An Econometric Analysis of Contracts between Pharmaceutical Firms and French Veterinarians: A Principal-Agency Theory Approach in the Context of Oligopolies

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Abstract

In France, veterinarians are allowed to both prescribe and deliver drugs, a questioned situation from the perspective of antimicrobial use (AMU) reduction in order to ovoid AM resistance (AMR). This situation places veterinarians in direct commercial relationships with the pharmaceutical industry. The present study aims to describe contracts between pharmaceutical companies and veterinarians during the period 2008-2014. 382 contracts related to 47 drugs belonging to the 8 main pharmaceutical firms (2,320 observations) in France were collected. The price per unit after rebate (PUR) was calculated for each drug and contract. The descriptive analysis demonstrated a high disparity between the content of contracts and the way in which they are presented. A linear regression was then used to explain the PUR with the explanatory variables, which were the yearly purchase objective, the year, the type of drug and type of rebate. The decrease in PUR for each extra €1,000 objective per drug category was established to be €0.061 per 100 kg body weight (BW) for anticoccidiosis treatments, €0.029 per 100 kg BW for anti-inflammatories, €0.0125 per 100 kg BW, €0.0845 per animal for antiparasitics, and €0.031 per animal for intramammary antimicrobials. Applying agency theory shows that veterinarians can be considered the agents in case of monopolistic or oligopolistic situations of pharmaceutical firms, they are considered the principals otherwise. Policies that focus on maintaining veterinarians as principals may help reach the better societal benefit since this helps them maintain access to veterinary services throughout the region at low public cost while being liable for AMU.

KEYWORDS: drugs; veterinarian; pharmaceutical firm; contract

Introduction

The antibiotic resistance observed in humans originates from the use of antibiotics in humans and is likely high in animals as well. From a simple point of view, 'higher antibiotic use leads to higher the antibiotic resistance'. During several decades, an inappropriate medical application has been pointed out as a primary factor of this global issue. Thus, ceaseless efforts, such as the ban of the use of antibiotic growth promotors (AGPs) and the establishment of surveillance systems, have been conducted to cope with this issue (Cogliani et al, 2011). France also participates in this movement through its Ecoantibio plan, which reduced the total consumption of antibiotics in livestock by up to 37% from 2012 to 2017. This decrease was by 75% for fluoroquinolones and by 81% for the last generation of cephalosporines (ECOANTIBIO, 2012).

In France, such drugs can be prescribed only by veterinarians, and drug delivery is restricted to veterinarians, pharmacists and farmer organizations, depending on drug class. In fact, a large part of drug delivery is performed by veterinarians, despite some variations between livestock systems. A recent study highlights that the share of income raising from drug delivery varies across veterinary offices but remains altogether high, regardless of whether small or large animal sectors were considered (Minviel et al., 2019). A recent law has limited veterinarian antimicrobial (AM) delivery to veterinarians and pharmacists. There is increasing concern regarding the conflict of interest due to the simultaneous prescription and delivery of drugs by veterinarians. However, countries that have decoupled prescription and delivery by veterinarians have not observed changes in the pattern of AM use (AMU). Moreover, the French situation shows that prescription and delivery by the same actors does not prevent a large decrease in AMU.

The drug value chain is composed of pharmaceutical firms (which can subcontract drug production), wholesalers, veterinarians (and other actors allowed to deliver drugs) and farmers or animal owners. This means that veterinarians have direct commercial relationships with both pharmaceutical firms and AM end users. The factors that may influence end-user drug

consumption have been recently reviewed (Lhermie et al., 2016). These factors include drug price and induced demand: extra demand may arise from the lack of disease prevention or end-user risk aversion (AMs are very good at handling damage, disease, and control). The price of AMs is known to represent a key driver of use in veterinary medicine (Chauvin et al., 2005, 2005). In human medicine, the link between AM price, AMU and increased AMR has been demonstrated. For instance, in Denmark, the increase in the number of drugs containing ciprofloxacin (from 3 to 10) was associated with a decrease in drug prices by 53%. The proportion of urinary *E. coli* that is resistant to ciprofloxacin increased by 200% in the 4 years that followed (Grundmann et al., 2011). Despite this link between AM price and use, AMs remain a regulated good in most countries.

The induced demand for drugs by patients or farmers and the way in which pharmaceutical firms may modulate prescriptions are not well understood in both human and veterinary medicine. The link between a prescriber's tendency to prescribe more profitable drugs for him/her and drug delivery rebates has been shown in China (Xu, 2012). On the one hand, the relationship between prescribers and pharmaceutical firms was reported to encourage inappropriate usage, to increase medical costs and to favour the propagation of resistance (Buckley, 2004), among others, through asymmetric information (Lee and Kwon, 2011). Prescribers with a frequent intercourse/meeting with a pharmaceutical salesperson tend to (i) more easily prescribe a newly arrived medicine and to (ii) overuse/overprescribe drugs due to the ease of his/her permission for a patient's request for the prescription, even if it is not medically advisable (Watkins et al., 2003; Watkins et al., 2003). The pharmaceutical industry is also known to use the push strategy (e.g., promotions, funding, and sponsorship) in its relation with prescribers (Moynihan, 2003; Buckley, 2004). On the other hand, the close relationships between the pharmaceutical industry and prescribers i) help prescribers access information in some areas, even if there is bias present (Black, 2005) (Prosser and Walley, 2003), ii) improve innovation due to the positive impact of sharing information (García et al, 2007), and iii)

optimize supply chain management (Schwarz and Zhao, 2011). Relationship marketing remains one of the primary drivers of sales in the pharmaceutical industry (Wright, 2003).

The prescriber is recognized as a strong filter to access drugs, which are regulated products. For instance, a recent study observed a change in prescription behaviour in the case of new drugs available on the market, but drug prescription substitution was observed only within the same drug category of the AM family (Lhermie et al., 2019). Because veterinarians and the pharmaceutical industry have commercial relationships, annual contracts are negotiated to define at least the quantity and prices, and a rebate system has been developed by pharmaceutical companies. This complex situation leads to the application of principal-agent theory to analyse the nature of the relation between these contractors and the potential outcome for public health. The central argument of contract theory (Coase, 1937) is that if agents encounter transaction costs, if they can enjoy informational advantages or if nonredeployable investments must be made (i.e., specific assets), then the same goods will not be exchanged at the same price, and the rules of a Walrasian market will not be followed. To make their activities compatible and to share the value surplus thus created, agents sign contracts that limit their behaviour and establish coordination mechanisms based on mutual obligations (Brousseau, 1997). Considering the frequency of drug purchase, both parties have an interest in establishing contracts to reduce transaction costs. Moreover, yearly contracts will also support the planning of their activities. Veterinarians will ensure drug availability and gain visibility for their pricing policy, which also helps increase income since the rebate obtained from pharmaceutical firms is often not passed on to the final price proposed to end users. Signing contracts with several firms allow for veterinarians to reduce information asymmetry regarding drug prices, as they can compare prices. Pharmaceutical firms will be ensured of their clients' willingness to pay, better define the yearly market expectation and will visibility regarding the drug supply chain (from local to international levels), which altogether supports production cost cutting (lean management). Competitive drugs with close medical indications are often differentiated on

marginal points, which could be seen as an attempt by the pharmaceutical firm to maintain asymmetric information related to prescribers and end users.

The aim of the present work is to describe the trade-off between the oligo-political position of pharmaceutical firms and the prescription freedom of practitioners in a situation of joint prescription and delivery. To do so, the French pharmaceutical contracts between pharmaceutical companies and veterinarians during 2008-2014 were analysed, focusing on the relationship between purchase objectives and rates of rebate. An agent-principal approach perspective is then proposed.

Materials and methods

Data

Thirty French veterinarian offices were randomly contacted to provide their purchasing contracts with pharmaceutical firms for the period 2006 to 2014. Data from 8 veterinary organizations, 5 veterinary offices and 3 common purchasing groups were collected. To be included, the purchase contracts should specify the drug or group of drugs to be purchased, the objective of the purchases required by the veterinarian and the rebate in which the pharmaceutical firm has engaged (in absolute value or percentage). A total of 498 contracts, 23 pharmaceutical firms and 125 drugs were included (Figure 1). The 382 contracts related to the 8 main pharmaceutical companies were related to bovine production, and the categories of drugs that were AMs, antiparasitics (APs; i.e., pest control), anti-inflammatories (AIs) and vaccines (VACs) were sorted out. They included 47 selected drugs and 2,320 observations. Each drug was coded according to the company (C1 to C8) and the drug (P1 to P47) to provide a combination from C1P1 to C8P47. For each drug, the drug price for the veterinarian when he/she bought it from the wholesaler (i.e., before the rebate from the pharmaceutical firm) was implemented.

A database was then created with the following variables: veterinarian, firm, year (of the contract), range (of the drug, i.e., how the drugs were grouped in the contract), drug name, yearly revenue from the veterinarian office for each firm, duration of the contract (trimestral, semesterly, yearly), monetary objective for the rebate, type of rebate (per drug, per range or global, as defined below), rebate value in percentage, price of the drug, type of drug (parenteral administration following body weight dosage (PerBW), intramammary syringe (SYR), VAC or per animal fixed dose (DOSE)), and category of drug (AMs, APs, AIs, or VACs). The type and category of drugs are as follows: VAC are DOSE and AIs are PerBW, but AMs are PerBW or SYR and APs are PerBW or DOSE. When the rebate was indicated in whole value or in free units, it was converted into the percentage of the rebate for a given objective. Three types of rebates were defined. When a drug was explicitly nominated in a contract (with an objective and a rebate), the type of rebate was defined as the drug. When a group of drugs was nominated in a contract (with an objective and a rebate), the type of rebate was defined as the range. For a given year, a drug can then have a first rebate with an objective linked to this drug only and a second rebate with an objective defined for the range of drugs. When the rebate was given when both the objectives of drug and those of range were achieved, the rebate type was defined as global. To allow for the comparison of the contracts, a standardization of the duration was made, since 67% of the contracts were based on full years. For the same drug, many presentations were available on the market, and the price per ml was different. Because the contract did not specify the presentation of the drug, the combination of the presentations expected to be purchased to achieve the objective was defined to be the same share as indicated in central average selling. When the objective to be achieved to reach the rebate was defined for multiple drugs, the share of drugs was defined as equal, except if the share was defined in the contract. When the objective was defined for multiple drugs belonging to various types of drugs (for instance, parenteral administration following weight dosage and vaccines), these drugs were excluded since prices cannot be standardized, as explained below.

Price per unit after rebate (PUR)

To standardize the way in which contracts may influence the final drug price paid by the veterinarian, a price per unit of drug after rebate (PUR) was calculated for a treatment of 100 kg BW of animal (parenteral administration drugs) or for a treatment per animal (per animal fixed dose, for vaccine, intramammary syringes and few others).

The weight of the animal treated (WAT, kg) for a given drug was calculated as indicated in Equation (1):

$$\mathbf{WAT = Qty/Dose} \quad \mathbf{(1)}$$

where Qty is the quantity of active substance per packaging unit (mg/g or mg/ml), and dose is the dose regimen to be administered (mg or IU per kg BW); the dose was reported from the Summary of Product Characteristics (SPC; https://www.ema.europa.eu/en). For ambiguous situations, the guidelines of the French National Veterinary Medicine Agency (ANSES) were followed. When the treatment duration was an interval, the longest duration was selected (ANSES, 2019). For instance, when the dose varied between species, the bovine dose was maintained. Then, the yearly quantity of BW to be treated with the yearly contract (WAT_Contract) was calculated as indicated in Equation (2):

$$\mathbf{WAT\_contract\ (kg) = WAT\ *Objective/Price} \quad \mathbf{(2)}$$

where Objective is the objective (€) mentioned in the contract, and price (€) is the price of the drug.

Then, PUR was expressed in euros per 100 kg BW treated as indicated in Equation (3):

$$\mathbf{PUR\ (€/100\ kg\ BW) = (Objective - Rebate)/WAT\_contract\ *100} \quad \mathbf{(3)}$$

where Rebate is the absolute rebate (objective multiplied by the rebate value in percentage).

For intramammary syringes, PUR was calculated for a whole treatment of mastitis, as indicated in the SPC. For dry-off, one treatment per teat was considered:

$$\mathbf{Nb\_Trt = Nb\_Syr\ \_Pack/Nb\_Syr\_Trt} \quad \mathbf{(4)}$$

where Nb_Trt is the number of animals treated for a given packaging, Nb_Syr_Pack is the number of syringes in the packaging considered, and Nb_Syr_Trt is the number of syringes required for the whole treatment, as indicated by the SPC.

Then, PUR was calculated in euros per animal, as indicated in Equation (5):

$$\textbf{PUR (€/animal) = (Objective – Rebate)/(Nb\_Trt*Objective/Price)} \quad \textbf{(5)}$$

Similarly, for vaccines, the PUR was calculated for 1 year of protection, as indicated in Equation (6):

$$\textbf{PUR(€/animal) = (Objective – Rebate)/(Objective/(Price\_Dose * Nb\_Doses)} \quad \textbf{(6)}$$

where Nb_Doses is the number of doses for annual protection, and Price_Dose is the price per dose.

Descriptive analysis

A descriptive analysis was first performed. The contracts were compared by year and by company to understand how they were built and how the rates and the types of conditions were determined. Dispersion graphs were drawn of the PUR on the rebate rates for all drugs separately and for all the possibilities of rebate rates when several were possible for a given drug. When appropriate, a comparison was conducted for the group of drugs with similar indications to draw the temporal pattern of the combinations among rebate, objectives and PUR.

Analytic statistics

Before the analytic step was performed, a second set of restrictions was presented (Figure 1). First, observations obtained with rebates defined in the contract for multiple drugs were not considered for this second step to limit the assumption being made. Second, exclusions were performed for specific drugs to exclude outliers or drugs with very different characteristics within each category of drug (AMs, APs, AIs and VACs). An AMs drug with a mean PUR of

€15 per 100 kg BW was excluded since it was up to twice the average PUR range (€1-10 per 100 kg BW) of other AMs. The higher PUR for this drug was in accordance with the specificity of its indication (mastitis treatment by parenteral route). Moreover, most of the objectives were within the range of € [0; 25,000], and others were excluded (195 out of 2,320 observations). Finally, the drugs expressed as doses before 2010 had very low PUR (€1 vs €3.25 per dose), suggesting the exclusion of these 5 observations.

Data were then analysed with R software (R core team, 1997). Linear regression was performed using the nlme package of R. The outcome variable was PUR, and the explanatory variables were objective, year, yearly revenue from the veterinarian office for each firm, type of drug (general administration, intramammary syringe, vaccine or per weight dose) and type of rebate (drug, range, or global). The variable type of PUR was also created (per 100 kg BW or per dose). A step-by-step procedure was used to include explanatory variables one by one, and then, final multivariate models were proposed based on Akaike information criterion (AIC) values. Both drug name and firm were considered random variables.

Results

Drug typology

The drugs were classified into 5 groups according to the relationship between the PUR and the purchase objective. Figure 2 summarizes the profile of each group, and the results for all drugs are proposed in supplemental data 1. Group 0 refers to drugs that have been little represented in the sample (data not shown, n=19). Group 1 includes drugs with PUR that linearly decrease with the objective. The PUR does not change with the objective for group 2. Group 3 refers to drugs with 3 additive rebates and is divided into 2 classes. The PUR changes according to the type of rebate (drug, range, or global) for group 3A, but such a relationship is not seen for group 3B. Finally, group 4 includes drugs with no relationship observed between PUR and objectives.

240 **Dynamics of 3 drugs with similar indications**

241 Three drugs indicated for respiratory diseases of cattle (C8P39, C4P11, and C7P37, by way of
242 their arrival on the market) were specifically analysed to better describe the place of the
243 contracts in the veterinary-firm relationship (Figure 3). The drug C8P39 arrived on the market
244 in 2003, and its PUR was €4 to €5 per 100 kg BW up to 2010. Similarly, the PUR of C4P11
245 was approximately €4 per 100 kg BW up to 2010. The drug C7P37 arrived on the market in
246 2011, and a decrease in PUR by €0.5 to €1 per 100 kg BW was observed for some veterinarians
247 for C4P11 and C8P39. This decrease in PUR was achieved through an increase in rebates:
248 C8P39 used to have a rebate of 5-10% for objectives above €4,000, whereas C7P37 and C4P11
249 arrived on the market with rebates of 10-25%. Then, the contracts observed for C8P39 reached
250 40%, but the objective was also increased, whereas the objectives for the other 2 drugs remained
251 very low. A rebate of 25% was finally offered to all veterinarians, i.e., with very low purchase
252 conditions, by C7 for C7P37.

253 **Factors influencing PUR: analytic statistics**

254 The distribution of the PUR per group and category of drugs is shown in Figure 4 and Table 1.
255 AIs and APs have low variability, whereas AMs has large variability. Coccidiosis-related
256 treatment has been classified separately (AP.C) since its PUR is higher than that of other APs.
257 One drug with high PUR is observed for AP, as the only deworming drug with a unique dose
258 per animal (not per 100 kg BW). The type of drugs VACs and SYR and, to a lesser extent,
259 DOSE are higher than INJ, in accordance with a PUR per animal for the first 3 types and per
260 100 kg BW for the fourth one.

261 In none of the models was the yearly revenue from the veterinarian office for each firm
262 significantly associated with PUR. The average value of PUR for a null objective, a drug per
263 100 kg BW and the type of rebate for that drug was €3.26 (Table 2). Compared to AM, drugs
264 from the categories AIs and APs were €2.1 and €2.0 lower than those from the categories AP.Cs
265 and VACs were €1.1 and €2.3 higher, respectively. For the category AM, an objective of €1,000

was associated with a decrease in PUR by €0.023, and a global rebate was associated with a decrease in PUR by €0.12. Finally, AMs expressed per animal had a PUR that was €0.74 higher than that of AMs expressed per 100 kg BW. Moreover, the 2 by 2 and 3 by 3 interactions were significant, but the interpretations were complex. To allow for a better understanding of these interactions, the analysis was performed per category of drugs (Tables 3 to 5).

For VAC, no explanatory variable was significantly associated with PUR. The mean PUR was €5.28 per dose. For AP.C, the average PUR was €3.50 per 100 kg BW for a null objective and a rebate on the drug (Table 3). An extra objective of €1,000 was associated with a decrease in PUR by €0.061, and a global rebate was associated with an increase in PUR by €0.97, compared to a rebate on the drug only. For AI, the average PUR was €1.07 per 100 kg BW for a null objective and a rebate on the drug (Table 3). An extra objective of €1,000 was associated with a decrease in PUR by €0.029, and a global rebate was associated with an increase in PUR by €0.15, compared to a rebate on the drug only. No significant interaction was observed for AP.C or AI.

For APs (Table 4), the average PUR was €1.15 per 100 kg BW for a null objective and a rebate on the drug. An extra objective of €1,000 was associated with a decrease in PUR by €0.0124 per 100 kg BW for drugs with a rebate on the drug. The PUR was €1.48 higher for drugs with PUR per animal compared to those with PUR per 100 kg BW, with all other things being equal. In other words, the PUR was €2.63 (i.e., 1.15+1.48) per animal for drugs with a rebate on drug for a null objective. A global rebate was associated with a decrease in PUR by €0.075 per 100 kg BW compared to a rebate on the drug only, but the decrease in PUR was €0.15 higher for drugs with PUR expressed per animal and a global rebate compared to drugs with PUR expressed per 100 kg BW and with a drug rebate. Moreover, the PUR decreased slower with the objective when a global rebate was applied (difference of €0.009 per €1,000 of extra objective). As a result, for a drug with a global discount, each €1,000 extra objective was associated with a decrease in PUR by €0.079 (-0.0124-0.0757+0.009) per 100 kg BW. Finally,

each €1,000 extra objective was associated with an average decrease in PUR by €0.072 per animal for drug with a global rebate.

For AMs (Table 5), the average PUR was €2.76 per 100 kg BW for a rebate on the drug. Drugs with PUR expressed per animal had a PUR that was €1.90 higher compared to others, leading to an average PUR of €4.66 per animal for a rebate on the drug. A global rebate tended (P=0.07) to be associated with an increase in PUR by €0.20 per 100 kg BW compared to a rebate on the drug only, but it was significantly associated with a decrease in PUR by €0.59 (-0.79+0.20) for drugs with PUR expressed by animal. For drugs with PUR expressed per 100 kg BW, the PUR was not associated with the objective, but it was decreasing by €0.031 per animal for each extra €1,000 objective for drugs with PUR expressed per animal.

Discussion

The present work is the first study focusing on contracts between veterinary practitioners and pharmaceutical firms in the context of linked prescription and delivery. The first part of the present work allows us to better understand the kind of relationship between pharmaceutical firms and practitioners. The second part quantifies the relationship between the PUR and objectives for different drugs.

Empirical considerations

For all categories except VAC, the objective is negatively associated with PUR. Because the variables drug and pharmaceutical firm were kept as random effects, this association means that for a given drug of a given firm, the real price paid by the veterinarian is decreasing when the objective increases, as expected. The decrease in PUR for each extra €1,000 of the objective ranges from €0.003 to €0.085 and even from €0.03 to €0.06 for most of the results. The present association is reported as linear since the other functions tested (squared, cube, etc.) were not significant. The relationship is unlikely to be linear: a maximum rebate rate is observed for

many drugs when the objective exceeds a threshold. Further research is needed to define with more precision the nature of the function linking the PUR and the objective. Even if the present study had not included real purchases but rather the objective of such purchases, the framework described here clearly demonstrates the relationship between drug price and quantity purchased for French veterinary practitioners for the studied period. The rate of contract completion is reported to be above 80% for this period. In summary, the decrease in PUR for each extra €1,000 of the objective per category of drug is established to be €0.061 per 100 kg BW for AP.Cs, €0.029 per 100 kg BW for AI, €0.0125 per 100 kg BW and €0.0845 per animal (only 1 drug) for APs and €0.031 per animal for intramammary syringe AMs.

Amazingly, PUR was not associated with the objective of the vaccine, which is in opposition to the expected results since vaccines represent a hot spot in the veterinary drug market, with high revenue. They are often reported from field actors as the subject of fierce competition in practice. The present lack of significant association may come from the fact that the majority of the observations (70%, i.e., 84 out of 120 observations) arise from the same pharmaceutical firm, performing 3 additive rebates.

As expected, PUR is negatively associated with a global rebate for APs and for AMs, which means that the extra rebate reduces PUR. However, this effect is limited for APs with a lower (even if negative) association between PUR and the objective when a global rebate is given by the firm. The association between PUR and the objective in the case of a global rebate is even lower (-€0.072) for animals as units of PUR (compared to per 100 kg BW), probably because of the higher (+€1.48) average PUR for animals as units of PUR (compared to per 100 kg BW)

Principal-agent approach

The present results also provide new and clear insight into the respective positions of the pharmaceutical firm and veterinarians in the French context. Agency theory considers the relationships between contractual parties as unequal: the principal is seeking to align the

342 behaviour of the agent, who provides particular information, with his/her own interests. In the
343 present situation, considering the gap in terms of firm size, pharmaceutical firms have market
344 power and thus are likely to be the principal, while veterinarians are likely to be the agent. Such
345 a superficial analysis suggesting that pharmaceutical firms play the role of the principal is
346 supported by evidence from the present work.

347 We demonstrated here that veterinary drugs, even if regulated, are subject to market
348 consideration, leading to changes in their use and in their prescription. The present results
349 clearly demonstrated the relationship between lower PUR and higher objectives as a potential
350 source of conflict of interest, with consequences for prescription patterns. However, this does
351 not mean that pharmaceutical firms are the principal of the relationship. In contrast, this
352 marketing power of the firm, clearly demonstrated here, supports the idea of the pharmaceutical
353 firm as the principal (in addition to supporting the idea of the conflict of interest). The results
354 highlight the marketing efforts and imagination provided by pharmaceutical firms to present to
355 veterinarians various kinds of contracts and different relationships between the rebate and the
356 objective, which may be considered a way to maintain information asymmetry. This includes
357 different types of rebates, different periods of eligibility, and different ways to present the rebate
358 obtained (percentage, absolute value, or free units). The present work also shows that this
359 includes different effect sizes (€0.003 to €0.085 for each extra €1,000 of the objective), even if
360 this relationship cannot be seen directly from the contract by the buyer. The rebates described
361 here also demonstrated multiconditional rules and are included by the firm in contracts (multi-
362 objective contracts), with varying conditions between different categories of drugs (3 types of
363 rebates) and even new extra conditions proposed during the year, which strengthens the
364 intention of veterinarians to buy drugs from the same firm to increase the rebate and to avoid
365 any sharing of what they bought between different pharmaceutical firms. This approach also
366 aims at preventing any reasoning by range of drug or by drugs technically equivalent (i.e., drugs
367 with the same indication and sold by 2 firms) from the veterinarian. Moreover, the fact that the
368 relationship between the objective and the rebate is limited to a maximum rebate rate per drug

or range of drugs clearly supports the pharmaceutical firm acting as the principal, which can even be seen as the final marketing strategy: stimulating the purchase through rebates but limiting the overall amount of rebate by complex rules that may limit the understanding and overview of veterinarians on this question of prices.

The analysis of the 3 drugs in direct competition (Figure 3) also clearly shows the marketing power of pharmaceutical firms and their ability to change rules. In a situation of an oligopoly, the drug C8P34 has a low rebate that seems to be imposed by the firm to most of its clients. The ease of use (long-acting) and technical innovation may be a reason for the high demand, and the situation can be qualified as an oligopoly since other drugs for the same indication face more difficult conditions of use. The drug C7P37 arrived on the market with a high rebate, but its PUR remained the highest of the 3 drugs. Veterinarian decisions based only on rebate will lead to bad decisions, but any systematic transformation of rebates into PUR remains impossible due to the heterogeneity of the contracts proposed by pharmaceutical firms. Here, pharmaceutical firms are clearly not transparent and reinforce information asymmetry. Interestingly, the first drug on the market maintained the lowest PUR for the whole period of the 3 drugs on the market, highlighting the complex relationship between PUR and objectives in cases of products with direct competition. Unfortunately, the present study did not allow us to perform a similar analysis for other drugs in direct competition due to inconsistency in contract collection and data availability.

Taken together, our results show that pharmaceutical firms can be considered the principal, based on the information asymmetry and the marketing power they can develop compared to the limited size of most veterinary offices. Bargaining power appears to be clearly unbalanced. In contrast, veterinarians have a specific position that allows them to counteract pharmaceutical firms' power, even leading them to ask whether veterinarians should not be considered the principal in this contractual relationship. Because of their close relationship with farmers and their field experience, veterinarians have some information superiority in the transaction. They

395 are the ones with the information regarding the farmers' willingness to pay and the consecutive
396 need for drugs. In addition to these arguments, the present work reinforces the conclusion of
397 considering the veterinarian as the principal.

398 A key argument is that the final decision of the purchase and on the prescription remain with
399 the veterinarian only and that veterinarians are using this tool to maintain and strengthen their
400 power. The present work clearly shows that in a situation of the oligopolistic position of a
401 pharmaceutical firm, the veterinarian is mainly a price taker. However, we observed that the
402 veterinarian clearly acts as principal in the case of free competition between drugs, which was
403 clearly highlighted when 2 new drugs arrived on the market (Figure 3), leading to a shift from
404 an oligopolistic position (no real competitor of C8P34 since real innovation) to a free
405 competition position. Veterinarians clearly use their prescription power to ensure that
406 pharmaceutical firms change their position, which is in accordance with a recent study that
407 highlighted the change in AMU in cases of market changes (new drugs) at the national and
408 regional levels, but this was observed only between drugs with similar medical indications
409 (similar technical characteristics) (Lhermie et al., 2019).

410 Seeing the veterinarian as the principal is also reinforced by the low incitation given by the
411 pharmaceutical firms. Amazingly, the decrease in PUR (€0.003 to €0.085 for each extra €1,000
412 of the objective) is low. Even if the absolute amount for veterinary offices can be high (because
413 of high revenue), there are increasing calls for the higher independence of veterinarians to
414 pharmaceutical firms by the veterinarians themselves (personal observations). The present work
415 gives credit to this statement, and all the results show that PUR is positively associated with a
416 global rebate for AP.C, AIs and partly AMs. This positive association can be interpreted as a
417 hidden relation within the contract and an application of an extra rebate in case of higher initial
418 PUR, in accordance with the fact that recent drugs (or medical innovation) are on average more
419 expensive than older drugs and receive extra rebates to gain or secure markets in a competitive
420 context. However, this interpretation makes sense only if an oligopoly applies since free

competition gives power back to veterinarians. In summary, the veterinarian can be considered the principal once the oligopoly on a drug is over and remains the agent in cases of a monopolistic or oligopolistic situation of the pharmaceutical firm. These findings are in line with the literature extensively highlighted by the major role of market structure (Sexton and Lavoie, 2001; Donald et al., 2006).

Agency theory highlights that both parties may have an interest in the principal compensating the agent in exchange for the abandonment of the informational advantage or consequences by the latter. Here, the situations may appear all the more complex, as the drug is a regulated private good and veterinarians jointly support public services through i) the collective dimension of animal health, including zoonosis, ii) limitation of the side effects of antibiotic use, iii) consolidation of animal and human welfare, and iii) securitization of high-level service access in areas where it is limited. These collective and public considerations lead to question-linked policy considerations.

Policy considerations

There are increasing calls to separate delivery from prescription in veterinary medicine. The efficiency of such a policy is not clear. Countries that had separate prescriptions and deliveries by veterinarians did not observe changes in the pattern of AMU. The income of veterinarians highly depends on delivery in France. A recent study highlights that the share of income raising from drug delivery varies across veterinary offices but remains altogether high, regardless of whether small or large animal medicine is considered (Minviel et al., 2019). The separation of drug prescription and delivery may lead to great changes in veterinary services, as many territories are lacking an adequate veterinary service offer. The present work sheds new light on this issue when analysing the recent impact of new regulations that occur after the period covered by this study. New limitations on drug prescription and delivery and on contracts and

446 veterinary drug prices, specifically for critical AMs, have been adopted in the context of
447 national plans to reduce AMU (ECOANTIBIO, 2012, 2017). Such an evolution has stressed
448 the marketing power of pharmaceutical firms and the freedom of practitioners, but in different
449 proportions, while globally strengthening the role of veterinarians as the principal. Another
450 example that reinforces the idea that the role of principal for the veterinarian may be facilitated
451 by institutional context is the emergence of suprastructures such as corporations that are
452 specifically in charge of drug purchasing. They establish contracts on behalf of veterinarian
453 offices and clearly move the ambiguous principal-agent relationship toward a principal role for
454 the veterinarian (or for the group of economic interest heads).

455 This finding clearly shows that regulation and power equilibrium between pharmaceutical firms
456 and veterinarians are closely linked and that adequate regulation may help within the bargaining
457 power of veterinarians, permitting them to provide common goods (animal health service in
458 low-density areas, for instance) while being in a conflict of interest. Even if the present situation
459 may be paradoxical, improving access to services at minimal public cost in areas in a context
460 of difficult service access may be an easy way to improve societal benefit. In other words, the
461 separation of prescription and delivery may not be as efficient for reaching societal benefit as
462 might providing an institutional context—including regulation if required—which strengthens
463 the bargaining power of veterinarians and makes sure they remain the principal in their
464 relationship with pharmaceutical firms or at least that they retain some power. However, recent
465 results from the application of transaction costs theory to the dairy sector (Ménard and
466 Valceschini, 2005; Royer, 2011; Royer et al., 2016) emphasize the contribution of the state to
467 the legitimatization and improvement of the efficiency of contracts. Public policies that focus
468 on maintaining the bargaining power of veterinarians may be the best public cost-benefit
469 strategy.

Conclusions

The present work is the first study focusing on contracts between practitioners and pharmaceutical firms in the context of joint prescription and delivery. Even if pharmaceutical firms may appear as the principal, evidence is provided here to consider the veterinarians as the principal in the French context. The bargaining power between the two clearly appears to be dependent on whether the pharmaceutical laboratory has an oligopolistic situation in the field or whether the drugs are subject to free competition. Policies that focus on maintaining veterinarians as the principal may help reach optimal societal benefit since this helps maintain access to veterinary services at low public cost.

		PUR (€ per dose or per 100 kg BW)			
		Unit	n	μ	σ
Category of drug	*AM*	Both	530	5.01	4.38
	AI	€ per 100 kg BW	198	1.28	0.49
	AP	Both	440	1.25	1.40
	AP.C	€ per 100 kg BW	43	4.22	1.26
	VAC	€ per animal	119	8.91	3.59
Type of drug	*PerBW*	€ per 100 kg BW	947	1.84	1.96
	DOSE	€ per animal	33	2.85	1.44
	SYR	€ per animal	226	7.07	2.19
	VAC	€ per animal	119	8.91	3.59

Table 1: Descriptive statistics of PUR.

AM: antimicrobials; AI: anti-inflammatories; AP: antiparasitics; AP.C: anticoccidials; VAC: vaccines; PerBW: drug administered with a dose per bodyweight; DOSE: drug administered with a fixed dose per animal; and SYR: intramammary syringe.

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488

		Estimate	(SE)	P value
Intercept		3.261	(0.284)	< 2e-16
Objective (per €1,000)		-0.0234	(0.00306)	4.4e-14
Category of drug	*AM*	Reference		
	AI	-2.094	(0.815)	0.0117
	AP	-1.977	(0.567)	0.0007
	AP.C	1.167	(1.24)	0.3494
	VAC	2.380	(1.04)	0.0247
Type of rebate	*Drug*	Reference		
	Range	-0.0702	(0.0882)	0.4265
	Global	-0.123	(0.0384)	0.0013
Unit of PUR	*Per 100 kg*			
	BW	Reference		
	Per animal	0.7412	(0.269)	0.0060

489

490 **Table 2: Final linear regression for all groups (without interaction)**

491 The outcome variable is PUR (€). SE: standard error; AM: antimicrobials; AI: anti-
492 inflammatories; AP: antiparasitics; AP.C: anticoccidials; VAC: vaccines; the type of rebate
493 can be applied to drugs only, to a range of drugs or on all the drugs for a given pharmaceutical
494 firm (global); per 1/100 kg BW: PUR expressed per 100 kg bodyweight; and per animal: PUR
495 expressed per animal.

496

		AP.C			AI		
		Estimate	(SE)	P value	Estimate	(SE)	P value
Intercept		3.50	(0.734)	0.0157	1.07	(0.168)	4.43e-05
Objective (per €1,000)		-0.0615	(0.0114)	3.75e-06	-0.0291	(0.00342)	4.43e-15
Type of rebate	*Drug*	Reference			Reference		
	Range	-0.248	(0.131)	0.0656	0.156	(0.0862)	0.0709
	Global	0.973	(0.289)	0.0017	0.144	(0.0559)	0.0106

Table 3: Final linear regression for anticoccidials (AP. C) and anti-inflammatories (AI)

The outcome variable is PUR (€). SE: standard error. The type of rebate can be applied to drugs only, to a range of drugs or on all the drugs for a given pharmaceutical firm (global).

		Estimate	(SE)	P value
Intercept		1.15	0.0193	3.31e-06
Objective (per €1.000)		-0.0124	0.00223	5.08e-08
Type of rebate	*Drug*	Reference		
	Range	0.0064	0.0622	0.917911
	Global	-0.0757	0.0213	0.000437
Unit of PUR	*Per 100 kg BW*	Reference		
	Per animal	1.48	0.0667	0.036096
Unit of PUR (per animal) x Type of rebate (global)		-.0.146	0.0690	0.034093
Unit of PUR (per animal) x Objective (per €1.000)		-0.0132	7.986e-06	0.100520
Type of rebate (global) x Objective (per €1.000)		0.0095	2.505e-06	0.000171
Unit of PUR (per animal) x Type of rebate (global) x Objective (per €1.000)		-0.0717	1.791e-05	7.57e-05

Table 4: Final linear regression for the category antiparasitics (AP)

The outcome variable is PUR (€). SE: standard error. The type of rebate can be applied to drugs only, to a range of drugs or on all the drugs for a given pharmaceutical firm (global); per 100 kg BW: PUR expressed per 100 kg bodyweight; and per animal: PUR expressed per animal.

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		Estimate	(SE)	P value
Intercept		2.76	0.457	2.97e-05
Objective (per €1.000)		-0.00721	0.0117	0.5411
Type of rebate	*Drug*	Reference		
	Range	0.133	0.251	0.5972
	Global	0.200	0.110	0.0701
Unit of PUR	*Per 100 kg BW*	Reference		
	Per animal	1.90	0.324	9.45e-09
Unit of PUR (per animal) x Type of rebate (range)		0.139	0.443	0.7538
Unit of PUR (per animal) x Type of rebate (global)		-0.788	0.134	9.31e-09
Unit of PUR (per animal) x Objective (per €1.000)		-0.0031	1.335e-05	0.0230

510 **Table 5: Final linear regression for the category antimicrobials (AMs)**

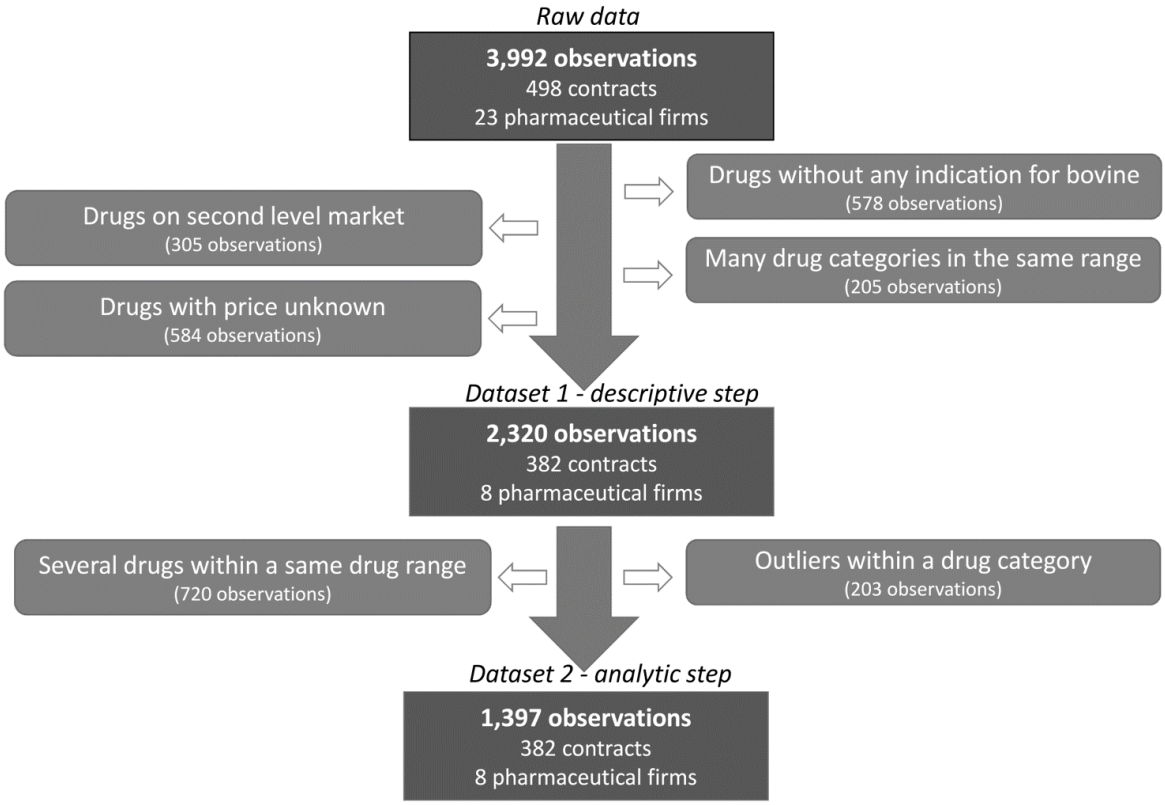
511 The outcome variable is PUR (€). SE: standard error. The type of rebate can be applied to drugs
512 only, to a range of drugs or on all the drugs for a given pharmaceutical firm (global); per 100
513 kg BW: PUR expressed per 100 kg bodyweight; and per animal: PUR expressed per animal.

514

515

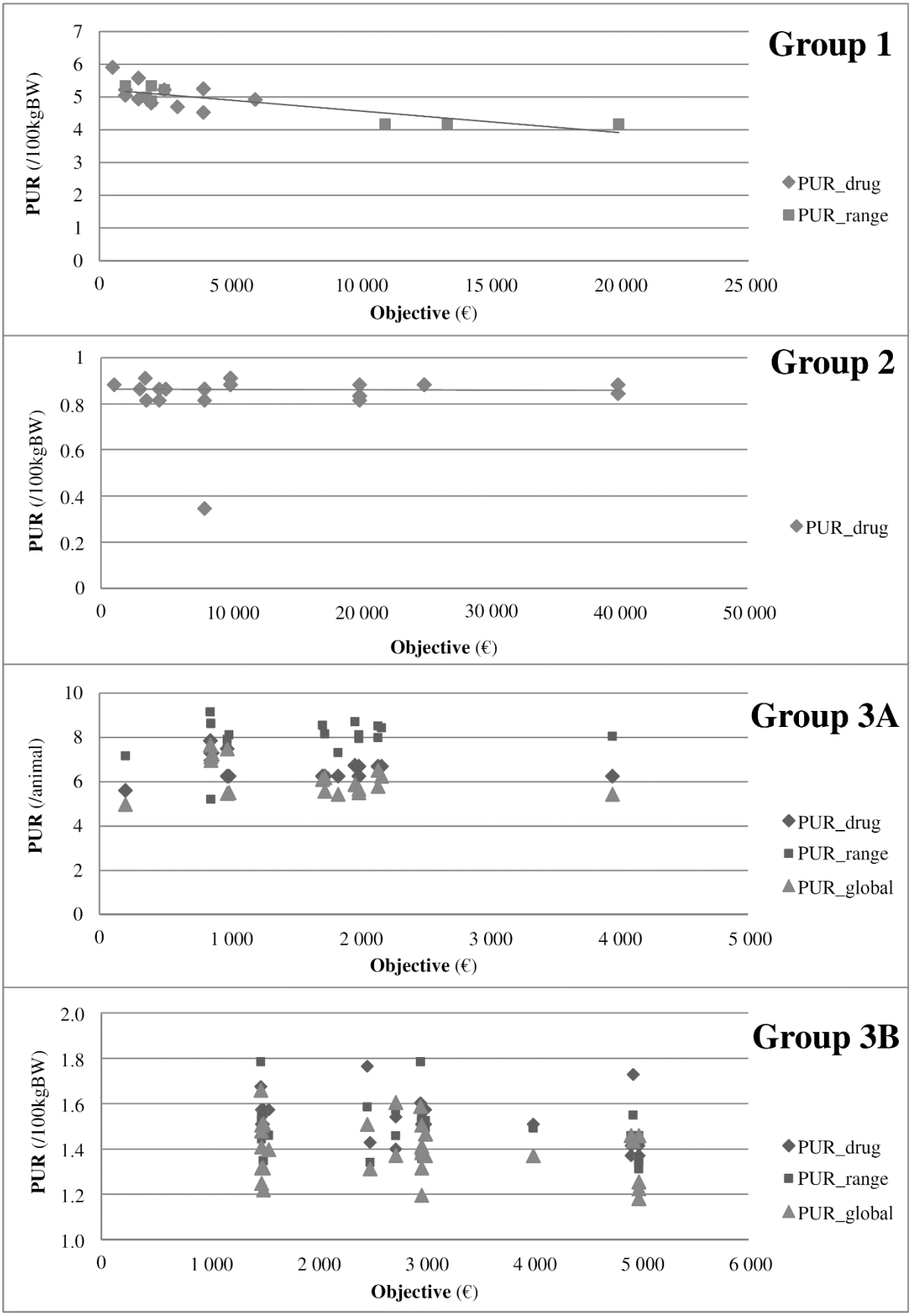
Figures

Figure 1: Chart flow for data selection



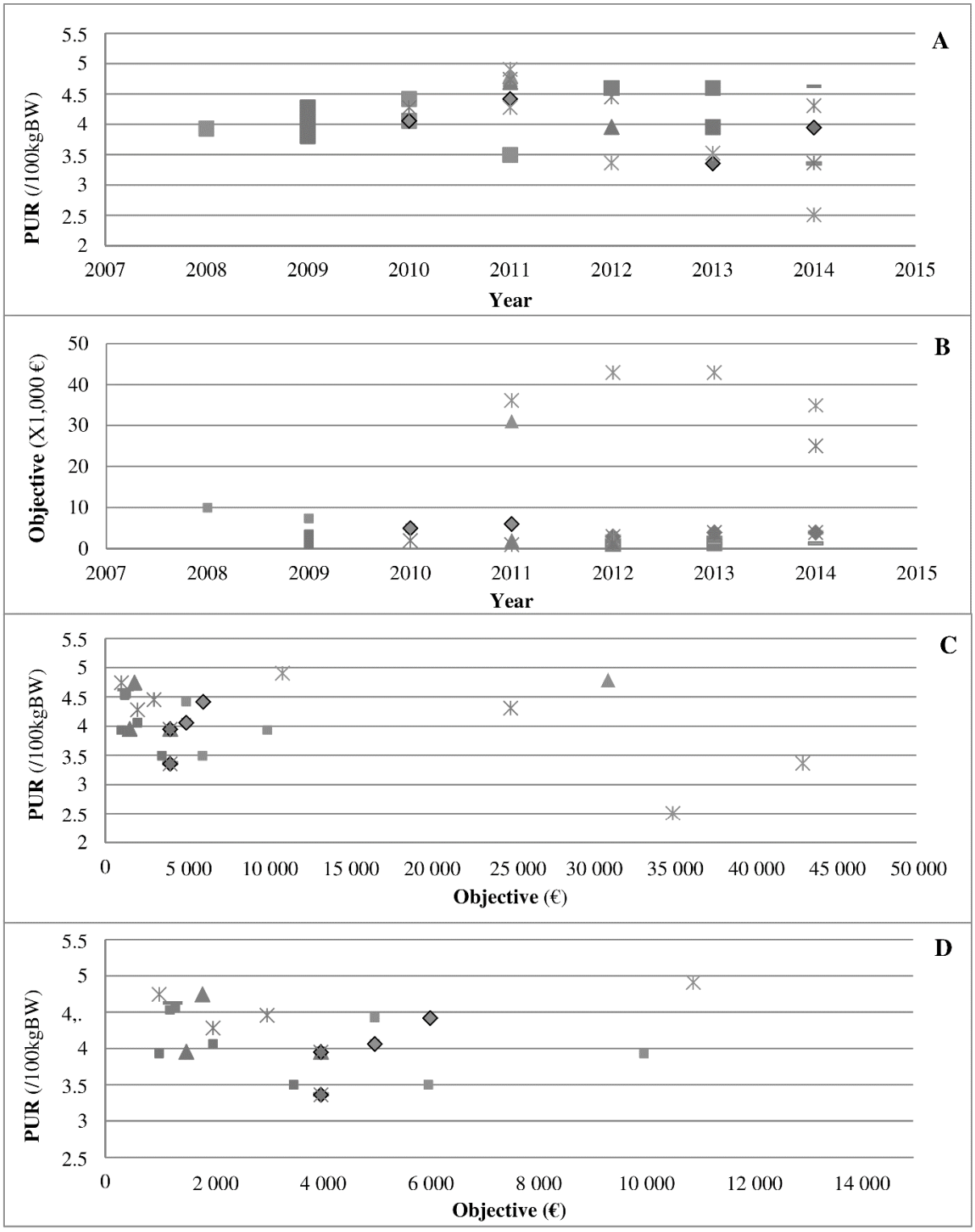
527 **Figure 2: Typology of drugs according to the relationship between PUR and purchase**

528 **objectives**

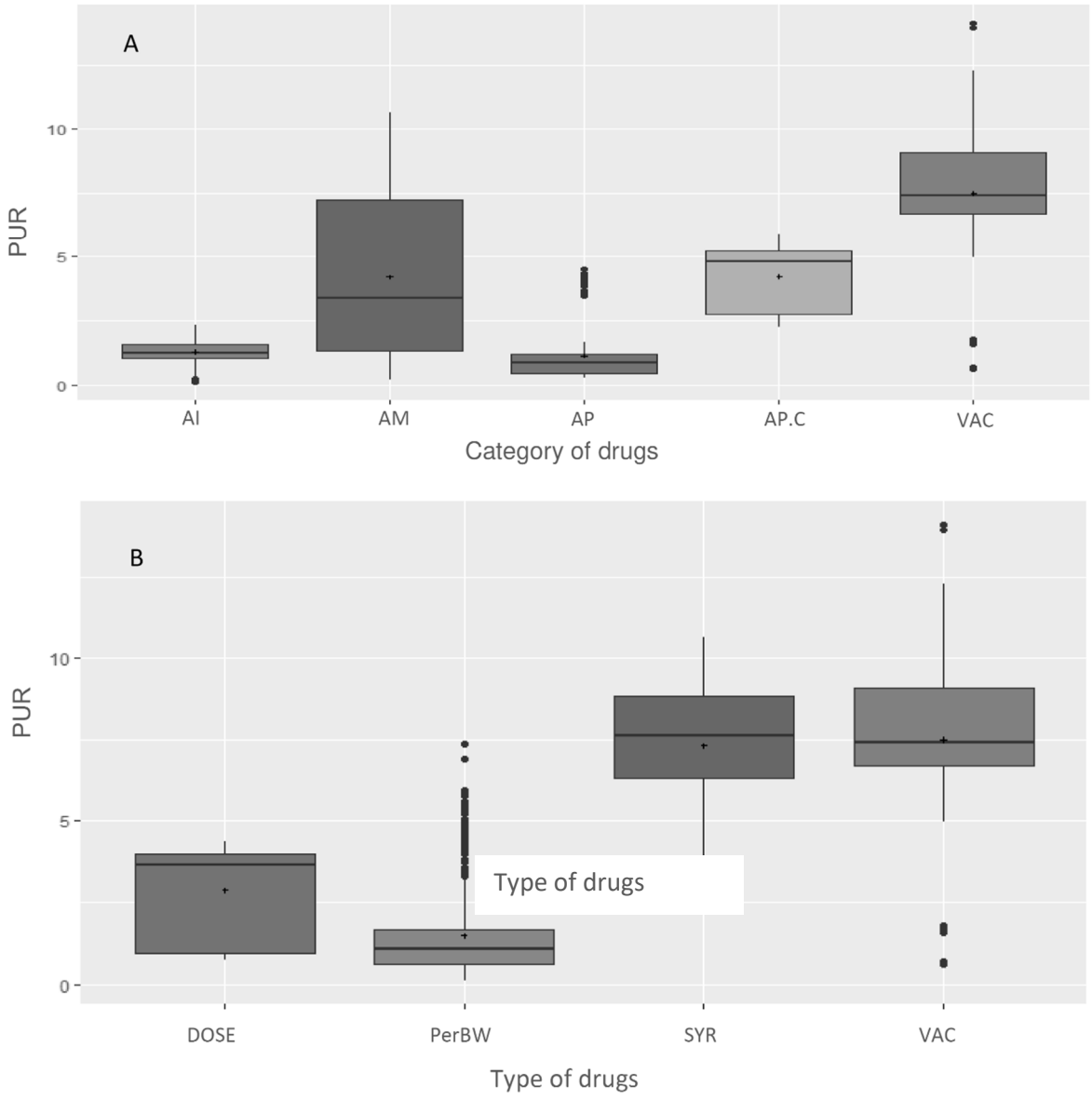


529

Figure 3: PUR depending on different years (A) and objectives (C and D for objectives < €15,000) and PUR objectives depending on different years (B) for 3 drugs (C8P39 in green, C4P11 in blue, and C7P37 in red) and 5 offices (square, triangle, star, diamond, and dash).



537 **Figure 4: Distribution of PUR for the different types and categories of drugs**



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