Predicting Market Outlook: Enhancing Market Forecasting via Application of Pharmacoeconomic Modeling Techniques

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KEY POINTS

Traditional stock and flow models have significant limitations when applied to complex and evolving markets, as they get unwieldy when needed to account for segmentation of the market based on patient characteristics, treatment history, patient preferences, or disease stage.

Pharmacoeconomic models are well suited to address limitations associated with stock and flow models, and they can improve the quality of market outlook predictions.

Within the health economics community, there is a wealth of scientific experience and know-how in the development of the analytical frameworks to address a wide range of research questions that also can be used to help improve the quality of forecasting models.

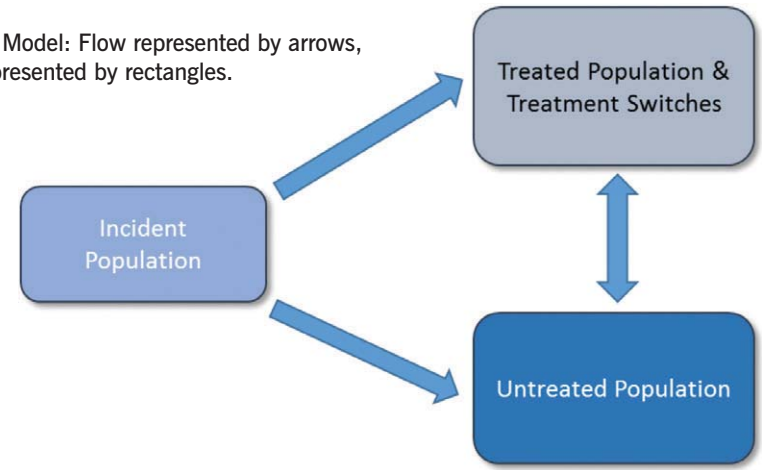
Models are tools to help understand complex systems through analytical frameworks. Hence, all models are implicitly an approximation to the reality, rather than a replica. That said, it is also important to keep in mind that the utility of a model is still highly dependent on how the reality is conceptualized and translated into an analytical framework. This can be a critical nuance, especially if results from a model are used to inform decisions that have substantial implications, such as reimbursement decisions for new therapies or budget and resource allocations across biotechnology and pharmaceutical organizations. Therefore, while all models are approximations, the required level of approximation should be considered and assessed carefully, as it may have significant consequences through the decisions they inform.

The organizations typically use mathematical models to optmize investment decisions by forecasting the market outlook in a given therapeutic area, and use model-produced results to inform both short- and long-term strategies. These strategic choices often have material implications on how organizations structure themselves and allocate their resources. The typical approach to conducting market forecasting has been to use stock and flow (S&F) models that conceptualize the market in relatively straightforward terms such as key patient segments, anticipated market changes, etc. However, as the health care markets evolve and new treatment options continue to become available at an unprecedented rate, traditional simplistic approaches to understanding market evolution may not be sufficient, as they often fail to capture nuances in increasingly complex markets, such as more detailed patient segmentation based on the patient preference and behavior and medical histories. More often than not, such critical market nuances are either over-simplified or ignored for the sake of low computational burden which, however, increases the risk of lowering the quality of predicted power. Hence, it may lead up to strategic decisions that are based on limited, or in some cases, wrong market expectations.

CONVENTIONAL APPROACH TO MARKET FORECASTING: STOCK AND FLOW MODELS

The concept of S&F goes back to the late 19th century,[1] where initially it was applied to problems in economics. In the original approach, the term "stock" referred to variables that do not have a time dimension and therefore can be measured at a given point in time, whereas the term "flow" represented the change in "stock" measured for a given time interval. When applying S&F models to market forecasting, the stock represents the size of each of the patient segments of interest, such as incident patients, diagnosed but untreated patients, or patients receiving certain treatments. The flow represents the

Figure 1: S&F Model: Flow represented by arrows, and stocks represented by rectangles.



rates at which patients move between defined stocks over time. The flow is usually dependent on market dynamics and events, such as market uptake of a therapy following its launch, the rate of diagnosis, treatment discontinuation rates, etc. (Figure 1). Using such estimates based on patient dispositions, this type of analysis provides insight into the anticipated evolution of the market regarding the size of the patient segments, and helps organizations identify future commercial opportunities and risks.

S&F models are simple to construct and are appropriate for markets where there are a limited number of variables and dynamics to consider. However, these models have limitations, which become more apparent in more complex market scenarios. S&F models may become harder to construct and manage when there are multiple key market dynamics, such as the impact of patient or physician preference on treatment selection, or when patient's age, sex, race, treatment history, disease activity, the location of service, etc. are important factors determining how patients may be managed in clinical practice. In such scenarios, the application of S&F models either becomes too complicated and loses transparency, or requires numerous assumptions to be able to approximate the reality into the simple framework.

Understanding market evolution is critical in ever-evolving and highly competitive healthcare markets. Therefore, to ensure the development of reliable strategies, it is necessary to employ flexible, sound modeling approaches that can capture the inherent complexity of the field.

AN ALTERNATIVE APPROACH: PHARMACOECONOMIC TECHNIQUES APPLIED TO MARKET FORECASTING

Pharmacoeconomic evaluations are tools designed to inform decisions to improve healthcare delivery and health outcomes.[2] Typically, such decisions require the development of analytical models to better understand short- and long-term health and economic consequences of new interventions compared to existing alternatives. This is especially important in the absence of long-term evidence from randomized clinical trials and/or head-to-head comparison of therapies in a trial setting. It requires a solid understanding of the interactions between key disease and management concepts: the epidemiology of the condition, natural disease progression, efficacy and safety profiles of therapies, treatment pathways, and pharmaceutical and medical costs associated with the management of the condition. This is, indeed, a much broader set of considerations than what S&F models would take into account for typical market forecasting.

When applied to market forecasting, pharmacoeconomic models can still use the same building blocks of traditional S&F market forecasting models (see Figure 2), but with greater flexibility that can help capture additional details around each concept, which in return can help address inherent challenges of S&F models.

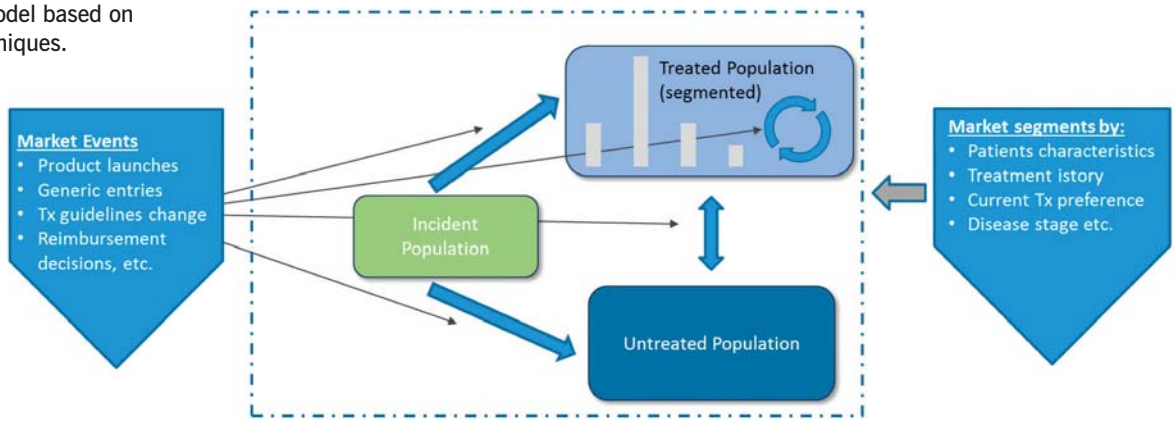
Market forecasting using pharmacoeconomic techniques relies on 3 concepts:

- **Market segments** that describe the patient populations of interest, which can be defined not only by the treatment that patients are on at a given time, but also other key variables such as treatment history, age, sex, race, underlying disease activity, etc. The size of each market segment is monitored throughout the simulation to represent how it may change over time. The advantage of the pharmacoeconomic technique is that it captures the complexity of the market segments using any relevant combination of descriptors, which can very quickly become unmanageable with a S&F model.
- **Patient flow** is the same as what it represents in a S&F model; that is the rate at which patients move between market segments. However, with pharmacoeconomic techniques, patient flows can be defined in greater detail for each market segment (eg, line of therapy, treatment history, disease activity, etc) so that market nuances and their impact on rates at which patients move can be reflected in the model framework.
- **Market events are** disruptions in the existing market dynamics that impact the rate of patient flow and hence impact the size of market segments. Examples of market events include the introduction of new therapies, changes in clinical treatment guidelines, or changing patient/physician preferences over therapy profiles (eg, mode of administration or efficacy/safety profile).

EXPLORATION OF UNCERTAINTY: SENSITIVITY ANALYSIS

Sensitivity analysis is an essential aspect of modeling, because it allows one to understand the uncertainty associated with the model inputs and the structure, hence the model results. S&F models typically address uncertainty in a fairly simplistic way; in addition to the base case, optimistic, and pessimistic sets of assumptions >

Figure 2: Forecasting model based on pharmacoeconomic techniques.



regarding the market events (eg, uptake of new products and other key model parameters). This approach is known as scenario analysis because it compares alternate scenarios that are constructed based on analyst expectations around how the market may evolve. However, pharmacoeconomic models are typically developed to employ 2 additional techniques that allow for a more sophisticated and rigorous assessment of parameter uncertainty, namely deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA). In DSA, each of the parameters of the model is varied one by one to both a low and a high plausible value, and the primary model outcome is evaluated with the new value. Then all of the parameters are ranked in terms of the impact on the primary outcome, and their effects are presented in a way that identifies the key parameters that have the largest impact on the outcome. In PSA, all of the parameters are varied simultaneously, drawing each parameter stochastically from a distribution, and the model outcome is evaluated for each parameter set. The scatter of outcomes is then plotted on a plane in order to give an assessment of the total parameter uncertainty in the model. Together, the tools of DSA and PSA, which are standard components of pharmacoeconomic analysis, provide much richer insight into the uncertainty of the model results than simple scenario analysis.

CASE EXAMPLE: COMPARISON OF S&F WITH THE PHARMACOECONOMIC APPROACH

To demonstrate the differences of the 2 aforementioned methods, we applied each method to a hypothetical problem, where we tried to predict the market outlook over the next 5 years for a slow-progressing chronic disease state. The example included the following specifications:

• **Available Therapies:** Three established therapies (E1, E2, and E3) are available in the market with varying efficacy, safety, and convenience profiles (Figure 3).

• **Patient Preference:** Patients prefer therapies with favorable safety/convenience profiles at earlier stages of disease management and trade off safety for efficacy as they progress on their treatment pathway.

• **Market Events:** Two new therapies, N1 and N2 are expected to launch in year 1 and year 2, respectively. The new treatments have the following profiles:

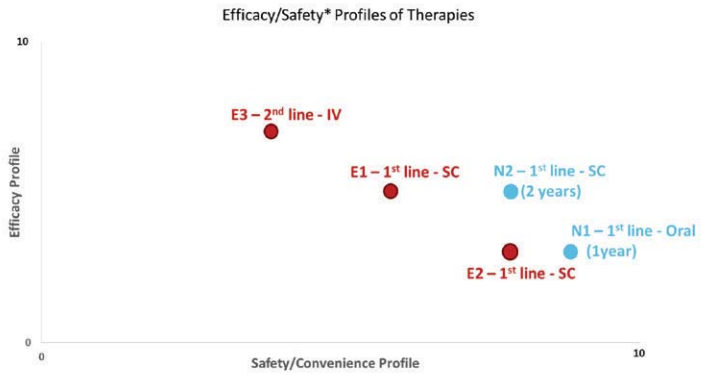
a) N1 improves the safety/convenience profile of E2, and at the same level of efficacy with E2;
b) N2 improves the efficacy profile compared to E2 and the safety profile compared to E1.

The new therapies are expected to impact the current market dynamics by offering new safety/efficacy trade-off options for the patients and physicians. The key questions of interest are:

- What would be the market share of each new therapy over the next 5 years, and
- What will be the magnitude of the change in the market share of each established therapy?

The key difference between the 2 models is that, the S&F model assumes that certain percentage of patients from each segment will "flow" (ie, switch from the segment) annually and the switching population will be distributed between other segments based on pre-determined ratios determined by the analysts. To illustrate the simplicity of the model, the S&F model does not track or account for patient preferences and/or medical histories (eg, previous treatments

Figure 3: Representation of the efficacy/safety/convenience profiles of the available (E1, E2, E3) and new (N1, N2) treatment options.



*Higher value on the efficacy and safety/convenience scale means more favorable profile. / Abbreviations: IV = intravenous infusion; SC = subcutaneous injection.

Table 1: Key differences in the case study among S&F and pharmacoeconomic-based models

S&F Model	Pharmacoeconomic Model
Stocks • Treated patients (by therapy) • Untreated patients	**Market Segments defined by** • Treated patients (by therapy) • Patients' treatment history • Untreated patients
Flows • Treatment switches • Incident patients • Treatment discontinuation • Death	**Patient Flow** • Treatment switches due to 1. Efficacy 2. Safety • Incident patients • Treatment discontinuation • Death
Market Events • New product launches	**Market Events** • New product launches

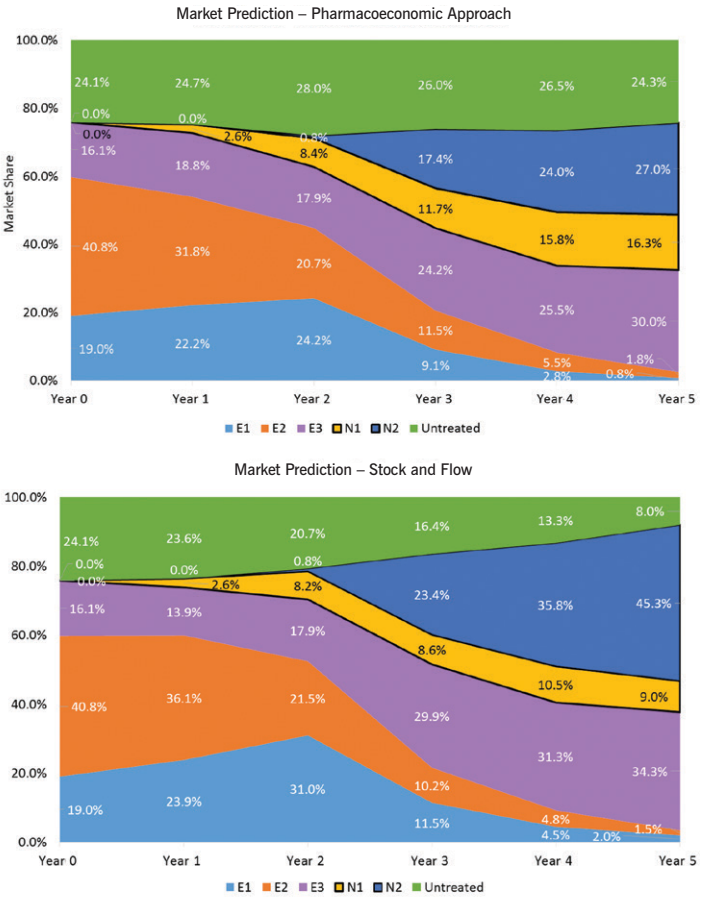
patients have been on), hence the market segments patients are assumed to join after leaving the previous segment does not play a role in determining the next segment. On the other hand, while it uses the same flow rates market segments as the S&F model, the pharmacoeconomic model tracks the patient preference and medical history, and determine the next segment a patient may join based on these considerations. More specifically, in the pharmacoeconomic model:

- Patients cannot go back to a therapy that they tried in the past, assuming that the reason for the original discontinuation still holds true.
- Patients who switch due to efficacy cannot be assigned to a therapy with the same or lower efficacy score, and
- Patients who switch due to safety/convenience cannot be assigned to a therapy with the same or lower safety/convenience score.

RESULTS FROM GROWTH

When we forecasted the growth of the market in this hypothetical disease using each of the models, there were substantial differences in the market outlook predictions (Figure 5). The S&F model estimated that the launch of N2 in year 2 would bring a majority of

Figure 5: Comparisons of market evolution results using the pharmacoeconomic model (A) an S&F model (B)



E1-E3: existing therapies, N1-2: new therapies.

untreated patients back into the market and will be used for their treatment, thus becoming the market leader by reaching a market share of 45% by year 5 in the model (Figure 5B). In contrast, the pharmacoeconomic-based model suggested that, while N2 would grow rapidly initially, by year 5 it would reach a market share of only 27%, which is less than the share of E3 (ie, 30%) at that time (Figure 5A). Its impact on bringing untreated patients back to the "treated" segment is estimated to be more moderate than the S&F model. Furthermore, while the S&F model predicted small growth for N1 with a market share of only 9% at year 5, the pharmacoeconomic-based model predicted more steady growth, reaching 16%.

IMPLICATIONS

Considering the questions set at the beginning, the results of the 2 models can lead to substantially different strategic choices due to differences on the expectations of market evolution. For instance, based on the pharmacoeconomic model, one of the considerations can be further investing in mobilizing the untreated patient population, as a third of the market is expected to remain "untreated" over the next 5 years. Whereas the S&F model would suggest a limited return of investment in such an activity, as new product launches would bring them to the "treated" segment anyway. Furthermore, based on the expected growth of N1 or N2, prioritization and level of investment towards either of the new therapies could differ by respective manufacturers, such as the size of the salesforce to hire for a particular product.

As can be seen from this simple example, while the direction of the results from both models is similar (ie, new therapies grow in market share, whereas existing therapies lose share), the magnitude of changes are substantially different, which can lead to significantly different strategic choices. Such examples of diverging implications based on future expectations can be expanded. Pharmacoeconomic models include all of the same capabilities as S&F models, but are more flexible and allow for more interaction between key variables. Given that markets are known to be highly complex and that models inform important investment decisions, it is reasonable to use a sophisticated tool that can more closely approximate the dynamic complexities of the market and explore scenarios in an interrelated way. While it would be unreasonable to expect that the market will behave exactly the same way that either of these models predicts—it is important to keep in mind that all models are approximations to the reality—how market dynamics are conceptualized and captured is key in conceptualizing the market dynamics as they may lead to substantially different conclusions and strategic choices.

CONCLUSION

Healthcare markets are changing at an unprecedented rate and planning for future market conditions has become critical for ensuring that organizations are prepared for what the future may hold. As markets evolve, they are becoming more nuanced and segmented, meaning that market outlook projections using traditional simplistic tools will no longer be adequate to inform strategic decisions. Pharmacoeconomic models employ well-established and validated methods, and are utilized to address complex questions. Within the pharmacoeconomics and outcomes community there is a wealth of scientific experience and know-how in the development of such analytical frameworks to address a wide range of research questions, which can also be used to help improve the quality of forecasting models. Given the increasing importance of such tools for decision-making purposes and evolving market complexities, pharmacoeconomic modeling methods can also be used to address this growing vital need.

Pharmacoeconomic models offer a sophisticated set of tools that allows for a more detailed representation of complex market dynamics, which can aid in making important strategic decisions via better understanding and hypothesizing how healthcare markets may evolve over time.

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2. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programmes. Oxford University Press; 2015.

Additional information

The preceding article is based on a workshop given at the ISPOR 21st Annual International Meeting.

To view Dr. Deniz's presentation, go to: https://www.ispor.org/Event/ReleasedPresentations/2016Washington#workshoppresentations