaches a similar structural conclusion while cataloging substantial heterogeneity in exactly which instruments individual countries have adopted, underscoring that "biosimilar policy" is not a single lever but a bundle of largely independent choices about pricing, tendering, prescribing incentives, and substitution rules that each country has assembled somewhat differently [21]. Lobo and colleagues' 2025 scoping review focuses specifically on individual prescriber-level incentives — financial gain-sharing tied to a prescriber's own biosimilar prescribing rate, in several European systems — and finds this instrument specifically, as distinct from system-level tendering, associated with faster uptake in the settings where it has been studied, a finding with direct relevance to United States value-based and accountable-care arrangements that are only beginning to experiment with comparable prescriber-facing incentives [22].

The comparative picture that emerges is that the United States sits at an unusual point in the policy space: it has, since 2021, a scientifically rigorous interchangeability pathway that in principle permits pharmacy-level substitution without prescriber intervention, but it lacks most of the demand-side and supply-side policy instruments — gain-sharing, prescribing quotas, coordinated tendering — that the European experience associates with high uptake, and it layers on top of that a patchwork of state substitution laws whose notification and documentation requirements add friction the European automatic-substitution regimes largely avoid. The clinical evidence reviewed in the preceding sections gives no reason to think the ambulatory substitution opportunity in the United States is clinically constrained; the comparative policy evidence strongly suggests it is instead constrained by the absence of the specific economic and procedural levers that have driven uptake elsewhere.

7. Open Challenges

Several gaps recur across the literature synthesized here and deserve to be named plainly rather than glossed over. First, the real-world switching evidence, while reassuring in aggregate, remains concentrated in a relatively small number of well-studied molecule classes — anti-TNF biologics, rituximab, and, to a lesser extent, insulin — with much thinner data on newer and more structurally complex biosimilar classes as they reach the market; extrapolating the reassuring pooled safety findings from Herndon et al. and Zheng et al. to every future biosimilar approval is a reasonable working assumption, not an established fact for products not yet studied at comparable scale [12,13]. Second, essentially none of the nocebo-mitigation intervention literature has been conducted specifically in the retail or community pharmacy setting; Car and colleagues' systematic review draws its strongest evidence from structured clinic-based consultation models, and whether a comparable counseling intervention is feasible within the time and staffing constraints of a typical retail pharmacy encounter is, to our knowledge, essentially untested [8].

Third, the pharmacist-preparedness survey literature is itself geographically uneven — the most detailed multinational preparedness data comes from Arnet and colleagues' European-centered survey, while the most detailed United States-specific data, from Ling and

colleagues, focuses narrowly on immunological-disease biosimilars, leaving a real gap in understanding whether the readiness pattern generalizes across therapeutic classes within American ambulatory pharmacy [15,1]. Fourth, and perhaps most consequentially for United States policy, there is essentially no controlled or quasi-experimental evidence isolating the effect of any single American policy lever on ambulatory dispensing behavior; the comparative international evidence from Vogler et al., Machado et al., and Lobo et al. is associational and cross-national, and translating a European finding into a confident prediction about a specific American policy change requires an inferential leap the current literature does not fully support [20,21,22]. Fifth, longitudinal, multi-switch ambulatory data that follows the same patients through several sequential formulary-driven product changes over years remains sparse across every therapeutic area reviewed here, and is arguably the single most practice-relevant evidence gap given how often ambulatory patients on chronic biologic therapy will, in practice, experience more than one switch over the course of treatment.

None of these gaps undermines the core, well-supported conclusion that biosimilar substitution is clinically sound; they are, read together, a fairly specific agenda for pragmatic, ambulatory-setting research that would let pharmacy leadership build substitution programs on direct rather than extrapolated evidence.

8. Conclusion

The literature reviewed here supports a reasonably confident, if qualified, claim about biosimilar substitution in ambulatory pharmacy care: the clinical case for switching is well established and consistent across the therapeutic areas that have been studied at scale, from the randomized NOR-SWITCH evidence in inflammatory disease through the large pooled meta-analyses spanning dozens of biosimilars and thousands of patients [10,12,13], while the practical, everyday success of a substitution program depends far more on factors outside the molecule itself: whether a state's substitution law makes the pharmacist's path to dispensing an interchangeable product straightforward or burdensome [1], whether the patient receives a structured, confidence-building conversation about the switch rather than a passive notice at pickup [5,8,9], and whether the surrounding reimbursement and formulary system rewards, rather than merely permits, the

substitution [19,20,21].

For ambulatory pharmacy practice specifically, this synthesis points toward a fairly concrete set of priorities that does not require waiting on new clinical trials: building a standardized, biosimilar-specific counseling protocol comparable in rigor to the counseling scripts pharmacies already maintain for generic substitution [15]; ensuring pharmacist and technician staff have current, state-specific knowledge of interchangeability and substitution notification requirements rather than general biosimilar familiarity alone [1]; and treating the switch conversation itself, not merely the underlying regulatory approval, as the clinical intervention that determines whether a scientifically sound substitution succeeds in practice. The remaining scientific uncertainty is real but narrow, concentrated in newer product classes, retail-specific counseling feasibility, and the causal effect of individual American policy instruments — a narrower and more tractable research agenda than the field faced a decade ago, when the foundational biosimilarity science itself was still being established, and one that ambulatory pharmacy is now well positioned to help answer directly rather than by extrapolation from hospital-based or European evidence alone.

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Ethical Approval

Not applicable. This article synthesizes previously published literature and did not involve human participants, animal subjects, or the collection of primary clinical data by the authors.

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