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Evolutions in both co-payment and generic market share for common medication in the Belgian reference pricing system

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Running title: Co-payment in Belgian reference pricing system

Key points for Decision Makers:

- As the maximum co-payment level decreased over time, patients pay an equal price for name brand and generic drugs, regardless of the reference price, leaving the Belgian reference pricing system meaningless.
- Increasing co-payment amounts can reduce growth in medicine use, but apparently only in the short term.
- Price regulations can attenuate the intended price advantage for generic drugs.

Abstract

Background: In Belgium, a co-insurance system is applied in which patients pay a portion of the cost for medicines, called co-payment. Co-payment is intended to make pharmaceutical consumers more responsible, to increase solidarity and to avoid or reduce moral hazards.

Objectives: To study the possible influence of co-payment on sales volume and generic market share in two commonly used medicine groups: cholesterol lowering medication (statins and fibrates) and acid blocking agents (proton pump inhibitors (PPIs) and H2 receptor antagonists (H^2RAs)).

Methods and data: The data were extracted from the Pharmanet database, which covers pharmaceutical consumption in all Belgian ambulatory pharmacies. First, the proportion of sales volume and costs of generic products were modelled over time for the two medicine groups. Second, we investigated the relation between co-payment and contribution by the national insurance agency using change point linear mixed models.

Results: The change point analysis suggested several influential events. First, the generic market share in total sales volume was negatively influenced by the abolishment of the distinction in the maximum co-payment level for name brands and generics in 2001. Second, relaxation of the reimbursement conditions for generic omeprazole stimulated generic sales volume in 2004. Finally, an increase in co-payment for generic omeprazole was associated with a significant decrease in omeprazole sales volume in 2005.

The observational analysis demonstrated several changes over time. First, the co-payment amounts for name brand and generic drugs converged in the observed time period for both medicine groups under study. Second, the proportion of co-payment for the total cost of simvastatin and omeprazole increased over time for small packages and more so for generic than for name brand products. For omeprazole, both the proportion and the amount of co-payment increased over time. Third, over time the prescription of small packages shifted to an emphasis on larger packages.

Conclusions: As maximum co-payment levels decreased over time, they overruled the reference pricing system in Belgium. The changes in co-payment share over time also significantly affected sales volume, but whether physicians or patients are the decisive actors on the demand-side of pharmaceutical consumption remains unclear.

Introduction

The National Institute for Health and Disability Insurance (NIHDI) in Belgium applies a co-insurance system in which patients pay a part of the cost for medicines, called co-payment [1, 2]. Between 1995 and 2005, the proportion of public expenditure for health care in Belgium (i.e., medicine consumption) decreased from 78.5% to 72.3%, which implies that the proportion of private expenditure increased from 21.5% to 27.7%. In 2005, patient co-payment for medicines comprised 77.3% of total private expenditures. Other private expenditures include private insurance (10.2%); supplementary insurance provided by health insurance companies, such as additional dental and hospital insurance (11.0%); and employers' contributions (1.5%). The proportion of patient co-payment in overall private expenditures decreased over time, from 80.4% in 2000 to 77.3% in 2005, in contrast to the share of private insurance, which increased from 7.3% in 2000 to 10.2% in 2005 [3]. In total expenditure for pharmaceuticals for consumption in ambulatory health care in Belgium, patient co-payment per defined daily dose (DDD) decreased from 22.1% in 1997 to 16.3% in 2010 [2, 4, 5]. According to the World Health Organization definition, "The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults" [6].

The use of co-payment aims to make pharmaceutical consumers more responsible, to increase solidarity and to reduce or avoid moral hazards [2, 3, 7]. Since 2002, a reference pricing system has been applied in Belgium. Currently, the reference price for reimbursement is set at 69% of the price of the reference product with an identical active ingredient (5^{th} Anatomic Therapeutic Chemical level (ATC)). The reference price has been adjusted several times since its introduction, from 84% of the reference product in July 2002 to 74% in January 2003, to 70% in July 2005 and to 69% since April 2011. When pharmaceutical companies decide to set a price above the reference price, patients pay an additional cost above the standard co-payment amount, also referred to as a supplement. This cost may motivate patients to ask their physicians to prescribe a less expensive product.

In Belgium, reimbursable pharmaceuticals are divided into four categories according to their medical-therapeutic value. Pharmaceuticals in Category A are life-sustaining medicines, such as for the treatment of diabetes, and are fully reimbursed (0% co-payment); Category B includes medicines for therapeutic treatment, such as antibiotics and antihypertensives (25% co-payment); and Category C includes symptomatic medicines, such as mucolytics (50% co-payment). Categories Cs and Cx include influenza-vaccine and contraceptive medicines, respectively (80% co-payment), and Category D includes all other pharmaceuticals, including over-the-counter medicines for which there is no reimbursement [2]. The percentages refer to the situation before 2010.

Co-payment is limited to a set amount for each prescribed pharmaceutical product, which is known as the Maximum Co-payment Level (MCL). Supplements for medicinal use are also assigned a MCL. The MCL depends on the financial means of the patient—a lower MCL applies for low-income patients—and the type of pharmaceutical. Category B pharmaceuticals are subject to a lower MCL than Category C pharmaceuticals (as from April 2010, the MCL for Category C is abolished), and Categories A, Cs, Cx and D are excluded from this

regulation. When co-payment for the prescribed product is higher than the set ceiling, additional costs are reimbursed. An overview of changes in the MCL is provided in the next section and in Table I.

Since 2002, the total annual co-payment amount for patients per household has been limited to a maximum bill. Supplements for medical use are included in the maximum bill. When co-payments accumulated over a year exceed the fixed maximum bill, all additional costs are reimbursed for the remainder of that year [8]. Only pharmaceuticals from Categories A, B and C are eligible for inclusion in the calculation of the maximum bill; Categories Cs, Cx and D are excluded [2]. Four types of maximum billing exist with different reimbursement levels and conditions, mostly according to household composition and income [4, 8]. The maximum covered amount is fixed, but ranges of eligible incomes are adjusted according to the index. In 2012, approximately 310,000 Belgian households received reimbursement as part of the maximum bill. Between 2005 and 2012, the amount of reimbursement increased from 380 euro to 515 euro per household [4, 9].
The ceilings in co-payment significantly affect costs incurred by patients with a chronic condition or on polypharmacy. The determination of the co-payment level is naturally crucial for its effectiveness, particularly for low-income patients [1].

During the period under investigation in this study, the Belgian government introduced several measures to control the growing costs for pharmaceutical consumption [10]. Table I provides a detailed overview of the regulations that were introduced regarding co-payment during the past 15 years.

We aim to study the potential influence of co-payment on sales volume and generic market share in two commonly used medicine groups: cholesterol lowering medication (statins and fibrates) and acid blocking agents (proton pump inhibitors (PPIs) and H2 receptor antagonists (H^2RAs)). Both groups have consistently featured among the top two prescribed pharmaceuticals in the ambulatory sector in the past ten years [11]. Together, these medications represent 4.2% of the number of packages sold and 10.5% of the overall pharmaceutical expenditure (IMS Health for Belgium, August 2010).

Data &Methods

Dataset

The data were extracted from the Pharmanet database, which is based on claims data from all Belgian ambulatory pharmacies for reimbursable medication, entailing 68% of overall national health insurance expenditure; the remaining 32% applies to hospitals [5]. The Pharmanet database is managed by the NIHDI and is considered to be reliable [12]. Drug consumption in hospitals and over-the-counter sales were not included in our dataset.

Based on the ATC classification number, data on acid blocking agents (PPIs: A02BC and H²RAs: A02BA) and cholesterol lowering medication (statins, C10AA and fibrates, C10AB) from January 1997 to December 2009 were selected from the Pharmanet database. Only substitutable products or those pharmaceuticals with an equivalent generic product on the ATC 4 level were included in the analysis. Each pharmaceutical product has a unique identification number, the CNK number (which translates to a Unique National Identification Code). The Pharmanet data include the monthly sales volume in terms of packages, units (e.g., pills or capsules) and DDD per CNK number. They also include the monthly cost per CNK number, distinguishing between costs for the NIHDI and co-payment costs for patients.

Methods for investigating generic proportion

To investigate the market share of generic pharmaceuticals and their cost relative to name brand products, the proportion of sales volume and cost of generic acid blocking agents and cholesterol lowering medication is modelled over time. The sales volume is expressed as the number of packages, DDDs and units sold, and the costs are split into co-payments and NIHDI contributions.

Although a logistic regression model is the default analysis for this type of data, we borrowed principles from quasi-likelihood theory [13] and used the logit of the proportion, i.e., the log-odds, as a response variable in a normal regression model because of the ability to include change points and to allow for overdispersion [14](see below). The logit scale has an advantage because it is not limited to values between 0 and 1 but rather ranges from minus infinity to plus infinity. The log-odds are modelled as a linear function of time.

To increase the flexibility of the model and to account for sudden changes in the evolution of the proportion, we included change points in the model [14, 15]. We allowed the intercept and slope to change at particular time points, i.e., the monthly change points. To identify change points that improve the model, a grid of possible change points from January 1997 to December 2009 (i.e., the time span of the available data) is used. A model expressing the logit of the generic proportion as a function of time is fitted for each possible change point. The best model, and thus the best combination of change points, is chosen based on Akaike's Information Criterion (AIC), a model selection criterion that is minimised to provide the optimal trade-off between the accuracy of the model and the complexity of the model, measured by the number of model parameters [16]. To allow for sufficient flexibility, additional quadratic and cubic functions of time were also considered. Change points were successively added to the model, up to a maximum of six change points to avoid over-fitting. Diagnostic plots were used to assess goodness-of-fit. The change points identified through the best fitting models would not necessarily correspond to months in which the observed evolution of the generic proportions also indicates a

clear visual change in trend. Finally, we compared the model-based change points with the national policy measures (see Table I).

Methods for investigating cost per DDD

To investigate the relation between co-payment and NIHDI contributions, we focused on costs per DDD. This ratio provides a fixed unit of measurement independent of price or dosage and, therefore, is more consistent over time than alternatives such as cost per package and cost per unit [6]. We applied the analyses to omeprazole and simvastatin because they are both commonly dispensed molecules with name brand and generic variants belonging to medication groups for which various changes in reimbursement conditions were made.
Because longitudinal data are available for different pharmaceuticals that contain the same active ingredient, a linear mixed model is appropriate [17]. This technique models the trend in the data while accounting for the variability within and between study objects, in this case, pharmaceutical products. The co-payment per DDD is modelled as a function of the NIHDI contribution per DDD and time. More precisely, co-payment is allowed to evolve over time and to depend on the NIHDI contribution in a time-dependent way. The time and NIHDI contribution effects are allowed to differ for name brand and generic products. Moreover, to account for sudden changes in co-payments as well as NIHDI contributions per DDD, change points are included in the model. The same procedure as above is applied: potential change points are drawn from a grid of dates from January 1997 to December 2009. The inclusion of change points continues until the decrease in AIC becomes marginal or the arbitrary number of six change points is reached.

Results

Several influential events were linked to the change points identified by fitting the models (full details of the models are included in Online Resource 1). We discuss events in generic proportion and cost per DDD in chronological order.

First, a change in MCL regulations in July 2001 was associated with stagnation in the growth of the generic proportion of DDDs, units and packages sold and NIHDI and co-payment costs for acid blocking agents (time points May and June 2001, see Figure 1). The prescription of generic drugs seems to have been discouraged after the MCL increase for generics.

Second, an increase in the generic proportion of the acid blocking agent medicine group was associated with a change in the reference pricing in 2003 (Figure 1) because the reimbursement base for generic drugs decreased from 80% to 74% of the reimbursement base of the reference product after January 2003. This change coincided with a change in sales volume in favour of generic drugs (time point November 2002, see Figure 1). A specific change in reimbursement conditions for generic omeprazole in 2003, whereby prior consent of an additional advising physician is no longer needed to prescribe generic omeprazole, has also strongly stimulated the generic sales volume of acid blocking agents. Since 2004, omeprazole sales have represented approximately 70% of total sales volume of PPIs (in DDDs).

[Insert Figure 1]

In the plots representing the logit of the generic proportion, the models corresponding to NIHDI, co-payment, packages, DDDs and units sold largely overlap with the data, which explains why the dashed data curves are not clearly visible.

Third, in the model for cost per DDD, a change point was identified in July 2005 (time point June 2005, see Figure 2), which was seen as an influential event in the evolutions for both simvastatin and omeprazole. This time point could be linked to two potential causes. First, a change in reference pricing occurred. After July 2005, the reimbursement base for generic drugs decreased from 74% to 70% of the reimbursement base of the reference product. As a result, a steep increase is visible in the proportion of co-payment relative to the total cost for name brand omeprazole and simvastatin (Figure 3 displays the results specifically for the 28x20 mg package size to avoid any incongruent comparisons). After this change, most manufacturers lowered prices, but some did not, which implies that patients paid a supplement in addition to the co-payment for products that did not become less expensive at that point. Although this steep increase in slope flattened again after two months, the overall proportion of co-payment remained higher compared to the period before 2005 for both simvastatin and omeprazole (Figure 3).

[Insert Figure 2 and 3]

The second causal factor could be the modified reimbursement conditions for the observed medicine groups. In July 2005, the Belgian government endorsed a modification in reimbursement conditions for all PPIs and H²RAs to increase patients' price consciousness. Generic omeprazole was partially placed in a category of medicines for which patients co-pay a higher percentage of the total cost, whereas name brand omeprazole remained under more strict reimbursement conditions (see details in Table I). This change most likely induced the steep co-payment increase for generics and the decrease for name brands (Figure 4).
Additionally, 2005 seems to be a breaking point in the sales volume of omeprazole. At the time point where co-payment rapidly increased for omeprazole, sales volume decreased steeply, reaching a low point in 2006 (see Figure 5).

[Insert Figure 4 and 5]

Although the proportion of patient contributions for pharmaceuticals increased (Figure 3), the amount of co-payment per DDD for simvastatin and omeprazole decreased, and the decrease was steeper for omeprazole than for simvastatin. Over time, these amounts converged for name brand and generic versions of both molecules (Figure 4).
Figure 5 illustrates that the number of DDDs sold exceeds the number of packages sold for omeprazole and simvastatin and increasingly does so over time, meaning that a shift occurred over time from prescribing small packages to large packages with the average number of tablets per package growing from 28 to 51 for omeprazole and from 28 to 67 tablets per package for simvastatin between 1997 and 2009 (and the overall average number of tablets per package is higher for name brand than for generic drugs).

Discussion

We studied the potential influence of co-payment on sales volume and generic market share in cholesterol lowering medication and acid blocking agents with a special focus on the molecules simvastatin and omeprazole. The change point analysis suggested several influential events. First, the generic market share in total sales volume was negatively influenced by the abolishment of the distinction in maximum co-payment level for name brands and generics in 2001. Second, the relaxation of reimbursement conditions for generic omeprazole stimulated generic sales volume in 2004. Third, an increase in the co-payment for generic omeprazole significantly decreased the sales volume of omeprazole in 2005.
The observational analysis indicated several evolutions over time. First, the co-payment amounts for name brand and generic drugs converged in the observed time period for both medicine groups studied. Second, the proportion of co-payment in the total cost of simvastatin and omeprazole increased over time for small packages, and more so for generic than for name brand products. For omeprazole specifically, both the proportion and the amount of co-payment increased over time. Third, a shift occurred over time from prescribing small packages to prescribing large packages.

Several potential weaknesses of this study must be discussed. The data used were limited to ambulatory pharmacies, excluding hospital sales data. The analysis was also limited to two commonly used medicine groups that represent only 10.5% of overall pharmaceutical expenditures in Belgium . However, these choices were made deliberately because hospital pharmaceutical policy and ambulatory pharmacy policy have significantly different regulations and bottlenecks. Regarding the choice for the two medicine groups; these have been subject to several experimental policies in the past and were therefore considered to be interesting cases for this study [10, 18, 19].

The arbitrary choice of limiting the number of change points to six in the model could be considered a weakness because not all deviations were captured in the model. However, the model highlighted the most abrupt changes, allowing an efficient comparison between the data and co-occurring policy regulations. Although this type of analysis does not allow for causal inference, the change points indicate where significant changes in the slopes or intercepts occurred. This approach has previously been used in epidemiological studies, for instance to detect distortions in age-dependent seroprevalence data [15]. Modelling the reimbursement data with change points facilitates moving beyond visual data inspection, which has till now been the common method for studies of the potential influence of policy regulation on pharmaceutical sales volume [10, 18].

The variety of regulations imposed on prescribers and patients and additional changes over time complicate the interpretation of our results. The Belgian health care market is characterised by relatively extensive freedom of choice for patients, who may consult any general or specialist practitioner directly. A generous basic health care package, which is mainly financed progressively through income-dependent social security payments, is available for all. Physicians are typically remunerated based on the fee for service and generally compete on the basis of quality of care and service. In addition to the classical phenomena of asymmetry in information,

necessitating the prescriber, who has more information on the subject, to act as an agent for the patient [20] and moral hazard, implying the insured patient may consume excessively if not held accountable [21, 22], supplier-induced demand for name brand medication exists [22]. Indeed, patients may interpret name brand medication as a trait of quality care. Patients may be able to influence a physician's choice between name brand and generic medication, particularly in long-term medical therapies.

By increasing the proportion of co-payment for medicines, patients are stimulated to contemplate their medicine use and the choice between name brand and generic medication. However, assigning full responsibility to the patient would be overly simplistic. To what extent is the patient involved in the prescription and delivery of medicines? Does the patient know in advance what he or she must pay for medicine? Does the prescriber consider the health care cost and the patient's co-payment when prescribing? Logically, physicians will prescribe more medicines from a less expensive equivalent group [21] when co-payment increases for one group of medicines. However, physicians may consider cost secondary to clinical effectiveness and safety, or they may simply be unaware of co-payment amounts for patients [23, 24]. In the case of omeprazole, the increase in co-payment was associated with a decrease in sales volume in 2005 and 2006. However, between 2006 and 2009, omeprazole utilisation increased from 25 to 40 DDDs per thousand inhabitants per day [18]. Therefore, we can presume that addressing the patient by increasing his or her co-payment share might not be a long-term solution to stem the growing sales volume of acid blocking agents.

Since the introduction of generic medicines, the distinction between name brand and generic medication has apparently diminished. The Belgian government focuses on the patient's price rather than whether the product is name brand or generic. Ten years ago, generic producers fulfilled a unique competitive position in the pharmaceutical market, and producers engaged in price competition as a result. Since then, prices, and to a lesser extent co-payments, have converged. However, further price reductions are still possible [18, 25]. Shareholders of pharmaceutical companies may dispute this fact because they have an important share in the Belgian economy and may unwillingly be forced to assume responsibility for curbing growing health care expenditures.
As this study demonstrates, the increasing proportion of generic drugs in sales volume is influenced by the entry of new generic competitors. An increase of pathologies or indications for acid blocking agents could also justify increasing the overall utilisation volume [19]. Compared to other European countries, Belgium, where generics represent a relatively low proportion (14.7%) of total drug sales volume [18], has a developing generic market, and an increased share of generics may stimulate price competition [25]. However, excessive regulation may prevent some generic producers from entering the Belgian market [25]. Our results reveal that the reference pricing system and specific reimbursement conditions can favour generic sales, but their overall volume remains low because Belgian price regulations often attenuate the intended price advantage of generics..

Over the years, the MCL has undermined the reference pricing system by shifting the focus from the reimbursement cost to the patient co-payment. When reference pricing began, patients and physicians were dissuaded from pharmaceuticals priced above the reference price (mostly name brands) because the patient paid the extra price, but reference prices have now become increasingly irrelevant to the patients' contribution. The

MCL has become equal for generic and name brand drugs, and it has diminished to the extent that the co-payment is fixed regardless of the reference price.
A reference pricing system where patients pay an equal cost for name brands and generics regardless of the public price of the drug reduces the reference pricing system to a meaningless system. For example, as of March 2013, the public price for Lipitor® 98*80 mg was 123.51 euro, and the price for Atorvastatin Mylan® (same package size) was 62.52 euro. The co-payment was 14.5 euro for both, which leaves the NIHDI to pay 109.1 euro for Lipitor and 48.02 euro for the generic. The difference in public price notwithstanding, both packages are considered low-cost medicines because the patient's contribution is equally low for both packages (as the price reaches the MCL of 14.5 euro) [26]. Therefore, no single incentive remains for the physician or the patient to choose a generic medicine, although the NIHDI is left paying a cost that is twice as high for the name brand. In this case, the reference pricing system is a vain attempt to curb public drug expenditures. The effectiveness of existing regulations to curb growing pharmaceutical expenditures requires urgent reconsideration, and the intended objectives of the maximum co-payment level must be clearly defined to avoid such counteracting effects.

The influence of patient contributions for pharmaceuticals on health care utilisation has been reported in various studies [27-30]. Originally, this contribution was intended to curb overuse and to control growing expenditures for health care. Research indicates that increased co-payment can have some of the intended effects [30, 31]. However, modifications in patient behaviour are influenced by patient characteristics and the organisation of the health insurance system [7]. The most troublesome effect that could be associated with an increasing share of patient contributions is treatment disruptions for chronically ill patients, as reported in the US [31]. Ultimately, this phenomenon can result in higher health care costs. A tension clearly exists between patients' access to medicine and the government's efforts to control growing pharmaceutical expenditures by sharing financial responsibilities [2]. The principle of value-based pricing may merit further consideration in this context to take health technology assessment one step further and use it as a tool to determine a value-based price, which reflects the maximum societal willingness to pay for a particular health technology [7]. However, in view of the uncertainties inherent in estimating such values based on a cost-effectiveness analysis, we cannot solely rely on this tool to set levels of co-payment. Important criteria that can be assessed with more certainty, such as affordability and lifesaving urgency, will also need to be considered.

Conclusion

A variety of regulations between 1997 and 2009 has limited the co-payment share in pharmaceutical spending. This change resulted in some unintended effects. As maximum co-payment levels decreased over time, they have overruled the reference pricing system in Belgium. The changes in co-payment share over time have also significantly affected sales volume. However, whether physicians or patients are the decisive actors on the demand-side of pharmaceutical consumption remains unclear. Simplification of these overly complex regulations and improved access for patients to price information could be a first step towards resolving the information asymmetry between patients and physicians and avoiding inequities in medicine access [32].

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The sponsors had no role in the study design; the collection, analysis and interpretation of data; the writing of the report; or the decision to submit the paper for publication.

Conflicts of interest

NH declares a possible conflict of interest: support from the University of Antwerp Scientific Chair in Evidence-Based Vaccinology, financed in 2009–2014 by a gift from Pfizer. The sponsors had no role in the study design; the collection, analysis and interpretation of data; the writing of the report; or the decision to submit the paper for publication.
HDL declares a possible conflict of interest because as owner of a pharmacy, he is employed 75% of the time as a pharmacist.

All other authors declare no conflicts of interest.

Author contributions

Fraeyman Jessica: Wrote the first draft, guarantor for overall content of the paper
Verbelen Moira: Contributed to the analysis and interpretation of the data, critically revised the article for important intellectual content
Hens Niel: Contributed to the analysis and interpretation of the data, critically revised the article for important intellectual content
Van Hal Guido: Critically revised the article for important intellectual content
De Loof Hans: Critically revised the article for important intellectual content
Beutels Philippe: Initiated the study, contributed to the analysis and interpretation of the data, critically revised the article for important intellectual content

Tables

Table I: An overview of regulatory changes in co-payment and the maximum co-payment level (MCL) in Belgium, 1997-2009

Application date	Event[a]	Remarks[b]
July 2001	RD 21/03/2001	Distinction in the MCL between name brand and generic drugs is abolished (25% of the reimbursement base for both)
January 2002	RD 21/12/2001	Introduction of the Reference Pricing Scheme
January 2002	RD 15/07/2002	Introduction of the maximum bill
January 2003	RD 19/12/2002	A distinction is made in the MCL for small and large packages (more than 60 units per package). The MCL is higher for larger packages.
May/July 2003	MO 9/04/2003 MO 16/06/2004	Change in reimbursement conditions for generic omeprazole: an a priori authorisation is no longer needed; all indications are reimbursed (only for 20 mg packages)
April 2004	MO 18/06/2004	Change in reimbursement conditions for statins: an authorisation from an advising physician is no longer needed a priori; only a verification a posteriori is required
July 2005	MO 14/06/2005	Change in reimbursement conditions for generic omeprazole: a verification 'a posteriori' from an advising physician is required; larger dosages (40 mg) are switched to Category B (more restricted) and smaller dosages (10 and 20 mg) to Category C (less restricted)
September 2005	RD 17/09/2005	A higher MCL is applied for pharmaceuticals with a molecular equivalent generic or copy on ATC[c] level 4 (substitutable pharmaceuticals). The MCL is further increased for larger packages.
April 2007	RD 06/03/2007	The MCL for large packages of non-substitutable pharmaceuticals is lowered.
April 2008	RD 27/03/2008	The MCL is lowered for large and small packages of substitutable pharmaceuticals but remains higher than for non-substitutable pharmaceuticals.
July 2009	RD 18/05/2009	The distinction between substitutable and non-substitutable pharmaceuticals is abolished. That is, the MCL for substitutables is further lowered to the level of non-substitutables.

a. RD: Royal Decree. MO: Ministerial Order

b. Regulations are discussed for patients in Category B with non-preferential insurance status

c. ATC: Anatomical Therapeutical Chemical classification system (by the World Health Organisation)

Figures

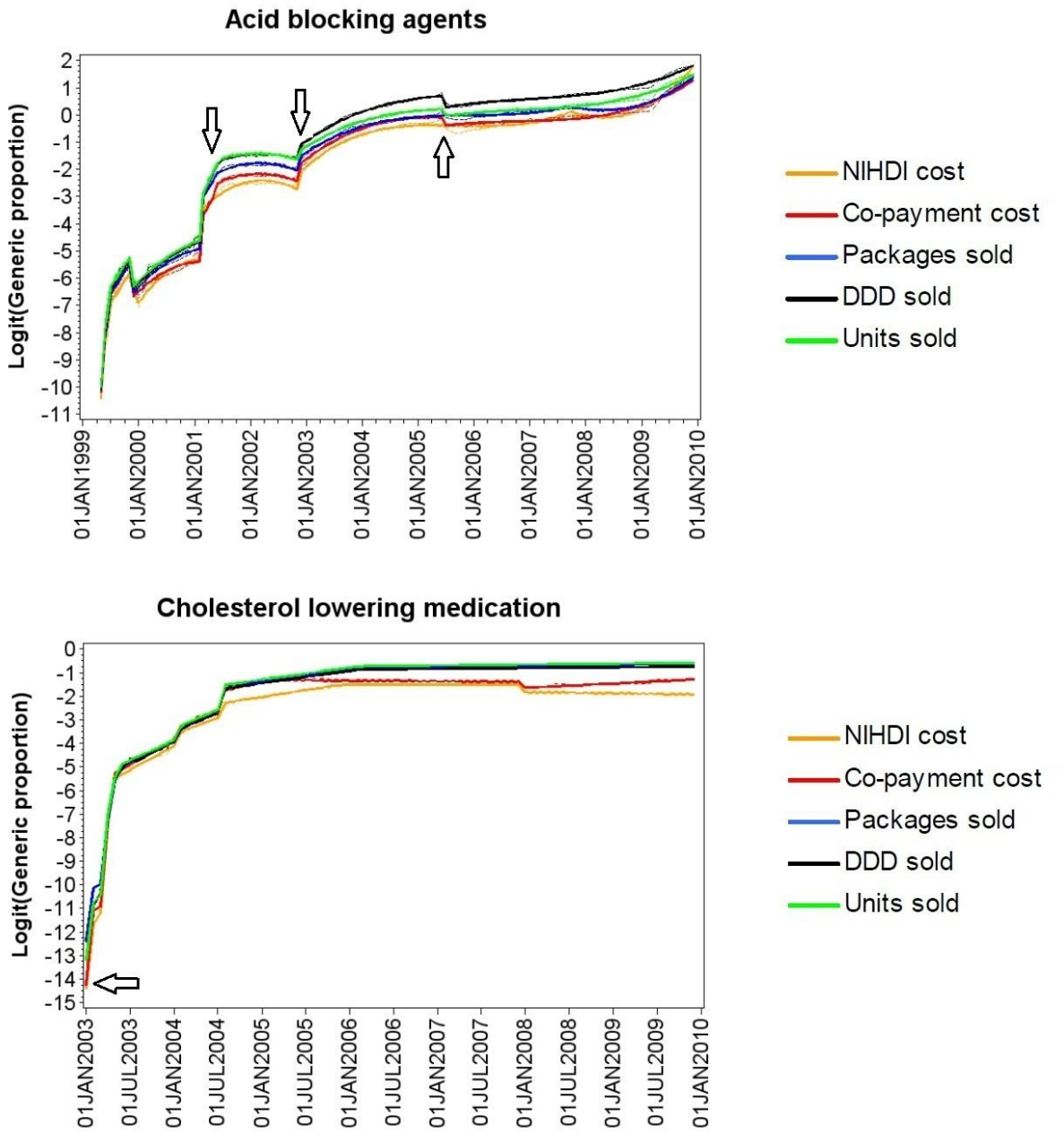

Figure 1: Logit of generic proportion in the contribution of National Institute for Health and Disability Insurance (NIHDI), co-payment, number of packages, Defined daily Doses (DDD) and units sold for acid blocking agents (upper panel) and cholesterol lowering medication (lower panel). Data are shown as dashed lines and the overlaid model as full lines. Change points that were linked to possible influential events were marked with an arrow.

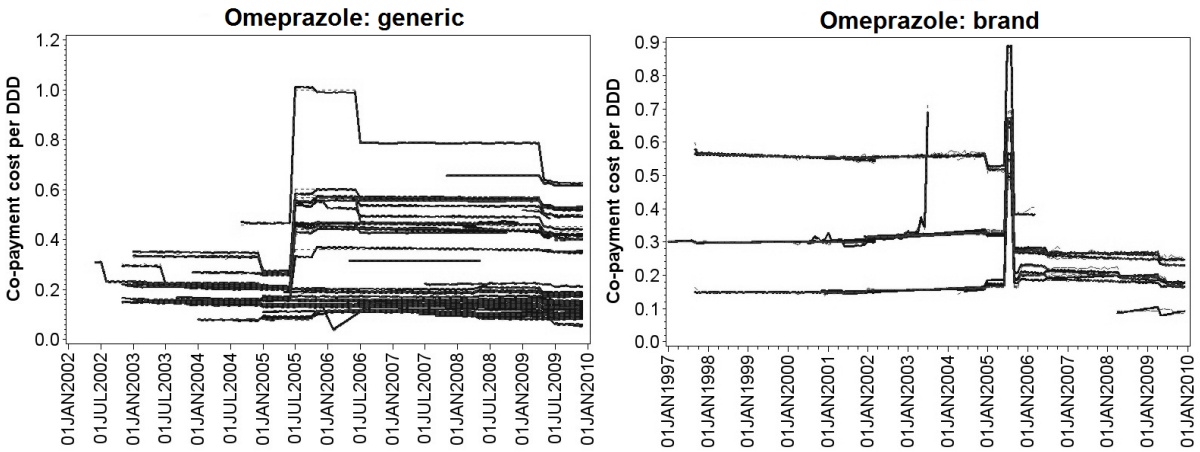

Figure 2: Estimated co-payment per DDD (in euro) for omeprazole distinguishing generic and brand drugs, as a function of time and NIHDI cost per DDD overlaid on observed co-payment costs. Data are depicted as dashed grey lines, the overlaid estimates from the model as full black lines.

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