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## Size and dynamics of order-of-entry effects in pharmaceutical markets

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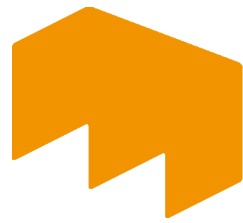
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## **Size and Dynamics of Order-of-Entry Effects in Pharmaceutical Markets**

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## **Abstract**

There is a wide consensus that the chronological order of firms entering new product markets can affect long-term market shares. Commonly, it is expected that early entrants are able to gain long-lasting competitive advantages over their followers. This is corroborated by a large body of research both on theoretical and empirical grounds, often discussing the conditions under which these so-called order-of-entry effects generally exist or do not exist. Knowledge about existence, size and dynamics of order-of-entry effects is especially important in industries driven by research and development, like pharmaceutical companies aiming at launching innovative, patented drugs. These companies sometimes deliver themselves virtual races for an early launch because they expect substantial advantages from early entrance. The literature on order-of-entry effects for pharmaceuticals indeed confirms advantages for the first mover (“first mover advantage” or “pioneer’s advantage”). Apart from this confirmation, however, the existing literature hardly gives any further guideline for companies planning the optimal moment for a new launch.

This paper identifies the shortcomings of the existing literature for measuring size and dynamics of order-of-entry effects for pharmaceutical drugs and tries to overcome them. Particularly, this paper advances the literature in the following aspects: First, the size of order-of-entry effects will not be restricted to follow a predefined pattern. Second, the effects will be measured directly in terms of average differences in absolute market shares, and not with proxies or average relative market share differences. This is accomplished by an innovative econometric method. Third, special attention will be given to the question how the order-of-entry effects change over time. This will be done by identifying and then testing the dynamic effects expected by the theoretical literature. Last, but not least, measurement will be carried out with a sample which to the best of the author’s knowledge is by far bigger and more representative for the most important pharmaceutical markets than those used in any other publication on the topic.

## **Keywords:**

Order-of-Entry Effects, First Mover Advantage, Pharmaceutical Drugs, Fractional Probit Regression, Panel Data

## 1 Introduction<sup>1</sup>

Pharmaceutical companies put much effort in forecasting sales before launching new, innovative drugs. They have good reasons for doing so, because the bulk of the costs for a launch, most notably the costs for research and development, have to be earned during the period that pharmaceutical drugs are under patent protection. Typically, once patent protection expires, biologically equivalent and much cheaper imitators, called generics enter the market and drag down the pioneer's market share. Patented drugs, however, do not necessarily enjoy a monopoly position during patent protection, because they often compete with biologically non-equivalent brands of the same therapeutic class. Therefore, market shares will be affected by the launch of new patented brands within the same therapeutic class and all these patented competitors within a therapeutic class will probably be affected by the launch of the first generic within the class. Usually, forecasters incorporate the information on competitors via an order-of-market entry effect (as for example Regnier and Ridley, 2015, do), where early entrants' long-term market shares are assumed to exceed those of the followers.

If companies expect advantages from launching brands earlier than their potential competitors they are advised to use this information for planning new launches. This is exactly what pharmaceutical companies seem to do. As pointed out by DiMasi and Paquette (2004) the opening of new markets in the pharmaceutical industry is not characterized by a sequential imitation, improvement or development of existing brands, but followers usually find themselves already in advanced stages of development when the first launch in a new class takes place. For this phenomenon DiMasi and Paquette have coined the term "race of development", illustrating the intensity of how competing companies try to market their products as early as possible. It is evident that this kind of race is induced by the expectation of a substantial order of entry advantage which is assumed to prevail at least until the first generic enters the market. The literature on the order-of-entry effects for pharmaceuticals generally confirms the existence of these advantages. Beyond that, however, the findings of the existent literature are hardly useful for guiding companies through this kind of race. Particularly, there is no answer to the question if the advantages from early entry are expected to be large and persistent enough to justify a participation in such a race and if they also exist for the later entrants.

The study presented here aims at shedding more light on these questions. In a nutshell, this implies a possibly most precise and representative measurement of the order-of-entry effects. Such a measurement requires a careful sample selection as well as a model specification which is able to capture the dynamics of the effects and at the same time is flexible enough not to impose any restriction on their size. It also requires a measurement of the effects in terms of absolute market share differences instead of some proxy. The following section 2 explains these requirements in more detail and justifies their importance on the background of the existing literature. After that, in section 3, a discussion of how to measure the dynamics of order-of-entry effects will follow, before the econometric model is presented in section 4. Section 5 is dedicated to the model specification and section 6 to the presentation of the data. Results are discussed in 7

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<sup>1</sup> I am greatly indebted to Benjamin Collins, Nich Guthrie and Nick Meilinger from Boehringer Ingelheim GmbH for their valuable comments and their help with the data. Without their discussions and support this paper would not exist.

and further summarized with an outlook on their contributions to theory and practice in the final section 8.

## 2 Literature Review and Shortcomings of Existing Research

Generally, the order-of-market entry effect can be defined as the causal effect of the chronological order of the competitors' product launches on discounted profits accumulated over the whole product life cycle (Lieberman and Montgomery, 1988).<sup>2</sup> This definition, however, is difficult to use, because discounted aggregated profits cannot be observed for a broad range of products. Therefore empirical studies replace this variable by market shares, sales or survival (Lieberman and Montgomery, 2013). In their surveys, Gómez-Villanueva and Ramírez-Solis (2013) and Lieberman and Montgomery (2013) find that the measure preferred by most researchers in the last decades is market shares. Therefore the common understanding is that entry order effects are the differences between the market shares of competing brands which are attributed to their different launch order position. It is expected that early launches are rewarded over their followers with higher market shares. The advantages expected from early market entry are assumed to play an important economic role, as they are considered as one of the main sources of innovativeness (Urban et al. 1986, Kalayamaran 2008).

Order-of-market-entry effects have been extensively studied for different kinds of consumer goods. Whereas early research dates back to the 1950ies (Bain, 1956), most of the seminal papers still referred to today are from the late 1980ies and 1990ies, for example Robinson and Fornell (1985) Urban et al. (1986), Lieberman and Montgomery (1988), Carpenter and Nakamoto (1989), Kardes and Kalyanaram (1992), Robinson et al. (1994) or Lieberman and Montgomery (1998). These papers have given stimulus to a still ongoing research. Gómez-Villanueva and Ramírez-Solis (2013) who present an overview and summary of the literature count a total of 274 related articles published in prestige journals between 1985 and 2012.

The theoretical reasons for the existence of order-of-entry effects can be subsumed under the three categories brand loyalty, technological leadership and preemption of competition (see the papers cited above for an overview, e.g. Lieberman and Montgomery (1988 and 1998)). Pioneers can create brand loyalty by imposing switching costs if buyers change to the competitor's brand. A different way of creating brand loyalty works through the way consumers learn and build up preferences. In their seminal paper Carpenter and Nakamoto (1989) show that consumers form their preferences based on the attribute combination of the pioneer. This favors pioneers in the long-run, because usually buyers are reluctant to adapt to products with different attributes. Technological leadership may arise through patent protection or because early entrants are more advanced on the learning curve and therefore benefit from a higher productivity. Preemption of competition can either be achieved by reserving scarce assets, like input factors or distribution channels or by product positioning: Pioneers can preempt the best market position(s), so that all followers have to reposition or offer "something extra" to gain market share (Carpenter and Nakamoto, 1989). However, there is no unanimity about the positive effects of early entrance neither in the theoretical nor in the empirical literature. Lieberman and Montgomery (1988)

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<sup>2</sup> When reducing the view to the first entrant, the order-of-entry effect is called pioneer's advantage or first-mover advantage.

enumerate the most important reasons why early entrants might be disadvantaged: First, when innovation costs are higher than imitation costs, it is possible that late entrants free-ride on the pioneer's efforts, e.g. in R&D, buyers' education, teaching of employees, or infrastructure development. Second, risks due to technological and market uncertainties generally are higher for pioneers than for followers. Third, pioneers may be less innovative than followers when in the course of time customers' needs or technology change. The possibility of later entrants to benefit from technological progress is called vintage effect of capital (Bohlmann et al, 2002).

For pharmaceutical drugs, many of the theoretical reasons for the existence of an either positive or negative order-of-entry effect are valid: For example, Coscelli (2000) argues that brand loyalty is important for pharmaceuticals, after having found empirical evidence for reluctance on behalf of patients and physicians to switch to new brands. Additionally, non-monetary switching costs may exist in some cases, for instance, if long-term medication includes a phase when the patient has to get used to the drug. Technological leadership also favors pioneers in the pharmaceutical industry, mainly through patent protection. Patent protection prevents competitors from simply imitating the drug during the period under protection. Without patent protection the imitation of drugs would be much easier than of most other consumer goods, so that competitors would have substantial advantages by free-riding on the pioneer's development costs. In fact, free-riding is regularly observed in the post-patent period, when much cheaper, biologically equivalent generics enter the market. Overall, the theoretical literature suggests that early market entries *ceteris paribus* create a benefit, at least in the time span before generics enter the market.

The empirical studies on pharmaceuticals seem to corroborate this suggestion, although the existing academic literature is less concerned with measuring order-of-entry effects, but more with studying the impacts of third factors on them, mainly for seeing how late followers can overcome their disadvantages. Such third factors are promotion (Bond and Lean, 1977), price (Gorecki, 1986, Berndt et al., 1995, Wilkie et al. 2012), product quality or innovativeness (Bond and Lean, 1977, Shankar et al. 1998, Fischer et al., 2010), or the type of market entry strategy (Fischer et al., 2005). Other studies analyze how the assumed advantage changes in different groups, like prescription drugs and over-the-counter drugs (Kalyamaran, 2008) or like before and after the introduction of the TRIPS agreement (Bhaskarabhatla and Chatterjee, 2013). Table 1 in the appendix gives an overview of the empirical academic literature on pharmaceuticals and their primary aim. All of the studies listed there involve estimations of order-of-entry effects and find that *ceteris paribus* early entries are rewarded. None of the studies, however, really focusses on the measurement of the size of these effects which is the aim of the present study.

The main motivation of this paper is to provide information on order-of-entry effects that can improve pharmaceutical companies' planning of new launches. My focus is on companies that develop innovative, branded products instead of generic imitations. These companies know about the existence of early entrance effects, but only have vague information about their size and persistence. I argue that such a situation can induce competitive companies to put much pressure on launching their products as early as possible without being able to justify the costs involved by such a strategy. If a company knew, for example, that the advantage of, say, being the 3<sup>rd</sup> entrant rather than the 4<sup>th</sup> is only small or not persistent, maybe it would reduce the effort for launching earlier. To measure size and persistence of the order-of-entry effects the following questions have

to be addressed: (i) How does the order-of-entry effect change with the order position (e.g. what is the difference of the effect for the second entrant compared to the sixth entrant)? (ii) How do the effects evolve over time (e.g. after how many years will they cancel out or will they cancel out after the first generic's market entry)? (iii) What is the role of launch time (e.g. what is the difference for the second entrant to follow early or late)?

Interestingly, in recent years, some high-quality empirical studies for practitioners have been published that partly address some of these questions. Table 2 (see appendix) presents the most recent empirical studies on order-of-entry effects for drugs that meet academic standards either because of their data selection or because of their estimation method. For example, Cohen (2006) discusses whether order-of-entry effects really exist, Regnier and Ridley (2015) try to quantify them, whereas Schulze and Ringel (2013) analyze how order-of-entry effects evolve over time. These studies are far from answering the questions addressed by the present paper, but they underpin their highly practical relevance and the need for further empirical evidence. In the remainder of this section I will explain why neither the academic literature cited in Table 1, nor the more practical literature listed in Table 2 are able to give answers to the three questions mentioned before.

First of all, all econometric studies reported in Table 1 assign a constant coefficient to the order of entry (or to its logarithm), so that the effect of the order of entry is restricted to be constant for all entry orders. While there is no theoretical reason for such a restriction, it obviously makes it impossible to see how the effects change for different entry order positions. Remarkably, only some of the studies cited in Table 2 (for example Regnier's and Ridley's (2015)) make an attempt of comparing higher order-of-entry effects without imposing restrictions on their size, which corroborates the high practical relevance of using a more flexible approach. I argue that for measuring order-of-entry effects no restriction on their size should be imposed, see section 5.

A second shortcoming of the existent literature is that order-of-entry effects are defined as market share differences, but not measured as such. As can be seen from Table 1 or Table 2 none of the econometric studies directly uses market shares as an independent variable. Some non-econometric studies do, but at the cost of ignoring control variables (Gorecki (1986) and Cha and Yu's (2014)). The econometric studies either replace market shares by proxies, such as sales (Bhaskarabhatla, Chatterjee (2013), peak sales (Fischer et al. (2010)) or peak market shares (Regnier and Ridley (2015)) or they transform it to the logarithm of the market share relative to the pioneer (Berndt et al. (1995), Fischer et al. (2005), Kalyamaran (2008) and Wilkie et al. (2012)). The latter transformation is part of the leading approach of studying order-of-entry effects proposed by Urban et al. (1986). In this approach the effects of entry order on market shares are estimated within a linear econometric model, but since market shares are bounded between the values of 0 and 1, a linear model would be inadequate. The transformation is used to "linearize" market shares, ie to make them compatible to a linear model. The cost of this linearization however is that order-of-entry effects are all measured as relative to the pioneer, ie coefficients measure the ceteris paribus impact of a 1% change in the entry order position on the market share relative to the pioneer. Such a result cannot be used to study the absolute effects of the entry order on market shares. I argue that instead of transforming market shares and



estimating a linear model it is preferable to analyze the levels of market shares and estimate a nonlinear model, see section 4.

A third shortcoming of the literature is the sample selection. With the exception of Cha and Yu (2014) all other studies cited in Table 1 or Table 2 clearly do not use datasets which are representative for the whole pharmaceutical market. In most cases, the results rely on data of few therapeutic classes only and data availability rather seems to be the main driver for the sample selection. It is therefore questionable if the results on the order-of-entry effects published so far can be generalized to other therapeutic classes. The only study using a larger sample of around 500 brands is that of Cha and Yu's (2014), but the representativeness remains unclear, because details about the selection (like countries, therapeutic classes) are not given. Even more, the 10-year horizon they use and the method of comparing average market shares of different groups preclude a precise measure of the order-of-entry effect and its dynamics. For the present study I take into account all therapeutic classes that seem appropriate and include the 7 worldwide largest pharmaceutical markets (USA, UK, Germany, Japan, France, Italy and Spain). The data selection is explained in more detail in section 6. The sample used in this paper includes 4,659 brands in 98 therapeutic classes and 7 different countries.

Finally, there is little doubt that order-of-entry effects are dynamic, for example it is assumed that early movers' advantages slowly decay in the course of time. However, the papers listed in Table 1 and Table 2 do not address these dynamics systematically, nor do they treat them in a uniform way: Some authors totally suppress dynamics by regarding cross sections at a given time horizon (Cha and Yu (2014) or Regnier and Ridley (2015)), others incorporate variables like time-to-market (Berndt et al. (1995) or Fischer et al. (2005)) or time between entries (Wilkie et al. (2012)). I argue that measures of order-of-entry effects are meaningless when the existing dynamics are ignored or not appropriately treated. Particularly, companies planning new launches need to know how long the possible competitive advantages persist on average. The following section is dedicated to a discussion of the dynamics of order-of-entry effects.

### **3 Time and Entry Order Effects**

As Lieberman and Montgomery (2013) point out, it is generally accepted that order-of-entry effects are dynamic, but the dynamics are normally not addressed at all or they are modelled inadequately. To better understand the effect of time on order-of-entry effects I review the relevant literature before presenting the way the dynamics are modelled in this paper.

In their influential paper Urban et al. (1986) use the time to the previous launch as control variable for the regression of launch order on the logarithm of relative market shares. They argue that followers can reduce the disadvantage from later entry by entering fast after the previous launch. In the following I refer to this effect as the lag time effect.

The seminal works discussing the impact of time on the order-of-entry effects, however, are those of Brown and Lattin (1994) and Huff and Robinson (1994). Brown and Lattin define time in market as the difference between the observation period and the period a product is launched. The relative time in market used in their regression divides the later entrants' time in market by that of the pioneer. They find that increasing relative time in market reduces earlier entrants'

advantages. This slow decay of order-of-entry effects in the long run has also been noted by many other authors, like for example Kalyamaran et al. (1995), Brown and Lattin (1994) and Fischer et al. (2005) for pharmaceuticals.

Huff and Robinson (1994) provide theoretical reasons for a causal effect of time in market on the dynamics of the order-of-entry effects. They argue that time in market is the sum of two components which they call pioneer's lead time and the time of rivalry. The pioneer's lead time is the period between the pioneer's launch and a later entrant's launch. The pioneer can use the lead time to build up advantages over the later entrant through productivity gains (technological leadership) and customers' loyalty. Vintage effects that may reduce or even reverse these advantages are not assumed to be dominant in the pharmaceutical industry (see Cohen 2006), so that overall, the effect of lead time is expected to increase the pioneer's advantage. The time of rivalry, as the second component of time in market is defined as the time that the pioneer and the later entrant(s) spend together in the market. During the time of rivalry the benefit from early entrance is assumed to decay, or to "be competed away". Therefore the time of rivalry is expected to decrease the pioneer's advantage.

Following this argumentation the impact of time in market on the market shares is positive in the initial phase of lead time and negative in the subsequent time of rivalry. However, the role of time in market in a market share model is even more complex, when supposing that part of the market share fluctuations common to all brands are independent of competition. Such dynamics, commonly referred to as product life cycle, may stem from the diffusion process of innovations. Diffusion of innovation, especially in the pharmaceutical industry, is believed to be a nonlinear process, because potential consumers behave differently (for example "innovators" and "imitators" in the famous model of Bass (1969)). The framework for modelling the diffusion of new drugs is called uptake curve or adoption model (see Cook, 2015). Although adoption models can incorporate competition and other factors (e.g. Guseo and Mortarino (2012) or Shankar et al. (1998)), they generally assume a nonlinear, S-shaped relationship between time and cumulated sales, where sales initially grow moderately, then accelerate and finally decay (see Cook, 2015). These dynamics from the diffusion process initially were ignored by the empirical literature on order-of-entry effects, presumably because as seen in section 2 most studies replace market shares by the logarithm of market shares relative to the pioneer and in this transformation the diffusion process of any later entrant is overlaid by that of the pioneer. Additionally, Frawley and Fahy (2006) point out that many studies use datasets containing only sales data for mature markets, so that the estimation of order-of-entry effects is biased. Some authors circumvent the problem by redefining order-of-entry effects as "long-run market share advantages" in mature markets (for example Urban et al., 1986, Kalyamaran et al. (1995) and Gómez-Villannueva (2013)).

Taking into account the lag and the lead time effect, as well as the effect of time of rivalry and the common effect of time in market independent of the order of entry I will proceed as follows: I will use absolute market shares as a dependent variable instead of the logarithm of relative market shares. This allows me to adjust the order-of-entry effects and their dynamics for the effects of time in market which are independent of the entry order. The adjustment is carried out by including dummy variables for time in market in the model. With this procedure the uptake is

not restricted to follow any specific functional form, so that the effects from diffusion have the same role as fixed (calendar) time effects in panel regressions. For identifying the dynamics of the order-of-entry effects I interact the time-in-market dummy with the entry order, which again does not impose any functional restriction. This allows me to test for evidence of lead time and time-of-rivalry effects: Under these effects the coefficients of the interaction dummies should change their sign with increasing time in market from positive (lead time effect) to negative (effect of time and rivalry). Finally they should be insignificant (decay of order-of-entry effects). The drawback of this flexibility is that it implicitly assumes equal lead times for all brands. This is clearly unrealistic, so I also include the actual lead time of each individual brand. The main purpose of this variable is to check if the assumption of equal lag times flaws the results. Additionally, a variable for the lag time effect is included.

The combination of time-in-market dummy variables and interaction variables partials out the dynamics attributed to the order-of-entry effects from the market share dynamics common to all entrants. However, it requires the introduction of some maximum time horizon into the estimation, because for each time-in-market value a separate coefficient has to be estimated. Such a restriction is also desirable from a theoretical point of view. As Lieberman and Montgomery (2013) point out, given that the effects of the entry order gradually decay in the course of the time their size cannot be determined in a meaningful way without a predefined maximum time horizon. In the following the maximum horizon is a time in market of 25 years where the value 25 will be selected on empirical grounds, see section 6. Additionally, an alternative maximum time horizon which is justified on theoretical grounds will be discussed: As pointed out in the introduction the entry of the first generic into a therapeutic class is assumed to structurally change competition. For example Vandoros and Kanavos (2013), Gonzalez et al. (2008), or Saha et al. (2006) analyze the effects of this event on price, sales or market sales. It seems likely that it will also change the order-of-entry effects, or maybe even abolish them. In such a case the maximum time horizon should be the entrance of the first generic to a market. The model presented in the next sections can be used to test whether this event really induces changes on the order-of-entry effect.

#### 4 Method

Market shares can only take values in the interval  $[0, 1]$ . As mentioned before, the literature on order-of-entry effects usually handles this problem by linearizing market shares with a sort of log-odds transformation

$$\log\left(\frac{ms}{ms_{pioneer}}\right) = \mathbf{x}\boldsymbol{\beta} + \mathbf{e}$$

where  $ms$  is the market share of a brand,  $ms_{pioneer}$  is the market share of the pioneer,  $\mathbf{x}$  is a vector of explanatory variables (where the first element is 1),  $\boldsymbol{\beta}$  is a vector of coefficients and  $\mathbf{e}$  is assumed to be the iid residual. This procedure, however, has several drawbacks for estimating order-of-entry effects. First, it is impossible to measure the effects of any variable included in  $\mathbf{x}$  (ie order of entry) on the market share. The coefficients  $\boldsymbol{\beta}$  measure the (approximate) ceteris paribus effects of a one-percentage change of an element of  $\mathbf{x}$  on the market share relative to the

pioneer, and these can no longer be retransformed to the effect of that element on  $ms$ . Second, all observations with  $ms = 0\%$  and  $ms = 100\%$  drop out, possibly creating a selection bias. Third, as seen in section 3, the dynamics of the diffusion process cannot be modelled in a meaningful way, because the diffusion of any brand is overlaid by that of the pioneer. To circumvent these problems I propose to estimate order-of-entry effects within a nonlinear model where  $ms$  remains untransformed. Such a framework is given with a fractional probit model. A fractional probit model takes the form

$$E(ms|\mathbf{x}) = \phi(\mathbf{x}\boldsymbol{\beta})$$

where  $\phi$  is the cumulative standard normal distribution and  $E(ms|\mathbf{x})$  is the expected market share for a given set of values for the variables  $\mathbf{x}$ . In this specification  $ms$  is bounded to values between 0 and 1 including the limits. For the estimation of  $\boldsymbol{\beta}$  Papke and Wooldridge (1996) propose a quasi-maximum likelihood estimator. It should be noted that just like in any binary probit model the size of the coefficients  $\boldsymbol{\beta}$  cannot be interpreted as ceteris paribus effect of an element of  $\mathbf{x}$  on  $ms$ , because their size depends on the levels of all elements of  $\mathbf{x}$ . A common practice for summarizing ceteris paribus effects is to calculate average partial effects (APE) from the  $\boldsymbol{\beta}$ . These are the individual (ceteris paribus) effects of a one-unit-change in an element of  $\mathbf{x}$  on  $ms$  averaged over the observations of the sample.

When dealing with panel data unobserved heterogeneity can bias the results. Assume  $ms$  and  $\mathbf{x}$  are measured for the cross section element  $i$  at time  $t$  where here  $i$  stands for a specific brand launched in a specific country and  $t$  is the time in market. Then unobserved heterogeneity arises through the individual effect  $c_i$  as well as through the time effect  $\tau_t$ . Including these effects, the model can be written as:

$$E(ms_{it}|\mathbf{x}_{it}, c_i, t_t) = \phi(\mathbf{x}_{it}\boldsymbol{\beta} + c_i + \tau_t)$$

As seen in section 3, the market share dynamics arising from the diffusion process are modelled with dummy variables for the time in market. These dummy variables are not only necessary for partialling out the order of entry dynamics from the overall market share dynamics, but they also wipe out unobserved heterogeneity arising from the time effect. To model the individual effects, Wooldridge (2010a) advocates the random effects model. In this type of model the individual effects are captured by individual-specific averages of all time varying variables (with an exception of the time dummies) which are included in the set of the explanatory variables. Hence, in the present context the random effects model is

$$E(ms_{it}|\mathbf{x}_{it}, \bar{\mathbf{x}}_i) = \phi(\mathbf{x}_{it}\boldsymbol{\beta} + \bar{\mathbf{x}}_i\boldsymbol{\psi})$$

where  $\bar{\mathbf{x}}_i$  is a vector containing averages of all time-varying variables of  $\mathbf{x}_{it}$  (apart from dummy variables for time in market) and  $\boldsymbol{\psi}$  is a vector of coefficients. Wooldridge (2010a) shows that for balanced panels (and under some additional assumptions on  $c_i$ ) the APE can be identified. However, the dataset used in this paper is unbalanced. In such a situation Wooldridge (2010b) proposes to allow the variance of  $c_i$  to depend on the number of time periods available for each individual. I follow this proposal for the estimations in this paper. Estimation of the fractional

probit random effects regression is carried out with the Stata procedure written by Bluhm and described in Bluhm (2013).

## 5 Selection of Variables

The elements of  $\mathbf{x}_{it}$  in the fractional random effects probit regression presented before contain variables measuring the order of entry, variables measuring the dynamics of the order of entry, other covariates, dummies for time in market and dummies for the different countries.

The order-of-entry effects are measured with a set of  $n - 1$  dummy variables of the form:  $order\_n_i = 1$  if the brand was the  $n$ th entrant in a specific therapeutic class of a specific country and otherwise  $order\_n_i = 0$ . The rationale for using dummy variables and not incorporating the order of entry as a single variable with a constant coefficient is that this specification does not impose any restriction on how the order-of-entry effect changes with the order position. This flexibility, however, comes with the cost that the order-of-entry effects have to be estimated in different samples. For estimating the order effect of entrant  $n$  over subsequent followers all data on the previous entrants have to be dropped out of the data set. With this procedure the coefficient of  $order\_n$  gives the (average) market share difference between the entrant  $n$  and all subsequent entrants.

As discussed in section 3 several time variables are included. These are the dummy variables for the time in market (for measuring the market share dynamics independent of competition) and interaction terms of time in market with the entry order (for measuring the dynamics of the order of entry effects). As order-of-entry effects are assumed to first build up (lead time effect) and then decay (effect of time of rivalry), the coefficients are supposed to be positive in the beginning and then negative and decreasing for an increasing time in market. The variable  $lagtime_i$  is defined as the time span between the launch and the previous launch in the same market and serves to measure the impact of lag time on the order-of-entry through the interaction variable  $order\_n_i * lagtime_i$ . As longer lag times should lower the advantage from early entry, the coefficient of the interaction variable is expected to be negative. Note that  $lagtime_i$  does not exist for the pioneer, so it will not be used in the regression for  $order\_1$ . The variable  $leadtime_{it}$  which is defined as time period prior to the subsequent launch in the same class is introduced together with  $order\_n_i * leadtime_{it}$  as a corrective for the assumption of equal lag times imposed by the interactions of  $order\_n$  with the time-in-market dummy variables. A significant impact of  $leadtime$  on market shares would indicate that the measurement of the lead time effect via time-in-market is imprecise.

The other covariates should control for promotional spendings and price. I define the variable  $avpromotion_{it}$  as the spendings for promotion divided by the average spendings of all brands in the same period and market and, similarly, the variable  $avprice_{it}$  as the price divided by the average price of all competitors in the same period.

## 6 Data

All data used in this paper is from IMS Health, a US American consulting company specialized in health care market research and data collection. The sales data are projections of a continual, periodic IMS market survey, measuring total purchases of pharmaceuticals by wholesalers, retail pharmacies and for most countries, by hospitals. Sales are measured in standard units, a standardized measure for the quantity of a drug, making different package sizes and forms, such as solid or liquid, comparable. Additionally the dataset contains information on price (list price in Euros adjusted for exchange rate changes) and promotional spendings. Promotional spendings cover sales representative visits and other direct or indirect advertising in various channels.

For calculating market shares and determining the order of entry, it is necessary to define what a market is. In this context a market is identified as a therapeutic class in a specific country. The therapeutic class is the aggregation level 4 from the Anatomical Therapeutic Chemical (ATC) classification system. Classes with only one competitor over the whole time are excluded as well as classes with herbal products (e.g. G4C9, G4D8, G4D9, N6A2, N5B5) or with products that are bought primarily by tender by governments (such as anti-malarias, flu vaccines, antibiotics, J5B4) and therefore not adhere to the usual market rules. Due to measurement problems some other therapeutic classes and brands had to be excluded.<sup>3</sup>

I calculated the market share of a brand as the annual sales divided by total annual sales of all brands of the same ATC4 class and country. Whenever dosing information was completely available for the entire ATC4 class in a country I transformed sales in standard units into sales in daily doses before calculating market shares, otherwise market shares were directly calculated from sales in standard units. The order of entry was calculated from the launch date measured on a monthly base. Contemporaneous launches were assigned the same (lower) number, subsequent launches were corrected for the multiple assignment of the same rank order. For example, if in a market with 3 competitors two new brands are launched at the same time, they will both obtain the order of entry number 4 – the subsequent launch then will obtain the order of entry number 6. The variable  $lagtime_i$  could be measured on monthly basis, whereas  $leadtime_{it}$  and the time in market are measured on annual basis.

For calculating market shares and order of entry, all brands available in the sales dataset between 2003 and 2014 were taken into account, but for the estimations, all brands older than 25 years and all generics were excluded. Generics were excluded because the goal of this paper is to estimate order-of-entry effects for patented drugs. A maximum time horizon is generally needed as shown in section 3. The threshold of 25 years can be justified empirically from Figure 1.

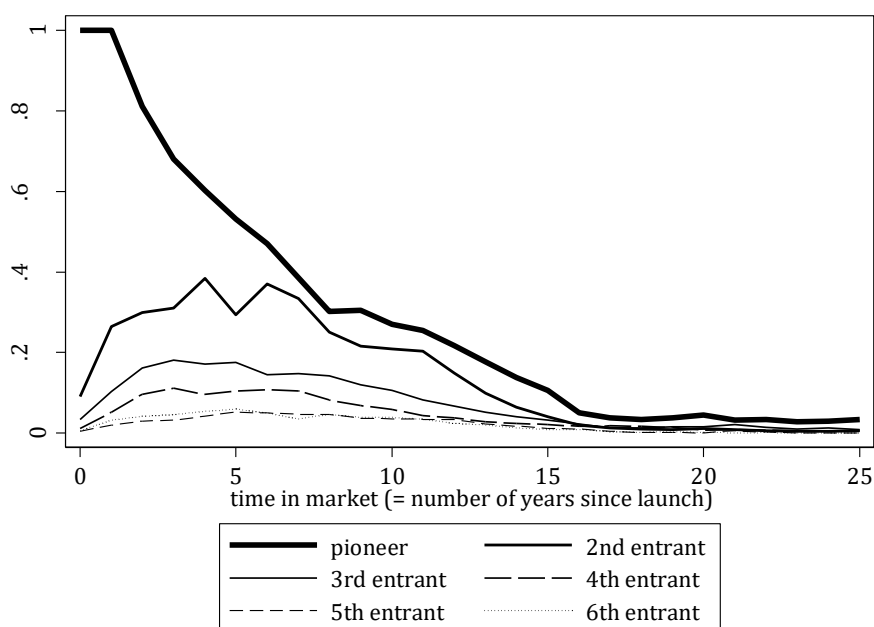
Figure 1 illustrates the development of the median market share for different times in market and the first 6 entrants. Here also, the observations are from pre-generic entry markets, ie observations are excluded after the first generic launch in a market. Although covariates, such as

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<sup>3</sup> These are (1) therapy areas with a significant over the counter (OTC) component (such as anti-diarrhoea, anti-tussives) because IMS data does not capture most of the OTC sales (2) topical medicines because it is difficult to quantify volumes, (3) antibiotics, since most of them are generics, (4) all L1, L2, L3 and L4 classes because these are oncology products and IMS data does not give the split by indication, (5) anything marketed by a generics company (e.g TEVA), (6) combinations of old products (e.g. Omeprazole and Naproxen), and (7) line extensions that are not new combinations (e.g. Nevaripine XR).

price or promotional spending are missing, the curves corroborate several hypotheses discussed so far. For instance, market shares – apart from the pioneer – seem to follow the shape of an uptake curve with an initial strong growth followed by a peak and then by a gradual decay. Also, in most cases median market shares of early entrants are higher than those of late entrants which can be taken as evidence for the existence of order-of-entry effects. As expected, these differences tend to diminish over time and with increasing number of competitors. After the 5<sup>th</sup> launch and after around 15 up to 20 years, the differences seem to have disappeared for all entrants except for the pioneer. The pioneer’s median market share seems to remain higher even after 20 years, but the difference to the subsequent 5 entrants is small. Thus, the exclusion of brands that are older than 25 years may slightly underestimate the pioneer’s advantage, but this can better be seen from the estimation results. For the other entrants’ estimation it is not expected to imply any loss of information.

**Figure 1: Median market share for different order of entry**



Many observations drop out because promotional data is not available. With all exclusions a total of 41,742 observations (4,659 different brands from 98 different therapeutic classes, 12 different years and 7 different countries) are available for the estimation. Table 3 lists the 98 therapeutic classes of the whole sample. To the best of my knowledge this is by far the biggest and most representative sample for non-generic prescription drugs used for estimation order-of-entry effects.

## 7 Results

The estimated coefficients of the random effects models and their corresponding p-values are given in Table 4. The table contains the results of the estimation for the first six different entry orders  $n$ . For example, the results entitled as “second entrants ( $n = 2$ )” refer to the model, where  $order\_n$  is  $order\_2$  and all observations on the pioneer are excluded. This estimation can be used for measuring the early entrant advantage of the second entrant over all followers. Similarly, the columns of the third entrants ( $n = 3$ ) contain the estimation results of  $order\_3$ . The underlying sample does not contain observations on the pioneer and the second entrants.

Like in all fractional probit models the size of the coefficients does not measure the size of the cause and effect relationships, but only the p-values and signs allow some conclusions. To begin with the order-of-entry effects, it can be noted that all coefficients of  $order\_n$  given in Table 4 are positive and highly significant which corroborates the hypothesis that early entrance is rewarded with higher market shares. Interestingly, the coefficient of  $order\_6$  still is significantly positive. This can be taken as evidence, that even the 6<sup>th</sup> entrant gains market share advantages over later (branded) followers. The impact of lag time on the order of entry effect can be seen from the coefficient of  $order\_n*lagtime$ . It is highly significant and negative for the first three entrants indicating that higher lag times lower the order of entry effects. For the later entrants it is not clear whether lag time changes the order-of-entry effects or not, because the coefficients of the interaction terms are insignificant on a 5% level. In none of the regressions the coefficient of  $order\_n*leadtime$  is significant on a 1% level. Only on a 10% level it is significant for the pioneer and on a 5% level it is significant for the sixth entrant. Obviously, there are no significant additional lead time effects which are not already captured by the interaction of  $order\_n$  with time-in-market. The coefficient of price ( $avprice$ ) is not significantly different from zero in any of the estimations at least on a 10% level. A possible explanation is the general low price elasticity of physicians and patients, due to the fact that costs of pharmaceutical drugs are reimbursed in many cases. As expected, the coefficient of promotion ( $avpromotion$ ) is positive and highly significant in all estimations indicating that ceteris paribus over-average promotional spending translate to higher market shares. To conserve space the 25 coefficients of the time-in-market dummies and their interactions with  $order\_n$  are not reported in Table 4. Overall their signs and significance is in line with the expectations on all standard levels of significance: For the dummies of time in market, the coefficients show a similar pattern in all regressions with an increase after the first year, followed by a decrease for around 12 years. After around 13 up to 16 years they are no longer significant. Such a pattern corresponds to the typical shape of an uptake curve. The interaction terms of time in market and  $order\_n$  which should measure the main dynamics of the order-of-entry effects are negative (when significant) as expected, but their effect on the early entrants advantage can better be seen from the APE.

The APE of the order of entry dummies are reported in Table 5. The values can be taken as the average market share difference of the entrant  $order\_n$  to all followers when controlling for lead time, lag time, time in market, promotion, price and country. The table contains the APE for some selected times in market plus the average APE over all times in market (“total average”). The p-values, also included in Table 5, show that these averages are highly significant and therefore indicating strong order-of-entry effects: For example the ceteris paribus market share



difference of the pioneer to the followers amounts to 33 percentage points on average. The averages sharply decline for the first four entrants (19% points for the second and 13% points for the third entrant), and afterwards they seem to remain stable at around 6 or 5% points. As the market shares of the sixth entrant still exceed that of the followers by 6% points (with a 95% confidence interval of 3% and 9%) there is no indication that the advantage cancels out for higher orders of entry. The effect of time in market on the order-of-entry effect can be studied by comparing the APE for the different times in market. In the first year (when time in market is zero) the average market share of the pioneer exceeds the first year's market share of competitors by 70% points. Whereas for the pioneer this is the maximal value, the other competitors seem to reach their maximum advantage later, at around 2 years in market. This initial increase can be explained by the effect of lead time during that the pioneer builds up advantages over followers. After having reached the maximum the APE strongly decay which is in line with the idea that during time of rivalry advantages from early entrance are competed away. For example, the pioneer's initial advantage of 70% points drops to 8% after 15 years and is insignificant after 20 years. After 20 years of competition none of the APE is significant any longer. For later entrants the order of entry advantage seems to die out earlier, as after 15 years the APE is insignificant for the 4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> entrant (and on a 5% level also for the 3<sup>rd</sup>). Since not all values of time in market are listed in Table 5 the exact time horizons where the p-values exceed the 10% level for the first time are mentioned here: 17 years for the pioneer and for the second entrant, 16 years for the third entrant, 13 years for the fourth and fifth entrant and 12 years for the sixth entrant.

Similarly, the effects of the variables *leadtime* and *lagtime* can be studied. The APE of the order of entry for different lead and lag times are given in Table 6. Here the total averages are the same as in Table 5, and since all of them are significant, to conserve space, p-values are not reported. As time horizons I selected values between 0 and 5 years. When overlooking the values, the effects of lead and lag time on early entrant's advantage both seem to be small: In many cases the (rounded) APE do not change at all or at utmost by 1 or 2 percentage points. The APE of entrant 3 and 6 display the greatest fluctuation for changes in lead time with only 4 percentage points. It should also be noted that the APE of a given entry order are almost all contained in the confidence intervals of all the other time horizons. Therefore the changes of the APE reported in Table 6 probably are not significantly different from zero. The low impact of lead time can be explained with the fact that the lead time effect is already measured by the APE of time in market, as observed in Table 5. The weak impact of lag time on market shares, on the other hand, indicates that lag time effects are small. Given the strong impact of the order of entry it seems that once the order of entry position is decided, the time of the launch is only of minor importance.

In order to test whether the first entrance of a generic to a market abolishes order-of-entry effects I performed Chow tests. More precisely, the estimations of Table 4 were interacted with an indicator variable which takes the value 1 for periods of generic competition and 0 otherwise. Table 7 reports the p-values of a joint test on the significance of these interaction terms. The first line gives the results from a test on all interactions terms. Here, with the exception of the 6<sup>th</sup> entrant, all p-values are very low, so the null hypothesis that the entrance of the first generic to a market has no effect on the market shares is clearly rejected for the first five entrants. The test

reported in the second line is only about the significance of the interaction terms related to the entry order effects. Here, the null hypothesis cannot be rejected on a 5% level of significance and on a 10% level the null hypothesis can be rejected for the first two entrants. This means that for the first two entrants the result is not very clear, but for the other entrants there is no evidence that generics have a reducing impact on the order-of-entry effects. Taken together both results suggest that the entrance of the first generic causes a structural break in the model, but there is scarce evidence that this break abolishes all order-of-entry effects.

## **8 Summary and Conclusion**

The estimations clearly confirm the existence of order-of-entry effects in pharmaceutical markets implying that early entrants indeed are rewarded with higher market shares. The market share advantages are sharply declining for later entrants but still exist at least for the 6<sup>th</sup> entrant to a market. Although the launch of the first generic to a market induces a structural break, the order advantages over the other branded products seem to partly carry over. Nevertheless the advantages do not hold in the long-run: In my estimations they are insignificant after around 16 to 17 years for the first three entrants, for later entrants they die out after around 12 to 13 years. Over these times the advantage of the pioneer over all later entrants (generics excluded) amounts to around 33 percentage points, whereas the corresponding value for the second entrant is 19 and for the third entrant 13. For the later entrants the average advantage is about 6 percentage points.

For the first followers to a new market the advantages over their subsequent followers increase in the first year(s) after launch and then slowly decay. This finding corresponds to the theory of the dynamics of the order-of-entry effect where the leading time can be used to build up advantages and during the subsequent period of competitive rivalry these advantages again are competed away. On the other hand, the effect of lag time on the early entry advantage is negligible in my estimations, suggesting that the order of entry position is more important than the time of market entry after the previous launch.

The information that order-of-entry effects exist is probably not too surprising for managers or academics. However, this knowledge alone is not sufficient for incorporating the effects in sales forecasts or in strategic decisions in more than a qualitative way. With the description of the average size of the effects in terms of absolute market shares and with the measurement of their speed of decay, this study provides the information necessary to implement order-of-entry effects in a quantitative way.

## APPENDIX

**Table 1: Empirical academic studies on order-of-entry effects in the pharmaceutical industry**

	major aim	target variable	no. of classes*	no. of drugs	countries	(econometric) method
Berndt et al. (1995)	effects of marketing and pricing	log of market share over market share of pioneer	1	4	US	nonlinear 2SLS
Bhaskarabhatla, Chatterjee (2013)	first-mover advantage before and after TRIPS	sales	3	73	India	random effects model
Fischer et al. (2010)	impact of quality and order of entry on peak sales	peak sales	2	73	France, Germany, Italy, UK	multi-level regression model
Fischer et al. (2005)	impact of market entry strategy on pioneer advantage	log of market share over market share of pioneer	2	73	France, Germany, Italy, UK	random-effects model
Gorecki (1986)	impact of price and quality on the pioneer advantage	market share		7	Canada	comparison of average market shares
Kalyamaran (2008)	difference of order-of-entry effect between prescription and over-the-counter drugs	log of market share over market share of pioneer	5	21	US	random effects model
Shankar et al. (1998)	impact of innovativeness on the pioneer advantage	sales	2	13	US	iterative nonlinear least square
Wilkie et al. (2012)	impact of low-price brands on the order-of-entry effect	log of market share over market share of pioneer	3	48	Australia	random effects model

\* not necessarily defined as in this study

**Table 2: Empirical non-academic studies on order-of-entry effects in the pharmaceutical industry**

	major aim	target variable	no. of classes*	no. of drugs	countries	(econometric) method
Cha and Yu (2014)	identify factors that impact on the pioneer advantage	market share 10 years after launch	131	492	not mentioned	comparison of average market shares
Cohen (2006)	existence of order-of-entry effect	sales	11	54	US	graphical analysis of sales
Regnier and Ridley (2015)	measurement of order-of-entry effect	peak market shares	29	81	US	OLS
Schulze and Ringel (2013)	impact of quality and time on the pioneer advantage	cumulated discounted sales	15	53	US	comparison of averages

\* not necessarily defined as in this study

**Table 3: List of ATC4 classes included in the estimations**

A10C1 H INSUL+ANG FAST ACT	C1B0 ANTIARRHYTHMICS	J5C9 OTHER HIV ANTIVIRALS
A10C2 H INSUL+ANG INTERMED ACT	C3A1 POT SPARING AGENTS PLAIN	M1C0 SPEC ANTIRHEUMATIC AGENT
A10C3 H INSUL+ANG INT+FAST ACT	C3A2 LOOP DIURETICS PLAIN	M4A0 ANTI-GOUT PREPARATIONS
A10C4 H INSUL+ANG INT+LONG ACT	C3A3 THIAZIDE+ANALOGUE PLAIN	M5B3 BISPHOSPH OSTEOPOROSIS
A10C5 H INSUL+ANG LONG ACT	C3A4 POT SPARNG+LOOP DIUR COM	M5B4 BISPHOSPH TUMOUR-RELATED
A10K1 GLITAZONE A-DIABS PLAIN	C3A5 POT SPARING+THIAZ COMBS	M5B9 OTH BONE CALCIUM REGULAT
A10K2 GLITAZONE & S-UREA COMBS	C3A7 VASOPRESSIN ANTAG DIURET	N3A0 ANTI-EPILEPTICS
A10K3 GLITAZONE & BIGUAN COMBS	C3A9 OTHER DIURETICS	N4A0 ANTI-PARKINSON PREPS
A10M1 GLINIDE A-DIABS PLAIN	C6A0 OTH CARDIOVASCULAR PRDS	N5A1 ATYPICAL ANTIPSYCHOTICS
A10N1 DPP-IV INH A-DIAB PLAIN	C9C0 ANGIOTEN-II ANTAG, PLAIN	N5A9 CONVNTL ANTIPSYCHOTICS
A10N3 DPP-IV INH & BIGUAN COMB	C9D1 AT2 ANTG COMB C2 &/O DIU	N5B1 NON-BARBITURATE PLAIN
A10S0 GLP-1 AGONIST A-DIABS	C9D3 AT2 ANTG COMB CALC ANTAG	N5B2 NON-BARBITURATE COMBS
A10X9 OTH DRG USED IN DIABETES	C9D9 AT2 ANTG COMB OTH DRUGS	N5B3 BARBITURATE PLAIN
A2B1 H2 ANTAGONISTS	C9X0 OTH RENIN-ANGIOTEN AGENT	N5B4 BARBITURATE COMBS
A2B2 ACID PUMP INHIBITORS	G3A1 MONOPHAS PREP<50MCG OEST	N6A3 MOOD STABILISERS
A2B3 PROSTAGLANDIN A-ULCERANT	G3A2 MONOPHAS PREP>=50MCG OES	N6A4 SSRI ANTIDEPRESSANTS
A2B4 BISMUTH ANTIULCERANTS	G3A3 BIPHASIC PREPARATIONS	N6A5 SNRI ANTIDEPRESSANTS
A2B9 ALL OTHER ANTIULCERANTS	G3A4 TRIPHASIC PREPARATIONS	N6A9 ANTIDEPRESSANTS ALL OTH
B1C0 ANTI PLAT.-NON ORAL SOLI	G3A5 PROGEST-ONLY PREPS,ORAL	N6B0 PSYCHOSTIMULANTS
B1C1 CYCLO-OX INH PLAT - OS	G3A9 OTH HORMONAL CONT,SYST	N6C0 PSYCHOLEPT-PSYCHOANALEPT
B1C2 ADP RECEP ANTAG PLAT -OS	G3F0 OESTROGEN + PROGESTOGEN	N7D1 ANTI-ALZ PROD CHOL INHIB
B1C4 PL CAMP ENH PLAT - OS	G4C2 BPH ALPH-ADREN ANTAG PLN	N7D9 ALL OTHER ANTI-ALZ PRODS
B1C5 PLATELET COMB - OS	G4C3 BPH 5-ARI PLAIN	N7E0 DRUGS USED IN ALCOH DEP
B1C9 OTHER PLATELET - OS	G4C4 BPH ALPH-ANTAG+5ARI COMB	N7X0 ALL OTHER CNS DRUGS
B1E0 DIRECT THROMBIN INHIBIT.	G4D4 URINARY INCONTINENCE PRD	R3A2 B2-STIMULANTS, SYSTEMIC
B1F0 DIRECT FACTOR XA INHIBS	G4E0 ERECTILE DYSFUNCTION PRD	R3A3 LONG-ACT B2-STIM,INHAL
B1X0 OTH.ANTITHROMBOTIC AGENT	J5B1 VIRAL HEPATITIS PRODUCTS	R3A4 SHORT-ACT B2-STIM,INHAL
C10A1 STATINS (HMG-COA RED)	J5B3 HERPES ANTIVIRALS	R3D1 CORTICOIDS INHALANTS
C10A2 FIBRATES	J5B9 ANTIVIRALS OTHERS	R3F1 B2-STIM+CORTIC INHALANTS
C10A3 ION-EXCHANGE RESINS	J5C1 NUCLEOS/T REV.TR.INH.	R3G3 ANTICHOLINER-PLAIN,INHAL
C10A9 OTH.CHOLEST&TRIGLY.REGUL	J5C2 PROTEASE INHIBITORS	R3G4 A-CHOL+B2-STIM COMB,INH
C10C0 LIP.REG.CO.W.OTH.LIP.REG	J5C3 NON-NUCLEO REV TRANS INH	R3J2 ANTILEUK ANTI-ASTHM SYS
C11A1 LIPREG.CV.MULT-TH.FX.COM	J5C4 HIV ANTIVIR ENTRY INHIB	

**Table 4: Estimated coefficients of fractional probit regressions**

	first entrant ( $n = 1$ )		second entrant ( $n = 2$ )		third entrant ( $n = 3$ )	
	coefficient	p-value	coefficient	p-value	coefficient	p-value
<i>order_n</i>	2.812	0.000	1.270	0.000	1.150	0.000
<i>lagtime</i>			0.004	0.000	0.005	0.000
<i>leadtime</i>	0.039	0.000	0.054	0.000	0.054	0.000
<i>order_n*lagtime</i>			-0.002	0.003	-0.004	0.000
<i>order_n*leadtime</i>	-0.026	0.071	-0.014	0.346	0.001	0.969
<i>avpromotion</i>	0.020	0.000	0.017	0.000	0.015	0.000
<i>avprice</i>	0.001	0.966	0.010	0.462	0.015	0.200
<i>number of obs</i>	41742		38830		36370	
	fourth entrant ( $n = 4$ )		fifth entrant ( $n = 5$ )		sixth entrant ( $n = 6$ )	
	coefficient	p-value	coefficient	p-value	coefficient	p-value
<i>order_n</i>	0.554	0.000	0.609	0.000	0.741	0.000
<i>lagtime</i>	0.005	0.000	0.005	0.000	0.005	0.000
<i>leadtime</i>	0.067	0.000	0.063	0.000	0.061	0.000
<i>order_n* lagtime</i>	-0.001	0.547	-0.003	0.054	-0.001	0.550
<i>order_n*leadtime</i>	-0.022	0.418	-0.047	0.133	-0.067	0.013
<i>avpromotion</i>	0.018	0.000	0.018	0.000	0.016	0.000
<i>avprice</i>	0.015	0.218	0.018	0.113	0.018	0.086
<i>number of obs</i>	33950		31727		29971	

Country dummies, time-in-market dummies, interaction of *order\_n* with time-in-market dummies, averages of *leadtime*, *avpromotion* and *avprice* are included in the estimation, but to conserve space, coefficients are not reported here. The variance depends on number of time periods available for each individual. Observations where time-in-market exceeds 25 years and generics are excluded.

**Table 5: APE for different times in market**

	time in market (in years)	APE	p-value	[95% confidence interval]	
<i>order_1</i>	0	70%	0.000	[63%	77%]
	2	56%	0.000	[50%	62%]
	5	40%	0.000	[35%	46%]
	10	22%	0.000	[17%	27%]
	15	8%	0.000	[5%	11%]
	20	3%	0.142	[-1%	6%]
	total average	33%	0.000	[29%	36%]
<i>order_2</i>	0	27%	0.000	[20%	34%]
	2	33%	0.000	[27%	39%]
	5	24%	0.000	[18%	30%]
	10	17%	0.000	[11%	22%]
	15	3%	0.034	[0%	6%]
	20	3%	0.150	[-1%	7%]
	total average	19%	0.000	[16%	23%]
<i>order_3</i>	0	21%	0.000	[14%	29%]
	2	26%	0.000	[19%	33%]
	5	19%	0.000	[14%	24%]
	10	8%	0.000	[5%	11%]
	15	2%	0.065	[0%	5%]
	20	-1%	0.635	[-4%	3%]
	total average	13%	0.000	[10%	17%]
<i>order_4</i>	0	6%	0.010	[1%	10%]
	2	13%	0.000	[7%	18%]
	5	9%	0.000	[5%	13%]
	10	5%	0.003	[2%	8%]
	15	2%	0.148	[-1%	5%]
	20	2%	0.265	[-2%	6%]
	total average	6%	0.000	[3%	9%]
<i>order_5</i>	0	5%	0.023	[1%	9%]
	2	9%	0.001	[4%	15%]
	5	5%	0.005	[2%	9%]
	10	4%	0.010	[1%	7%]
	15	1%	0.543	[-2%	4%]
	20	1%	0.617	[-4%	7%]
	total average	5%	0.001	[2%	7%]
<i>order_6</i>	0	8%	0.004	[2%	13%]
	2	10%	0.000	[4%	15%]
	5	9%	0.000	[4%	14%]
	10	3%	0.046	[0%	5%]
	15	3%	0.317	[-3%	8%]
	20	3%	0.467	[-6%	12%]
	total average	6%	0.000	[3%	9%]

APE from estimations of Table 4

**Table 6: APE for different lead times and lag times**

	lead time (in years)	APE	[95% confidence interval]		lag time (in years)	APE	[95% confidence interval]	
<i>order_1</i>	0	33%	[29%	37%]				
	1	33%	[29%	37%]				
	2	33%	[29%	37%]				
	3	33%	[29%	37%]				
	4	33%	[28%	37%]				
	5	32%	[28%	37%]				
	tot. av.	33%	[29%	36%]				
<i>order_2</i>	0	19%	[15%	23%]	0	20%	[16%	24%]
	1	20%	[16%	23%]	1	20%	[16%	24%]
	2	20%	[16%	24%]	2	20%	[16%	24%]
	3	21%	[17%	25%]	3	20%	[16%	24%]
	4	21%	[17%	25%]	4	20%	[16%	24%]
	5	21%	[17%	26%]	5	20%	[16%	23%]
	tot. av.	19%	[16%	23%]	tot. av.	19%	[16%	23%]
<i>order_3</i>	0	13%	[9%	16%]	0	14%	[11%	18%]
	1	13%	[10%	17%]	1	14%	[11%	17%]
	2	14%	[11%	18%]	2	13%	[10%	17%]
	3	15%	[11%	19%]	3	13%	[10%	16%]
	4	16%	[12%	20%]	4	12%	[9%	15%]
	5	17%	[12%	22%]	5	12%	[8%	15%]
	tot. av.	13%	[10%	17%]	tot. av.	13%	[10%	17%]
<i>order_4</i>	0	6%	[0%	3%]	0	6%	[3%	9%]
	1	6%	[0%	3%]	1	6%	[3%	9%]
	2	6%	[0%	4%]	2	6%	[4%	9%]
	3	6%	[0%	3%]	3	7%	[4%	9%]
	4	6%	[0%	3%]	4	7%	[4%	10%]
	5	6%	[1%	2%]	5	7%	[4%	10%]
	tot. av.	6%	[3%	9%]	tot. av.	6%	[3%	9%]
<i>order_5</i>	0	5%	[3%	8%]	0	5%	[2%	8%]
	1	5%	[2%	8%]	1	5%	[2%	8%]
	2	5%	[2%	7%]	2	5%	[2%	7%]
	3	4%	[1%	8%]	3	4%	[2%	7%]
	4	4%	[-1%	8%]	4	4%	[1%	7%]
	5	3%	[-2%	8%]	5	4%	[0%	7%]
	tot. av.	5%	[2%	7%]	tot. av.	5%	[2%	7%]
<i>order_6</i>	0	7%	[4%	10%]	0	6%	[3%	9%]
	1	6%	[3%	9%]	1	6%	[3%	9%]
	2	5%	[2%	8%]	2	6%	[3%	10%]
	3	5%	[1%	8%]	3	6%	[3%	10%]
	4	4%	[0%	7%]	4	7%	[2%	11%]
	5	3%	[-2%	7%]	5	7%	[1%	12%]
	tot. av.	6%	[3%	9%]	tot. av.	6%	[3%	9%]

APE from estimations of Table 4

**Table 7: P-values of Chow test on the effect of entrance of first generic**

	order_1	order_2	order_3	order_4	order_5	order_6
coeff. of all interactions are 0	0.0000	0.0000	0.0006	0.0018	0.0005	0.3009
coeff. of all interactions with <i>order_n*</i> are 0	0.0880	0.0574	0.3628	0.2228	0.1041	0.5581

From estimations of Table 4 augmented by interaction terms for markets with generic competition.

\*) Including *order\_n*, *order\_n\*time-in-market dummies*, *order\_n\*lagtime* and *order\_n\*leadtime*.



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