Biosimilar Prescribing Incentives: Results of a French Pilot of Gainsharing Between Hospitals and the National Health Insurance

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Abstract – This article evaluates an incentive for hospital prescriptions of biosimilars delivered in retail pharmacies, whereby gains are shared between hospitals and the French NHI and incentives are directly redirected to prescribing units. Using SNDS data, we compare the pre- and post- biosimilar prescription rates of treated public hospitals with those observed at similar facilities. Between October 2018 and September 2021, the pilot led to an increase in biosimilar use for insulin glargine (+6.0 percentage points) and etanercept (+10.8 ppt). The pilot generated 0.5% cost savings for insulin glargine and 0.1% for etanercept. Cost savings for the French NHI are modest even though the incentive dramatically boosted biosimilar use. The fact that medication price changes outpaced the rate at which incentives are adjusted is the primary reason for this, in addition to deadweight loss effects.

JEL: I18, D04, D61
Keywords: pilot, pay-for-performance, biosimilars, hospital, difference-in-differences

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Medicinal products are one of the largest items in the French healthcare budget, with costs of medication dispensed by retail pharmacies totalling €31 billion in 2021, or 14% of all healthcare expenditure (Arnaud *et al.*, 2022). Public authorities have controlled the prices of reimbursable medicinal products and adjusted reimbursement rates in order to restrict the impact of this increasing burden of spending on social security accounts. These two regulation methods preceded a third, which was introduced in the late 1990s, through which the French state encouraged the use of generic medicinal products and attempted to change physician prescribing behaviours (Lancry, 2007). The rise of generics has curbed the increase in medicinal product spending, to some extent, and now the emergence of biosimilar medicines harbours similar potential for substantial costs savings. In the same way that generics are therapeutically equivalent to chemical brand-name medicines, biosimilars are equivalent to brand-name biologics (or reference biomedicines).[1] A policy to boost biosimilar use was therefore introduced in the mid-2010s in a context of soaring spending on biological drugs: these accounted for €4.4 billion and more than 20% market share of outpatient medicinal products in 2018 (Dahmouh, 2019). In conjunction with lapsing biologic patents, the emergence of biosimilars provides a more diverse supply network and opens up major saving potential for the *Assurance Maladie* (French National Health Insurance, NHI), which are necessary to pursue the funding of medicinal innovations (Box 1).

Prescribing behaviours in hospitals, including for medicinal products provided in retail pharmacies, greatly determines the expansion of biosimilars. It is in the hospitals' interests to negotiate optimal terms when purchasing medicinal products to be dispensed by their internal pharmacies and therefore minimise costs. However, there is no automatic incentive for hospitals to prescribe less expensive biosimilars for medications dispensed by retail pharmacies. Physicians choose not to prescribe biosimilars for many reasons, regardless of whether they work in hospitals or primary care facilities. They may be more accustomed to prescribing brand-name drugs that are more established and reputable, or they may expect their patients to be reluctant to switch treatments or receive biosimilars. Without any incentive being put in place, maintaining the status quo remains the simplest approach for physicians to adopt. However, prescriptions issued by hospital practitioners have a heavy influence on retail pharmacies, given that hospital prescriptions of medicinal products dispensed by these pharmacies (*Prescriptions Hospitalières de Médicaments Exécutées en Ville*, or PHMEV) account for nearly a third of the reimbursable outpatient medicinal product market. There are also a number of biologics for which hospital practitioners are exclusively authorised to commence treatment (Dahmouh, 2019). GPs also tend to prescribe whatever product has been selected by the prescribing hospital physician when they provide patient follow-up. If physicians are authorised to switch from one biologic to another from the same biologically equivalent group, primary care practitioners will generally continue the treatment initiated in the hospital. The impact of this behaviour is even greater for long-term treatments (Gallini *et al.*, 2013). It is also worth noting that, while pharmacists can substitute generic medicinal products, they are not allowed to substitute biological medicinal products in the general case.[2]

To encourage hospitals to prescribe biosimilars for outpatient use, an incentive scheme

1. A biological process is used to derive the active substance in biologics (animal-produced protein, complex formulation derived from a bacterium, etc.). This ultimately produces compounds of greater complexity than those found in non-biological medicinal products, which are generally the product of simple chemical synthesis. Examples of biologics include antibodies, hormones, growth promoters and many vaccines.

2. In 2022, following the recommendation issued by the ANSM (the French National Agency for the Safety of Medicines and Health Products), the French Social Security Financing Act introduced the first two groups of substitutable biosimilars: filgrastim and pegfilgrastim (ANSM, 2022 – Ministerial Decree of 12 April 2022, OJ of 14 April 2022).

Box 1 – **Price Cuts in Hospital and Retail Pharmacies Following the Introduction of Biosimilars**

When patents lapse for biologics and their therapeutically equivalent biosimilars are introduced onto the market, a series of price cuts for the reference medicinal product, other biomedicines with similar therapeutic indications, and any associated biosimilars is triggered by means of competition and regulatory measures. In France, the national price-setting authority marks down reference biomedicine prices and sets lower prices for their biosimilars in retail pharmacies. Hospitals and hospital procurement groups are encouraged to tap into the competitive environment to negotiate discounts from their suppliers. These negotiations also give the authority responsible for setting retail pharmacy prices an indication of the medicinal product reserve price for future price cuts, thereby minimising the risk of the product being withdrawn from the market (Robinson & Jarrion, 2021).

was introduced into French common law on January 1st, 2018, whereby prescribing hospitals receive 20% of the price difference between the reference drug and the biosimilar[3] for every biosimilar delivered in retail pharmacies from these hospital prescriptions. This article examines a pilot scheme that ran from October 2018 to September 2021, the purpose of which was to trial a higher financial incentive (30%) which would also be intended to be redirected directly to hospital's prescribing unit(s). The scheme focused on two formulations upon its launch in 2018 – insulin glargine, a slow-release long-acting insulin, and etanercept, which is primarily used to treat inflamed joints. Both formulations have been available as biosimilars since 2016.

To measure the causal effect of the pilot on biosimilar use, we use exhaustive administrative data from SNDS (*Système National des Données de Santé*, French National Health Data System) and compare changes in biosimilar prescription rates among healthcare facilities in the pilot (treatment group) with similar facilities (control group), comparing the results obtained before and after the pilot (difference-in-differences model). Throughout the three-year pilot phase, we find that facilities receiving the incentive had a higher share of biosimilar prescriptions delivered in retail pharmacies for insulin glargine (+6.0 percentage points) and etanercept (+10.8 percentage points). These results are similar to the 9.7 percentage point increase estimated for etanercept following an evaluation of the first two years of the pilot using survey data (Tano *et al.*, 2023). We complement this study using exhaustive data to analyse the effect of the pilot on a second formulation, and we run the analysis over the entire three-year phase of the pilot. We also estimate the pilot's cost-effectiveness, considering all hospital prescription expenditure, including follow-up prescriptions by primary care physicians. All French NHI costs incurred as a result of the pilot (i.e. to cover incentives and the reimbursement of prescribed medicines) are compared with the costs that would have been incurred in the absence of a pilot, in order to assess the pilot's efficiency. We assume that the pilot does not affect effectiveness because biosimilars are therapeutically equivalent to their reference biomedicines. Our estimates indicate that the pilot would yield saving rates of 0.5% for insulin glargine and 0.1% for etanercept, modest savings for the French NHI. The pilot's design leads to reimbursement savings if there is a switch between biosimilars and reference biomedicines, such savings decreasing proportionally with the financial incentive rate, and to deadweight losses, which are a source of additional expenditure linked to incentives. The pilot's cost-effectiveness is dependent on the relative magnitude of these two counteracting effects. First, medication price changes outpace the rate at which incentives are adjusted. This can lead to higher financial incentives, reducing the profit that the French NHI gains from prescriptions of biosimilar medicines that are cheaper than reference biomedicines (substitution effects). Secondly, over the course of the pilot phase, biosimilars use for both formulations strongly increased, achieving a breakthrough comparable to previous biosimilars during their first few years on the market (Gouvernement, 2022). This led to more significant deadweight loss effects over time, since the higher incentive applies to all prescriptions, including those that would have been issued outside of a pilot.

This article contributes to the literature that examines pay-for-performance (P4P) arrangements for healthcare professionals. Since the 2000s, performance and quality-based payment programmes aiming to improve inpatient and outpatient care quality and effectiveness have been developed in several countries. Based on a summary of 14 programmes across 16 European countries and their evaluations, the OECD concluded that the programmes appear to have a moderate impact on process indicators (such as participation in programmes to help people stop smoking or manage diabetes). However, those evaluations do not reveal any progress in terms of health outcomes or healthcare security and the OECD found that their cost-effectiveness was inconclusive or even unfavourable (Eckhardt *et al.,* 2019).

In France, a target-based remuneration programme rolled out for primary care physicians[4] in 2012 features efficiency indicators in addition to quality indicators (Bras, 2020). The *Contrat d'Amélioration de la Qualité et de l'Efficience des Soins* (Contract for improved

3. The term "biosimilar" is used in this article for reasons of clarity despite the fact that the term is a misnomer since the pilot encourages prescriptions of cost-efficient biologics within comparable medicine *classes that do not necessarily correlate to the groups of* biosimilar *medicines as defined by the French Public Health Code (Decree of 31 March 2022 amending the Decree of 19 April 2021 on the pilot project to encourage hospital prescriptions of biologics dispensed by retail pharmacies – Légifrance, legifrance.gouv.fr).*

*4. The current programme is the ROSP (*Rémunération sur Objectifs de Santé Publique*, or Remuneration based on Public Health Objectives), which replaced the CAPI (*Contrat d'Amélioration des Performances Individuelles*, or Contract for Improving Individual Practices). In 2023, the ROSP is based on 29 indicators, 20 of which are quality scores (8 indicators for monitoring patients with chronic conditions, 12 indicators for prevention) and nine of which measure the efficiency of prescriptions.*

healthcare quality and efficiency, CAQES) is a P4P agreement for clinical facilities established in 2016 and which introduced an annual incentive when these meet fixed targets, including gainsharing agreements on healthcare savings. There are very few evaluations of these measures in France and the few existing studies focus on specific aspects of the programmes for primary care practitioners. No studies focus on the CAQES for clinical facilities. These studies have found no impact of these incentives on the quality of care or the uptake of preventive measures (Saint-Lary & Sicsic, 2015; Constantinou *et al.*, 2016; Sicsic & Franc, 2017). The only evaluation relating to prescription behaviour found that the incentives had a positive yet limited impact on benzodiazepine prescriptions (Michel-Lepage & Ventelou, 2016). Current quality and performance-based payment arrangements may hold a certain symbolic and educational value, yet their effectiveness remains somewhat inconsistent (Bras, 2020).

In France, the framework for structural innovation in healthcare ("Article 51" of the 2018 French Social Security Financing Act) allowed pilots to test funding methods that deviate from French common law. This framework creates the conditions to test the effectiveness of innovative financing solutions in a pilot and to perform evidence-based analyses prior to wider scaling. The pilot in which hospital are incentivised to prescribe biosimilars that are delivered in retail pharmacies was the first large-scale project of its kind to be carried out at the national level. Underpinned by a model of incentives that scale up based on the number of prescriptions issued, the pilot also focuses on hospital physicians, in that a percentage of the savings made in outpatient facilities as a result of the prescriptions issued by the physicians is filtered back to their hospital units directly. Another distinguishing feature of the pilot is that it is being trialled using a sample of facilities to establish a control group. This article expands on the existing literature by providing a quantitative evaluation of the impact of incentives on biosimilar prescriptions, measures the pilot's effect by using a counterfactual to compare pre- and post-pilot biosimilar prescribing patterns, and additionally includes an analysis of the pilot's cost-efficiency.

After setting out the pilot's principles and procedures in Section 1, we describe the empirical strategy followed to assess the pilot's effect and cost-efficiency for its first two formulations – insulin glargine and etanercept (Section 2) – and the data used (Section 3). We present the findings (Section 4) and conclude by discussing their limitations and implications.

1. Overview of the Pilot

Improved biosimilar uptake rates are one of the objectives of the 2018–2022 French national health strategy (*Stratégie nationale de santé*, SNS), which targeted a biosimilar uptake rate of 80% among prescriptions for biologics where a biosimilar is available, by 2022. A pilot was therefore launched in 2018 to encourage higher rates of biosimilar prescriptions for two formulations that are commercially available in pharmacies both within hospitals and in outpatient settings:

- insulin glargine: a slow-release long-acting insulin used to treat diabetes, which, despite being relatively affordable (average price of €45 (2018–2021) per standard box of the leading insulin glargine medication), is taken by many patients;
- etanercept: an anti-TNF immunosuppressive agent used to treat skin conditions such as psoriasis, or inflamed joints. A standard box of the leading etanercept medication costs €675 on average (2018–2021).

These two products are distinctive because they are prescribed in hospitals but mainly used on in outpatient settings and, having generated pre-tax sales revenue of €182 million (etanercept) and €145 million (insulin glargine) in the outpatient market in 2018, are the second and third most lucrative biologics among those with a commercially available biosimilar (Dahmouh, 2019).

When the pilot began in 2018, insulin glargine and etanercept biosimilars had respective penetration rates of 41% and 30% in the hospital market, and 13% and 14% in the outpatient market. The proportion of biosimilars among biologics for which a biosimilar is available increased from 16% to 32% in outpatient settings between 2018 and 2021 (Sécurité sociale, 2019; 2022). While hospitals receive incentives to switch to biosimilars to cut their medicine procurement costs, the limited penetration of biosimilars in the outpatient market may be explained by the relatively recent introduction of the incentives for primary care practitioners and hospitals to include biosimilars among prescriptions delivered in retail pharmacies.

Primary care practitioners in outpatient facilities are incentivised to prescribe biosimilars under the ROSP. The programme has a set target rate for biosimilar prescriptions. Insulin glargine was

the only formulation covered in 2017,[5] but others were included in 2022.

On January 1st, 2018, French common law introduced a financial incentive for healthcare institutions under the CAQES.[6] For eligible formulations, each clinical facility receives approximately 20% of the price difference[7] between the reference biomedicine and its biosimilar for each box prescribed by its physicians and delivered in retail pharmacies (PHMEV). However, this also applies to drugs prescribed by primary care practitioners providing patient care follow-up by continuing treatment with a biosimilar originally prescribed by a hospital physician. The hospital's legal entity is the final recipient of the incentive, which the *Agence Régionale de Santé* (Regional Health Agency, ARS) pays out on an annual basis.

A pilot initiated within the Healthcare Innovation Framework ("Article 51" of the 2018 French Social Security Financing Act[8]) aimed to trial a more extensive system of incentives for hospital units that rewards the latter for prescribing biosimilars that are delivered in retail pharmacies. There are two ways in which this initiative deviates from French common law. First, it duplicates the incentives provided for by the CAQES, albeit with a payment of approximately 30%[9] of the savings made by the French NHI as a result of a hospital's prescriptions, rather than the original 20%. Secondly, the terms of the pilot specify that any funds that a facility receives must directly accrue to its prescribing unit(s), in accordance with a framework defined by the facility (equipment, seminars or research, training, etc.), with the specific aim of promoting greater uptake of biosimilar medicines.[10] The pilot therefore provides a higher financial payout than the CAQES and also has an organisational aspect whereby the aim is to reward units for driving change. Application of the pilot is non-concomitant with application of the CAQES.

The principle behind this incentive-based pilot scheme was announced in early 2018, when the CAQES[11] was introduced, and the terms of the scheme were communicated in the decree concerning the pilot, issued on August 3rd, 2018.[12] The pilot start date was set for October 1st, 2018 for insulin glargine and etanercept, for an initial period of 3 years, for all selected clinical facilities.[13]

Following a call for submissions issued in the decree concerning the pilot, clinical facilities with an interest in applying and being selected were given a one-month deadline by which to submit their application files. Applications could be made for both target formulations, or just a single formulation. Evaluation of the files was delegated to the regional health agencies, which scored the files based on various criteria – the quality of biosimilar promotion measures already undertaken or planned for the future, the quality of the internal incentive-based scheme, and the target volume of biosimilar prescriptions, particularly for the target formulation. The French *Direction de la sécurité sociale* (Directorate of Social Security, DSS) and *Direction générale de l'offre de soins* (General Directorate of Healthcare Services) proceeded to select clinical facilities using the criteria and rankings of the regional health agencies as their primary source. However, consideration was also given to ensuring that hospitals were selected in such a way that a geographically consistent network covered mainland France.

The list of accepted facilities was notified in an order issued on October 2nd, 2018:[14] Of the 42 facilities that applied for insulin glargine, 23 were selected, and 40 of the 63 facilities that applied for etanercept were selected. Given that some hospitals were selected for both formulations, the pilot includes 45 different facilities in total (four facilities are geographical entities belonging to the AP-HP conglomerate of hospitals operating in Île-de-France). The selected facilities cover all 12 regions of mainland France. The whole pilot was extended in 2022.[15]

The pilot's stated aim was to increase by 15 percentage points the share of biosimilar prescriptions in treatment group facilities

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5. Initially 20% in 2017, the target biosimilar prescription rate was set at 40% of the total boxes prescribed in 2020. GPs that meet this 40% target gain 30 of the 940 points available under the ROSP, i.e. 3.2% of the total score. New entries have been added to the list of active substances qualifying for the programme since January 2022.

6. Decree of 19 March 2019 on the efficiency and relevance of hospital prescriptions of biosimilar medicines dispensed in retail pharmacies (https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000038268137).

7. Amounts are set by decree and vary according to the dosage on each box. The incentive rate may therefore vary over time to reflect any medicinal product price fluctuations.

8. Trials and innovation to improve care standards – French Ministry of Health and Prevention – https://sante.gouv.fr/systeme-de-sante/parcours-des-patients-et-des-usagers/article-51-lfss-2018-innovations-organisationnelles-pour-la-transformation-du/article-51

9. Under the pilot, amounts are also set by decree and vary according to the dosage on each box.

10. In reality, units primarily used the funds to purchase equipment, hire new staff, fund treatment programmes or improve financial standings.

11. Directive DSS/1C/DGOS/PF2/2018/42 of 19 February 2018. https://solidarites-sante.gouv.fr/fichiers/bo/2018/18-03/ste_20180003_0000_p000.pdf

12. https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000037316661

13. In early 2019, the pilot was expanded to include adalimumab, and this prompted a new selection phase in which 40 facilities were chosen from 78 applicants. (Decree of 12 February 2019 – https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000038129827).

14. https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000037477126

15. The Decree of 31 March 2022 extends the pilot project until September 2022. https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000045462658

compared to control group facilities. Biosimilars for insulin glargine and etanercept were widely available when the pilot launched and the biosimilar uptake rate for these two formulations increased sharply over the pilot phase, reflecting the trend observed for older biosimilars, which made a similar breakthrough during their first few years on the market (Gouvernement, 2022).

2. Empirical Strategy

2.1. Impact of the Pilot on Hospital Biosimilar Prescriptions

The empirical strategy initially aims to measure the pilot's effect on the rate of biosimilars. The rate of biosimilars among all PHMEV prescriptions issued by each hospital for a given formulation is the indicator of interest in order to capture the prescribing behaviours of hospital physicians, as it conveys the choice between the reference biomedicine and the biosimilar made by a hospital physician when writing a prescription. This rate, which is between 0 and 1, can be used to compare facilities, provides insight into the potential scope for improvement, and is independent of treatment durations and prescribed volumes.

It is possible to calculate this indicator over each period, provided that facilities prescribe a formulation on at least one occasion. As a result, we first verify that participation in the pilot has no bearing on the decision to prescribe the formulation. When modelling the probability that facilities record at least one prescription for the (reference biomedicine or biosimilar) formulation, the treatment effect is null for both insulin glargine and etanercept (model shown below in Table 1). We therefore subsequently focus exclusively on facilities that prescribe each of the formulations.

We use a difference-in-differences method to estimate the causal effect. The purpose is to use a time-series comparison of facilities in the treatment group and control group to estimate the pilot's effect. Selection of facilities in the treatment group is not random because they are all voluntary and have been selected after having submitted an application. In order to account for this as accurately as possible, we apply a doubly robust method to control for selection bias based on observed characteristics. This combines estimates for a propensity score and a conditional expectation (Sant'Anna & Zhao, 2020) (Box 2). However, selection bias cannot be completely eliminated and may also depend on unobserved characteristics of the facilities to some extent.

An advantage of this method is that it can be used to estimate a treatment effect for each month and consequently analyse the effect's dynamics as well as to estimate the mean effect over the entire treatment period. It makes it possible to ascertain whether the incentive appears to prompt temporary or sustained changes in prescribing patterns (over a 3-year period).

2.2. Efficiency Calculation Method

As biosimilars are therapeutically equivalent to their reference biomedicines, we assume that switching to a biosimilar from a reference biomedicine does not affect efficacy and that a cost analysis is sufficient to analyse efficiency.

The pilot is efficient if it generates positive net savings for the French NHI. French NHI expenditure incurred as a result of PHMEV for insulin glargine (or etanercept) issued by facilities in the pilot must therefore be subject to a comparison for pilot and non-pilot situations.

For both of these formulations, this expenditure consists of NHI reimbursements for medicines (reference biomedicines and biosimilars) and incentives to prescribe biosimilars. To quantify the differential for total pilot and non-pilot expenditure, it is compared with expenditure that would have arisen for treatment group facilities had there been no pilot.

A counterfactual value for the number of dispensed boxes of reference biomedicines and

Table 1 – **Effect of the treatment on the probability for facilities to record at least one prescription for the (reference biomedicine or biosimilar) formulation**

y	Insulin glargine			Etanercept		
	Effect	Standard error	p-value	Effect	Standard error	p-value
(ordo>0)	−0.01	0.06	0.99	−0.01	0.13	0.91

Notes: Linear regression estimate of the average effect of the pilot on the probability that the (reference biomedicine or biosimilar) formulation is prescribed on at least one occasion after its launch. This is calculated by comparing it with values for September 2018, the month immediately prior to the pilot's launch.
Sources and coverage: SNDS 2017–2021, SAE 2019 (facility categories); public facilities that include at least one hospital complex, long-term nursing home or healthcare cooperation association. PHMEV for insulin glargine and etanercept.

Box 2 – **The Econometric Model**

The econometric model uses the doubly robust method, which combines both an estimated propensity score and conditional expectation (Sant'Anna & Zhao, 2020).

First, it models the probability for facilities to be selected for the pilot using a logit model-derived propensity score (see Appendix A1). Non-treated clinical facilities are weighted in the calculation using this probability, with higher weightings being assigned to facilities with the highest selection propensity score. All non-selected clinical facilities are therefore included in the control group used for the estimate, albeit with a higher weighting if they are more likely to be selected[(a)]. The propensity score method is better suited than linear regression with the inclusion of covariates due to the high disparity between treated and non-treated facilities in terms of the variables observed, which increases the risk of omitted-variable bias[(b)].

Secondly, the conditional expectation of changes in the explained variable for the control group is estimated using an outcome regression. Calculating the "doubly robust" estimator then allows for the explained variable changes and propensity score to be modelled in order to obtain a more robust estimator than if the approaches were followed in isolation (Sant'Anna & Zhao, 2020)[(c)]. Estimates are made in R using the package (https://cran.r-project.org/web/packages/did/vignettes/did-basics.html) developed by Callaway and Sant'Anna (2021).

Strictly speaking, the average treatment effect on the treated $\boldsymbol{ATT}$ is estimated as follows:

$$\boldsymbol{ATT}(t) = \boldsymbol{E}\left[\left(\frac{\boldsymbol{G}}{\boldsymbol{E}[\boldsymbol{G}]} - \frac{\frac{p(X)C}{1-p(X)}}{\boldsymbol{E}\left[\frac{p(X)C}{1-p(X)}\right]}\right)\left(\boldsymbol{Y}_t - \boldsymbol{Y}_{T0-1} - \boldsymbol{E}\left[\boldsymbol{Y}_t - \boldsymbol{Y}_{T0-1} \mid \boldsymbol{X}, \boldsymbol{C}=1\right]\right)\right]$$

where $\boldsymbol{Y}_t$, the explained variable, is the rate of biosimilar prescriptions among prescriptions written by a facility in month $\boldsymbol{t}$, $\boldsymbol{G}$ is a dummy that indicates whether a facility is included in the treatment group, $\boldsymbol{C}$ is a dummy that indicates whether a facility is included in the control group, $\boldsymbol{T}0$ is the effective start date of the pilot, and $\boldsymbol{p}(\boldsymbol{X})$ is the propensity score, i.e. the estimated probability of selection in the pilot, which is calculated using covariates $\boldsymbol{X}$.

Thus, on average, the deviation $\boldsymbol{Y}_t - \boldsymbol{Y}_{T0-1}$ for a facility is compared to the average deviation for the control facilities $\boldsymbol{Y}_t - \boldsymbol{Y}_{T0-1}$ and conditionally to the covariates, by assigning either a constant weighting inverse to the probability of selection (i.e. $\boldsymbol{E}[\boldsymbol{G}]$) if the facility is a treatment group facility ($\boldsymbol{G}=1$) or the weighting $-\frac{\frac{p(X)}{1-p(X)}}{\boldsymbol{E}\left[\frac{p(X)C}{1-p(X)}\right]}$ if the facility is a control group facility ($\boldsymbol{C}=1$), with a higher weight being given to the facilities with the highest estimated probability of being selected on the basis of their observable characteristics.

If the covariates did not have an impact on the probability of selection in the pilot, in other words if the treatment and control group facilities had similar average characteristics, and if the common trend hypothesis between the groups was unconditional, in other words if the changes expected in the treatment group in the absence of treatment matched those of the entire control group, this would be simply expressed as the difference in changes in $\boldsymbol{Y}_t$ in the treatment group and the control group:

$$\boldsymbol{ATT}(t) = \boldsymbol{E}\left[\boldsymbol{Y}_t - \boldsymbol{Y}_{T0-1} \mid \boldsymbol{G}=1\right] - \boldsymbol{E}\left[\boldsymbol{Y}_t - \boldsymbol{Y}_{T0-1} \mid \boldsymbol{C}=1\right]$$

The average treatment effect on the treated $\boldsymbol{ATT}$ is estimated over the period from October 2017 (one year before the pilot began) to September 2021 (end of the three-year pilot phase). $\boldsymbol{T0}$ corresponds to the month of October 2018, which marks the beginning of the pilot. It is estimated separately for insulin glargine and etanercept.

The covariates $\boldsymbol{X}$ selected for sample rebalancing purposes measure the number of prescriptions, the size of the facility, the size of the prescribing unit (etanercept only), the mean proportion of prescriptions among deliveries of medication (a proxy for the validity period of a prescription and therefore patient follow-up intensity), and the proportion of first-time treatments among prescriptions (see the description of these variables in Section 3). Insofar as repeated cross-sectional data is used, the estimate for each month is based on the sample of facilities that issued at least one prescription for the formulation being studied. Facilities are clustered in the calculation of standard deviations so that intra-facility correlation is achieved without other covariates being correlated. Standard deviations are calculated by bootstrap (1,000 iterations).

(a) The study cannot be limited to applicant facilities that were not selected to form the control group, due to insufficient sample size (see Section 2). They are included in the control group because they share similar characteristics to the selected facilities. Their observable characteristics are similar to those of the treated facilities and their application was clearly motivated by an interest in actively boosting biosimilar prescriptions.

(b) When the standardised differences for the covariates are above 0.25, conventional difference-in-differences regression methods are considered to be highly sensitive to omitted variables (Imbens & Wooldridge, 2009). All the standardised differences exceed 0.6 here. Possible omitted variables could potentially characterise a clinical facilitie's medical team in terms of aspects such as qualifications, peer reviews, further training, inclusion in a network with a shared approach to biosimilars, prescriber age, etc.

(c) The OR (outcome regression) model requires efficient modelling of the conditional expectation of the changes in the explained control group variable, whereas the IPW (inverse probability weighting) model requires efficient modelling of the conditional probability of selection in the treatment group. The "doubly robust" model combines both methods by modelling explained variable changes as well as the propensity score. Results are accurate if at least one of these parameters is met and therefore the resulting estimator is more robust than if OR and IPW methods were used in isolation.

biosimilars is required to estimate the costs that would have been incurred had there been no pilot. To produce this, we econometrically estimate the effect of the pilot on the ratio of biosimilars to total boxes delivered, weighted[16] by dosage. Unlike the estimate in Section 2.1, this indicator refers to the number of boxes delivered as opposed to the number of prescriptions, in order to reflect the active substance volume and the prescribed treatment course duration. This estimate provides us with a counterfactual number of weighted boxes of reference biomedicines and biosimilars following PHMEV for each month and each facility (assuming that the number of dispensed weighted boxes of biologics is the same in pilot and non-pilot situations[17] and only the rate of biosimilars changes).

This then allows us to calculate pilot and non-pilot PHMEV-related spending. The incentives are calculated by multiplying the number of weighted boxes of biosimilars by the value of the incentive for a box with a weighting of 1. Reimbursements are calculated by multiplying the number of boxes by the price of boxes. A 100% French NHI reimbursement rate is assumed.[18] For the formulations in the pilot, the financial impact on households and supplementary health insurance is therefore assumed to be negligible.

However, the French NHI expenditure incurred as a result of PHMEV relates to all biologics delivered in retail pharmacies to patients who received a PHMEV, that is to say that biologics delivered following a subsequent prescription issued by a primary care physician are also included. This is because the incentives provided via the pilot scheme, just like those provided under the CAQES, apply to all medication delivered in retail pharmacies following an initial PHMEV. To shift from expenditure linked to boxes delivered following a PHMEV (reference biomedicines and biosimilars) to expenditure linked to all boxes delivered in retail pharmacies following a PHMEV or subsequent prescription issued by a primary care physician, in the counterfactual situation as well as in the pilot, we use two multiplicative coefficients (the total number of boxes delivered in retail pharmacies compared with the total number of boxes directly linked to a PHMEV, and the probability that the type of biologic prescribed in retail pharmacies is different from that prescribed as a PHMEV[19]) that are estimated on an annual basis using data from the pilot.

Annual expenditure is calculated by aggregating the expenditure for each month and facility, and total net savings are estimated by aggregating annual profits/losses over the entire period.

The pilot's design produces an effect which is caused by switching between biosimilars and reference biomedicines (a source of reimbursement savings) and a deadweight loss effect (a source of additional incentive-related spending). The pilot's efficiency is dependent on the relative magnitude of these two counteracting effects.

Net savings achieved via the pilot can more specifically be broken down as follows (see details of the calculation in Online Appendix S1 – link provided at the end of the article):

$$EXPENDITURE^{\text{Non-pilot}} - EXPENDITURE^{\text{Pilot}} = \underbrace{\Delta Price \times \left(1 - TI_{\text{Biosim}}^{\text{Pilot}}\right) \times \Delta Q_{\text{Biosim}}}_{\text{substitution effect}} - \underbrace{\Delta I \times Q_{\text{Biosim}}^{\text{Non-pilot}}}_{\text{deadweight loss effect}}$$

in which $\Delta Price$ is the difference between reference biomedecine and biosimilar, $TI_{\text{Biosim}}^{\text{Pilot}}$ is the pilot's incentive rate (defined as the ratio between the incentive paid out under the pilot and the price difference $\Delta Price$, i.e. $\frac{I_{\text{Biosim}}^{\text{Pilot}}}{\Delta Price}$), ΔQ_{Biosim} is the difference between the volumes of biosimilars delivered under the pilot and those delivered with no pilot, ΔI is the difference in incentives paid out for a box with a weighting of 1 under the pilot and those paid out with no pilot, and $Q_{\text{Biosim}}^{\text{Non-pilot}}$ is the counterfactual volume of biosimilars.

The substitution effect increases in line with the difference in price between reference biomedicines and biosimilars because when physicians prescribe biosimilars, the French NHI incurs lower costs due to the fact that they are more cost-effective than reference biomedicines if they both contain the same quantity of active substance. However, the gainsharing component minimises this positive effect on reimbursements since the price differential is partly redirected to the clinical facilities. The substitution effect therefore decreases when the incentive rate increases (assuming a fixed quantity of biosimilars).

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16. We apply a weighting that the Direction de la sécurité sociale *defined for each box of biological medicinal products in the decrees establishing the incentives under the CAQES and the pilot, which enables a shift from box counts to a total volume of active substance. Using etanercept as an example, 50 mg boxes of Enbrel brand (the reference biomedicine) will be assigned a weighting of 1, while 25 mg boxes of Enbrel brand will be assigned a weighting of 0.5.*

17. When the same econometric model described in Section 2 is applied to the total number of weighted boxes of biologics (reference biomedicines or biosimilars), the estimated effect is not significant at standard thresholds.

18. This is a reasonable hypothesis given that 90% of patients supplied with etanercept as well as insulin glargine in the first half of 2021 had a long-term medical condition for which their expenses were fully reimbursed.

19. Non-hospital physician prescriptions match the original prescriptions issued by hospital physicians in more than 97% of cases.

The pilot's higher incentive also creates a deadweight loss effect because it applies to all prescribed boxes, which, in turn, means that the French NHI redirects more incentive funds to treatment group facilities for boxes of biosimilars that would have been prescribed even in the absence of the pilot incentive (counterfactual). The higher the non-pilot biosimilar penetration rate and the greater the difference between the incentives under the pilot and under French common law, the more pronounced this deadweight loss effect.

The pilot's ability to deliver positive net savings and therefore its efficiency requires the deadweight loss effect associated with the pilot's higher incentive to be at least counterbalanced by the substitution effect caused by the increase in biosimilar prescriptions. The efficiency threshold value at which the pilot generates positive net savings for the French NHI can be calculated (see details of the calculation in Online Appendix S1):

$$EXPENDITURE^{\text{Non-pilot}} - EXPENDITURE^{\text{Pilot}} > 0$$
$$\Leftrightarrow \frac{\Delta Q_{\text{Biosim}}}{Q_{\text{Biosim}}^{\text{Non-pilot}}} > \frac{\Delta TI}{\left(1 - TI_{\text{Biosim}}^{\text{Pilot}}\right)}$$

where ΔTI is the difference between the pilot and non-pilot incentive rates.

The efficiency threshold increases in line with the pilot's incentive rate since this rate reduces the substitution effect. However, it also increases in line with the incentive rate differential on account of the deadweight loss effect.

Successive decrees set the amount of the incentive under the CAQES (French common law, no pilot) and the pilot at 20% and 30%, initially, of the price difference between standard boxes of the reference biomedicine and its biosimilar, i.e. boxes with a weighting of 1.

If $TI_{\text{Biosim}}^{\text{Non-pilot}} = 20\%$ and $TI_{\text{Biosim}}^{\text{Pilot}} = 30\%$, the efficiency threshold is about 0.14, which means that biosimilar volumes must increase by at least 14%[20] if the pilot is to yield positive net savings.

However, reference biomedicine and biosimilar prices may have varied over time while incentive unit amounts remained constant. This may have resulted in different incentive rates (see Section 3.2.3) and therefore different efficiency thresholds.

3. Data

3.1. Sources and Coverage

We use data from the French national health insurance reimbursement database (*Datamart de Consommation Inter-Regimes*, DCIR) of the SNDS, which comprehensively records services and items reimbursed by the French NHI. Every patient prescription delivered in a retail pharmacy includes the date on which the medication is delivered, the prescribing professional (clinical facility or primary care physician), the formulations and dosages (CIP code), and the number of boxes. Data concerning medication delivered in retail pharmacies is aggregated by formulation, prescribing facility and month of delivery. It should be noted that a pharmacy can repeatedly deliver medication under the same prescription if no further visit is required during the treatment period. Our analysis is limited to prescriptions (not deliveries), i.e. when a physician prescribes a first-time treatment or a different treatment, to calculate the monthly share of biosimilars among prescriptions issued by each facility, for each formulation[21] (explained variable).

We also use this data to construct multiple covariates. The patient population treated by a given facility is measured on the basis of the number of prescriptions it issues for each of the formulations. For each formulation, we also identify the proportion of first-time treatments among all of a given facility's prescriptions since initiating biosimilars as a first-line treatment is generally simpler than switching between reference biomedicines and biosimilars as a treatment. We use the historically extensive data up to 2012 to identify a first-time treatment, when the same patient receives a particular formulation for the first time (since 2012). Lastly, we include the percentage of deliveries for each prescription. A low percentage suggests that a facility is prescribing longer courses of medication between consultations. For these three covariates, we use the monthly average during the year preceding the pilot (October 2017 to September 2018) to account for seasonal patterns.

To characterise the facilities, we use the *Statistique Annuelle des Établissements de santé* dataset (Annual statistics of healthcare institutions,

20. This 14% increase applies to the total number of weighted boxes of biosimilars and cannot be compared with the estimated effect of the pilot on the percentage of biosimilars among all weighted boxes, which is given in percentage points.

21. Prescriptions are when a physician actively prescribes medication during a visit: the physician specifies the formulation, dosage and treatment course duration on the prescription. We only count prescriptions once, even if they have resulted in multiple instances of medication deliveries (for example, a single prescription for a 3-month course of treatment is recorded once, even if it has resulted in a pharmacy delivering medication for three consecutive courses of treatment each lasting one month). In practice, we use counts of medication being dispensed directly after a new prescription date in pharmacy reports to identify prescriptions in the data.

SAE 2019), in which each facility's size and legal category is provided. Facility sizes are measured on the basis of the number of beds available in medicine/surgery/obstetrics wards (and its square) and the FTE number of salaried physicians, with no distinction made for specialties (FTE and its square). The number of annual FTE dermatologists/venereologists/allergists and rheumatologists (and its square) provides the size of the units likely to prescribe etanercept. No equivalent indicator exists for insulin glargine because it is prescribed by physicians in many specialties.

Medicine prices and their changes over time are obtained from the monthly unit prices charged at retail pharmacies for each medicine (CIP), excluding sales tax, according to the data reported by the GERS (*Groupement pour l'Élaboration et la Réalisation de Statistiques* (Partnership to Collect and Prepare Statistics)). A 13% increase is applied to these prices (reflecting the estimated mean deviation between the pre-tax GERS prices and the prices inclusive of tax according to the *base publique du médicament* (public medicinal products database)) in order to derive the monthly prices, inclusive of tax, which correspond to the French NHI *base de remboursement*, or reimbursement rate. A price can be assigned to medicinal products under the pilot as their prescription data is known, whereas we are limited to the estimated weighted quantity of reference biomedicines and biosimilars for the counterfactual. For a specific facility, month and type of biomedicine (reference biomedicine or biosimilar), the average price of a box with a weighting of 1 is therefore used for boxes that have actually been prescribed (see Online Appendix S1). Lastly, to determine expenditure from PHMEV in retail pharmacies, the annual ratios of hospital/primary care prescriptions are calculated for the formulations.[22]

The analysis is carried out on prescriptions in clinical facilities using their legal entity as the unit. The legal identifier is the most reliable means of identifying a prescribing facility from the data, and it is this entity to which the incentive is redirected.[23] As individual physician identifier numbers are not always entered on hospital prescriptions, it is currently impossible to link prescriptions and prescribing physicians or units via the SNDS. The analysis therefore excludes facilities that have identifiers which are not recognised in the FINESS database – and that cannot therefore be matched with the *Statistique Annuelle des Établissements* (Annual statistics of healthcare facilities, SAE) dataset – as well as atypical facilities, and only includes facilities whose legal category includes at least one hospital complex, long-term nursing home or health cooperation association. We restrict the analysis to public sector hospitals because, in the private sector, it is not possible to comprehensively match physician prescriptions to the correct facility as physicians in for-profit facilities occasionally use their own prescribing books instead of the facility's books.

The analysis period used for the econometric estimate is from October 2017 to September 2021, that is to say the three years of the pilot plus the year preceding it. The statistics that describe prescription trends among the treatment and control groups are presented for the entire period during which biosimilars existed. The first biosimilars for insulin glargine and etanercept were marketed in January 2016 and October 2016, respectively.

3.2. Descriptive Statistics

3.2.1. Sample Description

The group of facilities selected for the pilot and used in the estimate (treatment group) consists of 18 or 19 hospitals for insulin glargine, depending on the month, and 36 hospitals for etanercept. Restricting the analysis to public hospitals effectively excludes four private hospitals selected for each of the formulations in the pilot.

The control group consists of approximately 530 facilities for insulin glargine and 270 for etanercept, taken from an initial sample of approximately 1,900 and 560 facilities that prescribe the formulations, respectively (Table 2). Less than 5% of facilities are excluded on account of their identifier being unknown (FINESS number not found in the database) or because of their legal category. The others are excluded on account of their private status. Although there are many excluded facilities, their prescription numbers are limited. Only 5% of prescriptions for the formulations studied were issued by private facilities.

The facilities selected in the pilot are predominantly large hospitals. They have for example more than a triple bed numbers in average

22. *The programs used by the* Direction de la sécurité sociale *(DSS) to calculate the amount of the incentives based on the SNDS are used to calculate this indicator.*

23. *Any legal entity that includes a cluster of geographical entities that may prescribe the formulations being studied is responsible for distributing the subsidies under the pilot or the CAQES among them. Four AP-HP geographical entities selected for the etanercept pilot are an exception to this, however. They are recorded here as separate entities (Pitié-Salpêtrière/Charles Foix, Cochin, Nord/Val-de-Seine and Mondor/Chenevier).*

Table 2 – **Facilities in the sample**

	Insulin glargine	Etanercept
Prescribing clinical facilities (initial sample):	1,924	561
Excluding:		
- Unknown identifier	27	10
- Atypical category	63	18
- Private sector (profit and non-profit)	1,288	227
Prescribing clinical facilities (final sample):	546	306
Including:		
- Accepted applicants (= treatment group)	**18***	**36**
- Non-pilot (= control group):	**528**	**270**
- Rejected applicants	10	12
- Applicants rejected but accepted for a different formulation	2	6
- Non-applicants	516	252

Notes: Prescribers are identified by the FINESS number of their facility's legal entity. The number of prescribers varies from month to month, as some facilities may not record any insulin glargine or etanercept prescriptions in a given month. These figures relate to facilities responsible for at least one dispensation of medication during September 2018. * 19 public facilities were selected, but only 18 recorded prescriptions in September 2018.
Sources: SNDS (prescribing facilities responsible for dispensing medication in September 2018), DSS (applications and rejections), SAE (facility categories).

than control group facilities. Their treated patient populations, which are measured using prescription numbers, are larger, irrespective of formulation (Table 3).

These observable characteristics can be linked to the ability of facilities to prescribe more biosimilars. We use the propensity score to make treatment and control group facility samples more comparable. This score enables to balance the treatment and control samples by assigning a higher weighting to those facilities that are closest to the treated facilities. This requires a common support assumption between both groups of facilities. Therefore, we ensure that there are sufficient control observations comparable to the treated facilities along the entire distribution of these characteristics (see Table S2-1, Online Appendix S2). We also make sure that the control sample features comparable characteristics to the treated sample once it has been weighted by the propensity score (see Table S2-2, Online Appendix S2).

3.2.2. Changes in Biosimilar Prescription Rate

The general trend observed for both formulations is an increase in prescriptions for biosimilars immediately after their introduction onto the market (Figures I and II). The very marginal upturn in 2018 coincides with the introduction of the CAQES on January 1st, 2018, for all facilities in France.

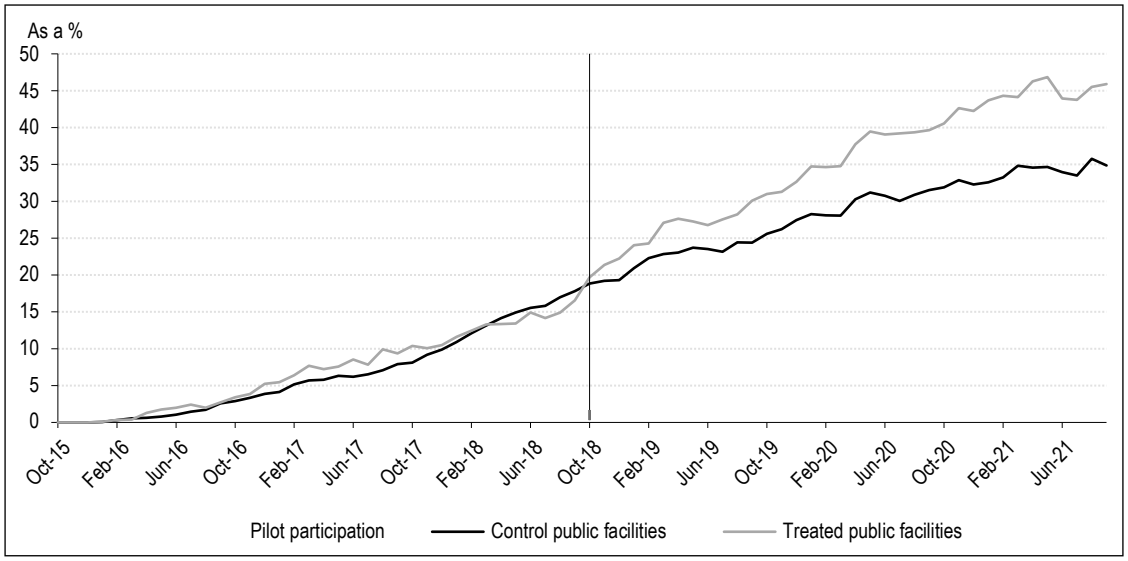
The patterns for insulin glargine prescriptions in treated facilities were similar to those in control facilities prior to October 2018 (Figure I). Over the three years of the pilot, biosimilar prescriptions among all prescriptions issued by treated hospitals increase by 7.0 percentage points, on average. Over the year preceding the pilot, the average biosimilar prescription rate for etanercept in treated facilities already exceeds the rate achieved by other facilities by 3.9 percentage points (Figure II). The mean difference is 9.7 percentage points over the three pilot years studied.

Table 3 – **Average characteristics of facilities in the sample**

	Insulin glargine		Etanercept	
	Treatment	Control	Treatment	Control
Number of prescriptions (monthly average)	169.7	39.7	44.6	6.6
% of first-time prescriptions	15.5	17.9	10.9	9.5
% of medication dispensed following a prescription	60.4	73.2	31.3	31.6
Unit size – salaried physicians	NC	NC	13.4	2.8
Facility size – salaried physicians	475.8	108.8	530.3	154.8
Facility size – beds	1,004.4	221.7	1,047.7	321.1

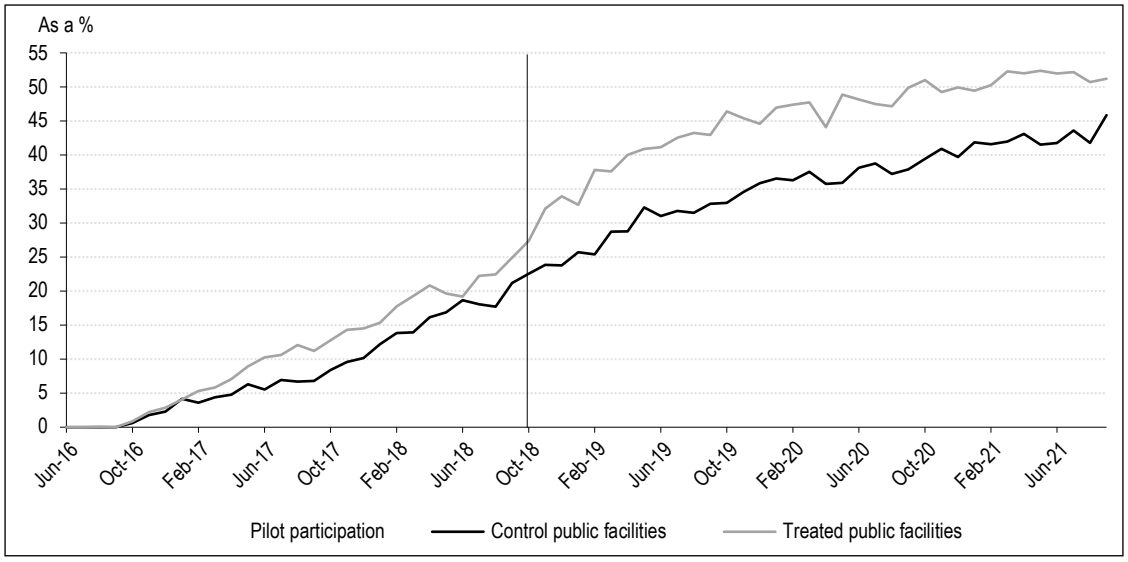
Notes: The size of the units is determined by the FTE of dermatologists, allergists, venereologists and rheumatologists. This is not calculated for insulin glargine.
Sources: SNDS (prescribing facilities responsible for dispensing medication in September 2018, indicators relating to dispensing of medication, repeat prescriptions and new first-time prescriptions), SAE 2019 (indicators relating to number of physician FTEs and beds in medicine, surgery and obstetrics wards).

Figure I – **Proportion of biosimilars among all insulin glargine prescriptions**



Reading note: The black (or grey) line shows the percentage of biosimilars among prescriptions issued in facilities excluded from (or included in) the pilot that resulted in medication being delivered in a retail pharmacy.
Sources and coverage: SNDS (2012–2021), DSS (applications), SAE 2019 (facility categories); public facilities that include at least one hospital complex, long-term nursing home or healthcare cooperation association and provide PHMEV for insulin glargine.

Figure II – **Proportion of biosimilars among all etanercept prescriptions**



Reading note: The black (or grey) line shows the percentage of biosimilars among prescriptions issued in facilities excluded from (or included in) the pilot that resulted in medication being delivered in a retail pharmacy.
Sources and coverage: SNDS (2012–2021), DSS (applications), SAE 2019 (facility categories); public facilities that include at least one hospital complex, long-term nursing home or healthcare cooperation association and provide PHMEV for etanercept.

The proportion of biosimilar prescriptions issued by treated facilities therefore increases sharply when the pilot begins, for both formulations. This suggests that the pilot has a positive effect.

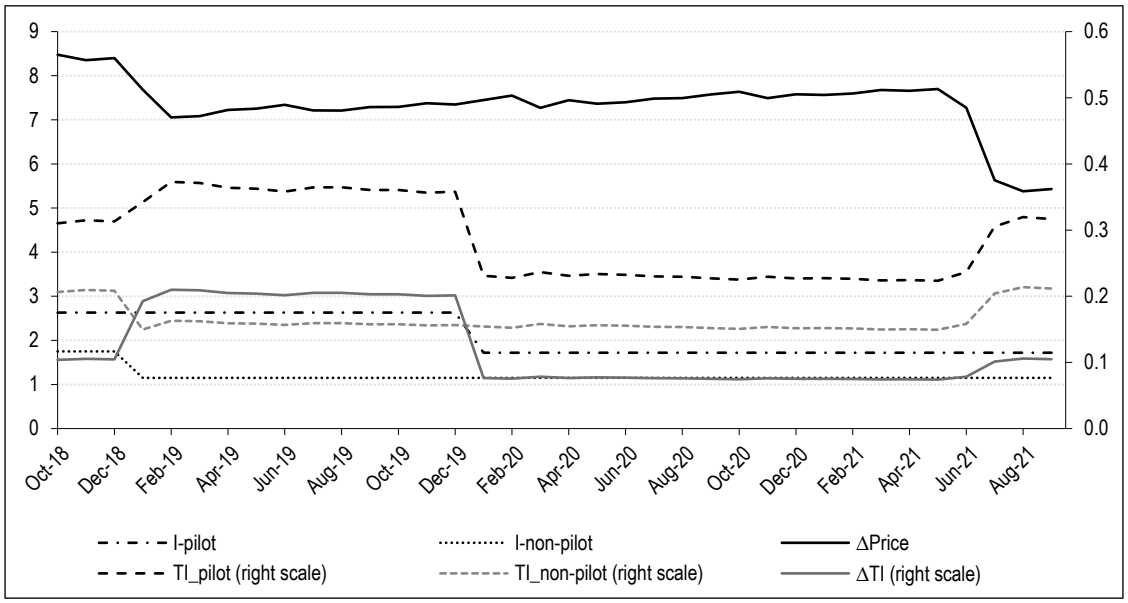
3.2.3. Changes in Incentives and Price Differences

At the start of the pilot, its incentives were set at 30% of the price difference between standard boxes of biosimilars and reference biomedicines with a weighting of 1. CAQES incentives were similarly set at 20% of the price differential. However, there is a fluctuating relationship between the incentives and the price differential as medicinal product prices change over time. As such, the amounts of the incentives were adjusted to reflect these price changes, albeit with a delay. CAQES incentive adjustments were more immediate than adjustments to incentives provided under the pilot (Figures III and IV).

These delays in adjusting incentives to reflect prices are not consistent between French

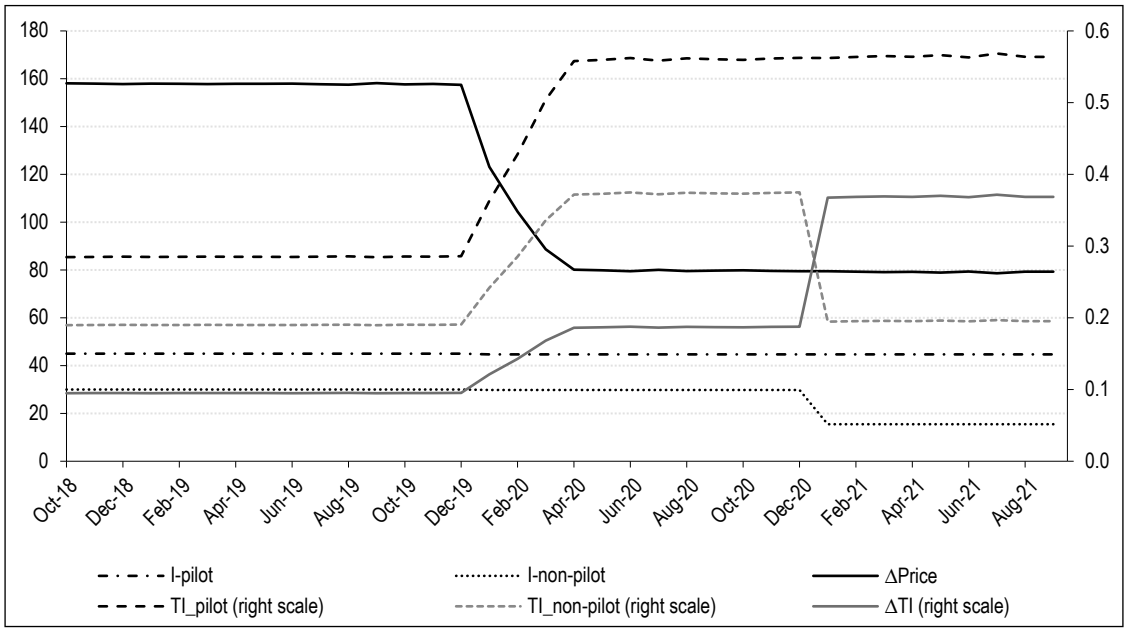
common law and the pilot and lead to variations in the incentive rates as well as the incentive rate differential between the pilot and common law over time. For insulin glargine, the pilot's incentive rate and the incentive rate differential increased in early 2019, following a reduction in the price differential, which was only passed on in the amount of the common law incentive.

Figure III – **Changes in financial incentives and difference between reference biomedicine and biosimilar prices for insulin glargine**



Reading note: In October 2018, the financial incentive for a standard box of insulin glargine is €1.75 under the CAQES (I_non-pilot), whereas it is €2.63 under the pilot (I_pilot). On the same date, the difference between the average prices (ΔPrice) of a box of reference biomedicine and a box of biosimilar (each with a weighting of 1) is €8.50. The CAQES incentive is equal to 0.21 of the difference between average prices (TI_non-pilot), i.e. 21% of the difference, and the pilot incentive is equal to 0.31 (TI_pilot), i.e. 31%. The difference in the pilot and non-pilot incentive rates is 0.1 (ΔTI).
Sources and coverage: Ministerial decrees relating to the CAQES and the pilot (incentives); GERS, French public medicinal products database and SNDS 2018–2021 (average box prices).

Figure IV – **Changes in financial incentives and difference between reference biomedicine and biosimilar prices for etanercept**



Reading note: In October 2018, the financial incentive for a standard box of etanercept is €30 under the CAQES (I_non-pilot), whereas it is €45 under the pilot (I_pilot). On this date, the difference between the average prices (ΔPrice) of a box of reference biomedicine and a box of biosimilar (each with a weighting of 1) is €158.10. The CAQES incentive is equal to 0.19 of the difference between average prices (TI_non-pilot), i.e. 19% of the dfference, and the pilot incentive is equal to 0.28 (TI_pilot), i.e. 28%. The difference in the pilot and non-pilot incentive rates is 0.09 (ΔTI).
Sources and coverage: Ministerial decrees relating to the CAQES and the pilot (incentives); GERS, French public medicinal products database and SNDS 2018–2021 (average box prices).

They then declined in early 2020 with the reduction in the pilot's incentive. Lastly, in mid-2021, a drop in the price differential led to an increase in the common law and pilot incentive rates and the incentive rate differential rose slightly. For etanercept, there was no quantitative adjustment of the incentives in early 2020 despite the sharp price differential drop that occurred, which led to an increase in the common law incentive rate, the pilot incentive rate, and also the incentive rate differential. In 2021, the common law incentive amount fell, further widening the difference in incentive amounts granted under the pilot and under common law.

4. Findings

4.1. Impact of the Pilot on Biosimilar Prescriptions

The primary factor associated with facilities' application and selection likelihood is their size and patient population size (see logit results in Table A1-1 in Appendix A1). Some variables have no significant effect on selection, such as the proportion of prescriptions among deliveries or the proportion of first-time treatments. The model still includes these variables given their differing distribution between the treatment and control groups and their tangible impact on the explained variable via the conditional expectation. Our reliance on a doubly robust estimator that combines two approaches to estimate the treatment effect means it makes sense for the estimate to include the covariates that allow changes in the explained variable (outcome regression) and conditional probability of inclusion in the treatment group (inverse probability weighting) to be modelled.

For comparable facilities, the estimated overall effect of the pilot between October 2018 and September 2021 for insulin glargine is a 6.0 percentage points increase in prescriptions filled by biosimilars (standard error of this mean effect over the 36 months of the pilot: 2.6). This is significant at the 5% threshold.[24] Although the estimated month-on-month effects of the pilot trend upwards over the study period (Figure V and see Table A1-2 in Appendix A1), these monthly estimates are less precise than a mean estimate that covers the entire pilot phase. Zero is included in the 95% confidence interval for each month. For example, the pilot's effect in June 2020 is estimated to be 10.6 percentage points, with a 95% confidence interval that ranges from −4.4 to 18.9.

For etanercept, the estimated overall effect of the pilot between October 2018 and September 2021 is 10.8 percentage points, which is statistically significant at a 7% threshold.[25] The standard error of this mean effect over the 36 months of the pilot (6.6) reveals widely varying results between clinical facilities.

Monthly effects vary between +3.3 and +17.4 percentage points for biosimilar prescriptions (Figure VI and see Table A1-2 in Appendix A1). However, the estimates for these effects are less precise. For example, the pilot's effect in June 2020 is estimated to be 17.4 percentage points, with a 95% confidence interval that ranges from −4.0 to 38.8.

4.2. Robustness Checks

4.2.1. Placebos

The model is estimated on the period preceding the pilot to confirm that it has not incorrectly inferred a causal effect of the pilot. Producing a zero effect thus enhances the degree of confidence that can be placed in the causal effect estimate, and more specifically in the rebalancing of non-treated facilities in the doubly robust method framework. For etanercept and insulin glargine, the effect of belonging to the treatment group is calculated for each month of the year that precedes the pilot (November 2017 to September 2018) as compared with October 2017 – the first month considered by the model.

The average estimated placebo effect is −0.1 percentage point for etanercept and 0.2 for insulin glargine. These values are close to zero and therefore not significant. These results can be considered with regard to the estimated causal effect of the pilot (see Figures V and VI): the estimated mean effect over the course of the pilot is 6.0 percentage points for insulin glargine and 10.8 percentage points for etanercept.

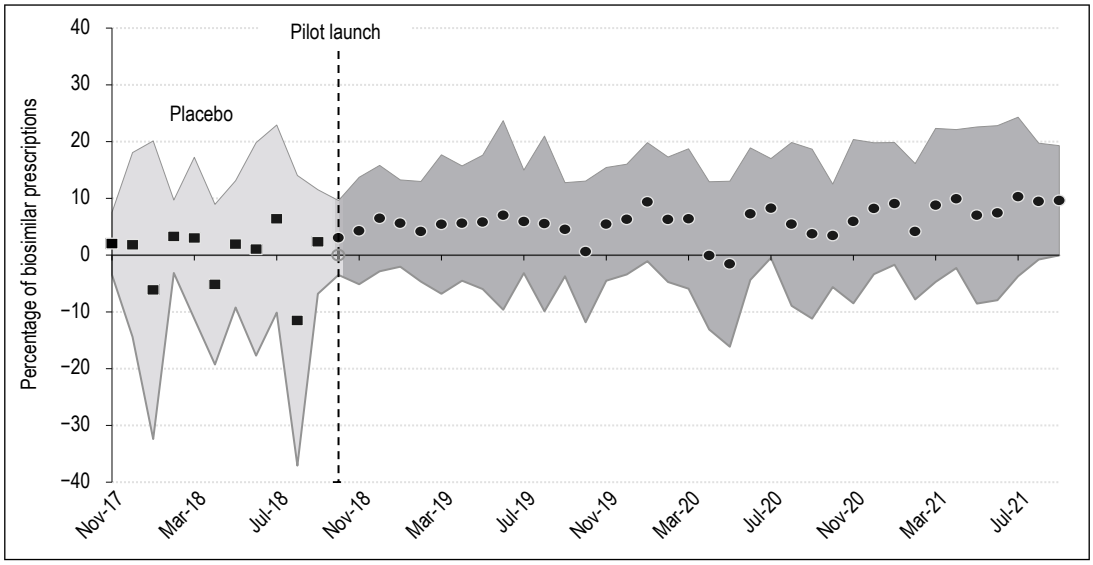
4.2.2. Private Sector

An alternative estimate is made by including private non-profit sector facilities. Since their physicians are typically salaried employees, the prescriptions they issue are generally registered with the facility.

167 private non-profit facilities are responsible for at least one delivery of insulin glargine in September 2018, four of which are treated facilities. The corresponding number of non-profit facilities for etanercept is 48, which includes three treated facilities.

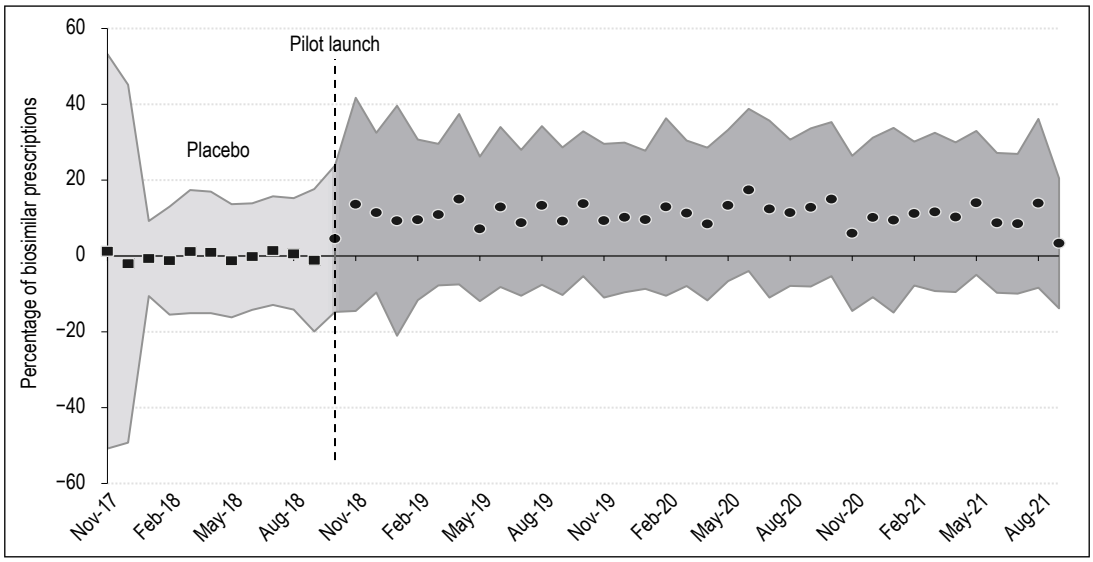
24. Significant at 5% for H0 = zero effect. The effect is significant at the 3% threshold where H0 = zero or negative effect.
25. Significant at 7% for H0 = zero effect. The effect is significant at the 4% threshold where H0 = zero or negative effect.

Figure V – **Insulin glargine – Estimated effect of the pilot on the proportion of prescriptions**



Notes: The dots starting from the vertical bar represent the estimate of the pilot's effect each month from its launch. This is calculated by comparing it with values for September 2018, the month immediately prior to the pilot's launch. The effect for the placebo is calculated for each month from November 2017 to September 2018 as compared with the month of October 2017. The greyed out areas represent the 95% confidence interval.
Sources and coverage: SNDS, SAE (facility categories); public facilities that include at least one hospital complex, long-term nursing home or healthcare cooperation association and provide PHMEV for insulin glargine.

Figure VI – **Etanercept – Estimated effect of the pilot on the proportion of prescriptions**



Notes: See Figure V.
Sources and coverage: SNDS, SAE (facility categories); public facilities that include at least one hospital complex, long-term nursing home or healthcare cooperation association and provide PHMEV for etanercept.

These facilities are generally smaller than those in the public sector and provide fewer first-time prescriptions. Among treated facilities, the highest increase in biosimilar uptake is observed in private non-profit facilities, for all formulations. Nevertheless, including private non-profit facilities in the econometric model leads to an estimate of +7.8 percentage points for biosimilar prescriptions attributable to the pilot for insulin glargine (significant at the 1% threshold), and +8.1 percentage points for etanercept (significant at the 10% threshold). These figures compare with +6.0 and +10.8 percentage points if only public facilities are included. Findings concerning the pilot's impact are therefore consistent with or without the inclusion of the private sector. The main reason for the lower impact for etanercept is a higher uptake rate of biosimilars among private non-profit control facilities.

4.3. Pilot Efficiency

Public treatment group facilities are used to calculate efficiency. The pilot's estimated effect on the total number of weighted boxes of biosimilars delivered following a PHMEV is slightly lower than the estimated impact on the proportion of biosimilar prescriptions alone (Tables 4 and 5). Aside from the scope selected (medication deliveries versus prescriptions), this difference can be explained by the fact that boxes are delivered following prescriptions that started before the pilot began in order to be consistent with the incentives that applied to all medication dispensed from October 2018 onwards. The model estimated to measure the effects on prescribing behaviour only applies to new prescriptions made from that date, however.

Table 4 – **Annual cost saving for insulin glargine**

Year	Insulin glargine						
	Effect of the pilot on the proportion of biosimilars among weighted boxes (ppt)	Estimated efficiency threshold	$\frac{\Delta Q\_biosim}{Q\_biosim^{non\text{-}pilot}}$	Cost saving (€)	Cost saving expressed as a share of non-pilot expenditure (%)	Estimated substitution effect (€)	Estimated deadweight loss effect (€)
2018 (1)	2.7	0.15	0.18	1,000	0.1	4,000	−3,000
2019	4.0	0.32	0.18	9,000	0.1	25,000	−45,000
2020	4.4	0.10	0.14	46,000	0.6	42,000	−30,000
2021 (2)	6.6	0.11	0.19	53,000	0.9	47,000	−27,000
All	4.7	0.17	0.17	109,000	0.5	117,000	−105,000

(1) from October 2018 to December 2018, (2) until September 2021.
Sources and coverage: Authors' calculations, details available in Online Appendix S1; public facilities included in the pilot.

Table 5 – **Annual cost saving for etanercept**

Year	Etanercept						
	Effect of the pilot on the proportion of biosimilars among weighted boxes (ppt)	Estimated efficiency threshold	$\frac{\Delta Q\_biosim}{Q\_biosim^{non\text{-}pilot}}$	Cost saving (€)	Cost saving expressed as a share of non-pilot expenditure (%)	Estimated substitution effect (€)	Estimated deadweight loss effect (€)
2018 (1)	4.2	0.13	0.18	23,000	0.2	82,000	−60,000
2019	11.2	0.13	0.37	623,000	1.2	954,000	−346,000
2020	11.6	0.35	0.30	21,000	0.0	383,000	−453,000
2021 (2)	9.8	0.85	0.23	−493,000	−1.4	200,000	−749,000
All	10.4	0.24	0.29	173,000	0.1	1,619,000	−1,608,000

(1) from October 2018 to December 2018, (2) until September 2021.
Sources and coverage: Authors' calculations, details available in Online Appendix S1; public facilities included in the pilot.

Over the course of the entire pilot, it is estimated that approximately 470,000 *weighted* boxes of insulin glargine and 230,000 *weighted* boxes of etanercept were delivered in retail pharmacies following a PHMEV issued in a treated public hospital, resulting in total spending of approximately €20 million (insulin glargine) and nearly €150 million (etanercept) (see Tables A2-1 and A2-2 in Appendix A2).[26] Over this period, the pilot is estimated to have generated total saving rates of 0.5% for insulin glargine and 0.1% for etanercept. These values are obtained by comparing values with the expected expenditure on biomedicines for public hospitals in the treatment group, had there been no pilot. Insulin glargine savings therefore exceed etanercept savings over the entire period, whereas the pilot's estimated effect on prescriptions is more pronounced for etanercept. However, this general finding masks contrasting annual effects for both formulations. Not only do these depend on the pilot's effect on prescriptions, they also depend on changes to biosimilar uptake rates in the counterfactual situation (with the overall proportion of biosimilars doubling for both formulations over the pilot) and to prices and incentives. To understand these effects more effectively, we provide the estimate of the substitution and deadweight loss effects for each year in addition to the net savings estimate.

For insulin glargine, the savings from the pilot represent an increasing proportion of non-pilot

26. Details of the calculations can be requested from the authors.

expenditure over time, rising to 0.9% in 2021. The deadweight loss effect peaks in 2019, when the difference between reference biomedicine and biosimilar prices narrows and the pilot incentive rate and differential between the pilot and French common law incentive rates increase (cf. Figure III). In 2020, the substitution effect increases due to a rise in the effect on prescriptions and a fall in the rate of incentives under the pilot. Deadweight loss effects also fall in 2020, coinciding with the fall in the differential between the pilot and French common law incentive rates.

The highest level of efficiency for etanercept is recorded in 2019, when the savings from the pilot reach 1.2% of non-pilot expenditure. The higher biosimilar uptake rate largely offsets the deadweight loss effect owing to the difference between biosimilar and reference biomedicine prices. This differential decreases in 2020 (cf. Figure IV), thereby increasing the pilot incentive rate and lowering the substitution effect. In 2021, there is additionally a steep rise in the deadweight loss effect, which follows from an increase in the incentive rate differential and leads to a negative estimated net saving.

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In this article, we examine the effect of a financial and organisational biosimilar prescribing incentive on hospital prescriptions for drugs delivered in retail pharmacies by comparing changes in biosimilar prescriptions within facilities taking part in the pilot with the same changes observed in facilities that are not taking part in the pilot and which share comparable observed characteristics. The findings show that, for public facilities, the pilot led to an increase in the rate of biosimilar prescriptions, estimated at 6.0 percentage points for insulin glargine and 10.8 percentage points for etanercept, all other things being equal, on average over the three years of treatment. This effect may perform below initial expectations of the pilot (+15 percentage points), but it does testify to the interest of the tested incentive design. Despite the fact that the pilot's financial incentive, which is notionally set at 30% of the gains generated through biosimilar prescriptions, is only 10 percentage points greater than the financial incentive paid out under French common law, the pilot seems to have led to a more substantial and faster increase in biosimilar prescriptions issued by hospitals in the treatment group. Although the quantitative evaluation does not allow us to identify to which extent these effects are attributable to the financial incentive or the organisational incentive, these positive results suggest that the incentive being redirected to the prescribing units was certainly decisive in altering the prescribing behaviour of hospital physicians. The fact that the effect for insulin glargine is more muted than for etanercept could also be due to prescriptions of insulin glargine being more widespread across many specialties and units, whereas etanercept is prescribed in fewer specialties. This makes measures that target prescribing units more effective. By way of example, it is easier in practice to distribute gains to units for formulations prescribed in hospital units that can be easily identified upstream. This is because reporting data cannot always be used to identify individual prescribers within hospitals at present. Due to etanercept's much greater price differential, its financial incentive is also much higher than the incentive for insulin glargine.

The findings of this evaluation mirror predictions made in the field of behavioural economics, as aspects of this pilot emulate some of its principles. This literature has shown that financial incentives, of any size, are more effective at boosting motivation when they are clearly distinct from standard remuneration (Emanuel *et al.*, 2016). Another way to boost motivation is to set incremental targets that reflect the starting situation and which do not have thresholds that may be too easily attainable for some and seemingly unattainable for others. Conversely, guidance resource support has been minimal during the pilot's roll-out, even though results from randomised controlled trials, particularly those involving healthcare professionals, underscore how important it is to provide frequent feedback to those involved in the pilot to keep their engagement levels high (Fox *et al.*, 2020).

The results from the econometric model then allowed us to model expenditure that would have been incurred had there been no pilot as part of an efficiency analysis in which expenditure and savings resulting from the pilot are compared. Compared to spending on biomedicines by treated public hospitals in a non-pilot situation, the estimated total saving rates are 0.5% for insulin glargine and 0.1% for etanercept over the entire pilot period. The pilot's efficiency changes over time, depending on the difference between reference biomedicine and biosimilar prices, the pilot's incentive rate, the difference between pilot and common law incentive rates, and the use of biosimilars in the counterfactual trend. The distribution of biosimilars leads to price cuts,

as could a large-scale pilot. Although it is not possible to measure this positive potential effect of the pilot in this study, it should be considered in any wider roll-out of a similar programme. In any case, these findings underscore the value of fine-tuning incentives provided via gainsharing arrangements so that they align with medicinal product price variations as closely as possible. However, even if incentive changes had mirrored price trends more closely, the deadweight loss effect on biosimilars that would have been prescribed even if there had been no pilot would have limited savings under the pilot, given the underlying significant growth in biosimilars.

There are a number of limitations to this evaluation, which stem from the fact that the pilot's treated hospitals took part voluntarily. Treated facilities are typified by their motivation and large size, two characteristics that correlate with the facilities' prescribing behaviours. Despite the fact that the econometric estimate factors this in to the maximum extent possible by using observed characteristics to control for selection, the estimated effect nevertheless remains a local effect that cannot be extrapolated to estimate what impact this measure would have on all French facilities. Furthermore, a lack of comprehensive data relating to the for-profit sector means that the calculations made do not include prescriptions issued by private clinical facilities.

This evaluation also covers the entire period of the pilot as initially envisaged, namely three years, and its findings show that the effects of the pilot on biosimilar prescriptions have been, at the very least, consistently stable (etanercept) or even progressive (insulin glargine) over this period. These incentives based on shared savings therefore appear to be effective in the medium term, but it is too early to determine their longer term efficacy. The incentives could generate lasting effects once prescribing habits change, in which case it may be preferable to gradually scale back or phase out incentives or to incentivise different formulations instead in an attempt to avoid financing deadweight loss effects. On the other hand, scaling back incentives could lead to a slowdown and justify their continuation instead, albeit at the expense of considerable deadweight loss effects. The required duration for a measure of this type and the optimal level of incentives therefore remain unclear at present.

Lastly, this pilot ran during a period of biosimilar distribution buoyed by a greater level of awareness among hospital physicians and primary care practitioners. The effect of the incentives for prescribing biosimilars is likely to be determined by the margin for growth: biosimilar uptake rates in clinical facilities that did not take part in the pilot have continually risen in recent years due to other factors, such as the French common law incentive provided under the CAQES. It may therefore be the case that rolling out the measure more broadly will lead to less pronounced effects on prescriptions due to the greater uptake of biosimilars in general. □

Link to the Online Appendix:
www.insee.fr/en/statistiques/fichier/8186110/ES542_Attia-et-al_OnlineAppendix.pdf

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APPENDIX A1

RESULTS OF THE ESTIMATES ON THE PILOT'S IMPACT ON BIOSIMILAR HOSPITAL PRESCRIPTIONS

The number of facilities in the sample varies each month because certain control group facilities may have no prescriptions in a particular month. Nearly 350 of the 530 insulin glargine-prescribing facilities have an insulin glargine prescription each month and are therefore routinely included in the sample. This is the case for just over 90 of the 270 etanercept-prescribing facilities in the control group. The stabilised panel is therefore much smaller than the non-stabilised sample used for the estimates. A logit model producing selection probabilities is run for each month of treatment, taking into account only facilities active in both the month examined and September 2018 (pre-treatment period). The logit results for the first month of the pilot (October 2018) are presented below.

Table A1-1 – **Results of the logit predicting the probability that a facility applied for inclusion in the pilot and was selected, for insulin glargine and etanercept, in October 2018**

	Insulin glargine		Etanercept	
	odds ratio	p-value	odds ratio	p-value
Constant	0.065	0.061.	0.020	0.003**
Average number of monthly prescriptions	0.999	0.715	1.074	0.001***
Proportion of prescriptions among monthly dispensations of medication	0.968	0.139	0.995	0.884
Proportion of new first-time prescriptions among monthly prescriptions	0.999	0.979	0.987	0.833
Number of beds	1.011	0.000***	1.000	0.942
square	1.000	0.047*	1.000	0.862
Number of salaried physicians	0.986	0.001***	0.995	0.283
square	1.000	0.057.	1.000	0.257
Number of dermatologists/venereologists/allergists and rheumatologists			1.672	0.000***
square			0.986	0.002**

Notes: Significance at the thresholds of 10% ".": 5% "*"; 1% "**"; 0.1% "***".
Reading note: The coefficients are odds ratios derived from a logistic regression, all other parameters being equal. Thus, for etanercept, an increase of 1 of the average number of prescriptions per month increases the probability of participating in the pilot rather than not participating of 7.4% (odds ratio of 1.074).
Sources and coverage: SNDS 2017–2018 (calculation of the monthly mean prescription numbers, the proportion of dispensations of medication following a prescription, and the proportion of new first-time prescriptions); DSS (list of treated facilities); SAE 2019 (bed and physician numbers); public facilities for which at least one prescription was recorded in September 2018 and in October 2018.

Table A1-2 – **Results of the estimate of the pilot's effect on the proportion of biosimilar prescriptions**

	Insulin glargine				Etanercept			
Month	ATT(g,t)	Standard error	Confidence interval at 95%		ATT(g,t)	Standard error	Confidence interval at 95%	
November 2017	2.0	2.0	−3.5	7.5	1.2	19.1	−50.8	53.3
December 2017	1.8	5.8	−14.4	18.1	−2.0	17.3	−49.2	45.1
January 2018	−6.1	9.3	−32.4	20.1	−0.7	3.6	−10.6	9.2
February 2018	3.3	2.3	−3.1	9.7	−1.2	5.2	−15.5	13.0
March 2018	3.0	5.1	−11.2	17.2	1.2	6.0	−15.1	17.4
April 2018	−5.2	5.0	−19.3	8.9	0.9	5.9	−15.1	17.0
May 2018	1.9	4.0	−9.2	13.1	−1.3	5.5	−16.2	13.7
June 2018	1.1	6.7	−17.7	19.8	−0.2	5.2	−14.2	13.9
July 2018	6.4	5.9	−10.1	22.9	1.4	5.3	−12.9	15.7
August 2018	−11.5	9.1	−37.1	14.0	0.6	5.4	−14.1	15.2
Sept. 2018	2.4	3.3	−6.8	11.5	−1.1	6.9	−19.9	17.6
October 2018	3.1	2.3	−3.5	9.6	4.6	7.1	−14.7	23.9
November 2018	4.3	3.3	−5.1	13.7	13.6	10.3	−14.5	41.7
December 2018	6.5	3.3	−2.8	15.8	11.4	7.7	−9.6	32.5
January 2019	5.6	2.7	−2.0	13.3	9.3	11.1	−21.1	39.6
February 2019	4.2	3.1	−4.7	13.0	9.5	7.8	−11.7	30.7
March 2019	5.4	4.3	−6.8	17.7	10.9	6.9	−7.8	29.6
April 2019	5.6	3.6	−4.5	15.7	15.0	8.2	−7.5	37.4
May 2019	5.8	4.2	−6.0	17.6	7.1	7.0	−11.9	26.2
June 2019	7.0	5.9	−9.6	23.7	12.9	7.7	−8.2	34.0
July 2019	5.9	3.2	−3.2	15.0	8.7	7.1	−10.5	28.0
August 2019	5.5	5.5	−9.9	21.0	13.3	7.7	−7.6	34.2
Sept. 2019	4.5	2.9	−3.7	12.8	9.2	7.1	−10.3	28.6
October 2019	0.6	4.4	−11.8	13.1	13.8	7.0	−5.3	32.9
November 2019	5.5	3.5	−4.5	15.4	9.3	7.4	−11.0	29.6
December 2019	6.3	3.4	−3.4	16.0	10.2	7.2	−9.6	29.9
January 2020	9.4	3.7	−1.1	19.8	9.6	6.7	−8.7	27.8
February 2020	6.3	3.9	−4.7	17.3	12.9	8.6	−10.5	36.3
March 2020	6.4	4.4	−5.9	18.7	11.3	7.0	−7.9	30.5
April 2020	−0.1	4.6	−13.1	12.9	8.4	7.4	−11.7	28.6
May 2020	−1.6	5.2	−16.1	13.0	13.3	7.3	−6.6	33.3
June 2020	7.3	4.1	−4.4	18.9	17.4	7.8	−4.0	38.8
July 2020	8.3	3.1	−0.5	17.0	12.4	8.6	−11.0	35.7
August 2020	5.4	5.1	−8.9	19.8	11.4	7.1	−7.9	30.7
Sept. 2020	3.7	5.3	−11.2	18.7	12.8	7.7	−8.0	33.6
October 2020	3.4	3.2	−5.6	12.5	15.0	7.5	−5.3	35.3
November 2020	5.9	5.1	−8.5	20.4	6.0	7.5	−14.5	26.4
December 2020	8.2	4.1	−3.4	19.8	10.2	7.7	−10.9	31.2
January 2021	9.1	3.8	−1.7	19.8	9.4	8.9	−14.9	33.8
February 2021	4.2	4.2	−7.8	16.1	11.2	7.0	−7.8	30.2
March 2021	8.8	4.8	−4.7	22.3	11.6	7.7	−9.3	32.5
April 2021	9.9	4.3	−2.3	22.1	10.2	7.2	−9.5	30.0
May 2021	7.0	5.5	−8.5	22.6	14.0	7.0	−5.0	33.0
June 2021	7.4	5.5	−7.9	22.8	8.7	6.8	−9.7	27.2
July 2021	10.3	5.0	−3.7	24.3	8.5	6.8	−9.9	26.9
August 2021	9.5	3.6	−0.8	19.7	13.9	8.2	−8.4	36.1
Sept. 2021	9.6	3.4	0.0	19.3	3.3	6.3	−13.8	20.5
Aggregate ATT	6.0	2.6	0.8	11.1	10.8	6.6	−2.2	23.9
Pre-treatment parallel trend test p-value:				0.88				1.00

Notes: The ATT provides an estimate of the pilot's effect each month from its launch. This is calculated by comparing it with values for September 2018, the month immediately prior to the pilot's launch. The effects for the period prior to the start of the pilot are calculated, for the placebo, between November 2017 and September 2018 in comparison with the month of October 2017. They are not taken into account in the calculation of the ATT.

Sources and coverage: SNDS 2017–2021, SAE 2019 (facility categories); public facilities that include at least one hospital complex, long-term nursing home or healthcare cooperation association and provide PHMEV for insulin glargine and etanercept.

APPENDIX A2

BREAKDOWN OF TOTAL PILOT AND NON-PILOT EXPENDITURE OVER THE ENTIRE PILOT PHASE

Table A2-1 – **Insulin glargine**

Insulin glargine		Non-pilot (counterfactual)	Pilot
Reference biomedicines	Number of weighted boxes	336,000	314,000
	Mean price of a box with a weighting of 1 (€)	45	
	Reimbursements (€)	15,089,000	14,000,000
Biosimilars	Number of weighted boxes	134,000	157,000
	Mean price of a box with a weighting of 1 (€)	38	
	Reimbursements (€)	5,074,000	5,904,000
Incentives (€)		156,000	306,000
Total expenditure (€)		20,319,000	20,209,000
Cost saving (€)		109,000	
Cost saving expressed as a share of non-pilot expenditure		0.5%	

Notes: Reimbursement amounts have been estimated on the assumption of a 100% rate of reimbursement by the French NHI.
Reading note: Between October 2018 and September 2021, a total of €14,000,000 is spent to cover reimbursements for reference insulin glargine biomedicines linked to PHMEVs issued by facilities in the pilot. This expenditure, under non-pilot conditions, is estimated to be €15,089,000 during the same period.
Sources and coverage: Authors' calculations; public facilities included in the pilot, October 2018 – September 2021.

Table A2-2 – **Etanercept**

Etanercept		Non-pilot (counterfactual)	Pilot
Reference biomedicines	Number of weighted boxes	149,000	125,000
	Mean price of a box with a weighting of 1 (€)	675	
	Reimbursements (€)	100,983,000	84,712,000
Biosimilars	Number of weighted boxes	83,000	107,000
	Mean price of a box with a weighting of 1 (€)	557	
	Reimbursements (€)	46,302,000	59,704,000
Incentives (€)		2,106,000	4,801,000
Total expenditure (€)		149,390,000	149,217,000
Cost saving (€)		173,000	
Cost saving expressed as a share of non-pilot expenditure		0.1%	

Notes: Reimbursement amounts have been estimated on the assumption of a 100% rate of reimbursement by the French NHI.
Reading note: Between October 2018 and September 2021, a total of €84,712,000 is spent to cover reimbursements for reference etanercept biomedicines linked to PHMEVs issued by facilities in the pilot. This expenditure under non-pilot conditions is estimated to be €100,983,000.
Sources and coverage: Authors' calculations; public facilities included in the pilot, October 2018 – September 2021.