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Choosing among competing blockbusters: Does the identity of the third-party payer matter for prescribing doctors?[1]

by

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May 14, 2009

Abstract

TNF-alpha inhibitors represent one of the most important areas of biopharmaceuticals by sales, with three blockbusters accounting for 8 % of total pharmaceutical sale in Norway. With use of a unique natural policy experiment in Norway, this paper examines to what extent the identity of the third-party payer affects doctors choice between the three available drugs. We are able to investigate to what extent the price responsiveness of prescription choices is affected when the identity of the third-party payer changes. The three dominating drugs in this market, Enbrel, Remicade, and Humira, are substitutes, but have had different and varying funding schemes - hospitals and the national insurance plan. We find that treatment choices are price responsive, and that the price response increases when the doctor's affiliated hospital covers the cost instead of a traditional fee-for-service insurance plan.

JEL classification: C35, D43, I 18, L11.

Keywords: Pharmaceuticals, discrete choice model, funding schemes.

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1. Introduction

Health care expenditure makes up a large and increasing share of GDP in many developed countries. For example, in the U.S. health expenditure as a share of GDP amounted to 8.7 percent in 1980, but had risen up to 15.3 percent in 2006.[5] This is often held to reflect a combination of rapid technological progress in health service provision, an aging of the population, and the incentive structure within the health care sector. As one of the most research intensive industries, the pharmaceutical industry is an important contributor to health care innovation. Pharmaceutical firms invest as much as five times more in research and development, relative to their sales, than the average U.S. manufacturing firm.[6] The success of this research shows up in the health care expenditure data. In 1980, pharmaceutical expenditure represented 9 percent of total health care expenditure in the U.S. In 2006, the share amounted to 12.6 percent.

In a survey for the U.S. by the National Institute for Health Care Management (NIHCM (2002)) it is reported that only 17% of all the drugs approved by the FDA in the period 1989-2000 can be classified as drastic innovations, where as much as 51% could be classified as modifications of existing compounds. One reason for this is likely to be the extensive health insurance plans that protect patients from the full cost of treatment. Insured patients do not pay for the prescription choices doctors make on their behalves. Price responsive choices can only occur to the extent that doctors internalize the real cost of the treatment as opposed to just internalizing the preferences of their insured patients.

The agency problem faced by the insurance company or the government is often referred to as "moral hazard" in the health economics literature (Arrow, 1963, 1968, Pauly, 1968, Zeckhauser, 1970), and its importance and consequences for health care financing has been subjected to extensive theoretical and empirical research (see McGuire (2000) for an extensive review). The moral hazard problem arises due to the introduction of a third-party payer. In an insurance based health care system, however, there are several candidates for being the third-part payer of drug expenses. When prescribing a drug on behalf of an insured patient, the cost may be covered by traditional insurance plans – private or public – on a fee-for-service basis or by the hospital with which the doctor and patient are affiliated.

[5] OECD – Health data 2008.
[6] CBO (2006).

With use of a unique natural policy experiment in Norway, this paper examines to what extent the identity of the third-party payer affects doctors choice of treatment. More precisely, we are able to investigate to what extent the price responsiveness of prescription choices is affected when the identity of the third-party payer changes. There are reasons to believe that the agency problem with hospital funding of pharmaceutical expenses is reduced compared with the fee-for-service approach adopted by traditional insurance plans. Treatment costs covered by the national insurance plan do not represent a direct cost for the doctor and the hospital. To the extent that treatment costs affect the choice of drug under a pure national insurance plan funding, this is explained by doctors' understanding and adherence to national guidelines for cost-effective treatment choices. When treatment costs are covered by the hospital, the opportunity costs becomes more "tangible" to the doctors. Increased treatment costs on one patient reduce available resources for other activities at the affiliated hospital. Due to this, treatment choices may be under a tighter control or monitoring when costs are covered by the local hospital instead of a national, and tax funded, insurance plan.

To date TNF-alpha inhibitors represent the most important way to treat arthritis and other autoimmune diseases (Feldmann and Maini, 2003). Treatment choices with TNF-alpha inhibitors in Norway are made by hospital doctors, and all patients receiving treatment are insured against the cost, but the funding source, i.e. the identity of the third-party payer, has differed between the three available drugs and over time.

When the market for TNF-inhibitors opened in Norway in 2000, the first entrant Enbrel was fully covered by the obligatory national insurance plan. The treatment with Enbrel is initiated by the hospital doctor, but the cost was automatically covered by the national insurance plan. The second entrant Remicade did not obtain the same type of coverage. Instead the treatment cost had to be fully covered by the doctor's affiliated hospital. Importantly, the hospitals' budget did not include earmarked grants for these patients. Cost of treatment with Remicade, therefore, competed with other expenses within the hospital. This sharp asymmetry in funding scheme reflects a quality attribute of the two drugs. Enbrel is administrated by the patients themselves (pump injections), while Remicade requires several hours infusion at hospitals. In fall 2002 the government modified the plan for Remicade by reducing the hospitals' share of treatment cost to 20 %. Choosing Remicade after fall 2002, the government required a copayment of 20% from the doctor's affiliated hospital. Enbrel maintained its full insurance

plan coverage. The third entrant Humira is also administrated by pump injections by patients, and received the same funding plan as Enbrel when the drug entered in January 2003.

The important policy change exploited in our study, however, took place in 2006. Then the asymmetry of financing between Enbrel and Humira, and Remicade was entirely removed by returning the entire funding responsibility to the hospitals for all three drugs. Since then all costs of treatment with TNF-alpha inhibitors have to be covered by the doctors' affiliated hospital. By creating large and exogenous variations in hospital and insurance plan treatment costs, these funding switches becomes the crucial source of identification in our empirical model.

We specify a discrete choice model in which the doctor's choice among the available of TNF-alpha inhibitors depends on prices. The price response is allowed to vary with the identity of the third-party payer. Our main result shows that doctors' choice of TNF-alpha inhibitor is responsive to price differences, and that this price response becomes stronger when hospitals cover the costs. Running counterfactual experiments, we derive the economic magnitude of changes of the third-party payer. Remicade, which is the cheapest of the three drugs, gains 8 percentage point increase in market share by moving from insurance plan funding to hospital funding. This materializes as a 3-5 percent reduction in total treatment cost. Since these drugs are all on the top five sale value list in Norway[7], the choice of the third-party payer has a non-trivial economic impact. Savings are shown to be far larger than the reduction in expected consumer surplus for these doctor-patient couples.

In a related paper Hellerstein (1998) provides evidence of the importance of insurance plans for the agency problem in prescription choices. She finds that doctors with a higher fraction HMO-patients relative to patients who are enrolled in traditional insurance plans, more often prescribe generics instead of the brand-name drug. Since her data did not contain prices, however, she is not able capture the effect on doctors' price responsiveness. Iizuka (2007) is a recent contribution to the literature on agency problems in prescription drug market. In the Japanese market, doctors make profit from selling prescribed drugs. Using data with both prices and doctors' own mark-up, Iizuka finds that doctors' prescription decisions are influenced by the size of mark-up, but that they care more about patient welfare than their

[7] Norwegian Association of Pharmaceutical Manufacturers (2009)

own profit. Other papers studying the importance of doctor and prices in prescription choices are Coscelli (2000) and Lundin (2000). The main contribution of Lundin is to show how the level of patients' co-payment influences doctors choices (between generics and brand-name). He finds that doctors' are more responsive to patients' co-payment than the cost of the insurance provider.

Another study related to ours is Berndt et al (2003). They do not study the effect of insurance on prescription choices, but estimate a demand model for a growing market with competing brand names available. They use data for H_2-antagonist antiulcer, and their data starts at the entry of the first patent Tagament. Similar to our study, therefore, they investigate the pharmaceutical demand in a market with several competing brand-name (patented) drugs. They develop a rich model that includes a dynamic component of diffusion. Their market share model allows the drug choice to depend on prices, in addition to marketing. Doctors' are found to respond to prices, with own-price elasticity in the range of about -0.3 and -0.6.

The reminder of the paper is organized as follows. In Section 2 we briefly describe the market for TNF-alpha inhibitors. In Section 3 we describe the data used in the analysis. Section 4 presents the econometric model. The results are presented in Section 5, and we conclude in Sections 6.

2. The market for TNF-alpha inhibitors

Biotechnology is considered to be one of the most important technologies that emerged in the last decades of the 20th century. The biotechnological revolution was expected to yield significant benefits to the pharmaceutical sector through improvements in drug discovery and development (Lawrence, 2006; Lawrence 2007; Walsh 2003). The biopharmaceutical market is now characterized by competition among few firms that act at a global level, and biotech drugs claim an increasing share of novel treatments approved by the regulatory authorities (Kneller, 2005). The number of biotech blockbusters, i.e. drugs on the market that have sales over 1 billion USD per year, is rapidly increasing. Recombinant therapeutic proteins represent the main business sector of biotechnological drugs, followed by monoclonal antibodies. Several proteins and antibodies are used in the treatment of arthritis and other autoimmune diseases, and the most important subgroup is described as tumor necrose factor (TNF) alfa inhibitors.

There are three biotechnological drugs acting as TNF alpha inhibitor in the treatment of RA. The first is Enbrel (etanercept), a recombinant protein of human origin: it was approved by the FDA in 1998 for the reduction of signs and symptoms of moderate to severe rheumatoid arthritis, and in Europe by EMEA in 1999; it is administered twice a week by subcutaneous injection. At the time of introduction, it was indicated for use by patients who had an inadequate response to one of the other disease-modifying anti-rheumatic drugs (DMARD) (Moreland et al., 1997), and in combination with Rheumatrex (methotrexate): clinical trials proved that the addition of etanercept to methotrexate therapy resulted in rapid and sustained improvement (Weinblatt et al., 1999). Enbrel gained approval also for the treatment of juvenile RA and psoriatic arthritis, and further studies demonstrated its effectiveness as compared with methotrexate in patients with early active RA (Bathon et al., 2000), making it a first-line treatment for RA and a leading brand within the new class of DMARDs. Enbrel was developed by Immunex, a biotechnology company that in 2001 was acquired by Amgen. The product is marketed jointly with Wyeth Takeda.

The second TNF-based RA product on the market is Remicade (infliximab), a chimeric (human and mouse) monoclonal antibody that proved to be safe and effective with persistently active RA not responding to methotrexate therapy (Lipsky et al., 2000). It is marketed by Centocor together with Schering Plough and the Japanese company Mitsubishi

Tanabe Pharma. In Europe EMEA granted marketing authorization in March 2000. It is administered every four to eight weeks via an intravenous infusion that may take several hours to complete and requires qualified personnel monitoring of adverse reactions: this is considered as a disadvantage in comparison with Enbrel. Nevertheless, Remicade progressively increased its sales gaining high market shares. Price of Remicade is lower than Enbrel.

The third TNF alpha inhibitor in the market is Humira (adalimumab), a fully human monoclonal antibody approved by FDA in December 2002 and by EMEA in September 2003, and marketed by Abbott in the form of subcutaneous injection every two weeks, setting the drug price in parity with Enbrel. Its attracting dosing profile was considered a key success factor, but relatively short after its launch, the growth of sales slowed and it seemed not to threaten significantly the market position of its competitors.

Since these drugs are expensive, and the leading products show also some important side effects, like tuberculosis (Antoni and Braun, 2002), other products than TNF-alpha inhibitors are used to treat the disease (like Rituxan, Orencia and Kineret). The profitability of the market stimulates new research – a number of pharmaceutical and biotechnological companies are currently trying to develop new products that may threaten the market leaders Enbrel and Remicade in the future (Sheridan, 2008).

Market penetration in terms of sales value has been highly successful in Norway. Sale of Enbrel, Remicade and Humira accounted for 8 % of total pharmaceutical sale in Norway in 2008.[8]

3. Data

The dataset consists of monthly wholesale sale value and quantity sold, expressed in defined daily doses (DDD), for each of the three drugs Enbrel, Remicade and Humira. The data set covers the months from January 2000 to March 2008, indicated as running from t=1 to t=99 in Figures 1 and 2 below. The price per DDD is constructed from combining the value and quantity information.

[8] Norwegian Association of Pharmaceutical Manufacturers. Facts and Figures (2009).

The following figure shows the monthly wholesale value of sale.

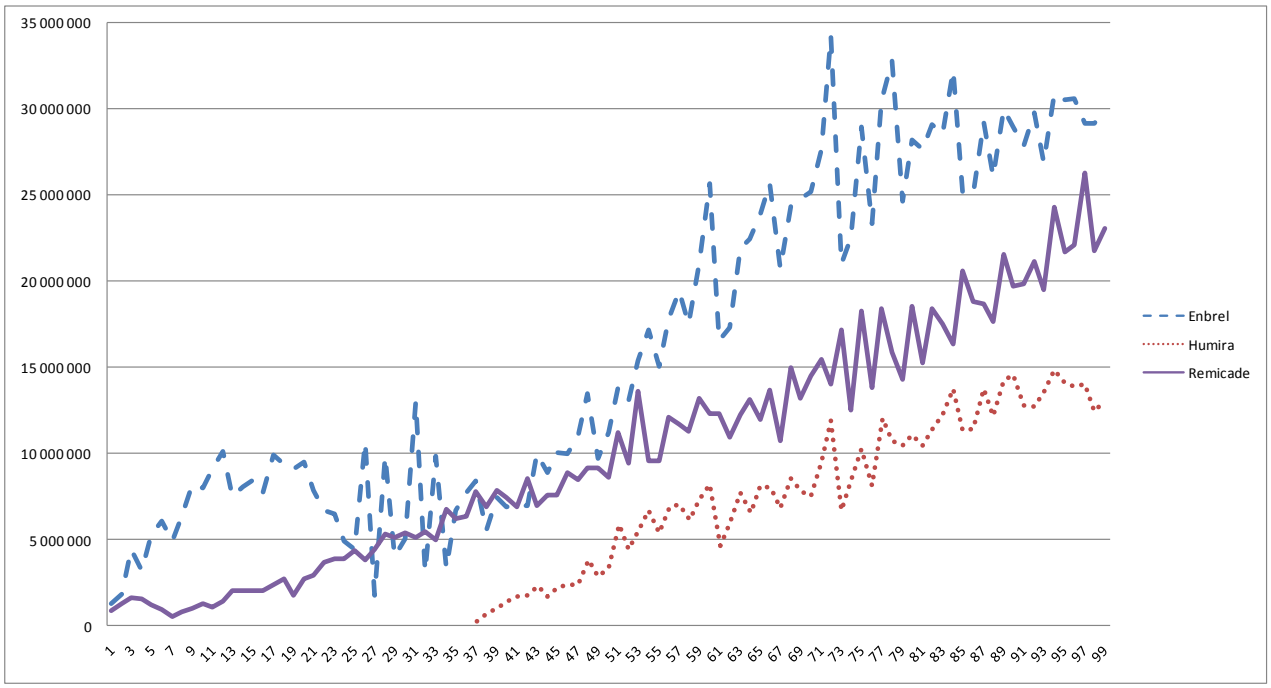

Figure 1: Monthly wholesale value of sale; 1000 NOK. As of April 2009 1€~NOK 8.7

The market opened early 2000, with the entry of both Enbrel and Remicade. Enbrel had a far stronger growth during the first year, and became soon the leading drug. In 2001-2002 Enbrel experienced problems of supplying the market. World wide capacity shortage forced the producer to reduce the sale of Enbrel in Norway. This explains the drastic reduction in sale value for Enbrel, and its volatility shown in Figure 1. In the fall 2003, the third drug, Humira, entered. Although Humira experienced a steady growth in the fast growing market, it never succeeded in capturing a larger market share.

The figure below shows the development of market shares.

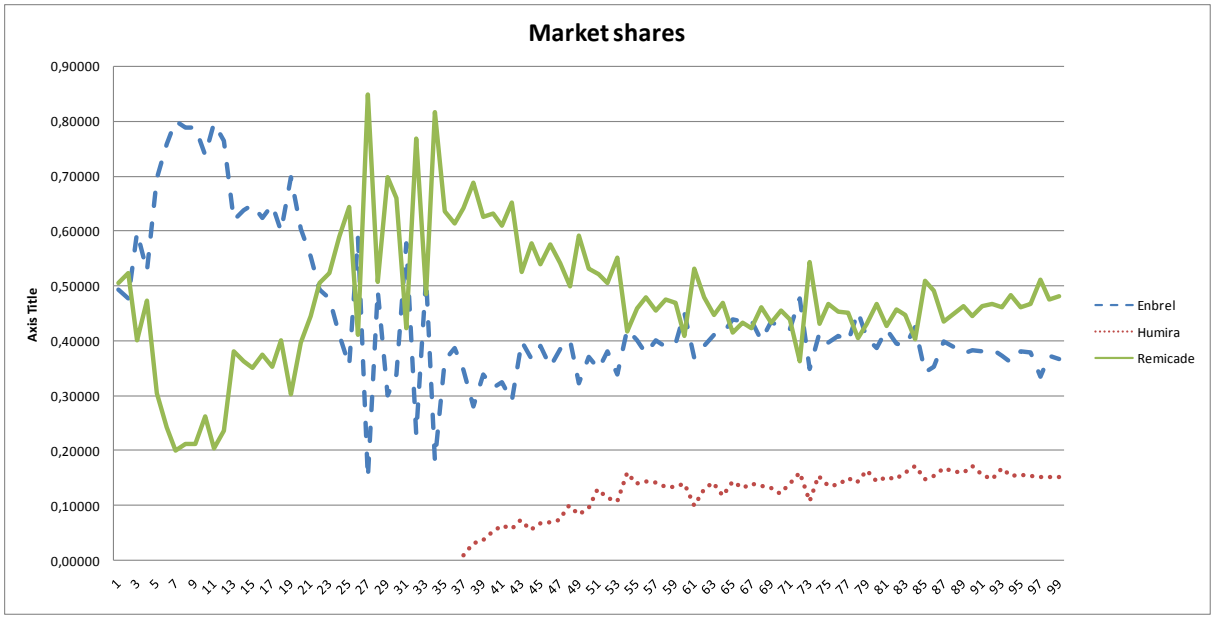

Figure 2: Market shares for the three drugs (DDD).

Within the first year, Enbrel reached a market share of 80 percent. The market share dropped rapidly, most triggered by the abovementioned shortage of production capacity. Since Remicade was the only alternative TNF-inhibitor in this period, it experiences an equivalent rise in its market share. Humira reached a market share close 9 percent after a few months.

The price of Enbrel has always been very high relative to Remicade. Except for the first couple of months, the wholesale price of Enbrel per DDD stayed between 350 and 400 NOK until late fall 2001. Then the price dropped to a level closer to 300 NOK per DDD. Remicade started out with a price of 200 per NOK, but came down to a level between 160 and 170 NOK per DDD after a few months. Humira entered with a price much above the price of Enbrel. Although Humira has kept its position as the price leader, the price gap (compared with Enbrel) has been narrowed during the sample period.

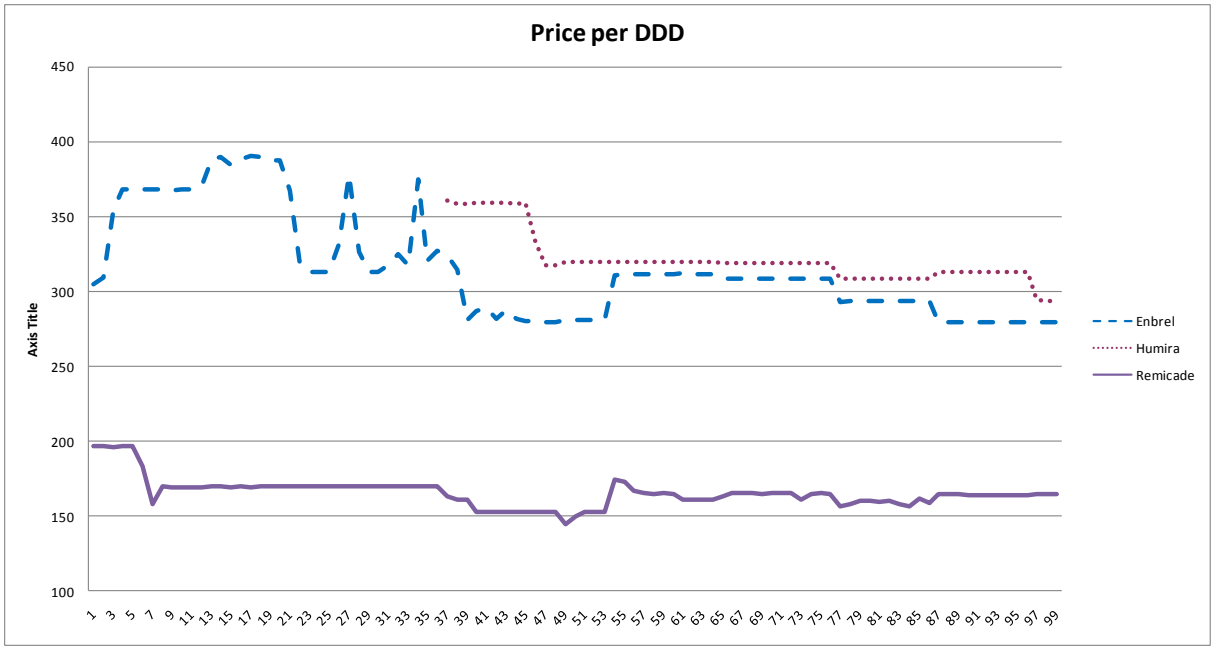

Figure 3. Wholesale price, NOK per DDD.

Note that pharmaceutical prices in Norway are regulated by a price cap. The cap is set to reflect the average of the three lowest prices on the similar drug in selected European countries, such as Sweden, Finland, Denmark, Germany, the UK, the Netherlands, Austria, Belgium and Ireland. The Regulation of 1999 mentioned that to some (minor) extent and in certain cases one should pay attention also to prices on related (but different substances) drugs sold in the Norwegian market and with the same treatment effect and to the cost of producing and distributing drugs. For practical purposes, however, the regulation implied that maximal prices on drugs in the Norwegian pharmaceutical market are set according to an international reference pricing system.

Summary statistics for the sample used in estimating our model is provided in Table 1.

Table 1: Summary statistics

Enbrel (obs: 99)	Mean	Median	Std. Dev.	Kurtosis	Asymmetry	Min	Max
DDD	53 249.77	46 557.00	34 755.95	-1.40	0.34	4 287.00	111 829.00
Price	315.39	308.30	34.98	-0.33	0.93	279.37	390.66
Market share	0.44	0.40	0.13	0.91	1.08	0.15	0.80
Humira (obs: 66)							
DDD	25 739.75	25 076.00	14 090.69	-1.18	-0.12	717.00	47 531.00
Price	321.20	319.00	16.90	1.31	1.38	293.55	360.60
Market share	0.13	0.14	0.04	0.62	-1.22	0.01	0.17
Remicade (obs: 99)							
DDD	62 542.05	58 247.00	42 225.41	-1.00	0.31	3 360.00	159 655.00
Price	165.41	164.78	9.56	3.72	1.40	144.63	196.55
Market share	0.48	0.47	0.12	1.34	0.29	0.20	0.85

We have chosen to restrict the sample period in our empirical analysis to t=38-99. The data reveals several reasons for this.

First, there are reasons to expect demand behavior – and in particular price responses – to be different in the early stage of a new pharmaceutical market compared with the more maturated market. In the early stage, doctors are unfamiliar with the particular technology of treatment (TNF-alpha inhibitors) – both its efficiency and its possible side-effects. In a more mature market, doctors have gained experience with the drug, and will be better able to make treatment choices for the individual patients.[9] Gaining experience with TNF-inhibitors, the doctors will better able to take treatment costs into account when choosing between the available alternatives. Second, capacity shortage for the manufacture of Enbrel during the first years distorts demand. As seen from the data section, Enbrel experienced a sharp decline in sale 2001-2002 that was due to a global capacity problem of the manufacture. After a period of decline, sale and market shares were very unstable, until problems were resolved some months before the entry of Humira.

[9] See Berndt et al. (2003).

4. Econometric model

The decision-making unit on the demand side is the physician, who acts as the patient's agent (Arrow, 1963). In making decisions, however, the physician needs to take into account the situation of each individual patient. In the formal model of demand, therefore, consumers are represented by physician-patient couples, *i=1,..I*. The model is derived from a random utility model (see Train, 2002 for an overview of such models) in which consumers chooses among the available drugs, *j=1,..,J*, to maximize utility. Utility is given by

$$U_{ijt} = U(\nu_{it}, p_{jt}, A_{jt}, \mu_{jt}, \varepsilon_{ijt}), \quad (1)$$

where v_{it} represents a vector of individual characteristics, p_{jt} is the price variable associated with drug j, A_{jt} and μ_{jt} are the observed and unobserved product characteristics, and t is the time index. ε_{ijt} is a random variable distributed across individuals, alternatives and time. Consumer i chooses product j at time t if:

$$U(\nu_{it}, p_{jt}, A_{jt}, \mu_{jt}, \varepsilon_{ijt}) = \max_{r} U(\nu_{it}, p_{rt}, A_{rt}, \mu_{rt}, \varepsilon_{ijt}) \quad (2)$$

The utility function is assumed to be linear with an additive error term that is independently distributed among consumers and product characteristics:

$$U(\nu_{it}, p_{jt}, A_{jt}, \mu_{jt}) = \mu_{jt} - b_{jt} p_{jt} + \varepsilon_{ijt} \quad (3)$$

μ_{jt} is an indicator of perceived treatment quality of drug j at time t. This is a common quality-indicator that applies to all patients that can benefit from TNF-alpha therapy. We will allow perceived quality to be time-dependent.

The costs of treatment with TNF-alpha inhibitors are covered by a third-party. There are two third-party payers. One is the National Insurance Plan (NIS) (termed "I"), and the other is the hospital with which the prescribing doctor is affiliated (termed "H"). As described in Section 1, the funding split between the insurance plan and the hospital varies. At a given time t the drug costs are fully paid by the hospital, fully covered by the insurance plan, or split between the two.

Let p^H be the price covered by the hospital and p^I the price covered by the national insurance plan. The linear utility function is now written

$$U(\nu_{it}, p_{jt}, A_{jt}, \mu_{jt}) = \mu_{jt} - b_H p_{jt}^H - b_I p_{jt}^I + \varepsilon_{ijt} \tag{4}$$

b_H and b_I represent the doctor's perception of drug costs covered by the two different funding parties. The main objective of this paper is to investigate to what extent doctors' perception of drug costs is sensitive to the identity of the third-party payer – the social insurance plan or the hospital. p_{jt}^H and p_{jt}^I are not independent of each other since they represent a particular split of the full drug cost p_{jt}.

The particular funding plans used implies

$$\begin{aligned} p_{jt}^H &= \alpha_{jt} p_{jt} \\ p_{jt}^I &= (1-\alpha_{jt}) p_{jt} \end{aligned} \tag{5}$$

Inserting into (4), we get

$$U(\nu_{it}, p_{jt}, A_{jt}, \mu_{jt}) = \mu_{jt} - b_{jt} p_{jt} + \varepsilon_{ijt}, \tag{6}$$

with

$$b_{jt} = \alpha_{jt} b_H + (1-\alpha_{jt}) b_I \tag{7}$$

When the market for TNF-apha inhibitors opened in 2000, Enbrel was fully covered by NIS (i.e. α=0), whereas Remicade was covered by the hospitals (α=1). In the fall 2002, the funding of Remicade changed. Hospital was to pay 20%, whereas NIS paid the remaining 80% (α=0.2). When entering in 2003, Humira was given the same funding plan as Enbrel, i.e. fully coverage by NIS (α=0). In June 2006, the government then gave the full funding responsibility to the hospitals for all three drugs (α=1).

Since hospitals face budget constraints, the hospital's opportunity costs of drug treatment is strictly positive when α=1. Reduced treatment costs will benefit other activities and patients at the same hospital. With coverage by the national insurance plan, the direct opportunity cost of the hospital will be zero. Choosing a drug that is fully paid by the insurance plan has no impact on the resources available for other activities at the hospital.

We have the following hypothesis:

$$H_0: \ b_H = b_I$$
$$H_1: \ 0 < b_I < b_H$$

Doctors have guidelines that require cost consciousness in their choices of treatment. Therefore, we expect doctors to be price responsive also in the case of insurance plan coverage. However, in the case where the hospital pays the treatment costs, we expect doctors to become more concerned about these costs. This might be due to the personal incentives of doctors' to economize on costs in other to being able to spend extra resources on other patients, or just due to the fact that the hospital management has stronger incentives to monitor the individual doctor's treatment choices when these involves hospitals own budgets.

By assuming ε_{ijt} to be independently, identically distributed extreme value (i.i.d. or type I extreme value) across individuals and products, the probability that consumer *i* will choose drug *j* at time *t* is given by:

(8) $$\varphi_{jt} = \varphi_{jt} = \Pr(U_{ijt} = \underset{k=1}{Max} U_{ikt}) = \frac{e^{\mu_{jt} - b_{jt} P_{jt}}}{\sum_k e^{\mu_{kt} - b_{jt} P_{jt}}}$$

We choose Enbrel to be the base product, here denoted product 1, and if we assume there is no outside good whose utility can be normalized to zero, these probabilities can be written

(9) $$\varphi_{jt} = \frac{e^{\mu_{jt} - \mu_{1t} - b_{jt} P_{jt} + b_{1t} P_{1t}}}{1 + \sum_{k=2}^{3} e^{\mu_{kt} - \mu_{1t} - b_{kt} P_{kt} + b_{1t} P_{1t}}}, \ (j=2,3)$$

and

(10) $$\varphi_{1t} = \frac{1}{1+\sum_{k=2}^{3} e^{\mu_{kt}-\mu_{1t}-b_{kt}P_{kt}+b_{1t}P_{1t}}}$$

The observed parallel to the probability that product *j* is chosen is the market share of the product, m_j. Because we only exploit aggregate data, our observed variable will be the market share, which gives us the following log-odd ratios:

(11) $$\ln(\frac{m_{jt}}{m_{1t}}) = \mu_{jt} - \mu_{1t} - b_{jt}P_{jt} + b_{1t}P_{1t},$$

Doctors' perception of quality may change over time. There are several reasons for this. Manufactures may adopt different marketing strategies, both in terms of size and type, which change doctors' preferences over the three drugs over time. We do not have information about marketing resources in the Norwegian market, but if we assume that the market strategy is not changed frequently, a time trend will be able to capture changes in demand that are due to differences in the marketing strategy for the three drugs.

Following the analysis of Berndt at al. (2003), we also allow quality perception to depend on accumulated sale. We expect doctors to be more willing to prescribe a certain drug the greater is the acceptance of that *drug class* in terms of the drug class' acceptance, measured with cumulative sale. This link between general acceptance and perceived quality might differ between the three drugs. We therefore consider the importance of local acceptance, by allowing perceived quality of drug *j* depend on past sale of the same drug $\mathrm{AX_j}$. These effects are introduced into the demand model by the following assumptions

(12) $$\mu_{jt} = \tilde{\mu}_{jt} + \tilde{c}_j t + d \cdot AX_{jt-1},$$

With this assumption, the demand equation to be estimated is

(13) $$\ln(\frac{m_{jt}}{m_{1t}}) = a_{jt} - b_{jt}P_{jt} + b_{1t}P_{1t} + c_j t + d \cdot \left(AX_{jt-1} - AX_{1t-1}\right)$$

where $a_{jt} \equiv \tilde{\mu}_{jt} - \tilde{\mu}_{1t}$, $c_j \equiv \tilde{c}_j - \tilde{c}_1$.

The parameter a_{jt} is assumed to determined by two elements: $a_{jt} = a_j + \mu_{jt}$. μ_{jt} is a random i.i.d. term (white noise with zero expectation and constant variance), while a_j is a deterministic drug-specific coefficient, that represents attributes and aspects that remain constant over time.

We have three funding plans: α=1, α=0.2, and α=0:

(14)
$$b_{jt} = \begin{cases} b_H \\ 0.2b_H + 0.8b_I \\ b_I \end{cases}$$

To capture these three regimes, we constructed two indicators:

(15)
$$A_{jt}^{I} = \begin{cases} 1 \text{ if drug j at time t has } \alpha = 0 \\ 0.8 \text{ if drug j at time t has } \alpha = 0.2 \\ 0 \text{ if drug j at time t has } \alpha = 1 \end{cases}$$
$$A_{jt}^{H} = \begin{cases} 1 \text{ if drug j at time t has } \alpha = 1 \\ 0.2 \text{ if drug j at time t has } \alpha = 0.2 \\ 0 \text{ if drug j at time t has } \alpha = 0 \end{cases}$$

Using these variables, we reformulate the model to be estimated as

(16)

$$\ln\left(\frac{m_{2t}}{m_{1t}}\right) = a_2 - \left[A_{2t}^{I}P_{2t} - A_{1t}^{I}P_{1t}\right]b_I + \left[A_{1t}^{H}P_{1t} - A_{2t}^{H}P_{2t}\right]b_H + c_3 t + d\cdot\left(AX_{2t-1} - AX_{1t-1}\right) + \mu_{2t}$$
$$\ln\left(\frac{m_{3t}}{m_{1t}}\right) = a_3 - \left[A_{3t}^{I}P_{3t} - A_{1t}^{I}P_{1t}\right]b_I + \left[A_{1t}^{H}P_{1t} - A_{3t}^{H}P_{3t}\right]b_H + c_3 t + d\cdot\left(AX_{3t-1} - AX_{1t-1}\right) + \mu_{3t}$$

Note that the product of the indicators A^I and A^H, and the prices P, defines the prices faced by the insurance plan and the hospital, respectively. Crucial for identification of the price response coefficients is the exogenous variations in relative (i.e. between the three available drugs) insurance plan and hospital prices. We have no reason to believe that the extensive changes in the funding plan are correlated with changes in drug specific attributes.

5. Empirical results

The model (16) was estimated with 3SLS, and the results are reported in Table 2 below. As explained in the data section, we have estimated the model on a restricted period (t=38-99). Model 1 includes the price variable and time trends, and in model 2 cumulative sale is included among the regressors.

Table 2: Results from the 3-stage least-square estimation, t=38-99 (t-values in parentheses).

	Model 1	**Model 2**
Price – ins b_I	0.0026	0.0037
	(2.90)	(3.84)
Price – hosp b_H	0.0045	0.0054
	(3.93)	(4.70)
Time trend- Humira	0.0144	0.0164
	(11.30)	(10.93)
Time trend- Remicade	-0.0110	-0.0105
	(-4.77)	(-4.56)
Accum sale (j)		3.54e-06
		(2.35)
R^2 (Humira)	0.7476	0.7700
R^2 (Remicade)	0.2351	0.2357
# observations	62	62

The price effects are highly significant and negative, implying that an increase in the price of a drug reduces the probability that doctors prescribe the drug.[10] This is the case in both specifications. We also see that the estimated price response under hospital funding always exceeds the estimated price response under insurance plan funding. The results, therefore, support our main hypothesis that doctors become more price conscious when hospital covers the cost of treatment.

The time trend is significant and positive for Humira and significantly negative for Remicade (relative to Enbrel). This effect is also robust to model specification. As expected, past sale of

[10] Note that with our specification a positive price coefficient *b* implies a negative price response on demand.

a drug (Accum sale (j)) has positive effect on doctors' current willingness to prescribe that drug.

In order to better evaluate the economic magnitude of the price effect, we have calculated the elasticity of demand. The price response differs according to the funding source.

The own-price elasticity is given by

$$E_{jt}^{H} = \frac{\partial \hat{\varphi}_{jt}}{\partial p_{jt}} \frac{p_{jt}}{\hat{\varphi}_{jt}} = \hat{b}_{jt} \cdot p_{jt} \cdot (1 - \hat{\varphi}_{jt}) \tag{18}$$

Using the results from Model 1 as the basis for calculation, we have

$$E_{jt}^{H} = \left(\alpha_{jt} 0.0026 + (1 - \alpha_{jt}) 0.0045\right) \cdot p_{jt} \cdot (1 - \hat{\varphi}_{jt}) \tag{19}$$

The figure below plots the point estimate of the elasticity with respect to the price covered by the hospital. The time is running from t=38 to t=99, which in the figures below is indicated by t running from t=1 to t=61.

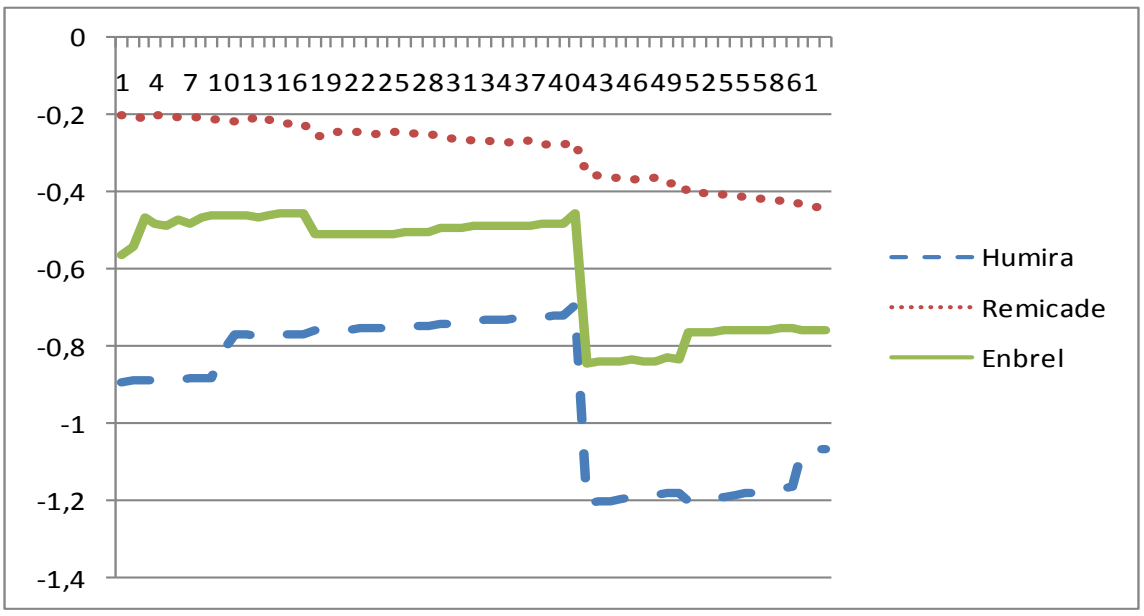

Figure 4: Price elasticity of demand (Model 1).

The sharp increase in the price response in June 2006 is due to the shift in funding source. The shift in price coefficient when moving from pure social insurance funding to pure hospital funding has the effect of increasing the price elasticity for Humira (absolute value) from 0.69 to close to 1.2. In absolute value, Remicade comes out with much lower price elasticity.

In order to gain insight into the economic importance of the funding plan, we have also calculated the expected market share and total treatment costs under different plans.[11] Figure 5 shows the predicted market share for the three drugs, using the true funding plan for each drug in each month.

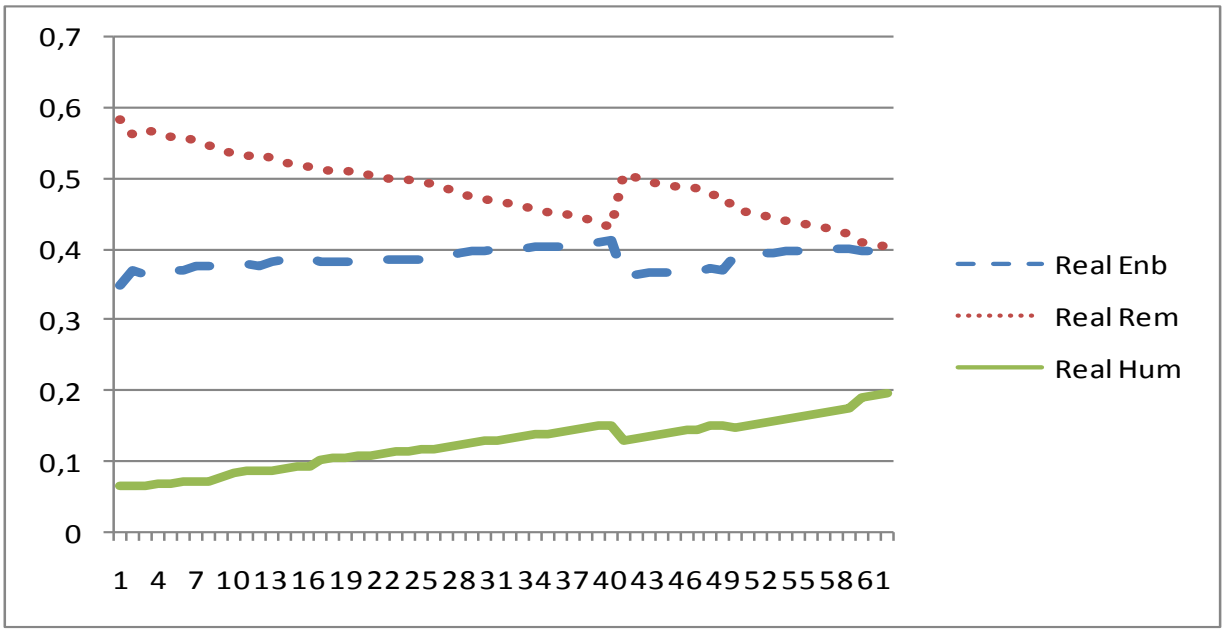

Figure 5: Predicted market shares under different funding plan (Model 1).

According to the results of model 1, Enbrel lost a market share of 5 percentage point when the funding of Enbrel and Humira shifted from the national insurance plan to the hospitals. Humira's loss of market share was smaller –2-3 percentage point. Remicade which always has the lowest market price, gain market shares when doctors become more cost conscious. The predicted increase in market share due to the change in June 2006 amounts to 7-8 percentage point.[12]

[11] The prices of these drugs are regulated by price caps set equal to the average of three lowest prices in a selection of other European countries. Since the Norwegian market represent only a small part of the European market, changes in funding plans here will not affect the prices.
[12] Since the model does not introduce an outside good, there is no effect on market size.

Using predicted market shares with pure hospital funding and insurance plan funding, we have computed the difference in expected total treatment costs. These are reported in the Figure 6 below.

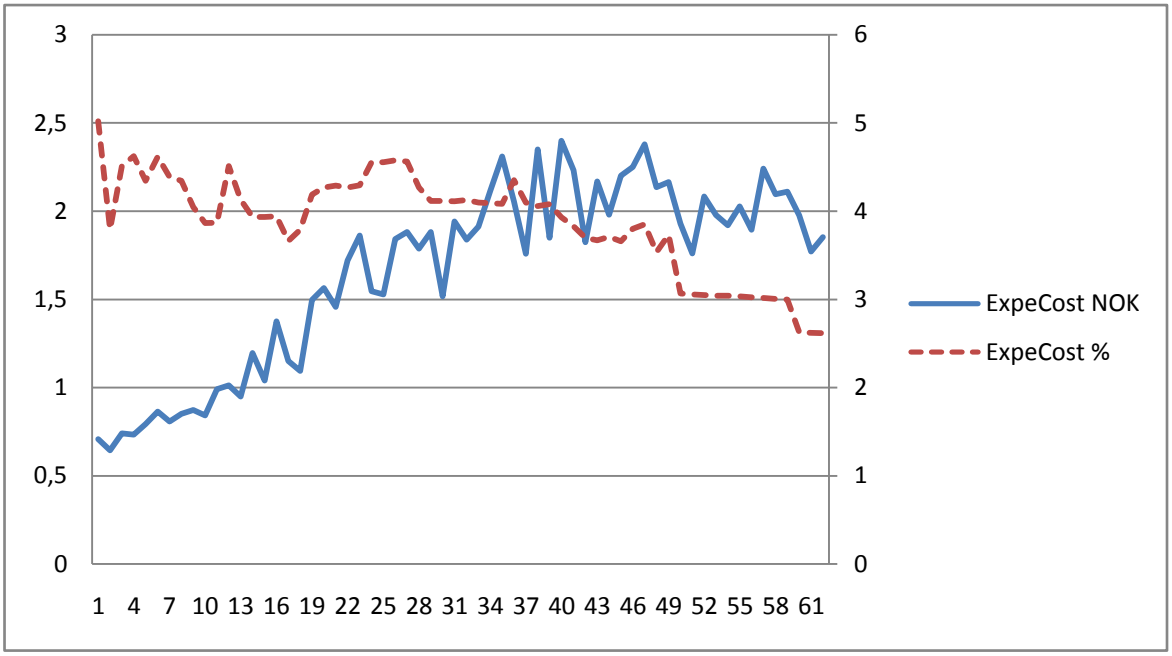

Figure 6: Predicted reduction in total treatment cost per month by moving from pure insurance plan funding to pure hospital funding. Mill. NOK (left axis) and percentage reduction (right axis).

Cost savings turn out be extensive. Monthly reduction in treatment costs amounts to up to 2.5 mill. NOK per month (the solid line - left axis). Relative to treatment costs, monthly savings amounts to between 5 to 3 percent (dotted line – right axis).

When doctors become more cost conscious, and change their prescription choices, the consumer surplus of the doctor/patient couples will – for given prices – fall. If utility is linear in income (so that price coefficient is constant with respect to income), then the expected consumer surplus becomes[13]

$$E(CS) = \frac{1}{b} \ln\left(\sum_{j=1}^{J} \exp^{V_j} \right) + C \tag{20}$$

where V_j is the deterministic part of the linear utility function in (3), C is an unknown constant that represents the fact that the absolute level of utility cannot be measured. Using this

[13] See Williams (1977), Khajavi (1981), Small (1983) and Trajtenberg (1990) for demonstration and application of this.

expression we can compute the change in expected consumer surplus under different funding plans – insurance plan and pure hospital funding.

$$\Delta E(CS) = \frac{1}{b_I}\ln\left(\sum_{j=1}^{J}\exp^{V_j^I}\right) - \frac{1}{b_H}\ln\left(\sum_{j=1}^{J}\exp^{V_j^H}\right) \tag{21}$$

where the superscripts I and H refer to two funding plans. Since the unknown constant C enters expected consumer surplus both before and after the change, it drops out of the difference and can therefore be ignored when calculating changes in consumer surplus. In other to get total consumer surplus we need to determine the number of consumers each month. The exact number of patients is unknown, but following Sorisio and Strøm (2008) we have computed this to be the total number of defined daily doses used per month divided by 30 (the number days). Total surplus is then simply given by the number of consumers times the expected consumer surplus in (19). Using Model 1, the difference between total consumer surplus under national insurance plan and hospital funding is given Figure 7.

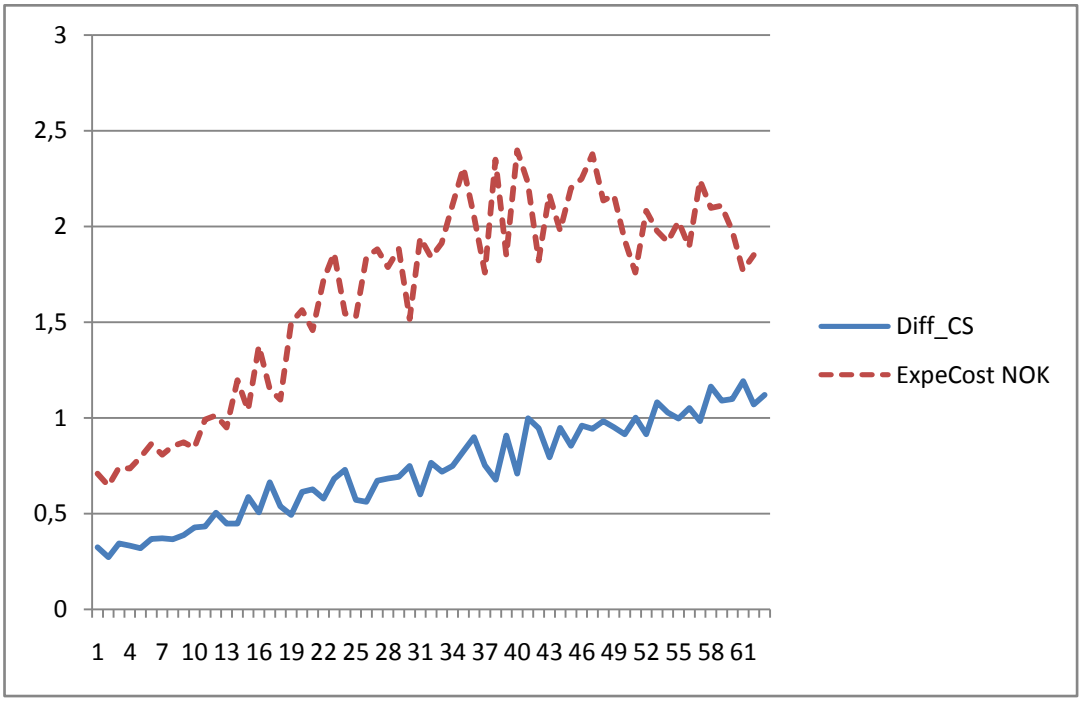

Figure 7: Difference in total consumer surplus under insurance plan and hospital funding (solid line), and reduction in total treatment cost (dotted line). Mill. NOK per month.

We thus see that the change in consumer surplus is economically important. Due to the steady increase in the number of patient, the difference is increasing over time, and reaches a level of

1-1.2 million NOK per month. However, comparing with monthly savings in treatment costs by moving from insurance plan funding to hospital funding, the net gain to the society is around 1 million NOK per month (reduction in treatment costs minus loss in consumer surplus).

6. Conclusion

With use of a unique natural policy experiment in Norway, we have examined to what extent the price responsiveness of prescription choices is affected when the identity of the third-party payer changes. A discrete choice model is employed to capture the doctor's choice among TNF-alpha inhibitors. The price response is allowed to vary with the identity of the third-party payer. Our main result shows that doctors' choice of TNF-alpha inhibitor is responsive to price differences, and that this price response becomes stronger when hospitals cover the costs. The policy change is found to yield a 3-5 percent reduction in total treatment cost. Because these drugs are all on the top five sale value list in Norway[14], the choice of the third-party payer has a non-trivial economic impact. Savings are shown to be far larger than the reduction in expected consumer surplus for the doctor-patient couples.

[14] Norwegian Association of Pharmaceutical Manufacturers (2009)

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