System Dynamics in New Product Forecasting: Collaborative Use of Patient Based Forecast Model for an Oncology Drug

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Abstract

This paper presents a solution with a System Dynamics model structure for a prototypic new cancer drug embedded in a corporate intranet for collaborative use of a restricted community. Patient flows modelled with SD overcome the limitations of classical spread sheet models that are observed at incidence based oncology models. Furthermore, SD combined with a web client not only provides the opportunity to work collaboratively but also to use them for business simulations in a multinational business environment. The SD model is segmented into 3 lines of therapy. Further lines can easily be added aided by the modular design. The model contains modules for competition, cross line reduction (probability of drug reuse in the subsequent treatment line), early access (so called compassionate use)e and for converting drug use into revenue. The latter is the prerequisite for determining the commercial value of the new drug by finance teams, e.g. by calculating expected profit and loss (P&Ls) and net present value (NPV).

Introduction

For new product forecasting in a multinational environment it is ideal to collaboratively work with one centrally provided forecast model structure, while maintaining the necessary confidentiality. The consolidation of such multiple local forecasts is expected to result in a robust regional consensus revenue forecast. Furthermore, after launch of the product the same models can be used as well for local as for central business simulations.

New product revenue forecasts are the base for asset valuation and feed into net present value evaluation. In the case of the pharmaceutical products the potential market size is determined by the epidemiology and actual market size is determined by the number of (drug) treated patients. Revenue generated by a specific product can be determined well via market shares and achieved price. In the majority of cases causal models (for further explanation see Cook 2005) based on the above can be formulated in hierarchic static models with spreadsheet software like Excel. Models are calibrated against actual market sales, which are usually obtained from global market research suppliers. Besides the information on market size (here: incident cancer patients) modelling of the effect of competing drug treatments on the use of the drug to be valuated is crucial for a new product forecast. The conversion of treated patients to revenue is the result to be delivered to financial teams calculating expected P&L and net present value for decision making.

There have been attempts to also apply Systems Dynamics for drug valuation in the pharmaceutical industry (Paich et al. 2009 and 2011). But still hierarchic patient based spreadsheet models are the most common type of model for evaluating new products in the pharmaceutical industry in particular when the model is based on prevalence. However, in the case of cancer drug models starting with incident patients and patients starting a specific treatment flow models can become very bulky and slow in spreadsheet software. This is

particular the case when monthly time resolution is desirable or necessary. System Dynamics embedded in a restricted space of a corporate intranet is expected to be a superior alternative to spreadsheets sent by mail and consolidated offline.

Features of the System Dynamics Model

The System Dynamics model(s) are built with the iThink software (isee-systems 2015a)

Flow of Incident Patients:
The evaluation of cancer drugs usually starts with the flow of incident patients (patients/year) undergoing several lines of treatment. The model presented here starts with incident drug treated patients and segments into 3 lines of therapy (Fig.1). Data can be obtained from global market research organizations or by own epidemiologic research.
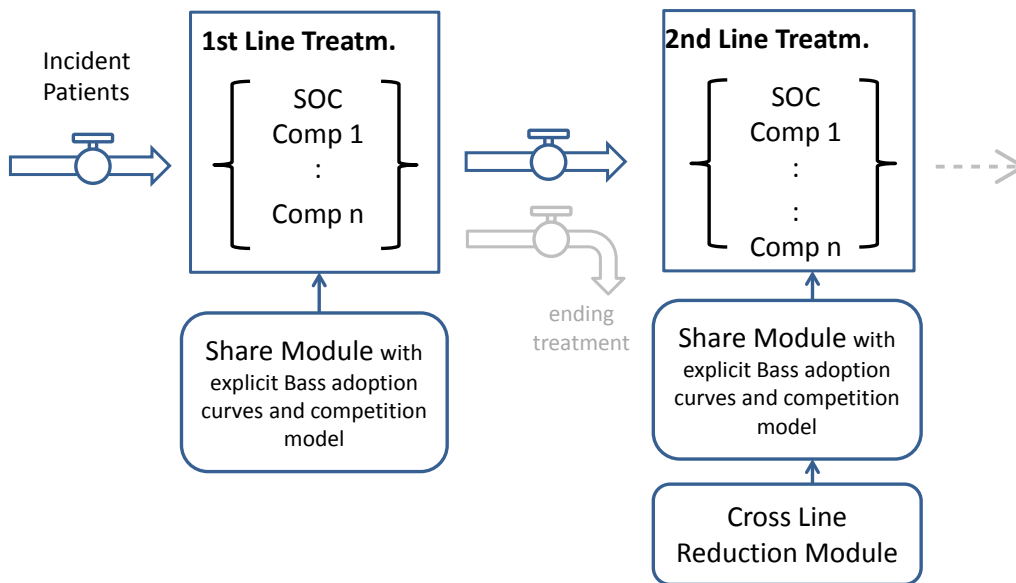

Fig 1: Basic patient flow of the SD model and its modules.

Early Access to New Drugs by Named Patient Programs:
Several governments have created early access to drugs for those patients with a life-threatening disease, for which a satisfactory treatment is not available. Under such regulations patients can receive innovative drugs (short) before the drug is authorized by drug administration agencies like the FDA (USA) or EMA (European Union). Compassionate use is granted by individual EU member states. Usually drugs must be given free of charge until marketing authorization (see EMA 2010).
The consequence for a forecast model is that it must consider patients already treated with the new drug before the official launch and that the drug is provided free of charge. Their treatment is supposed to continue and will usually be delivered from commercial supply after marketing authorization.

Competitive Landscape in the Share Module:

After patients have entered the frontline stock they are spit by the different drug treatments. Adoption of drug treatments can be modelled with System Dynamics (see Chichakly 2010 on ISEE website). However, we chose an alternative approach compatible with the way we model competitive landscapes in spreadsheet models. Such a model starts with the assumption that drug treatment have started with the advent of the originator drug treatment. The originator has per definition 100% share until the first competitor arrives. This competitor starts to adopt and to displace the originator from the market until reaching its specific maximal adoption characterized by its adoption share. The peak adoption share is a measure of the medical and commercial attractiveness of the new product compared to the originator. In pharmaceutical markets attractiveness primarily is the function of its relative effectiveness, its safety profile, its relative price and/or its probability to be reimbursed but also the launch sequence (see Johnson 2005)

Several methods have been proposed to estimate such peak shares. Subsequent drugs compete with the previous with the same principles. – Mathematically the adoption curves can be described well with the explicit Bass function (for applications see Johnson 2005), an exponential type of algorithm first described by Bass (see Bass 2004). For illustration see Fig. 2. Users can select from multiple imported Bass curves to allow for different adoptions times and run different scenarios.

Cross Line Reduction:

Patient treated with drugs in cancer can relapse after the previous treatment. For the subsequent line of treatment the physician will have to decide whether to change the drug treatment. The probability of reuse for each of the drugs of the previous line determines the amount of the so called cross line reduction. It can be an important factor for the commercial forecast of cancer drugs. This becomes even more relevant in the case of a drug initially only being indicated for later lines of treatment. It may have achieved a steady share after a certain time. If then the same drug also gets a label for frontline and is also rather efficient there, a reduced probability of reuse will start to reduce the previously higher share in later lines of therapy. Crossline reductions and the patients moving from one line treatment to the next capture the dynamic nature of patients flow particularly well in SD models. This represents one of the major advantages over hierarchic spreadsheet models.

Calculation of Revenue:

Cumulated month of treatment are multiplied with adherence, gross price per month and gross to net to yield revenue by single country.
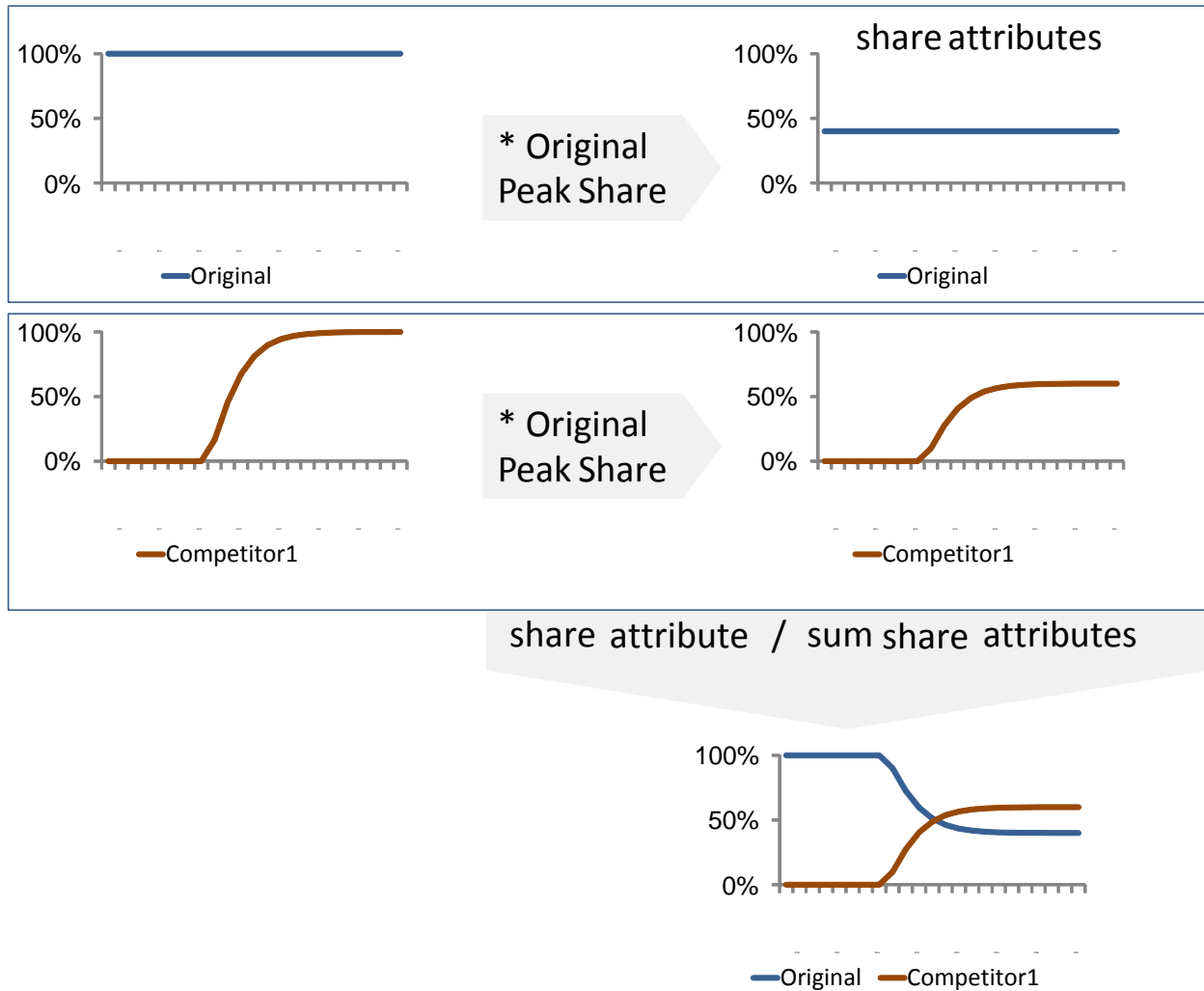
Fig 2: Schematic presentation of the calculus in the share module. The originator drug initially has a share of 100%. However, the relative final competitive weight after competitors have reached their maximal adoption is only "good" enough to show an equilibrium share of 40% in this example (share attributes over time shown at the right part of the graphic). The adoption of the first competitor is assumed to follow a classical Bass uptake curve approaching 100% adoption (red curve in the second box). Again the competitive weight is attractive enough to yield 60% in this example. The resulting adoption shares in the competitive landscape are calculated for every time point by dividing single share attributes by the sum of share attributes.

Collaborative use in a multinational environment and implemented software:
Objective of the described development was to collaboratively work with a uniform forecast model structure. In this case representatives from the 5 major European countries (France, Germany, Italy, Spain and UK) had access to 5 model of the same structure but filled with country specific data. The five models were uploaded to a Netsim Server version (isee-systems 2015b) residing on a virtual server of the Johnson & Johnson (JnJ) intranet.

To allow for cross country comparison and to store different scenarios a custom modification of a Whole Systems Partnership (WSP) client software (Domdouzis et al. 2013) was also installed on the same JnJ intranet server as Netsim.

The WSP client generates export files in Excel, which can be copied into specific Excel files providing convenient tools for analyzing results and for calculating the ramp-up from a G5 consolidation to total regional sales.
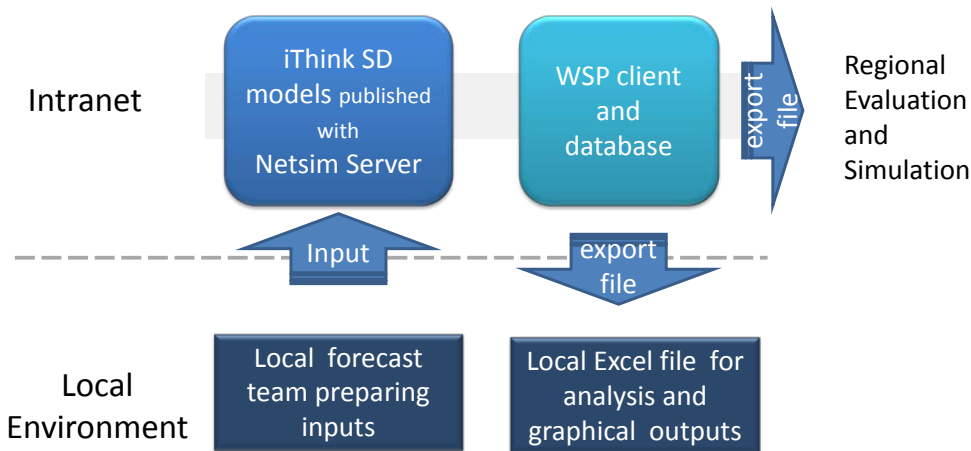

Fig. 3: Information flow and basic IT architecture

On business requirements and model build process

The benefits of using a System Dynamics solution in this business environment include factors such as the models' transparency and openness to challenge leading to higher consistency in business forecasting by using one commonly shared "cloud"-type of model; also the creation of an environment in which 'what if' scenarios can be created in a more intuitive and accessible way than equivalent spreadsheet solutions. However, in order to achieve these benefits initial confidence in the model outputs needed to be generated amongst end users, who had already used an Excel based model with typical spreadsheet drawbacks. The development of the model did not, therefore, follow a 'traditional' group model building process, although engagement with end uses remained an important feature of the process. The model build therefore followed a sequence of:

1.   Replicating the outputs from the spreadsheet modelling tool as far as was mathematically possible within an SD model, given the constraints within spreadsheets in the handling of 'over time' calculations. This makes it possible to be consistent with previous efforts.
2.   Adopting specific and identifiable improvements to the SD model build that could demonstrably improve the quality of forecasts due to its ability to deal with time delays in particular.
3.   Making the model structure explicit during the period of model adoption so that people could 'make sense' of what was happening 'under the bonnet'.

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4.	Ensuring an intuitive and easy to use model interface with carefully selected variables that were material to the sensitivity of the model outputs and reasonable in terms of people's ability to influence.

Conclusions and outlook to future developments

Two different types of models serving 2 different indications were successfully implemented in the JnJ network and have been used by local and central teams. They work stable and are the only means to calculate monthly time resolution forecasts for a cancer drug.
There was some central assistance to local teams necessary until they could work with the models. For regional forecast functions the approach is a convenient opportunity to quickly run scenarios or business simulations in particular for estimating the potential impact of competition.
For the future it is very desirable to replace the final offline evaluation in Excel by an online intranet approach.

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