Working Paper Series, N. 5, April 2013

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Emergence of a Pharmaceutical Drug as New Entrant in a Category: Ex Ante Diffusion of Innovation Modeling and Forecasting

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UNIVERSITÀ DEGLI STUDI DI PADOVA
DIPARTIMENTO DI SCIENZE STATISTICHE

Final version (2013-04-03) .

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1 Introduction

Theoretical and empirical research in diffusion of innovations has raised a growing interest in the past four decades. Basic ideas and perspectives stimulated by Rogers [29] were developed in many disciplines such as sociology, marketing, operations research, management, physics of complex systems, biology, epidemiology, science of networks, statistics, etc. Relevant reviews in the area of quantitative marketing may constitute a litmus paper of the increasing advancements in a context that is open to different and complementary contributions. See, among others, [21], [22], [23], [25], [28].

A pioneering paper by Bass [1] gave a sound formal approach to Rogers' intuitive ideas concerning the timing of the adoption events in a system (marketplace). Relevance of the social network of relationships was expressed by considering only two different sources of information that characterize two basic sub-classes of adopters (or adoptions). Innovators introduce to the system a seeding effect determined by an external force, an institutional communication channel. Imitators expand the adoption process through an internal independent information channel related to

word-of-mouth or social signals. The differential equation characterizing the standard Bass model, BM, is a restricted version of an autonomous Riccati equation whose solution is positive for $t > 0$ and zero elsewhere.

The limitations of the standard Bass model, which is locally symmetric, unimodal, insensitive to the heterogeneity of agents, independent upon external dynamic control factors, and not able to describe variations in market potential over time, suggested different directions of research. The most important perspectives may be focused on the following topics: heterogeneity of agents, control tools on life cycle dynamics, treatment of latent dynamics in market potential modulation, competition among few product or services in a common market, competition-cooperation among a large number of partially substitute products entering the market in different instants, etc.

Heterogeneity of agents may be represented by different approaches that distinguish the discrete case (see, for instance, Karmeshu and Goswami [19]) from other unimodal approaches with continuous mixing functions such as in the Bemmaor approach [3], [4].

An extremely important advance in including control factors in the life cycle dynamics modeling was proposed by Bass et al. [2] through the Generalized Bass model, GBM. The pioneering paper emphasizes a special version of the controlling function $x(t)$ based upon relative changes in prices and advertising efforts. Nevertheless, the proposed solution – again a special non-autonomous member of the Riccati family with some added constraints – is quite general and allows the recognition of local discrete interventions, mean-reverting or not, that are very flexible.

Both models, BM and GBM, assume a constant market potential over the entire life cycle, and in particular, the intervention function modifies the time-allocation of adoption events, and not the scale aspect over time. In other words, the market potential m in BM and GBM is constant, and the intervention function $x(t)$ cannot modify it.

A quite general treatment of latent dynamics in market potential is proposed through the Guseo-Guidolin model, GGM, [10], [11], and [12] that assumes a complex system approach followed by a mean-field approximation in order to represent an aggregate dynamic. The model, which has a closed form solution for a general market potential $m(t)$ and a substantially free control function $x(t)$, extends the GBM, emphasizing the distinction between a communication component, that affects the potential, and an adoption component, which defines the final decision stage of the diffusion process. Both components are time-dependent.

Competition modeling through systems of differential equations, within the field of diffusion of innovations, has received limited attention in literature, usually referred to few competitors due to the complexity of involved interactions. Recent closed form solutions may be found in Savin and Terwiesch [30] and Guseo and Mortarino [13], [14].

If the competition-cooperation dynamic is defined for a large number of partially substitute products entering the market at different times, then the study of the corresponding differential systems may be extremely difficult. For example, this situation emerges when we describe a wide category of pharmaceutical drugs with similar active principles and partially overlapping products that entered the market

of a pathology in different times, generating different life cycles.

Within this more complex framework, where interaction among life cycles is not easily estimable, there is a further issue of central interest for the management: the *ex ante* estimation of the features of a new entrant for which no data are available. In this context, a prediction based on analogies or, more properly, a meta-estimation based on the dynamic sequence of similar parameters describing successive life cycles, may be a reasonable proposal.

The focus of this paper is two-fold: the *ex ante* estimate of the launch date and the individual dynamic character definition of a new entrant by examining the sequential properties of older members active in the category. The underlying theoretical hypothesis assumes a patterned evolution of the parameters in a family of homogeneous life cycle models where each member of the category may take a special shape under competition. To our knowledge, this problem is not addressed in diffusion of innovation literature.

The paper is organized as follows. In Section 2, we introduce the rationale for a patterned evolution of competing products in a category and some details on BM, GBM, and GGM models. In Section 3, we examine a special category of pharmaceutical drugs in Italy: the *ranitidine*. We limit the time window in order to estimate *ex ante* the properties of a "future" entrant in the category. Section 4 studies the dynamics of the involved parameters and proposes a "meta-estimate" for the new entrant: Ulkobrin. A comparison between predicted and observed sales for Ulkobrin is discussed. Section 5 is devoted to concluding remarks and final comments.

2 Some diffusion of innovation models

The diffusion of innovations in a social system has always been of relevant interest in very different contexts. The basic assumptions that determine a particular evolutionary process may be summarized by the following conditions:

a) An innovation such as a new technology, a new service, a new cultural paradigm, a new pharmaceutical treatment, etc., exhibits, at the aggregate level (over space), a limited horizon (a limited life cycle), i.e., the relevant time interval is finite. Rogers [29], among others, separates different sub-populations such as "innovators," "early adopters," "early majority," "late majority," and "laggards." These are non-overlapping sub-categories over a finite life cycle. Communication channels are partially independent and characterize previous sub-classes.

b) Heterogeneity of agents is not systematically embedded in basic diffusion models by assuming perfect mixed sub-populations. This reduction may force dynamics within special unimodal distributions over time.

c) The communication channels, such as advertising and internal word-of-mouth, may be insufficient. External control functions may interact with the adoption process by including relevant environmental, cultural, legal, political actions

that usually define a third party with respect to firms' communication efforts and internal systems of signals and word-of-mouth among agents (final adopters).

d) The description of a category of partially substitute products with different entry times usually highlight a patterned structure over time. This structure may be recognized when competitors/collaborators are very few. See, for instance, Savin and Terwiesch [30] and Guseo and Mortarino [13], [14]. For a more complex context with a large number of competitors, the direct study, via a meta-analysis, of the sequence of the parameters characterizing the subsequent life cycles may be much more flexible.

In the following sub-section we highlight the basic features of three hierarchical models: BM, GBM, and GGM.

2.1 Standard Bass model, BM

The standard Bass model is characterized through a differential equation that defines the hazard of the adoption process at time t. It is a mixture of three sub-populations: innovators, imitators (through word-of-mouth), and neutrals characterized by p, q, and $1-p-q$ shares, respectively, with different but stable conditional preferences toward adoption within the life cycle. These preferences are conditional probabilities defined by 1, $F(t)$, and zero, respectively,

$$\frac{z'(t)}{m-z(t)} = \frac{f(t)}{1-F(t)} = p \cdot 1 + q \cdot F(t) + (1-p-q) \cdot 0 = p + qF(t), \qquad (1)$$

where $z(t) = mF(t)$ denotes the observed cumulative sales up to time t, $z(0) = 0$ is an initial condition relevant for counting processes, and m is the asymptotic fixed market potential. $F(t)$ represents the corresponding normalized distribution function, $F(t) = z(t)/m$, for $t > 0$ with the further constraint $F(t) = 0$ for $t < 0$, and the rate function $f(t) = F'(t)$ is the density related to the distribution function $F(t)$. Equation (1) may be simplified as follows:

$$f(t) = (p + qF(t))(1 - F(t)), \qquad F(0) = 0, \qquad t \geq 0, \qquad (2)$$

and zero elsewhere.

Equation (2) is an autonomous Riccati equation, and its constrained solution is

$$F(t) = \frac{1 - e^{-(p+q)t}}{1 + \frac{q}{p}e^{-(p+q)t}}, \qquad F(0) = 0, \qquad t \geq 0, \quad p, q > 0, \qquad (3)$$

and $F(t) = 0$ for $t < 0$.

The Bass density, $f(t)$, is a local symmetric function in the interval $[0, 2t^+]$,

$$f(t) = \frac{p(p+q)^2 - e^{-(p+q)t}}{(p + qe^{-(p+q)t})^2}, \qquad t \geq 0, \qquad (4)$$

where $t^+ = (\ln(q/p))/(p+q)$ is the time to peak. A useful approximation of density $f(t)$ in Equation (4) is

$$f(t) \simeq F(t+0.5) - F(t-0.5), \qquad t \geq 0. \tag{5}$$

The standard Bass model, introduced by Bass in 1969 (cfr. ref. [1]), has had an outstanding position in emphasizing the strategic role of sales forecasting within current life cycles. Nevertheless, it suffers from strong limitations, for example, local symmetry of sales, unimodality, and risk of underestimating the life cycle features if the initial time series of sales is short and very far from the peak time. Further limitations are related to some omissions in the definition of the equilibrium function (2), in particular, the unrealistic assumption of invariance and independence upon external controls or interventions, and the coarse assumption of a constant market potential over the entire life cycle.

2.2 Generalized Bass model, GBM

The dependence of a diffusion process upon external control functions was developed by Bass, Krishnan, and Jain in 1994 (cfr. ref. [2]) after about 25 years of fruitless attempts. The modeling setting is elegant and efficient. For simplicity, we use again previous notations for density $f(t)$ and distribution function $F(t)$ in the new context to avoid cumbersome symbols. The new equation that integrates exogenous time-dependent covariates is:

$$f(t) = (p + qF(t))(1 - F(t))x(t), \qquad F(0) = 0, \qquad t \geq 0, \tag{6}$$

where the function $x(t)$ describes a very general intervention function acting on the residual normalized market $(1 - F(t))$.

For $x(t) = 1$ uniformly, Equation (6) reduces to the standard Bass model. Deviations from the equilibrium level 1 have different interpretations. For $0 < x(t) < 1$, we observe a slower dynamic in adoption and, vice versa, for $x(t) > 1$, the adoption process is accelerated over its life cycle.

The general solution for the GBM with initial condition $F(t) = 0$ and the further constraint $F(t) = 0$ for $t < 0$ is:

$$F(t) = \frac{1 - e^{-(p+q)\int_0^t x(\tau)d\tau}}{1 + \frac{q}{p}e^{-(p+q)\int_0^t x(\tau)d\tau}}, \qquad t \geq 0 \quad p, q > 0 \tag{7}$$

and zero elsewhere.

The modulation of the intervention function $x(t)$ may be performed through different strategies. Function $x(t)$ may collect and combine various time-dependent covariates that are supposed to affect the diffusion process. A different perspective may be considered when controls or interventions are thought to describe rare events, for instance exponential shocks:

$$x(t) = 1 + c_1 e^{-b_1(t-a_1)} I_{t \geq a_1}, \tag{8}$$

where $I_{(e)}$ is an indicator function equal to 1 if proposition e is true and zero in the opposite case, c_1 measures the amplitude of the impulse starting at time a_1, and

$b_1 > 0$ denotes a memory effect that is decaying over time. For $b_1 < 0$, the proposed intervention is not mean reverting to the stationary equilibrium represented by the neutral factor 1 and describes a permanent modification of the system over time.

A quite different control may describe an essentially stable behavior within a limited time window. It is usually a regulatory regime:

$$x(t) = 1 + c_2 I_{t \geq a_2} \cdot I_{t \leq b_2}. \tag{9}$$

The ability of a GBM to consider covariates or local shocks has proved its performances in different contexts where policies, marketing strategies, advertising campaigns, etc. exert possibly significant effects. Such models may test these exogenous components in a simple and efficient way. For recent applications, see, for instance, [8], [9], [7], and [6].

2.3 Guseo-Guidolin model, GGM

The GGM defines a special approach in formalizing an important characteristic omitted by both the standard BM and the related extension, the GBM, which integrates control factors modifying adoption allocation over time. The relevant feature is the general shape of latent market potential, $m(t)$, as contrasted with the constant assumption m in BM and GBM. The topic was treated in literature by modifying the residual market, $(m(t) - z(t))$, or the word-of-mouth component. See, for instance, [24], [15], [18], [32], [16], and [27]. Sometimes, the shape of $m(t)$ is determined by exogenous control variables. See, for example, [24], [17], and [15]. In a limited number of papers the market potential is assumed to follow exponential function of time. See, for example, [32], [5], and [26]. The basic idea of GGM is the inclusion of a general function $m(t)$ for the market potential description, which is a direct function of a variable awareness on the relevance, fitness, efficiency, and efficacy of the product of interest. If we omit, for simplicity, a decay component in the original model, its general aggregate differential form is:

$$z'(t) = m(t) \left\{ \left(p_s + q_s \frac{z(t)}{m(t)} \right) \left(1 - \frac{z(t)}{m(t)} \right) \right\} x(t) + z(t) \frac{m'(t)}{m(t)}, \qquad z(0) = 0, \qquad t \geq 0, \tag{10}$$

with the usual constraint, $z(t) = 0$ for $t < 0$, where $z(t)$ denotes the cumulative sales, $m(t)$ the variable potential, $x(t)$ an intervention function, and $z(t)m'(t)/m(t)$ a collective reinforcing effect that emphasizes or depresses sales on the basis of the sign of $m'(t)$. Parameters p_s and q_s denote the local dynamics of the adoption process.

Equation (10) was obtained in [10] as a mean-field approximation of a Cellular Automaton. The general solution to Equation (10) with initial condition $z(0) = 0$ and $z(t) = 0$ for $t < 0$ is:

$$z(t) = m(t) \frac{1 - e^{-(p_s + q_s) \int_0^t x(\tau) d\tau}}{1 + \frac{q_s}{p_s} e^{-(p_s + q_s) \int_0^t x(\tau) d\tau}}, \qquad t \geq 0 \quad p_s, q_s > 0, \tag{11}$$

and zero elsewhere. Solution (11) does not depend upon special choices of $m(t)$ and $x(t)$. The issue of a realistic definition of a variable potential $m(t)$ for specific

problems was treated in [10] and [12] through the dynamic description of an evolutionary network among individuals in a social system with autonomous expression and saturation of awareness, which allows a better understanding of the parallel potential. A Cellular Automaton for the description of the increasing relationships was implemented and reduced with the aid of a mean-field approximation. The special result for this particular approach is:

$$m(t) = K\sqrt{\frac{1 - e^{-(p_c+q_c)t}}{1 + \frac{q_c}{p_c}e^{-(p_c+q_c)t}}}, \tag{12}$$

where p_c, q_c denote the communication parameters generating the non-constant market potential, and K is the asymptotic market potential. The proposed approach in [10] and [12] is quite interesting because the separation of two main forces, communication and adoption, may give rise to different prevalent allocations over time of the two components. See, in particular, [12], where some explicit examples in pharmaceutical drug diffusions may exhibit saddle or slowdown effects relevant for marketers because the temporal dominance of one factor during the launch stage may suggest convenient strategies of support.

2.4 Statistical inference

In previous sub-sections we have introduced the standard Bass model, BM; a relevant extension, the GBM, and a further extension, the GGM.

A reasonable and robust inferential methodology for the estimation and testing the performance of the proposed models may be described through a nonlinear regressive model, i.e.,

$$w(t) = \eta(\beta, t) + \varepsilon(t), \tag{13}$$

where $w(t)$ represents the observed cumulative sales data, $\eta(\beta, t)$ denotes a systematic rescaled cumulative distribution function of time t and some parameters β typical of BM, GBM, GGM; and $\varepsilon(t)$ is usually a white noise or a more complex stationary process if seasonality and/or autoregressive components are included as stochastic components. For estimation purposes, we use a two-phase procedure.

Firstly, we apply a robust nonlinear least squares algorithm, NLS, which ignores the stochastic structure of $\varepsilon(t)$, under the well-known Levenberg-Marquardt correction of the Gauss-Newton recursive procedure. See, for instance, Seber and Wild [31].

Secondly, the prediction $\eta(\hat{\beta}, t)$ based on an NLS solution, $\hat{\beta}$, may be used in a SARMAX framework (Seasonal, Autoregressive, Moving Average process with an input X) in order to improve short-term prediction. This second stage is implemented if the residuals of the first one do not follow a standard white noise. The Durbin-Watson statistic may be an exploratory test.

The proposed nonlinear models in Section 2 are essentially nested. The significance of an extended model, M_2, as compared with a simpler one, M_1, may be studied through a normalized squared multiple partial correlation coefficient $\tilde{R}^2$ within the interval $[0; 1]$, namely,

$$\tilde{R}^2 = (R^2_{M_2} - R^2_{M_1})/(1 - R^2_{M_1}), \tag{14}$$

where $R^2_{M_i},\ i = 1, 2$ is the standard determination index. An equivalent statistic, normalized in the interval $(0, +\infty)$, is the corresponding F-ratio. Let n denote the number of observations, v the number of parameters involved in the richer model M_2, and u the number of parameters that generalize model M_2 with respect to the reduced model M_1. The dual F-ratio, which is a standard tool in linear models, has a one-to-one correspondence with $\tilde{R}^2$, i.e.,

$$F = [\tilde{R}^2(n - v)]/[(1 - \tilde{R}^2)u]. \tag{15}$$

Under stronger assumptions on $\varepsilon(t)$ term in Equation (13), namely, i.i.d. and normality, the F-ratio is a statistical variable with Snedecor's F distribution, $F \sim F_{u,n-v}$. A common upper threshold for the F-ratio (15), without strong assumptions on error distributions, is 4.

The above-mentioned SARMAX improvement for short-term predictions rests on the following equation based on polynomial function of backward operators, namely,

$$\Psi(B)\,\Phi(B^s)\,[z'(t) - c\,\eta(\hat{\beta}, t)] \;=\; \vartheta(B)\,\Theta(B^s)\,a_t, \tag{16}$$

with a_t a WN process; B, B^s the standard and seasonal backward operators; and $\Psi(B)$, $\Phi(B^s)$, $\vartheta(B)$, and $\Theta(B^s)$ the usual backward polynomials of order p, P, q, and Q, respectively. The calibration parameter c allows a global assessment on the stability of the predicted regressive values stemming from model $\eta(\beta, t)$.

2.5 Ex ante modeling of a new entrant

In previous sub-sections we presented some univariate models for the description of the temporal trajectory of a product. It is a common experience to observe possible competition among few products pertaining to the same category. Savin and Terwiesch [30]; Guseo and Mortarino [13], [14]; Krishnan, Bass, and Kumar [20]; among others, examined directly the competition among few products by means of a system of related differential equations with interesting closed-form solutions. Nevertheless, previous approaches assume a sufficient development of the observed series to provide reliable response or parameters' estimates. When competition involves a large number of partially substitute products, the direct differential description may appear cumbersome, awkward, or not applicable. Moreover, the complete lack of information on the future series of a new entrant product highlights a non-standard class of inferential problems.

The latter limitation, summarized by the lack of data for a new entrant, may suggest a different approach based on the recognition of possible patterns of sequential life cycles in a common product category.

The main issues to deal with are:

a) the definition or estimate of the launch time for the new entrant;

b) the *ex ante* estimate, with no specific information, of the parameters characterizing a new entrant under reasonable assumptions.

For point **a)** we may follow different strategies. A possible way is to study the birth events over time within specific classes. For instance, the antidiabetic type 2 drugs

are classified through ATC codes (Anatomical Therapeutical Chemical classification system): A10BA (biguanides), A10BB (sulfonamides), A10BD (combinations or oral glucose lowering drugs), etc. Within previous homogeneous sub-classes or at the general level, some estimate of the birth time of a new entrant may be performed by implementing a BM, GBM or GGM model within common or equivalent active principles. Following, for simplicity, a Bass model $F(t)$, as defined in Equation (3), under the hypothesis of a good performance, where $\hat{m}$, $\hat{p}$, and $\hat{q}$ are the usual estimates and t_{LO} the time of the younger observation, we may solve the following equation in δ,

$$1 = \hat{m}\,[\hat{F}(t_{LO} + \delta) - \hat{F}(t_{LO})], \tag{17}$$

in order to obtain an estimate for the new birth time: $t_{LO} + \hat{\delta}$.

For point **b)**, a different path to define the time of a new entry may be obtained within a model that exhibits a slowdown or a saddle. This special time period may be interpreted as a kind of pause in the evolutionary behavior of the last competitor that entered the category. During that pause a new entrant has a limited number of difficulties in sustaining and increasing its market share. The Guseo-Guidolin model allows for a bimodal performance with a better understanding of the reasons motivating such a saddle.

Usually, the communication component that determines the shape of market potential is positioned in the first part of a product's life cycle. In some cases, especially for products that are of wide interest for a community, we observe a different order. Adoption is the first driver and communication efforts take place in a second moment in order to reinforce or stabilize the performance. The latter modality is normally associated with particular pharmaceutical drugs that are well known by patients affected by serious illness.

After the launch time determination for a new product, the second issue to be solved is the *ex ante* evaluation of plausible parameters' estimates within a common univariate model for each competing product in a category. A simple idea, proposed in this paper, rests on the evolutionary study over time of each parameter of the competing products. The basic proposal is to determine at a first step a convenient time-dependent function (polynomial or other) and evaluate their estimated values at the predicted launch date of the new entrant.

3 An application: the ranitidine diffusion in Italy

Ranitidine is a histamine H_2-receptor antagonist that normalizes stomach acid production. It is currently used in the treatment of gastroesophageal reflux disease, heartburn, and peptic ulcers. It was developed by Glaxo in the summer of 1976 as a response to Smith, Kline and French which introduced, in 1976, the first histamine H_2-receptor antagonist, cimetidine, launched in the UK with the trade name Tagamet.

The main difference of ranitidine was the substitution of the imidazole-ring of cimetidine with a furan-ring. The new active principle introduced a significant improvement in terms of tolerability with a reduction of adverse drug effects, a longer-lasting action, and an excellent activity as compared with cimetidine. Ranitidine

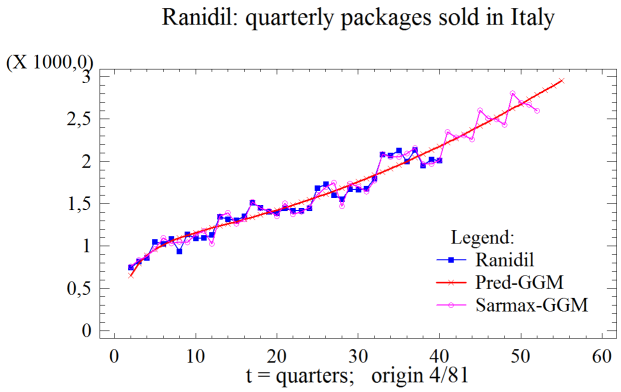

Figure 1: Ranidil, Italy: quarterly packages sold (in thousands). GGM and Sarmax-GGM models. Launch: 4/1981.

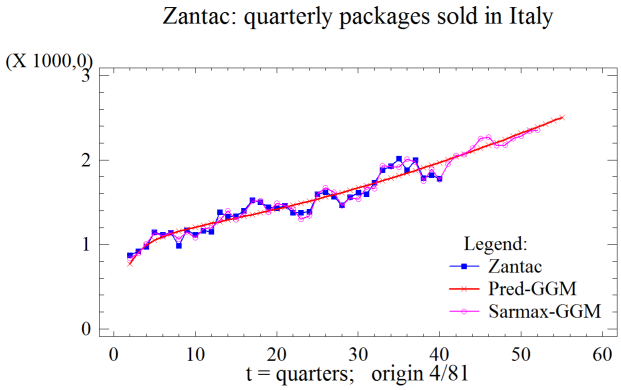

Figure 2: Zantac, Italy: quarterly packages sold (in thousands). GGM and Sarmax-GGM models. Launch: 4/1981.

was introduced worldwide in 1981 and was the "winner" in this area.

The launch in the Italian market dates back to the fourth quarter of 1981, 4/81 for brevity. Zantac by Glaxo (now GlaxoSmithKline) and Ranidil by Menarini (now Menarini Industrie Farmaceutiche Riunite) were the first two members of the ranitidine category. Further competitors entered the market with new launches in the subsequent years, namely, Trigger (4/83), Ulcex (4/83), Ranibloc (2/85), Raniben (4/86), and Mauran (4/86). A further drug for acid-related disorders based on ranitidine was Ulkobrin, launched in the fourth quarter of 1988 by Salus Researches.

The data, provided by IMS-Health, Italy, refer to the cumulative quarterly number of packages sold in Italy and are available until the third quarter of 1991.

In the sequel, we examine the dynamics of the above-mentioned drugs excluding Ulkobrin that plays the role of new entrant in the proposed analysis.

Ranidil was launched by Menarini as a parallel product. Zantac was the main driver sustained and promoted by Glaxo. A comparison between the twin products may be of interest.

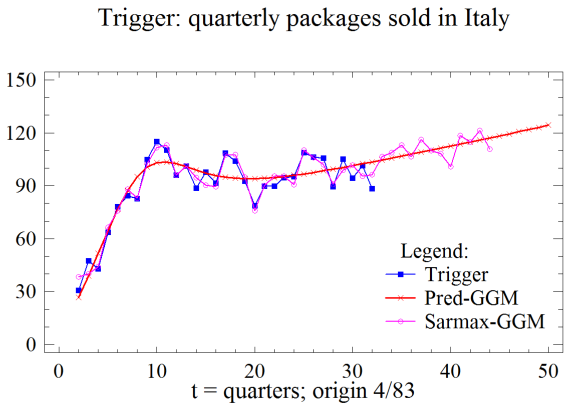

Figure 3: Trigger, Italy: quarterly packages sold (in thousands). GGM and Sarmax-GGM models. Launch: 4/1983.

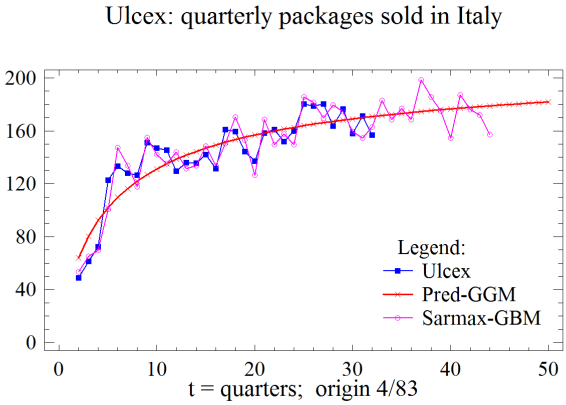

Figure 4: Ulcex, Italy: quarterly packages sold (in thousands). GGM and Sarmax-GGM models. Launch: 4/1983.

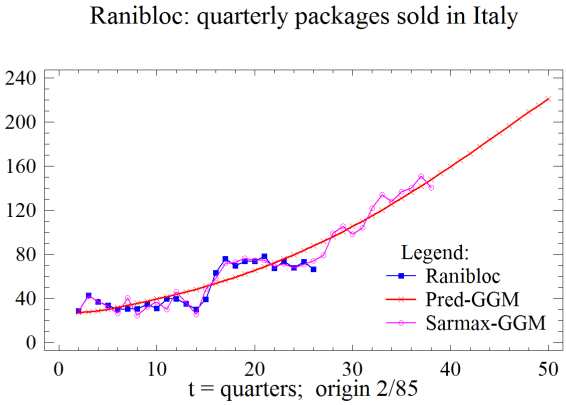

Figure 5: Ranibloc, Italy: quarterly packages sold (in thousands). GGM and Sarmax-GGM models. Launch: 2/1985.

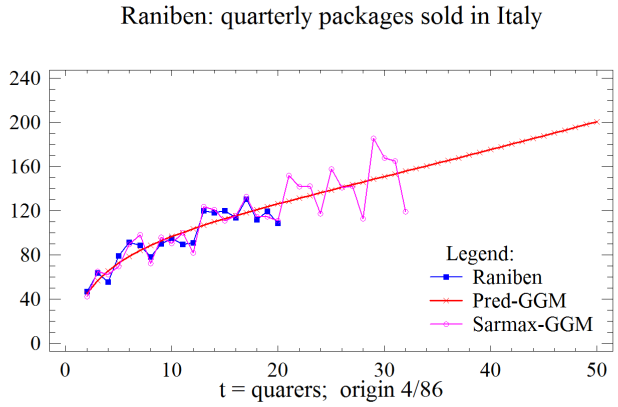

Figure 6: Raniben, Italy: quarterly packages sold (in thousands). GGM and Sarmax-GGM models. Launch: 4/1986.

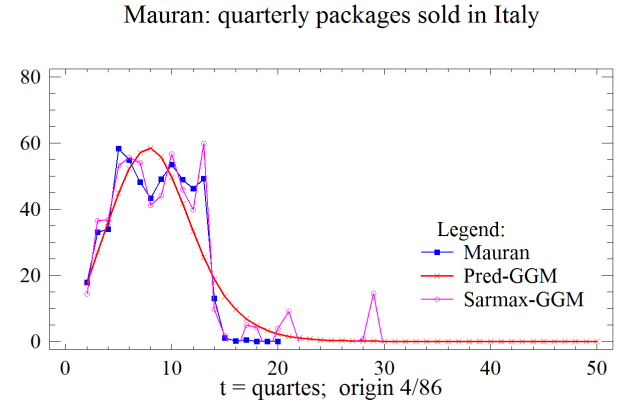

Figure 7: Mauran, Italy: quarterly packages sold (in thousands). GGM and Sarmax-GGM models. Launch: 4/1986.

The introductory analysis is based on the BM which tends to underestimate the life cycle of both products. The determination index in Table 1 defines a good approximation, $R^2 = 0.99967$ for Ranidil and $R^2 = 0.99968$ for Zantac, but the rigidity of the assumed fixed market potential is not able to recognize a kind of learning effect within the system.

The idea that market potential may present a structure that is time-dependent is well described by the GGM as denoted by Equations (11) and (12). They define an evident advantage over BM. We observe in Table 1 good levels of determination indexes, $R^2 = 0.999926$ for Ranidil and $R^2 = 0.999894$ for Zantac. What is much more relevant is the significance of the squared partial coefficients, $\tilde{R}^2_{B|GG} = 0.77$ for Ranidil and $\tilde{R}^2_{B|GG} = 0.67$ for Zantac. A confirmation of the significance of the extended GGM with respect to BM in both cases is highlighted by the high values of F-ratios, $F_{B|GG} = 59.6$ for Ranidil and $F_{B|GG} = 35.2$ for Zantac.

The performance of the GGM is satisfactory even if we observe some instability in the definition of the approximate confidence limits for the parameters. However, what is more important is the global stability of the system response.

Some remarks may be of interest. The asymptotic potential of Zantac is greater, 1509820 versus 937643. Nevertheless, the levels of p_c, 0.206 for Ranidil and 0.113 for Zantac, are relevant. This is an evident signal of the effort spent, at the communication level, by Menarini in sustaining Ranidil as compared with Zantac, where Glaxo obtained an optimal performance without forcing the market. The negative values of q_c denote a non-significant effect of imitative component within the communication factor.

A subsequent analysis through SARMAX models, where the X component is the estimated mean trajectory based on GGM, gives good results. For both models we observe a confirmation of the GGM over the BM, where parameter c equals 1.0002 and 0.99968, with a high value of t-statistic, 1483.01 and 880.51, respectively. The improvement generated by SARMAX with respect to GGM is denoted by the high values of $\tilde{R}^2_{GG|S}$, namely 0.913 and 0.946, versus $F_{GG|S} = 35.4$ and 38.2, respectively.

We observe in Figures 1 and 2 that the slowdown is positioned at 2/1985 and 2/1986, respectively. This is a typical effect of the GGM and usually describes a change of regime between the prevalence of the communication driver in promoting sales in a first phase followed by a more standard dynamic due to the adoption process in itself.

In the fourth quarter of 1983, we register the introduction of two new members within the ranitidine principle, namely, Trigger by Polifarma (licensed by Glaxo) and Ulcex (Laboratori Guidotti and Lusofarmaco).

Trigger is characterized by a typical GGM behavior: a wide effort during launch phase; a deep slowdown, which is a kind of saddle, and a subsequent takeoff. See, in particular, Figure 3. Its absolute dimension is not very high as compared with Zantac and Ranidil. It captures only a particular niche. A confirmation of the GGM relevance, with respect to BM, is given in Table 1 by two fundamental tests: $\tilde{R}^2_{B|GG} = 0.961$ and $F_{B|GG} = 441.04$. We observe a further improvement of SARMAX for short-term predictions, i.e., $\tilde{R}^2_{GG|S} = 0.86$ and $F_{GG|S} = 17.48$. The specific firm's effort during the introduction of Trigger in the market category is well described by the parameters $q_c = 0.33$ and $p_c = 0.026$. The subsequent adoption phase is quite normal. SARMAX analysis for short-term prediction is quite effective as determined by the estimate $c = 0.99983$ with t-statistic $t_{GGM} = 1167.13$ and $\tilde{R}^2_{GG|S} = 0.86$ or, equivalently, $F_{GG|S} = 17.48$ to confirm the global improvement.

Also, Ulcex is characterized by a particular GGM behavior even if the separation between the launch communication effect and the adoption process is small so that the latter is nearly superimposed on the former. The global performance under BM is not satisfactory, while GGM improves the fitting with $\tilde{R}^2_{B|GG} = 0.73$ and $F_{B|GG} = 47.49$. See, in particular, Figure 4. The asymptotic performance of the market potential is about 1/10 of Ranidil or Zantac considered as a benchmark. SARMAX improvement is quite satisfactory.

Ranibloc, introduced in the second quarter of 1985 by GlaxoSmithKlein, has a special behavior in the introductory phase. The commercial communication effort is

quite limited, and the observed takeoff is comparatively slow. This behavior is well described by a standard BM with a reasonable determination index $R^2 = 0.9972$. The contribution of GGM in this case is not relevant because $\tilde{R}^2_{B|GG} = 0.10$ and $F_{B|GG} = 1.97$. See, in particular, Figure 5. The improvement due to SARMAX framework is significant as expressed by $F_{GG|S} = 66.66$.

Raniben, introduced by Firma in the fourth quarter of 1986, has a limited share, and its behavior is well described by a GGM as compared with a BM. See, in particular, Figure 6. The F-ratio is significant, $F_{B|GG} = 18.9$, and a SARMAX improvement is well determined.

Mauran, introduced by Coli in the fourth quarter of 1984, reached a very limited expansion, and its life cycle was very short. In this case a BM is sufficient for interpretation. A confirmation is given by $F_{B|GG} = 0.35$ that excludes the appropriateness of a GGM. See, in particular, Figure 7. The particular short-term history of Mauran, very far from the previous ones, and very limited in time, suggests an exclusion of this product from the subsequent meta-analysis.

An important aspect of the GGM applied to Ranidil, Zantac, Trigger, Ulcex, Ranibloc, and Raniben is that the slowdown period of the products is related to the launch of successive competitors. The particular choice is quite reasonable because a local depression on sales allows the introduction of a new entrant with minor difficulties. For this reason we estimate the fourth quarter of 1988 as the possible entry time of a new competitor. This date was actually the launch date of Ulkobrin.

4 Meta-analysis point estimate of a new entrant: Ulkobrin

The key idea for the estimation of the main features of a new entrant in the category of ranitidine in the fourth quarter of 1988 is grounded in the hypothesis that the subsequent competitors may evolve according to the local opportunities and constraints of the category. The sequential introduction of competitors that develop with specific characteristics may give information about the expandability of the category or its evolutionary contraction. We have modeled all competing products with a common-model GGM, which is usually particularly suitable in describing the life cycle of pharmaceutical drugs dynamics. We express the pattern of the subsequent products by modeling the common five parameters K, p_c, q_c, p_s, and q_s over time through convenient regressive models.

In Table 2, we have summarized, for each parameter, the selected model under suitable restrictions. For instance, the K parameter exhibits two large values related to Ranidil and Zantac that may be considered outliers with respect to the followers. In this case the suggested model $K = (a + b/t)^2$ is limited to the four younger series. A similar discussion was reserved to the q_c dynamical evolution where Ranibloc may be considered as an outlier. For the other parameters we introduced specific functions that are (with some exception) quite reasonable in estimating the observed temporal evolution. The parameter q_s is quite stable over the examined period, and the low level of R^2 is a confirmation.

The last column of Table 2 includes the suggested estimates, computed at entry time 4/88, for the new entrant, Ulkobrin. In Figure 8, we propose a graphical com-

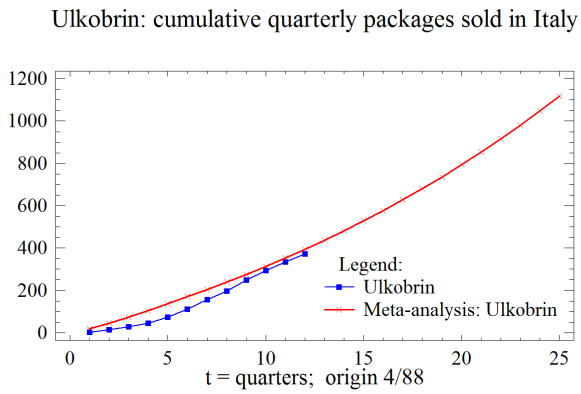

Figure 8: Ulkobrin, Italy: quarterly packages sold (in thousands). GGM and Sarmax-GGM models. Launch: 4/1988.

parison between observed Ulkobrin cumulative sales and the meta-estimate obtained by induction. The agreement appears quite good even if stability of single models is sometimes not very high and the number of older competitors is limited to few actors.

5 Conclusions

The proposed strategy in estimating *ex ante* the launch data and specific features of a new entrant in an existing category of pharmaceutical drugs is not an easy issue. There are many sources of uncertainty that may affect the procedure.

A basic assumption and, therefore, a limitation, is due to the necessity of implementing a single family of models for the individual description. The second constraint is a consequence of an informative assumption on the existence of a pattern of the subsequent trajectories that define the global properties of the category evolving over time.

In a certain sense we consider that the sequence of the alternative product is not a random white noise, but exhibits a kind of meta life cycle.

The statistical precision and stability of estimates strongly depends upon a kind of local minimal stationarity in order to estimate with few data some plausible future for a new entrant. Obviously, orphan pharmaceutical drugs cannot be examined with the proposed methodology because the learning component is totally absent. In this case, a common strategy is usually defined through a mean value determination of the parameters pertaining to similar or affine products.

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Table 1: Parameter estimates of standard Bass model, BM, and Guseo–Guidolin model, GGM. SARMAX model is an improvement of GGM. ( ) marginal linearized asymptotic 95% confidence limits. [ ] t statistic. $*$: significant, 95%. $**$: strongly significant, 99%. The subscripts of $\tilde{R}^2$ and F define the involved nested models, in particular, $B|GG$ denotes the comparison between BM and GGM, and $GG|S$ the comparison between GGM and SARMAX models.

Model	par.	**Ranidil** 4/81	**Zantac** 4/81	**Trigger** 4/83	**Ulcex** 4/83	**Ranibloc** 2/85	**Raniben** 4/86	**Mauran** 4/86
BM	m	164414	158686	3708.88	7121.4	4281.0	3117.39	568.25
		(126543)	(120224)	(3299.71)	(6062.42)	(283.294)	(2673.98)	(553.159)
		(202285)	(197147)	(4118.06)	(8179.86)	(8278.7)	(3560.8)	(583.342)
	p	0.004693	0.005443	0.012323	0.01023	0.005109	0.013332	0.018308
		(0.00376)	(0.00428)	(0.01148)	(0.00931)	(0.00089)	(0.01219)	(0.01353)
		(0.00563)	(0.00660)	(0.01317)	(0.01114)	(0.00933)	(0.01448)	(0.02309)
	q	0.041373	0.003590	0.087470	0.072470	0.073000	0.124238	0.386722
		(0.03643)	(0.03077)	(0.07166)	(0.06010)	(0.04662)	(0.10703)	(0.33306)
		(0.04632)	(0.04114)	(0.10329)	(0.08483)	(0.09938)	(0.14144)	(0.44038)
R^2		0.999674	0.999681	0.997668	0.998678	0.997247	0.999403	0.995978
RSS		3838820	3613170	56628.2	78091.2	10319.3	3822.47	3293.39
GGM	K	937643	1509820	78329.0	128682	111266	97912.2	571.673
		(-4402630)	(-13227000)	(76993.8)	(-146673)	(-280439)	(-95968.2)	(548.821)
		(6277920)	(16246700)	(79664.2)	(404036)	(502971)	(291793)	(594.525)
	q_c	-0.025046	-0.276337	0.332404	-0.046149	-1.897870	-0.06918	0.366790
		(-0.24212)	(-0.37853)	(0.29164)	(-0.17577)	(-14.0876)	(-0.16757)	(-7.36113)
		(0.19293)	(-0.17415)	(0.37316)	(0.08347)	(10.2919)	(0.02920)	(8.09471)
	p_c	0.20603	0.11343	0.02617	0.03898	0.061233	0.04454	0.28390
		(0.14324)	(-0.22530)	(0.02096)	(-0.13444)	(-17.5480)	(-0.14030)	(-1.45413)
		(0.26883)	(0.45216)	(0.03137)	(0.21241)	(17.6705)	(0.22938)	(2.02193)
	q_s	0.02535	0.02003	0.01233	0.00321	0.055216	0.016790	0.358643
		(0.00896)	(-0.00834)	(0.01114)	(-761.281)	(-392774)	(-386.07)	(0.13730)
		(0.04170)	(0.04839)	(0.01352)	(761.288)	(392774)	(386.102)	(0.57998)
	p_s	0.00093	0.000999	0.00093	0.00144	0.001185	0.001254	0.02152
		(-0.00436)	(-0.00998)	(-14436.4)	(-9091.18)	(-1.4057E6)	(-3043.57)	(-0.01641)
		(0.00622)	(0.01198)	(14436.4)	(9091.19)	(1,4057E6)	(3043.58)	(0.05944)
R^2		0.999926	0.999894	0.999911	0.999644	0.997526	0.999713	0.996058
RSS		875222	1206230	2161.89	21010.9	9276.26	1835.46	3228.53
$\tilde{R}^2_{B\|GG}$		0.77301	0.66771	0.96183	0.73071	0.10108	0.51982	0.01968
$F_{B\|GG}$		59.6	35.165	441.04	47.49	1.97	18.945	0.35
Sarmax + prGGM	AR1	1.17015*	1.33057*	-0.519946*	1.58315*	1.50803*	1.58483*	0.763015
	AR2	-0.04423	-0.79038*	—	-0.90740*	-0.972585*	-1.00913*	-0.135526
	AR3	-0.400743	—	—	—	—	—	0.347262
	AR4	—	—	—	—	—	—	0.078015
	SAR1	1.15990*	1.30197*	0.35227	1.14969*	0.863138*	0.908757*	-0.03024
	SAR2	—	-0.97882*	0.610592*	—	-0.814298	—	1.00052
	SAR3	—	0.628512*	—	—	0.975279	—	0.032378
	SAR4	—	—	—	—	—	—	—
	MA1	-0.0607202	-0.0553874	-1.38737*	—	0.903295*	0.989182*	-1.51889*
	MA2	0.473702*	-0.864262*	-0.954608*	—	—	—	-0.603104*
	MA3	0.822918*	-0.0458505	—	—	—	—	—
	MA4	—	-0.749604*	—	—	—	—	—
	SMA1	1.12057*	1.60100*	1.29839*	0.272824	0.59379*	-0.493494*	0.451533
	SMA2	—	-0.828773*	-0.597629*	0.902611*	-0.433146*	—	0.521321
	SMA3	—	—	—	—	—	—	-0.18182
	SMA4	—	—	—	—	—	—	—
RSS		76158.9	65202.84	303.761	1527.128	220.768	164.23	221.091
$\tilde{R}^2_{GG\|S}$		0.912983	0.945945	0.859493	0.927317	0.972601	0.910526	0.931596
$F_{GG\|S}$		35.41**	38.18**	17.48*	56.14**	66.66**	20.35*	3.40
prGGM	c	1.0002**	0.99968**	0.99983**	1.0034**	0.98901*	0.99741*	1.0388*
t_{GGM}		[1483.01]	[880.501]	[1167.13]	[223.94]	[675.91]	[610.86]	[14.62]

Table 2: Meta-analysis for Ulkobrin.

Par.	function: $g(t)$	Conditions	Ulkobrin (4/1988)
K	$(a + b/t)^2$ $R^2 = 0.9954$	$t > 830$ observations: 4	81466
q_c	$a + bt + ct^2$ $R^2 = 0.465$	outlier: Ranibloc observations: 5	-0.65
p_c	$1/(a + b\ln(t))$ $R^2 = 0.2015$	— observations: 6	0.031
q_s	$a + bt + ct^2$ $R^2 = 0.07$	— observations: 6	0.046
p_s	$a + bt$ $R^2 = 0.3005$	— observations: 6	0.0014

Acknowledgements

This work has been supported by Ministero della Salute and Regione Veneto, Italy. Bando Giovani Ricercatori 2009; A forecasting model for drug utilization and expenditure integrating a Cellular Automata model with the Budget Impact Analysis approach. GR-2009-1580488

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