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Chapter 7
The Successful Launch and Diffusion of New Therapies

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Abstract The successful launch and diffusion of new drugs is an essential factor of survival for many pharmaceutical firms. Sophisticated managers in this industry are in need for decision support tools that they can implement to increase the success of a new and approved pharmaceutical drug. In this chapter we present a review of such strategic and analytical tools. The review is based on significant contributions by marketing scientists, and is organized according to the components of a *launch and diffusion decision chain* we define. This chain represents the sequence of decisions managers must make with regard to the launch and diffusion of new drugs. The first element of the chain includes decisions regarding the specific methods by which pharmaceutical firms can gauge the commercial potential of a new treatment over time. Second, as pricing and promotion are prime instruments for pharmaceutical firms to extract maximum value, we review the means by which a manager can decide to extract the new treatment's commercial potential and generate value for

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the firm either by stimulating unit sales or through per-unit pricing. Third, pharmaceutical firms often operate in multiple markets. We therefore present an overview of the strategies that can be used to leverage the new treatment's potential across countries taking into account the different regulations, spending power for healthcare, prescription practice, among other factors, of different geographic markets. We conclude by reviewing possible directions for future advances in methods across the three chain elements.

For many large pharmaceutical firms that sell branded drugs, the successful launch of new therapies remains the key to profitable growth. New therapies are essential in enabling pharmaceutical companies to overcome the challenge of generic substitution—the replacement of branded drugs with generic alternatives, at the initiative of either physicians or pharmacists—as the patents of older drugs in their portfolios expire. Generic drugs enter the market at much lower prices compared with the original branded drugs they replace, as generic drugs do not need to go through the risky, costly, and lengthy process of new drug development. Grabowski and Vernon (1992) show that an original brand typically loses half of its market share 1 year after patent expiration. Generic substitution is ever increasing in scope and speed, given government regulations in many countries that promote generic dispensing at the pharmacy, in an attempt to control drug spending. Granted, there are multiple ways in which pharmaceutical firms that produce brand-name drugs can fight the trend of generic substitution. Some companies (e.g., Pfizer) own their own generic subsidiaries, others (e.g., Bayer, Merck Serono) offer diagnostics and other types of services in addition to their drugs or try to convince patients or physicians to be brand loyal, for instance, through social media (e.g., Johnson & Johnson). Nevertheless, the successful launch of new branded drugs remains crucial to the survival of such pharmaceutical companies and continues to be their primary means of differentiation.

Seemingly at odds with pharmaceutical firms' dependence on the success of new treatments, the number of newly approved treatments is declining. Grabowski and Wang (2006) review the decrease in the number of newly approved molecular entities in the period 1982–2003. Grewal et al. (2008) estimate that only 1 out of 50,000 molecules that receive initial investigation develops into a marketable drug. In 2010, only 21 molecular entities were approved (Jack 2011). The cost of developing such new drugs is enormous, between $500 million and $2 billion. Government agencies such as the FDA and the EMEA are increasingly critical of new drug applications, and are specifically attentive to the effectiveness/safety tradeoff. Furthermore, in several domains the need for new treatment has diminished, as many common diseases have long been treatable with effective drugs with few side effects, such as antihistamines, statins, beta blockers, and antibiotics. Several areas, such as oncology, neurodegenerative diseases, and autoimmune diseases, remain in high need of new drug development from a societal perspective, because existing therapies are not sufficiently effective for a large proportion of patients. However, drug development in these areas has presented few breakthroughs. Thus, given the high strategic importance of the launch of new pharmaceutical drugs and the lower frequency at

Fig. 7.1 The launch and diffusion decision chain

which approvals for such drugs occur, the successful execution of a new product launch has gained importance in the pharmaceutical industry.

This chapter gives a broad overview of the strategic and analytical tools that pharmaceutical firms can use to increase the success of a new product launch, given that these firms have attained the enviable position of having a new drug approved by regulatory authorities. Marketing scientists have made significant contributions to thought leadership in this area, and we will review those contributions in the following sections (also see, Stremersch and Van Dyck 2009).

We organize our discussion according to the components of the *launch and diffusion decision chain*. This chain, depicted in Figure 7.1, represents the sequence of decisions that managers must make with regard to the launch and diffusion of new drugs.

The decisions include the following:

- Decisions regarding the specific methods for the assessment of a treatment's commercial potential. In step 1, we will review several ways in which pharmaceutical firms can gauge the commercial potential of a new treatment over time. Developing a clear vision of a new treatment's commercial potential is essential for making sound decisions in subsequent steps.
- Decisions aimed at optimally extracting the new treatment's potential. In step 2, we review the means by which a manager can decide to extract the new treatment's commercial potential and generate value for the firm, either by stimulating unit sales or through per-unit pricing. Pricing and promotion are prime instruments for pharmaceutical firms to extract maximum value.
- Decisions regarding the strategy that will be used to leverage the new treatment's potential across countries. Pharmaceutical firms are often global firms. Therefore, launch teams are global teams that consider a worldwide launch strategy to successfully diffuse their drug in as many markets as possible. However, the international realm is complicated in pharmaceutical markets. Different geographic markets have different regulations, spending power for healthcare, prescription practices, and the like, and therefore differ in their attractiveness to firms from a new drug diffusion perspective. Moreover, different geographic markets may not be independent. For instance, prices may spill over from one market to another, because of gray trade or because of government regulations. A pharmaceutical firm needs to take such spillovers into account in its launch strategy. An important characteristic of launch strategies in the pharmaceutical industry is that the launch of new pharmaceutical drugs is never a "sprinkler launch" (i.e., launching in all countries at once) but rather is always a "waterfall strategy" (i.e., countries are staggered one after the other). Note, however, that this does not imply that all

innovations are launched first in the USA or in even in the domestic market of the manufacturing firm. We review these considerations in step 3.

This review is based on an exhaustive search across major scholarly journals in marketing, economics, and health.

7.1 Step 1: Assessing the Potential of a New Treatment

Marketing scientists have developed several methods to assess the potential of new treatments. Broadly, we can discern six different methodological frameworks to evaluate the commercial potential of new treatments (for an overview of the main characteristics of each framework, see Table 7.1). These frameworks can be divided into two main categories, distinguished according to the level at which they study the acceptance of a new treatment. Models in the first category, comprising diffusion models and sales models, study new product acceptance at the level of a group of people (region, segment, total market), whereas the models in the second

Table 7.1 Methodological frameworks for assessing new treatments' commercial potential

	Dependent variable	Level of model	Type of data
Aggregate-level models			
Diffusion models	Number of adopters of the new drug (cumulative across time periods)	Across groups of physicians	Observed behavior in panels across time (e.g., IMS Health physician panel) or stated behavior gathered from surveys or interviews (e.g., the Coleman et al. 1966 Medical Innovation study)
Sales models	Amount of active ingredient of the new drug sold (per time period)	Across groups of physicians or pharmacies	Observed behavior (e.g., IMS Health pharmacy audits)
Disaggregate-level models			
Prescription count models	Number of new or total prescriptions written	Physician-level	Observed behavior (e.g., IMS Health physician panel)
Learning models	Utility of the new drug (choice likelihood)	Physician-level/ Physician-patient-level	Observed behavior (e.g., the IPCI panel of Erasmus MC)
Consideration and choice models	Utility of the new drug (choice likelihood)	Physician-patient-level	Observed behavior (e.g., IMS Health physician panel)
Conjoint analysis	Utility of the new drug (choice likelihood or preference)	Physician- or physician-patient level	Stated preference (e.g., experimental conditions imposed on a sample of physicians)

category study acceptance at the level of an individual person (Table 7.1). The former models are therefore called aggregate-level models, whereas the latter are disaggregate-level models.

Diffusion models capture and forecast the cumulative number of new adopters (i.e., the cumulative number of physicians prescribing the new drug for the first time), whereas sales (growth) models capture the amount of the new drug's biologically active ingredient that is sold in a given market or region. This distinction between diffusion models and sales (growth) models—i.e., the distinction between the types of data they rely on—is important. The estimation of diffusion models in the tradition of Bass (1969) is known to create estimation bias when estimated on sales data rather than cumulative adoption data (see Van den Bulte and Lilien 1997; Van den Bulte and Stremersch 2004).

A different type of method aims to predict the behavior of an individual physician (towards an individual patient) regarding a new treatment. Unlike aggregate-level models, models that are based on this approach rely on disaggregate-level data, evaluating the acceptance process of new drugs from the perspective of the individual physician or patient. We, here, focus on models that are estimated on experimental or behavioral data, not attitudinal data as often gathered in surveys. The use of such individual-level (disaggregate) models requires technical sophistication and programming skills, and they are mostly suitable for heterogeneous social systems, for social systems with unusual network structures, and for products involving complex adoption decisions (Muller et al. 2010). Accordingly, such models fit the complex and unique structure of the pharmaceutical industry very well. Four types of models can be used to assess treatment potential on the basis of disaggregate-level data: prescription count models, learning models, consideration and choice models, and conjoint studies.

Prescription count models predict the number of new prescriptions or the total number of prescriptions dispensed for a drug. These models' predictions are typically based on drug characteristics, past prescription levels, drug prescription levels of other physicians, and (own and competitive) detailing levels, among others. Learning models predict the utility physicians will perceive in a treatment for a particular patient. These models emphasize the dynamic nature of physicians' perceptions regarding the quality of a new drug, and the important role of these dynamics in the choice process. Physicians' perceptions are estimated according to the physicians' initial beliefs regarding the drug's quality and their eventual prescription behavior. Consideration and choice models use past observations of physicians' choice (i.e., prescription) behaviors to predict whether a physician will prescribe the new drug to a particular patient. Conjoint analysis predicts the utility of a new drug to a physician for a particular patient and derives the likelihood that the physician will prescribe the drug to that patient.

7.1.1 Diffusion Models

Typical models in the diffusion literature predict the dynamic process of new product adoption. The Bass diffusion model (1969) has been used extensively to

investigate diffusion patterns and to forecast demand. This model investigates the aggregate first-purchase growth process in a given social system. In this model, also called the mixed-influence model, an adopter of a new product is potentially subject to two types of influence: internal influence, i.e., influence that occurs within the social system, and external influence, i.e., influence that is external to the social system. Internal influence results from interactions between adopters (e.g., physicians or patients who have adopted in the past) and potential adopters (e.g., physicians and patients who will adopt in the future) in the social system. External influence includes all influence outside the social system, such as, for instance, commercial efforts by the firm (i.e., detailing, sampling, advertising, conferences, etc.).

The basic premise underlying the Bass model is that the conditional probability of adoption at a given time in a given social system is increasing in the portion of the social system that has already adopted the new product:

$$n_t = \frac{\mathrm{d}N_t}{\mathrm{d}t} = p(m - N_t) + q\frac{N_t}{m}(m - N_t) \tag{7.1}$$

where m represents the potential number of eventual adopters, N_t represents the cumulative number of adopters by time t, and n_t is the number of adopters at time t. The parameter q in (7.1) reflects the influence of past adopters (i.e., internal influence), and the parameter p reflects an influence that is independent of previous adoption (i.e., external influence). The internal influence parameter can reflect word-of-mouth effects between physicians (which also includes opinion leadership), as well as the adoption of common treatment standards across physicians. For a review of the literature on the Bass model and a meta-analysis of the estimates produced by prior research (including in the field of pharmaceuticals), see Van den Bulte and Stremersch (2004).

Several extensions of the original Bass model have been introduced over the past 4 decades in order to reflect a number of market complexities. Such extensions incorporate, for instance, the notion of the influence of marketing-mix variables on the diffusion process (Krishnan et al. 1999; Lehmann and Esteben-Bravo 2006; Mesak and Darrat 2002; Libai et al. 2005), product replacement and repeat purchases (Islam and Meade 2000; Lilien et al. 1981), substitution between generations (Bayus 1992; Danaher et al. 2001; Islam and Meade 1997; Mahajan and Muller 1996; Padmanabhan and Bass 1993), competition among products (Kim et al. 1999; Givon et al. 1995; Eliashberg and Jeuland 1986), and heterogeneity in the social system (Goldenberg et al. 2002; Moore, 1992; Van den Bulte and Joshi 2007).

Beyond its many applications across a wide variety of industries, the Bass model and its successors have been repeatedly used in the study of the diffusion of new medical treatments. Berndt et al. (2003), for instance, studied the diffusion of antiulcer drugs in the USA. They used the Bass (1969) model to characterize network effects in drug diffusion. In another diffusion study, Vakratsas and Kolsarici (2008) distinguished between early market and main market adopters in a diffusion model for a new pharmaceutical drug. This notion of differentiating between two segments of adopters is similar to the dual-market approach suggested for technological markets (e.g., Goldenberg et al. 2002; Moore, 1992). However, in the context of the adoption of a new pharmaceutical drug, Vakratsas and Kolsarici (2008) associate

this dual-market phenomenon with the early adopters being patients who have severe health problems and whose latent demand has accumulated prior to the new drug's introduction, whereas the later adopters are patients with milder conditions whose adoption may have been triggered by the launch itself.

Marketing scholars have also used diffusion models other than the Bass model to characterize market penetration of pharmaceutical drugs. For instance, Desiraju et al. (2004) examined the effect of market characteristics on the maximum penetration potential and diffusion speed for a new category of prescription drugs in both developing and developed countries, using a logistic specification as in Van den Bulte (2000). Van den Bulte and Lilien (2001) used a discrete-time hazard model to show that several studies analyzing the diffusion of the drug tetracycline confounded social contagion with marketing effects. That is, they showed that when marketing efforts were controlled for in diffusion models, contagion effects disappeared, underscoring the importance of controlling for potential confounds when studying the role of social contagion in new drug diffusion.

The breakthroughs discussed above have helped to provide a better understanding of the determinants of new drug diffusion. The developed models can be helpful in gauging the commercial potential of a new treatment in two main ways. First, after a new drug is launched, these models can assist in making predictions of the drug's future commercial potential (for instance, see Ofek's (2008b) application of the Bass model in forecasting the future diffusion of drug-eluting stents). However, these forecasts are most reliable only after the inflection point—the point at which the growth in the cumulative number of adopters starts to decline—has passed. A second way in which one can use these diffusion models is to *guesstimate* the commercial potential of a new drug using the diffusion path of a similar drug. Such a similar drug should resemble the focal drug in its product characteristics, and the diffusion process must occur in similar market conditions (see Ofek's (2005) application of the Bass model for this purpose in the case of e-books and the background note in Ofek (2008a); while some of us have used this method inside pharmaceutical firms, unfortunately, no pharmaceutical application exists in the public domain, to our knowledge).

7.1.2 Sales Models

Overall sales differ from adoption in that they encompass repeat purchases. Whereas in durable markets (e.g., microwave ovens or refrigerators), for instance, repurchase frequency is quite low, in many pharmaceutical markets (e.g., drugs for chronic conditions, such as high cholesterol or hypertension) the repurchase rate is very high. Given the high repurchase frequency in some markets, marketing scientists have also developed models to forecast sales rather than adoption. The development of models for sales rather than for adoption can assist in understanding the overall dynamics in the market, and such models can potentially provide insight into the relative roles of repeat purchase versus initial adoption in the sales of a new product. The development of market-level sales models to forecast the commercial potential of a new drug is also driven by the availability of data. Often, data on past sales are

more readily available than data on past adoption by physicians or by patients. One type of sales model, using observations of aggregate sales, explicitly accounts for the trial and repeat-purchase process by identifying distributions for trial rates and for repeat-purchase rates (Hardie et al. 1998; Shankar et al. 1998). Parametric sales models typically rely on the assumptions that there is a linear relationship between the model variables and that the repeat-purchase rate for a given brand is constant. Shankar et al. (1998), for instance, propose a model in which the sales of a new product are decomposed into trial and repeat purchases as follows:

$$S_t = T_t + \rho \mathrm{CT}_{(t-1)} \tag{7.2}$$

where S_t represents the sales of the new product at time t, T_t represent the trial purchases at time t, $\mathrm{CT}_{(t-1)}$ represent the cumulative trial purchases until $t-1$, and ρ is the repeat-purchase rate. The authors further model trials as affected by both contagion and marketing-mix effects.

Several researchers have implemented trial-repeat models to investigate sales growth of new pharmaceuticals, incorporating, for instance, the influence of detailing visits (i.e., sales calls by pharmaceutical representatives), word-of-mouth effects, and competition (Ding and Eliashberg 2008; Hahn et al. 1994; Lilien et al. 1981; Rao and Yamada 1988; Shankar et al. 1998).

The validity of the interpretation of trial-repeat models critically hinges upon the validity of the models' identifying assumptions with regard to the trial-repeat-purchase process. Therefore, in forecasting the sales of new drugs, other scholars have preferred semi-parametric methods, which do not entail any assumptions on the underlying purchase process. For instance, Stremersch and Lemmens (2009) used regression splines to model new drug sales across the world. This flexible approach can be viewed as a compromise between linear regression and nonparametric regression sales models. The advantage of splines compared with other specifications lies in the fact that splines do not impose any assumption (linear, quadratic, or cubic) regarding the interactions among explanatory variables over time. Such flexibility is important in the case of sales growth models of pharmaceuticals. Stremersch and Lemmens (2009) investigated the role of regulatory regimes in explaining differences in the sales growth of new drugs across 55 countries all around the world. Their model is of the following form (with REG_{rt} representing r regulatory conditions and OTHER_{pt} representing p other variables, such as other country or drug characteristics):

$$sales_{it} = \beta_{rt} \times REG_{rt} + \beta_{pt} \times OTHER_{pt} + \varepsilon_{it} \tag{7.3}$$

The general idea behind splines is to represent the evolution of a smoothly varying function through a linear combination of basis functions. These functions are usually polynomial functions of low degree. The time-varying coefficients of any explanatory variable of drug sales (such as the REG or OTHER vectors in (7.3)) can then be expressed as follows (Stremersch and Lemmens 2009):

$$\beta_t = \beta_0 + \beta_1 t + \sum_{k=1}^{K} u_k^{\beta} (t - k_k)_+ \tag{7.4}$$

Where K is the number of linear spline basis functions, and k_k is the truncation point or knot where the broken lines are tied together. The combination of linear spline basis functions described in (7.4) gives a piecewise linear function called a spline.

Additional sales-derived metrics have previously been developed and can be used to build forecasting models. One such metric is new product takeoff, which refers to the first strong increase in sales after an initial period of low sales. The metric of takeoff has been developed for and applied to high-tech products and durables (Agarwal and Bayus 2002; Golder and Tellis 1997; Tellis et al. 2003; Van Everdingen et al. 2009), although it has not been tested, let alone used for forecasting purposes, in pharmaceutical markets. Another sales-based metric is third-quarter sales level, which Corstjens et al. (2005) proposed as a good measure for the ultimate success of new drugs. According to their logic, third-quarter sales could be used as a predictor for long-term commercial success.

The use of sales models in forecasting is similar to the use of diffusion models. First, like diffusion models, sales models can be used to make forecasts once the product is available in the market, and initial sales patterns can be used to reliably calibrate the model. Often, at least 1 year of monthly data needs to be available to be able to achieve a reliable calibration of the model. Second, one can use the pattern of sales growth of another molecule to predict the growth pattern of a soon-to-be launched molecule that is similar in terms of clinical support and market conditions (e.g., market structure and spending).

7.1.3 Prescription Count Models

The number of prescriptions written for a given drug is essentially a count variable with a considerable number of zeroes and a relatively small number of frequently occurring outcomes (Manchanda et al. 2005). Thus, the distribution across physicians of a new drug's prescriptions can be captured in individual-level prescription count models. Accordingly, several marketing scholars have used such models to investigate physicians' prescribing behavior and the factors affecting it. The standard count model is the Poisson regression model. In this model, the conditional mean and variance are specified as identical.

$$\Pr(\mathrm{RX}_{pt} = k \mid \lambda_{pt}) = \frac{\lambda_{pt}^{k} \exp(-\lambda_{pt})}{k!} \tag{7.5}$$

In this equation, λ_{pt} is the mean prescription rate, p represents the physician, and t represents the time period. Manchanda and Chintagunta (2004) use a Poisson model to examine the influence of detailing on the number of prescriptions written. The Poisson parameter in their model is allowed to be physician-specific and a function of detailing efforts, and the effect of detailing is also allowed to be physician-specific and a function of the characteristics of detailing directed to the physician, observed physician characteristics, and unobserved factors.

The negative binomial (NBD) regression model is another count model widely used in pharmaceutical marketing. One of the main advantages of the NBD

regression model is its ability to accommodate a wide range of over-dispersion degrees. An NBD distribution with mean $\lambda_{pt}^{\mathrm{RX}}$ and over-dispersion parameter α^{RX} is represented by:

$$\Pr(\mathrm{RX}_{pt} = k \mid \lambda_{pt}^{\mathrm{RX}} \alpha^{\mathrm{RX}}) = \frac{\Gamma(\alpha^{\mathrm{RX}} + k)}{\Gamma(\alpha^{\mathrm{RX}})\Gamma(k+1)} \left(\frac{\alpha^{\mathrm{RX}}}{\alpha^{\mathrm{RX}} + \lambda_{pt}^{\mathrm{RX}}} \right)^{\alpha^{\mathrm{RX}}} \left(\frac{\lambda_{pt}^{\mathrm{RX}}}{\alpha^{\mathrm{RX}} + \lambda_{pt}^{\mathrm{RX}}} \right)^{k} \tag{7.6}$$

This flexible count model has been used in several studies investigating physicians' prescribing behavior (e.g., Manchanda et al. 2005; Stremersch et al. 2013; Venkataraman and Stremersch 2007). In these studies, the most common specification for the conditional mean of the number of prescriptions is a log-link function that specifies the log of the mean of the conditional distribution as linear in the parameters.

In the case of new pharmaceutical drugs, time dynamics in the adoption process can be integrated into the NBD regression model through the specification of the conditional mean. Specifically, the mean number of prescriptions can be modeled as a function of the number of time periods, *t*, since the introduction of the new drug, as follows:

$$\ln(\lambda_{pt}^{\mathrm{Rx}}) = \beta_{0p} + \beta_{1p} t + \gamma_p \bar{X}_{pt} + \zeta_{pt}^{\mathrm{Rx}} \tag{7.7}$$

where $\bar{X}_{pt}$ includes a set of time-varying physician-level covariates such as the volume of detailing to the physician. Moreover, time in this specification can also take a nonlinear form.

Count models can be used for prediction purposes in at least two ways. First, they allow extension of the horizon for the prescriptions a physician writes. Once the model parameters are estimated on past data, one can calculate predictions of future states for each physician in the data set given the physician's past behavior. For instance, the number of detailing visits the firm expects the physician to receive can be used to predict the expected number of prescriptions for that physician, on the basis of the estimated model parameters. In other words, knowing the prescription history of a given physician for periods 1 through *T* (but not for any time after *T*), researchers can develop probabilities for some future time period $T + t$. Once these individual predictions are aggregated across all physicians in the data set for each time period in the investigated timeframe, they provide a predicted pattern of the total number of prescriptions. The aggregated predictions can serve as a diagnostic tool that depicts not only to what extent a new drug is expected to be prescribed across physicians, but also the differential effects that various factors, such as marketing efforts or the prescription volume of other physicians (e.g., word-of-mouth) or opinion leaders, have on this process. Second, "analogical" count models can be used in a similar fashion as "analogical" diffusion models, discussed above. In essence, given two drugs (drug A and drug B) that are similar in terms of category, administration method, etc., one could use response parameters retrieved for drug A (e.g., the responsiveness of new drug prescriptions at the physician level to detailing over time) to forecast physicians' responsiveness to drug B. This forecasting strategy works better for "follow-on" drugs (non-bioequivalent drugs in the same therapeutic category) than for radically new

drugs. As an example, given that Nexium was a clear follow-on drug of (Pri)Losec, one could have used physician response parameters of time, detailing, etc. on historical data on (Pri)Losec to estimate physician response to Nexium.

7.1.4 Learning Models

Learning models in particular exploit the uncertainty physicians perceive regarding the quality of a new pharmaceutical drug. Physicians reduce their uncertainty about the quality of a new drug over time on the basis of feedback from patients as well as the firm's marketing efforts. Several studies have specified models to capture physicians' learning with regard to new pharmaceutical drugs as these drugs diffuse into the market (Camacho et al. 2011; Coscelli and Shum 2004; Crawford and Shum 2005; Narayanan et al. 2005; Narayanan and Manchanda 2009). Coscelli and Shum (2004) suggest that the slow diffusion time of a new pharmaceutical drug in an existing product category is due to slow learning by risk-averse physicians. The only source of information in their model is patient feedback. Narayanan et al. (2005) investigated how the role of marketing communication for new products changes over time in the presence of learning. They specified a learning model in which marketing communication by firms as well as physicians' accumulated usage experience contribute to physicians' learning about a new drug. Narayanan et al. (2005) found that marketing efforts by pharmaceutical companies—i.e., detailing—have a primarily indirect effect (i.e., learning) in the early stages of the new drug's life cycle and a primarily direct (i.e., persuasive) effect at later stages. Narayanan and Manchanda (2009) find significant heterogeneity across physicians in learning rates and show that there are asymmetries in the evolution of physicians' responsiveness to detailing over time. Chintagunta et al. (2009) suggest that the information physicians retrieve from patients who were prescribed a new drug is subsequently used in the physicians' learning process to update their beliefs regarding both the drug's overall quality and a patient's idiosyncratic match with the drug. Their results suggest that physicians are influenced by many sources of information, including patient satisfaction, Medline articles, reports in the mass media and direct-to-consumer advertising (DTCA).

Camacho et al. (2011) developed a generalized quasi-Bayesian learning model that allows for decision-making biases that occur in physician decision making. In essence, they argue that physicians can retrieve some pieces of information from memory more easily than they can retrieve others. They show that physicians' belief updating, and thus the speed of their new drug adoption process, is strongly influenced by the salience of patient feedback. They find that negative patient feedback—feedback from patients whom the physician needed to switch to a different drug—receives 7–10 times more weight than positive feedback does in the physician's quality belief formation. The authors show that this effect greatly reduces the speed of diffusion of the new drug.

Firms can use learning models to gain knowledge about patterns in physician adoption of new drugs, and they can subsequently take such patterns into account

when planning the launch and forecasting the sales of a new pharmaceutical drug. The model by Camacho et al. (2011) can even be used to adjust predictions downwards after taking into account early switch-outs of patients from the new drug to other drugs in the market. Their model can also be used to predict, using counterfactual experiments, what would happen if a firm could reduce the number of patients abandoning the new pharmaceutical drug shortly after its launch. In addition, one can use the estimated parameters of a learning model for a given drug to predict the speed at which physicians would switch patients to a new, similar drug.

7.1.5 Consideration and Choice Models

In most diffusion models, the diffusion process is viewed as a single-stage, binary-state process in which at any point in time, individuals are either adopters or non-adopters. A few diffusion studies consider diffusion as a multistate, macro-flow process and thus take into account heterogeneity in customers' pre-adoption states, e.g., by incorporating awareness stages (Dodson and Muller 1978; Kalish 1985; Mahajan et al. 1984) or consideration stages (Weerahandi and Dalal 1992). However, in these models, heterogeneity is not reflected at the individual adopter level but rather at the aggregate level. To address heterogeneity among consumers in pre-adoption states, one can also build an individual-level model that separates different stages in the adoption process. For instance, Landsman and Givon (2010) proposed an individual-level model of a two-stage process of the diffusion of a service. In the first stage, customers decide whether to "consider" joining the service. This (Consideration) stage is modeled by a hazard model. Customers who decide to consider the service move on to the Choice stage, wherein they choose among the service alternatives and an outside No Choice option. This stage is modeled by a conditional multinomial logit model.

The model proposed by Landsman and Givon (2010) was developed for services or durable goods outside the pharmaceutical industry. Taking into account the unique features of the pharmaceutical market environment (Camacho et al. 2010; Stremersch and Van Dyck 2009), one could also apply such a model to these markets at the physician level. In this setting, in contrast to the setting of a new service, once a new drug is introduced, physicians can prescribe either the new drug or one of the other therapeutic alternatives already existing in the category. Accordingly, we must distinguish between physicians' initial adoption decision (the decision to first prescribe the drug) and their consequent process of integrating the new drug into the choice set until the new drug reaches its ultimate share in the category.

The time-dynamic process of initial adoption can be represented using a proportional hazard model, where the hazard function is decomposed into two multiplicative components:

$$h_{pt} = h_{p0t} \cdot \psi(X_{pt}) \tag{7.8}$$

The first component, h_{p0t}, defines the baseline hazard function. This function reflects the longitudinal patterns in the duration time dynamics. The second

component is a function of a vector of physician and/or market covariates that affect the adoption hazard rate. Thus, $\psi(X_{pt})$ adjusts h_{p0t} up or down proportionally to reflect the effect of the covariates.

The post-adoption stage can be modeled as a physician-level *choice* process, where P_{pjt} represents the probability that a physician p chooses drug j ($j=1, \ldots, J$) at time t, conditional on drug j's adoption by physician p by t. This probability can be specified as a multinomial logit model:

$$P_{pjt} = \frac{e^{V_{pjt}}}{\sum_{j=1}^{J} e^{V_{pjt}}} \tag{7.9}$$

where V_{pjt} is the deterministic part of the utility obtained from choosing drug j at time t. V_{pjt} can be specified as a function of a set of covariates that can characterize the drug, the physician, or the combination of both, and a *time dynamic* element affecting physician choice of the new drug (Coscelli and Shum 2004). To explain the dynamic adoption process, at least some covariates in the two model functions must vary over time.

7.1.6 Conjoint Analysis

The methods we have reviewed so far only use observed data either from the new treatment's own prescribing behavior or from the past prescribing behavior of other drugs that have been available in the market for a longer time. They do not use so-called primary data. Nonetheless, the use of primary data in the estimation of the commercial potential of a new pharmaceutical may yield valuable insights. Conjoint analysis is a particularly useful method to assess physicians' and patients' preferences and unmet needs before the launch of a new drug. Conjoint analysis is a method to estimate the structure of consumers' preferences, given their overall evaluations of a set of alternatives that differ with respect to several attributes. The main advantage of this research tool is that it can be used before a new product enters the market. Since its introduction (Green and Rao 1971), conjoint analysis has been widely adopted by marketing scientists and practitioners as a method for preference measurement. Conjoint analysis can assist firms in developing and launching new products, as it can be used to integrate knowledge on potential adopters' expected reactions to these products. This ability facilitates prelaunch sales forecasts for a new product, thus avoiding the high costs and time investments required for the use of test markets. Conjoint analysis is most appropriate when new levels of attributes are being introduced or when new attributes can be described well to potential customers (Urban et al. 1996). Figure 7.2 describes the different steps in setting up a conjoint study.

The basic premise of conjoint analysis is to present physicians or patients with several variations of attribute levels for a new product and to assess their choices, rankings, or ratings. This is typically done in a survey setting (Cattin and Wittink

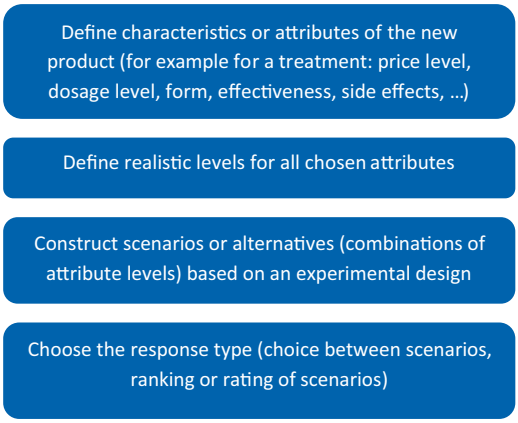

Fig. 7.2 Setting up a conjoint study

1982). Recently, web-based methods, together with efficient algorithms and more powerful computational capabilities, have yielded new interactive conjoint methods that generate more accurate knowledge with far fewer questions compared with traditional methods (Dahan and Hauser 2002; Hauser and Toubia 2005; Toubia et al. 2003, 2004).

By executing a conjoint analysis, companies observe the importance of the different attributes to physicians or patients as well as the preference for specific levels of these attributes. The complex payment structure of the pharmaceutical industry complicates the ability to assess market sensitivity to the price of a new pharmaceutical drug. In many cases, one of the attributes in a conjoint study is price (or, the co-pay of the patient), as incorporating this attribute allows companies to make statements about patients' or payers' willingness to pay or physicians' willingness to prescribe. In a conjoint study, every product—which is a combination of attribute levels—gets assigned a value based on assessments of attribute-level preferences. By letting consumers evaluate different products, conjoint studies enable inferences to be made with regard to the expected market share of different products. Furthermore, conjoint analysis also allows companies to discern different segments in the markets. Segments are groups of respondents that attach similar importance to attributes and share a preference for specific attribute levels. This type of information has proven to be very valuable when developing a new product and forecasting the demand for that product (Dolan 1990). To forecast the demand for a new product, the results of the conjoint analysis are incorporated into a model based on mathematical representations of each consumer's preferences alongside the specific attribute composition of the product. An aggregate-level diffusion or sales model can then be used to aggregate these individual forecasts into an overall prediction of the new product's sales (Gupta et al. 1999; Lee et al. 2006; Roberts et al. 2005; Urban et al. 1990).

The complex structure of demand in the case of pharmaceutical drugs forces pharmaceutical firms to identify patients' needs, either through direct means or through the mediation of physicians. Accordingly, prelaunch sales forecasts for new

products must consider several dynamic factors such as the discovery of new uses for the drug, the drug's dosing, efficacy, and side effects, and the price of the drug. Conjoint analysis can provide pharmaceutical companies with this type of information.

Several studies have focused on conjoint analysis in the context of healthcare. Kontzalis (1992), for instance, proposes a model to forecast the potential market share of a new pharmaceutical drug for Sandoz Pharma AG. The model considers physicians' decision-making process, taking into account their attitudes and needs as well as the drug's clinical profile. In this paper, the author first identified the key attributes physicians consider important in selecting drugs that treat certain conditions, and then, using a conjoint analysis, measured the relative importance of each attribute. Specifically, for the therapeutic category investigated in this study, the attribute "low irreversible toxicity" was found to be 3 times more important than of the attribute "low side effects," while the latter was found to be 5 times more important than of the attribute "easy to administer." In the next step of the study, the author simulated the therapeutic category market shares based on the clinical profile of the new product and its competitors.

In another study, Kellett et al. (2006) used a conjoint analysis to investigate patient preferences for acne vulgaris treatment. The conjoint analysis examined five different attributes of such treatment: form, storage, product life once opened, method of application and regimen. Although this research was conducted with the purpose of enhancing patient compliance, it demonstrates the applicability of patient-based conjoint analysis in predicting the adoption of new pharmaceutical drugs.

Conjoint analysis has also been used to assess the tradeoffs young girls make between various aspects of HPV vaccination, such as protection against cervical cancer, protection duration, risk of side effects and age of vaccination (de Bekker-Grob et al. 2010a). De Bekker-Grob et al. (2010b) have also looked at patients' preferences for both labeled and non-labeled screening tests. Kruijshaar et al. (2009) examined the trade-off patients make between the burden of testing and the expected health benefits in the context of regular endoscopic surveillance. Studies such as these guide managers as well as policy makers in the pharmaceutical industry.

If one of the product attributes affecting customer preferences is price, conjoint analysis can assist pharmaceutical firms in assessing patients' willingness to pay and thus provide them with a valuable tool in determining the price of a new drug. Singh et al. (1998) have conducted a conjoint analysis among patients for growth augmentation therapy. One of the five attributes they assessed was the yearly out-of-pocket cost of the drug ($100, $2,000, or $10,000). Their findings suggest that cost is among the most important factors in patients' preferences, outweighed only by long-term side effects. Moreover, once the utility partworths are derived from the conjoint analysis, the preference trade-offs among the different drug attributes can be used to assess consumers' willingness to pay for different drug profiles, as well as to simulate market shares given those profiles for different price levels.

7.2 Step 2: Extracting the Potential of a New Treatment

In assessing the potential of a new treatment, pharmaceutical companies gain insight into the types of decisions they need to make to extract value from the new treatment. Marketers have studied two main methods of extracting the commercial potential of a new treatment: setting the price of the new treatment and increasing unit sales through promotional expenditures.

Many studies (e.g., Kremer et al. 2008; Mizik and Jacobson 2004; Stremersch et al. 2013; Venkataraman and Stremersch 2007) have looked at the effect of promotional expenditures (e.g., DTCA, direct-to-physician advertising, detailing) on demand for pharmaceutical drugs, obtaining mixed results. Pricing strategies of new treatments have been studied to a lesser extent (e.g., Berndt 2000; Ekelund and Persson 2003; Lu and Comanor 1998). Researchers have also shown increasing interest in the threat of generic substitution and its consequences for the pricing of drugs (Frank and Salkever 1997; Hariharan et al. 2013).

Pharmaceutical companies' decisions regarding drug price levels and promotional expenditures, which are crucial for extracting value from the commercial potential of a new treatment, are often a source of controversy in the pharmaceutical industry. In the following subsections we discuss each of these two types of decisions.

7.2.1 Pricing New Treatments to Maximize Profits

Pharmaceutical companies' pricing decisions with regard to new treatments are often cause for debate. Opponents of current price levels claim that the prices of new drugs are too high given the low marginal cost of producing them. Hence, they conclude that high price levels of new drugs only serve companies' profit motives (Berndt 2000). However, pharmaceutical companies state that these prices are justified given the high research and development (R&D) costs and the high risk involved in the development of a new drug (Lu and Comanor 1998). Furthermore, industry executives claim that in many international markets, drug prices are no longer sufficient to reward companies for taking these high risks. Indeed, sufficiently high price levels are necessary to guarantee a society's access to innovative life saving drugs in the future (Santerre and Vernon 2005). Economists support this claim by showing that innovation is threatened by low price levels (DiMasi et al. 2003). Notably, however, pricing decisions have been found not to depend exclusively on past R&D expenses (Verniers et al. 2011; Vernon et al. 2006; Wagner and McCarthy 2004).

Lu and Comanor (1998) examined drivers of launch prices of new drugs relative to the average prices of existing brand-name substitutes (in the same categories) in the USA over the period 1978–1987. Unsurprisingly, they found that drugs with a larger therapeutic potential were priced higher than drugs that constituted smaller therapeutic advancements. Furthermore, a higher number of branded substitutes

decreased the launch price level of a new drug in the category. "Follow-on," or "me-too," drugs have more difficulty obtaining a higher price because they have to demonstrate their superiority in comparison with existing substitutes (DiMasi and Paquette 2004). DiMasi (2000) studied price levels of new entrants in an existing therapeutic class in the USA and found that 65 % of the observed drugs had an introductory price that was 14 % lower than the category's average price. Ekelund and Persson (2003) also studied new drugs' launch prices in Sweden, where regulations are stricter than in the USA, between 1987 and 1997. Similarly to Lu and Comanor (1998), they found that the extent of a drug's therapeutic innovation positively affects its relative introductory price. However they found that, competition does not influence launch prices. In addition to the extent of therapeutic benefit and number of substitutes, another factor influencing price is therapeutic indication: drugs indicated for acute conditions have larger premiums than those indicated for chronic illnesses (Ekelund and Persson 2003; Lu and Comanor 1998).

The evolution of new drugs' prices over the product life cycle—or price dynamics—has also received some attention. Lu and Comanor (1998) observed a price-skimming strategy, i.e., a high introductory price and then a decrease in price level, for drugs that constitute a substantial therapeutic advancement, whereas they found that pharmaceutical companies apply a penetration pricing strategy—low introductory price and then an increase in price level—for drugs that offer a small therapeutic gain (Lee 2004). Price increases were smaller if more brand-name substitutes were available in the market. In contrast to Lu and Comanor, who studied pricing strategies in the USA, Ekelund and Persson (2003) observed higher relative introductory prices and a price-skimming strategy across all drugs in the regulated country Sweden. The main source for the differences between the results of Lu and Comanor (1998) and those of Ekelund and Persson (2003) is likely the difference in the regulatory environments in the USA and in Sweden. Regulators in Sweden seem to compensate the pharmaceutical manufacturers' limitation of a price cap by allowing a relatively high introductory price before price decreases, and competition seems to matter less in a regulated country.

Many countries worldwide enforce price regulations, and a pharmaceutical company in such countries can only launch a new drug once price negotiations with local health regulators have ended. Price regulations can include price cap mechanisms that limit the price a new drug can attain. For example, a country's public health administration might enforce an ex-manufacturer price cap, i.e., a maximum price or reservation price that a manufacturer can charge to the wholesaler of a pharmaceutical product (Danzon et al. 2005). Belgium, Greece, and Portugal are examples of countries with strict ex-manufacturer price regulations. Verniers et al. (2011) find no direct effect of these price regulations on launch price. When setting a launch price, pharmaceutical companies often also take into account whether a new drug will get reimbursement or not.

At the moment of patent expiration in the product life cycle of a drug, generic drugs—drugs that are bioequivalent to the brand-name drug—enter the market. This generic entry poses a challenge for brand-name pharmaceutical companies, as generic manufacturers' drugs enter the category at lower prices. Morton (1999)

states that prices of generic drugs are 30–50 % lower than brand prices, and that these prices decrease further after introduction as the number of generic manufacturers increases. In addition, generic entry may also affect branded drugs' prices. Caves et al. (1991) found that prices of branded drugs fall when generics are introduced. This could be a strategy of branded manufacturers to safeguard their market share. However, Frank and Salkever (1997) and Lexchin (2004) found that branded drug prices may increase when generic entry occurs. Brand-loyal customers could drive this result, as these customers are willing to pay more for the branded drug, whereas other customers will choose the cheap generic drugs. On average, the price of an off-patent drug is lower than that of the patented version because of market competition. Danzon and Chao (2000b) find that generic competition is significant in countries that do not have strict regulations, such as the UK, the USA, and Germany. Generic competition is much fiercer in regulated countries such as France and Italy.

7.2.2 Promoting New Treatments to Maximize Unit Sales of a New Treatment

Pharmaceutical firms use several types of marketing tools, including free samples, detailing visits, professional magazine advertising, and DTCA to support the launch of new treatments. An important challenge marketing scientists have had to overcome is how to calculate the optimal allocation of marketing investments.

When a pharmaceutical firm launches a new treatment, it typically spends the largest portion of its marketing budget on physician detailing visits. Accordingly, numerous marketing research studies have focused on the effectiveness of these visits. Early endeavors by marketing scholars in this field used aggregate data to examine the effect of detailing visits on drug sales (Lilien et al. 1981; Parsons and Vanden Abeele 1981). In the past decade, several studies have used panel data to investigate the effect of detailing visits on the demand for pharmaceutical drugs (e.g., Kamakura et al. 2004; Gonul et al. 2001; Manchanda and Chintagunta 2004; Venkataraman and Stremersch 2007). While some of these studies (e.g., Gonul et al. 2001) find that detailing has a positive and significant effect on the number of prescriptions, other studies find that detailing has only a very modest effect (Mizik and Jacobson 2004; Stremersch et al. 2013; Venkataraman and Stremersch 2007) or even no effect (Rosenthal et al. 2003) on prescriptions or sales.

One possible explanation for these contradicting findings is that brands may in fact differ in the extent to which their detailing efforts evoke physicians' response (Leeflang et al. 2004). Venkataraman and Stremersch (2007) find that drug characteristics are a source for brand-specific differences in physicians' responsiveness (as reflected in their prescription behavior) to marketing efforts by pharmaceutical firms. Specifically, they find that physicians tend to be more positively affected by detailing visits when the drug is more effective or has more side effects. Typically, detailing visits for a newly launched drug are effective, as physicians still have a great deal of uncertainty with regard to the effectiveness, side effects, and safety of

the new drug. Gradually, this uncertainty declines due to past detailing visits or patient feedback that allow the physician to learn (see discussion of learning models above). As a result, detailing visits become increasingly ineffective. A general lesson for the pharmaceutical industry is to maximize their detailing spending at launch and shortly afterward, and to cut the detailing budget when the new drug starts maturing. Typically, models find that pharmaceutical managers may underspend at launch or shortly afterward, whereas they may overspend in maturity.

Narayanan et al. (2005) suggest that this variation in findings regarding detailing effectiveness is rooted in the difference between the role of detailing at the introduction stage of a drug versus its role in subsequent stages. In early stages of the drug's life cycle, physicians' experience with the drug is limited, and they are likely to be uncertain about its efficacy. Thus, in the introductory phase, detailing is assumed to have a primarily indirect effect by helping physicians reduce their uncertainty about the efficacy of the drug. However, as physicians learn about the drug and gain experience with it, they have less uncertainty about the drug's efficacy, and the effect of detailing becomes more direct (i.e., reminder effects influencing preferences through goodwill accumulation).

Another important aspect of the effectiveness of detailing visits is the information content that is provided in sales calls. Kappe and Stremersch (2013) investigate the responsiveness of physicians to information provided across different drug attributes. They also examine whether firms present positively biased information to physicians, and whether this bias has an influence on the responsiveness of physicians. In their study, they use data on the drug attributes presented in detailing visits, and they find that pharmaceutical firms do not provide information on the right product attributes at their optimal frequency. They also find that detailing visits that include discussion of positively biased information in the long run have a lower detailing effectiveness. These results imply that firms must optimally adjust their messaging in order to improve physicians' responsiveness to detailing.

Pharmaceutical firms' spending on DTCA has increased dramatically in recent years, from less than $1 billion US dollars in 1996 to $4.3 billion in 2010 (AdAge 2011). This increase has drawn attention from both practitioners and marketing scholars, who have made efforts to analyze the effects of DTCA on demand and the ROI from such marketing activities. As in the case of detailing, academic studies on the effect of DTCA on prescriptions yield contradictory results. Some studies claim that DTCA spending has a large effect on prescriptions (Atherly and Rubin 2009; Bell et al. 1999; Fischer and Albers 2010; Iizuka and Jin 2005; Koch-Laking et al. 2010; Kolsarici and Vakratsas 2010; Ling et al. 2002; Meyerhoefer and Zuvekas 2008; Weissman et al. 2004; Wilkes et al. 2000), whereas others claim it has no effect, or a very limited one, on brand-level prescriptions (Calfee et al. 2002; Donohue and Berndt 2004; Manchanda et al. 2008; Rosenthal et al. 2003; Stremersch et al. 2013; Zachry et al. 2002). Kremer et al. (2008) even find that DTCA has a negative effect on prescriptions in the fields of skin disease, neurology, and psychiatry. Another set of studies on DTCA focuses mainly on studying the ROI from such marketing activities by pharmaceutical firms (Wittink 2002; Narayanan et al. 2004). These studies find that the ROI for DTCA is quite low. Narayanan et al. (2004) further find a lower level of ROI for DTCA than for

detailing. None of these studies, however, focuses on the role of DTCA in supporting newly introduced pharmaceutical drugs (which may be one reason for the small effect found by prior studies).

Sample dispensing by physicians is rarely addressed in academic studies despite being an important physician decision. From the perspective of a pharmaceutical firm, samples that are dispensed by physicians may lead to prescribed long-term treatment (Morelli and Koenigsberg 1992). Thus, sampling can be a valuable tool to support the launch of new pharmaceutical drugs, especially for chronic conditions. Venkataraman and Stremersch (2007) find that physicians' prescription behavior in response to firm's marketing efforts and to patients' requests may differ from their sample-dispensing behavior in response to such factors. They also find that when a marketed drug is more effective or has more side effects, physicians tend to provide more samples in response to firms' marketing efforts.

7.3 Step 3: Leveraging the Potential of a New Treatment Across Countries

The international realm brings interesting challenges to global pharmaceutical launch teams. Probably among the most important challenges are differences across countries in new drug sales growth and the interdependence of international launch timing and pricing, generating a need to develop sophisticated global launch strategies.

7.3.1 Variance in the Market Potential and Speed of Diffusion Across Countries

Marketing research on international growth of new products in various industries has identified several key drivers of variation across countries in market potential and diffusion speed (Dekimpe et al. 1998; Gatignon and Robertson 1989; Helsen et al. 1993; Stremersch and Tellis 2004; Talukdar et al. 2002; Tellis et al. 2003; Van den Bulte and Stremersch 2004; Van Everdingen et al. 2009). For instance, the wealth of a country was found to have a positive effect on the diffusion process in terms of reducing the time before the country tries the innovation and speeding up the diffusion within the country (Van Everdingen et al. 2009). Other studies show that additional country characteristics, such as national culture, affect new product growth differentially across the product's life cycle (e.g., Stremersch and Tellis 2004; Tellis et al. 2003). Moreover, several studies have found evidence for cross-country learning effects (Dekimpe et al. 2000, Dekimpe et al. 1998; Mahajan and Muller 1994). Countries that introduce an innovation later than others seem to have faster within-country diffusion patterns.

Desiraju et al. (2004) examined the relative attractiveness of various countries in terms of maximum penetration potential and diffusion speed for a new category of

prescription drugs across both developing and developed countries. Their results, which are consistent with earlier findings from outside the pharmaceutical industry, indicate that developing nations tend to have lower diffusion speeds and lower maximum penetration levels compared with developed countries. They also find that per capita expenditures on healthcare have a positive effect on diffusion speed, and that this effect is stronger among developed countries. Stremersch and Lemmens (2009) have investigated the role of regulatory regimes in explaining international sales growth of new drugs, while controlling for introduction timing, economic and cultural factors, among others. In their paper they used a time-varying coefficient model to analyze the sales of 15 new molecules in 34 countries. Stremersch and Lemmens (2009) found that differences in regulation substantially contribute to cross-country variation in sales, emphasizing the importance of incorporating local regulatory constraints into pharmaceutical manufacturers' global launch plans. For instance, drug volumes were found *ceteris paribus to be* higher in countries with manufacturer price regulation, and lower in countries with DTCA or prescription budget restrictions. In addition, this study confirms that the cultural and economic characteristics of countries affect their attractiveness to pharmaceutical firms.

Table 7.2 displays the early sales volume (less than 3.5 years after launch) and late sales volume (more than 3.5 years after launch) for a sample of the following brands across 15 molecules (molecule name in parentheses; several molecules are marketed under multiple brands): Lipitor (atorvastatin), Baycol/Lipobay (cerivastatin), Lescol (fluvastatin), Crestor (rosuvastatin), Vesicare (solifenacin), Detrol (tolterodine), Caverject/Muse/Viridal (alprostadil), Uprima/Ixense (apomorphine), Viagra/Revatio/Caverta (sildenafil), Cialis (tadalafil), Levitra (vardenafil), Clarinex (desloratadine), Elestat (epinastine), Allegra/Telfast (fexofenadine), Mizollen (mizolastine). For each country Stremersch and Lemmens (2009) have calculated the percent deviation from the mean sales level. In countries where this deviation is high, the molecule reaches high sales levels compared to the mean sales level across all countries. Correspondingly, in countries where this deviation is low, the molecule reaches only low sales levels compared to the mean sales level across all countries. From Table 7.2, we can conclude that new molecules in the USA, Sweden, Norway, and Japan reach high sales levels. New molecules reach only low sales levels in many developing countries, such as Mexico, Eastern European countries, the Philippines, and South American and African countries. Some countries show very fast adoption (very high early sales level as compared to the late sales level): Sweden, Netherlands, and Belgium. Other countries show very slow adoption (very low early sales level as compared to the late sales level): Australia, Norway, and United Kingdom.

7.3.2 International Launch Timing and Pricing

Research on international launch of new drugs has identified several drivers of launch timing (Danzon et al. 2005; Kyle 2006, 2007; Lanjouw 2005; Verniers et al.

Table 7.2 Variation in early and late sales growth of a sample of 15 new molecules, launched between 1994 and 2004[a]

Early sales (<3.5 years after launch) per 1,000 inhabitants			Late (>3.5 years after launch) sales per 1,000 inhabitants		
Country	% Dev. from mean	Rank	Country	% Dev. from mean	Rank
North America	*79*			*74*	
U.S.	270	1	U.S.	305	1
Canada	87	8	Canada	94	9
Puerto Rico	34	17	Puerto Rico	−18	23
Mexico	−74	39	Mexico	−87	45
Oceania	*44*			*77*	
Australia	70	10	Australia	153	3
New Zealand	18	20	New Zealand	1	21
Europe	*23*			*17*	
Western Europe	*65*			*56*	
Sweden	202	2	Norway	163	2
Luxemburg	188	3	Sweden	139	5
Norway	114	5	Luxembourg	106	6
France	100	6	Greece	99	7
Netherlands	98	7	United Kingdom	97	8
Greece	75	9	Finland	77	10
Belgium	70	11	Portugal	56	11
Germany	61	12	Spain	49	12
Spain	56	13	Netherlands	42	13
Finland	54	14	Ireland	35	14
Portugal	42	15	Switzerland	32	15
Switzerland	31	18	Belgium	26	17
Italy	21	19	France	25	18
Austria	4	22	Germany	18	19
Ireland	1	23	Denmark	10	20
United Kingdom	−1	24	Austria	−1	22
Denmark	−15	25	Italy	−26	24
Eastern Europe	*−65*			*−66*	
Slovakia	−27	27	Slovakia	−28	25
Hungary	−51	30	Hungary	−33	27
Estonia	−64	34	Czech Republic	−60	31
Czech Republic	−65	35	Estonia	−78	40
Lithuania	−77	40	Poland	−81	43
Poland	−82	43	Lithuania	−88	48
Latvia	−86	48	Latvia	−92	51
Asia	*−27*			*−35*	
Japan	139	4	Japan	146	4
Korea	37	16	Korea	29	16
Saudi Arabia	6	21	Lebanon	−31	26
United Arab Emirates	−21	26	Turkey	−42	28
Lebanon	−31	28	Kuwait	−52	29

(continued)

Table 7.2 (continued)

Early sales (<3.5 years after launch) per 1,000 inhabitants			Late (>3.5 years after launch) sales per 1,000 inhabitants		
Country	% Dev. from mean	Rank	Country	% Dev. from mean	Rank
Kuwait	−40	29	Israel	−53	30
Israel	−56	31	Saudi Arabia	−61	32
Turkey	−68	36	United Arab Emirates	−69	35
Jordan	−83	45	India	−77	39
India	−84	46	Jordan	−80	41
Philippines	−94	53	Philippines	−96	52
South America	*−80*			*−79*	
Venezuela	−58	32	Uruguay	−63	33
Chile	−72	37	Chile	−64	34
Argentina	−74	38	Argentina	−70	36
Brazil	−79	41	Venezuela	−80	42
Uruguay	−82	42	Brazil	−86	44
Ecuador	−88	49	Colombia	−87	46
Colombia	−91	51	Ecuador	−87	47
Peru	−93	52	Peru	−91	50
Africa	*−80*			*−83*	
Tunisia	−60	33	Egypt	−72	37
South Africa	−82	44	Tunisia	−75	38
Egypt	−86	47	South Africa	−89	49
Morocco	−90	50	Morocco	−97	53

[a]Based on joint work of Stefan Stremersch and AurélieLemmens

2011). Kyle (2007) investigated the effect of price regulation on the number of new drug launches and the timing of launch and found that price regulation causes pharmaceutical companies to delay launch and leads to fewer launches. She also finds that drugs are 1.5 times more likely to be launched in countries that share a language border with the country in which the headquarter of the pharmaceutical company is located (Kyle 2007). In addition to these effects, Kyle (2006) also investigated other drivers such as the number of competitors, corruption index of a country, and administrative costs in a country. Danzon et al. (2005) examined launch timing of new drugs in 25 countries worldwide and observed an effect of expected drug price and expected market size (the data they evaluated included lagged average price and market size of drugs in the same therapeutic class). After controlling for a home country effect and global experience, the researchers found that pharmaceutical companies launch fewer new drugs and that they launch them at a later time in countries with a lower expected drug price and lower expected market size. Lanjouw (2005) also focused on drivers of launch timing and showed that price regulation tends to lower the launch speed, whereas she found mixed results for patent protection regulation (results were dependent on the specifics of the regulation).

When launching a new drug in an international context, pharmaceutical companies also need to decide on the launch prices in different countries. Like launch time, launch price is an important determinant of the evolution and distribution of cash flows across time and countries. As different countries have different characteristics (regulation, population size, GDP per capita, number of competitor drugs, etc.), launch prices are expected to differ across countries. Some studies have looked at drug prices across countries, without explicitly focusing on launch price. Chintagunta and Desiraju (2005) studied drug price levels across five geographic markets and showed that the USA is less price sensitive than European markets. Danzon and Furukawa (2003) examined drug prices in nine countries and showed that Japan and the USA have the highest drug prices. Other countries' drug prices are 6–33 % lower than drug prices in the USA. Danzon and Chao (2000a) examined bilateral drug price indexes between seven countries and found that older molecules had lower prices in countries with strict price regulations than they did in less strictly regulated countries. Price differences on a worldwide level have been the cause for parallel trade, which occurs when a third party purchases drugs in lower-priced countries and then resells them in higher-priced countries (Onkvisit and Shaw 1989). Although prices are quite heterogeneous across countries, many countries worldwide (mainly in the European Union) have an external reference pricing regulation. This regulation requires that, before launching a drug in a certain country, the pharmaceutical company supplies that country's health regulators with information on the drug's prices in selected foreign countries. Regulators then cap prices on the basis of that information (Dukes et al. 2003; Verniers et al. 2011).

Several studies have examined drivers of launch timing, and other studies have looked at differences in international launch prices. Verniers et al. (2011) investigated 58 molecules in 50 countries worldwide to empirically evaluate the regulatory drivers of both launch timing and launch price. They examined the effect of ex-manufacturer price control, profit control, internal reference pricing regulation, external reference pricing regulation, pharmacoeconomic evidence, and patent protection strength on launch price. Although they did not observe a direct effect of regulation on launch price, they did find an effect of regulation on launch timing. Apparently, regulatory restrictions are more useful to regulators in constraining the price of mature drugs rather than the price of newly launched drugs (Stremersch and Lemmens 2009; Verniers et al. 2011).

Table 7.3 presents the mean lead or lag in launch window (the launch window is defined as the difference in months between the first launch worldwide and the subsequent launch in a specific country) and the percent deviation from the mean price at launch for countries across seven world regions. Column 3 in Table 7.3 shows each country's deviation from the mean launch price across drugs. This is calculated according to the following steps: (1) construct the mean launch price for each drug across the countries; (2) calculate the percentage of deviation of the country-specific price from the mean price over all countries; (3) average these percentages of deviation for each specific country over all drugs launched in that country. A negative deviation for a given country means that a drug is typically launched at a relatively

Table 7.3 Mean lead (−) or lag (+) in launch window and % deviation from mean price at launch by world region and country[a]

World region and countries	Mean lead (−) or lag (+) in launch window (in months)	% Deviation from mean price at launch per gram
North America	*−8.95*	*37.87*
USA	−17.17	37.79
Canada	−7.50	−1.57
Puerto Rico	−7.21	93.09
Mexico	−3.94	22.16
Western Europe	*−5.81*	*−8.15*
Germany	−15.59	−9.17
Denmark	−10.65	−5.35
U.K.	−9.82	−0.14
Austria	−9.13	−9.92
Switzerland	−8.97	0.21
Ireland	−8.08	−5.22
Sweden	−7.11	−8.48
Netherlands	−6.95	−6.93
Finland	−6.44	−4.39
Norway	−5.87	3.83
Spain	−4.03	−17.22
Belgium	−3.45	−13.61
Luxemburg	−2.22	−12.78
Portugal	−1.66	−11.47
Italy	−1.01	−13.26
France	−0.46	−12.44
Greece	2.06	−12.21
South America	*−0.43*	*7.93*
Brazil	−6.79	14.43
Argentina	−6.36	0.89
Colombia	−3.12	33.67
Chile	−2.27	−8.19
Venezuela	1.97	17.49
Uruguay	3.95	12.72
Peru	4.29	−4.20
Ecuador	4.91	−3.39
Oceania	*0.10*	*−8.02*
Australia	−1.55	−11.82
New Zealand	1.75	−4.21
Asia	*5.16*	*11.01*
Philippines	−2.17	−12.15
Japan	6.89	47.89
Korea	10.75	−2.71
Eastern Europe	*8.74*	*−1.62*
Czech Republic	5.03	1.58
Estonia	5.21	−3.51
Hungary	5.68	−5.54
Poland	8.91	1.71
Latvia	9.55	−5.78

(continued)

Table 7.3 (continued)

World region and countries	Mean lead (−) or lag (+) in launch window (in months)	% Deviation from mean price at launch per gram
Slovakia	12.77	0.78
Lithuania	14.02	−0.61
Africa and the Middle East	*14.51*	*−13.31*
Kuwait	4.42	−1.81
South Africa	5.14	−26.11
United Arabic Emirates	6.49	4.33
Lebanon	6.77	−16.32
Jordan	12.37	−7.89
Egypt	17.86	−29.10
Saudi Arabia	19.40	−13.37
Morocco	20.88	−8.67
Tunisia	37.28	−20.82

[a]Based on the work of Isabel Verniers, Stefan Stremersch, and Christophe Croux

low price in that country, whereas a positive deviation indicates that a drug is typically launched at a relatively high price in that country.

Table 7.3 shows that the USA, Germany, and Denmark experience the largest lead in launch. Tunisia, Morocco, and Saudi Arabia experience the largest lag in launch. North America and Western Europe show similar (small) launch delays. Launch delays are largest in Eastern Europe, Africa, and the Middle East. There is a marked difference in launch timing between Western Europe (fast) and Eastern Europe (slow), despite many of these launches having occurred recently. Puerto Rico, Japan, and the USA have the largest positive deviation from the average launch price worldwide, whereas Egypt, South Africa, and Tunisia show the largest negative deviation from the worldwide average launch price. North America, South America, and Asia show positive deviations from the worldwide average launch price, while the other world regions—including Europe—show a negative deviation from the average launch price worldwide (Verniers et al. 2011).

When a pharmaceutical firm launches a drug in multiple countries worldwide, it needs to decide on the sequence of countries in which the launch will take place. As the launch price is a decision that is being made simultaneously, Verniers et al. (2011) examined whether launch timing is interrelated with launch price. They found that launch timing has a curvilinear effect on launch price, whereas launch price has a U-shaped effect on launch timing. This means that launch occurs fastest at moderate price levels. One can therefore infer that for pharmaceutical companies, a tradeoff is being made between the amount of time left under patent protection and the price needed to recoup R&D investments. Health regulators make a tradeoff between access of new drugs to society and the level of health expenditures.

7.4 Future Research on Launch and Diffusion Excellence

While the above overview shows that much work has been done in marketing science towards assessing the potential of new treatments, extracting value from a new treatment, and leveraging the value of a new treatment across countries, much work still remains. Below, we review some of the themes we consider important.

7.4.1 Future Research on Assessing the Potential of a New Treatment

Over the past 2 decades, marketing scholars have pointed out the need for a more elaborate framework for the study of diffusion processes that takes into account the usage of an introduced innovation (Anderson and Ortinau 1988; Hahn et al. 1994; Lewis and Seibold 1993). Several models in the life sciences, marketing, and economic literature have considered the process of post-adoption learning about a new drug (e.g., Camacho et al. 2011; Coscelli and Shum 2004; Hahn et al. 1994; Narayanan et al. 2005). These models, however, do not specifically account for physicians' initial adoption decisions and the factors that influence them. Furthermore, the models focus on the development of market shares rather than on drug sales and do not fully integrate patient behavior into the modeling framework. A promising avenue for future research is therefore to develop an individual-level model that integrates both the role of time dynamics in physicians' adoption decision processes and the role of patient compliance in the sales patterns of new drugs. This can be done by integrating information on refill prescriptions for previously diagnosed patients, corresponding to patients' compliance with therapeutic regimens, into an individual-physician-patient adoption model.

In addition, more work is needed that integrates the richness of primary data with the behavioral regularity identified in secondary data (such as from physician prescription panels). Integrating or fusing such data sources can yield great value, particularly for pharmaceutical companies have demonstrated the usefulness of primary and secondary data fusion in examining policy shifts in detailing by pharmaceutical firms. They found that when the market leader in a drug category dramatically reduces detailing, all firms in the category make more money, and the category shrinks only to a minor extent. Similar models can be developed for pharmaceutical forecasting, integrating information from conjoint analysis and information on past physician behavior from physician tracking panels.

Finally, there is a need for more work that examines the adoption of marketing science models by pharmaceutical managers. While marketing scientists have developed "heavy artillery" to assess the commercial (future) potential of new drugs, little of that artillery is used in practice. Rather, managers typically use linear or nonlinear extrapolation as well as traditional conjoint models. Examining the reasons that underlie the limited usage of sophisticated models in practice can yield important insights that can lead to better model development in the future.

7.4.2 *Future Research on Extracting the Potential of a New Treatment*

Pharmaceutical firms spend considerable sums on marketing activities and in particular on detailing visits. Over the past decade, some US states have initiated legislation limiting marketing spending by pharmaceutical firms, mostly in response to the growing concern regarding the effects that excessive marketing budgets might have on the costs of drugs. In the state of California, for instance, a new bill was signed in 2004 (going into effect in June 2005) requiring pharmaceutical firms to adopt a *Comprehensive Compliance Program* (CCP) that includes policies on marketing interactions with health care professionals. This program implements limits on gifts and other incentives to medical or healthcare professionals. More specifically, the CCP includes "specific annual dollar limits on gifts, promotional materials, or items or activities that the pharmaceutical company may give or otherwise provide to an individual medical or health care professional." In other parts of the world, governments have begun to take increasingly restrictive actions with regard to pharmaceutical marketing. An interesting question to investigate is whether legislation concerning the marketing of drugs alters the supply of detailing and/or the impact that marketing efforts have on the physician's final choice. More specifically, one may wonder whether such restrictions restrain the diffusion of new drugs in physician and patient populations. Another related development is the pending shift to virtual detailing, currently under experimentation in several major firms. What is the difference in effectiveness between a virtual versus a real-life detailing visit in promoting new drugs to physicians?

On the patient side, there is growing evidence suggesting a fundamental shift in the role of the patient in the medical decision-making process (Camacho et al. 2010). Specifically, there is evidence for more participatory decision-making involving patients and their physicians, in which both parties bear responsibility for medical decisions that concern the patients. This change indicates a dialogue between physicians and their patients, wherein physicians apply their medical knowledge in order to best suit their patients' needs and preferences (Emanuel and Emanuel 1992; Epstein et al. 2004). Stremersch et al. (2013) find additional evidence for such participatory decision-making interactions. They find that drug requests, especially those made to primary care physicians and to a lesser extent to specialists, have a substantial influence on brand prescriptions. Nowadays, digital and social media (e.g., Twitter, Facebook, PatientsLikeMe) are an important factor in drug requests in countries around the world. We know very little about the role of digital and social media in the diffusion of new drugs.

In terms of pricing new treatments, it would be beneficial to develop more insight into the evolution of price over the life cycle of a new drug. Lu and Comanor (1998) and Ekelund and Persson (2003) examined price dynamics in the USA and Sweden. However, more interesting insights could come from studying pricing strategies across multiple countries. In addition, the influence of regulation throughout the life cycle of a drug has also remained unexamined so far. Verniers et al. (2011) showed

that regulation does not influence launch price but conjecture this not to be true for prices across the product life cycle. In addition, all studies so far have focused on the ex-manufacturer drug price (e.g., Verniers et al. 2011), which is the price charged to wholesalers. However, it is crucial to also understand the proportion of the drug price that is truly paid by the patient. Data on copayment for drugs and reimbursement levels could provide useful insights. In addition, volume and bundle discounts are increasingly offered to payers. This is another topic that, to our knowledge, has not been the subject of systematic inquiry.

7.4.3 Future Research on Leveraging the Potential of a New Treatment Across Countries

To optimize their profits at a global level, pharmaceutical companies need to account for the extent to which the price of a drug in one country has an effect on the price of the same drug in other countries. There may be different reasons for such cross-country spillovers of price, such as the geographical proximity of countries, the trade relationships between countries, and the extent to which countries enforce a cross-country reference pricing system. Governments often see price spillover as a way to reduce or maintain drug prices at justifiable levels. To stimulate such spillover, many (European) governments have regulations in place by which they require companies to submit their products' prices in a predefined set of reference countries. The prices in this predefined set of reference countries are used to derive a reference price (often the minimum or average price across all reference countries). In both cases, the reference price becomes a ceiling price, and a drug's price can typically not exceed it (Gregson et al. 2005). Most reference pricing systems are asymmetric, in the sense that countries that are included in a specific country's reference set do not necessarily include that specific country in their own reference set. Governments and insurers (commonly referred to as "payers") consequently take prices in other countries into consideration in their own price negotiations with the firm. Managers need to account for price spillover, as agreeing to an excessively low price in one country may "infect" the price levels they obtain in other countries, and thus impact their global profits. So far, no rigorous model exists to optimize pharmaceutical managers' decisions on global pricing, even though this issue is the focus of thriving consulting businesses. Such models would also provide pharmaceutical companies with an optimal launch sequence across countries.

The successful launch and diffusion of new drugs remains the life blood of many pharmaceutical firms. While it is clear from our review that some questions are answered by past research in marketing science, it is equally clear that sophisticated managers are short of decision support tools (i.e., marketing models) that they can implement successfully to make a difference in their respective markets. We hope the present chapter has provided a stimulus for the development of such tools.

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