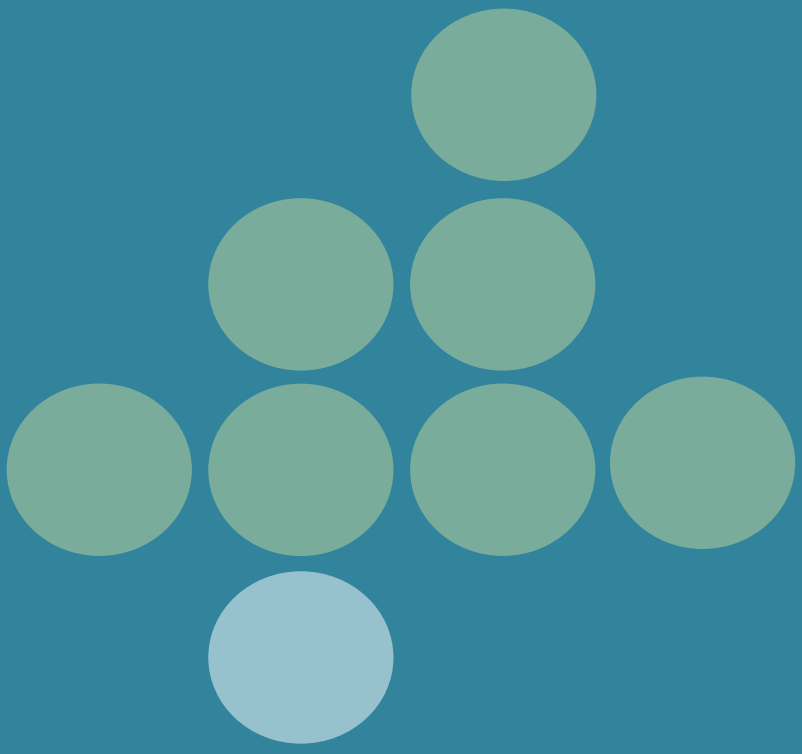
WHITE PAPER

Difference Engine™ FROM HEALOGIX

Scope Matters When Predicting Decisions



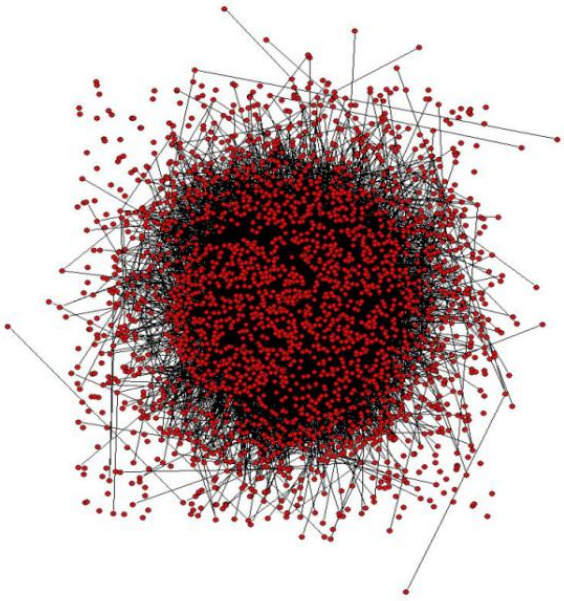
HEALOGIX

PARSIMONY IS STILL ESSENTIAL

"Make everything as simple as possible, but not simpler." – Albert Einstein

Over the last 10 years the challenge of assessing the opportunity for a new biopharmaceuticals, medical devices, or diagnostics has increased substantially. These challenges include:

- Patent expirations in combination with new entrants that offer minimal incremental improvement have made most categories extremely competitive.
- Multiple stakeholders with wide ranging preferences and priorities participate in each treatment decisions.
- Economic and political forces are in the initial stages of drastically changing the entire systems.



While it is reasonable to consider simplification as a solution to assessing complex market dynamics, there is real peril in making predictions bases on an over-simplified evaluation. Simple solutions are often discredited by simple questions. All it takes is an informed query that includes the words "what about?"

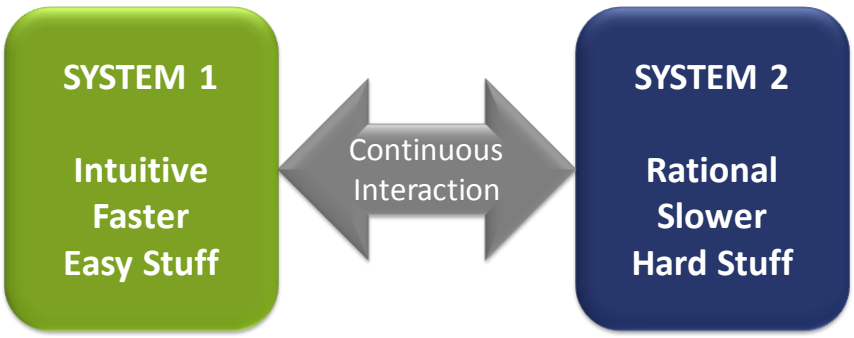
But how can we possibly account for everything that might impact the adoption of a new product without making the assessment overwhelming?

The challenge for contemporary marketing planners and commercial analytics is to create an assessment that is appropriately parsimonious without being overwhelming. Current best practices not only make this possible but add critically important values to the assessment of demand for a new product. This white paper outlines the details of these best practices starting with an important distinction from Behavioral Economics.

WHEN IT COMES TO DECISIONS, WE ARE OF TWO MINDS

Over the last 40 years a large body of research from contemporary psychology has challenged classic economic theory to establish a broader view of decision making and a new discipline called Behavioral Economics. We now understand that decision making can be accomplished by two distinctly different types of thinking or systems. These systems have been unimaginatively been dubbed System 1 and System 2 and they work together to process internal needs and drives along with external stimuli to make decisions[1].

Empirical evidence now overwhelming supports the idea that the majority of decisions are accomplished by System 1 using heuristics (i.e., decision rules that can be invoked quickly and habitually without much effort). The critical feature of System 1 is its ability to make fast and functional decisions. However, System 1 will sacrifice accuracy for speed and effort, which can result in mistakes. A wide range of irrational behavior can be accounted for, and potentially correct, when the behavior of System 1 is carefully studied.



System 2 reserves for itself for those decisions that require our more deliberate, rational capacity. The cost is substantial cognitive effort and time. Importantly, System 2's analytic capacity is only engaged when absolutely necessary. This typically happens when System 1 makes mistakes or when there are strong incentives to be deliberate.

While we embrace the lessons of Behavioral Economics and have expanded our practice to

[1]Nobel Laureate Daniel Kahneman has popularized these names, most recently in his 2011 book "Thinking Fast and Slow".

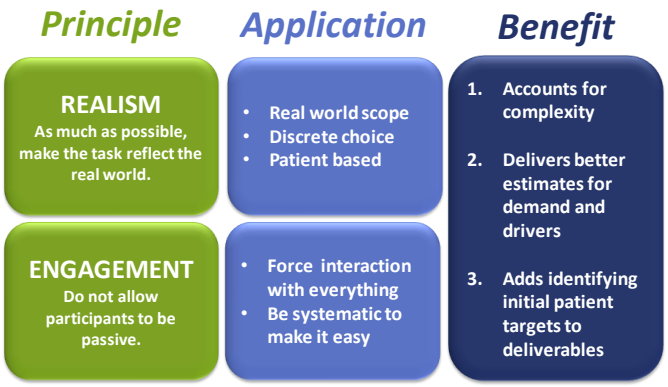
fulfill the opportunity it provides for market research[2], decisions related to healthcare have long been presumed to provide sufficient incentive to require deliberate decision making. This means that any assessment of an emerging opportunity, separate from any System 1 activity, must include a careful study of System 2.

REALISM AND ENGAGMENT

Two principles drive our ability to successfully account for both complex markets and the activities of System 2. The first principle is ***realism***, where as much as possible we make our research task reflect what happens in the real world. The application of this principle has three implications.

First, we have to take on a scope that realistically reflects what is happen in the market, not a scope that we arbitrarily deem as realistic. This requires careful consideration and extensive pretest to make sure we are testing everything that matters and nothing that doesn't.

Second, we use a discrete choice take to more closely reflect what participants do in real life. Physicians do not make treatment decisions in groups, so we shouldn't ask them to do it in our research[3].



To clarify the fundamental nature of this point, imaging two physicians, one is standing by the bedside of a patient about to review their chart; the other is standing in their waiting room, which is full of patients. Which image do you think is a more accurate image of physician about to make a treatment decision?

Third, because we use discrete choice, we have to provide sufficient patient level information to make the choice coherent and credible. Careful consideration of three options for testing patient profiles clarifies the fundamental difference in our approach to discrete choice. This distinction is described in detail in the next section.

The second principle that drives our approach is ***engagement***, where we significantly increase our ability to test a broader scope forcing research participants to interact and not be passive. The application of this is simple but powerful. We field very dynamic and carefully programmed surveys that are laid out systematically and coherently and then force interaction with all materials[4].

THE DIFFERENCE IN THE DIFFERENCE ENGINE

How we test patient profiles is the critical difference in our approach. We strongly advocate testing what we call hypothetical patient profiles over two other options, prototypical profiles or actual patient records. To be clear these are the define properties of each type of profile:

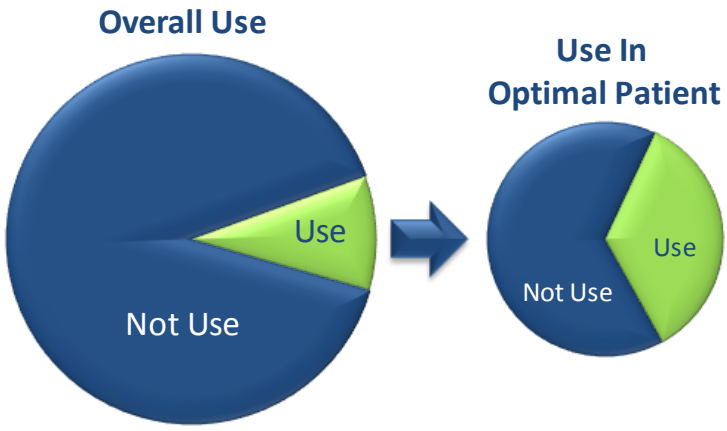
Hypothetical patient profiles define the details of the patient in terms of attributes and levels so that we can test those details in the same way we test the details related to products in a discrete choice task. This approach allows us to account for all possible patients during the analysis, which provides a significant incremental value to the results. We can execute optimizations to establish which patients are the best candidates for a new product.

Prototypical patient profiles are established in advance of the research and remain static throughout the study. The fundamental limitation is the research is limited to only what is tested; there is no option to estimating expected adoption to other potentially relevant patient types.

Actual patient profiles are based on actual patient records and have two inherent flaws. First, the logistics of research become very cumbersome and time consuming. Second, and more importantly, it is hard to avoid idiosyncratic chart pulls and obtain representative sample.

[2] See our Adaptive Toolbox™ white papers.
[3] See Tim O'Rourke's 2008 PMRG presentation on this topic.
[4] See case study below for examples.

There is a tangible benefit to testing hypothetical patient profiles that can't be under rated. Patient profiles based on a systematic test across a wide range of key attributes and levels allow us to explore all possible patients to find the combination of patient characteristics where use of new product is expected to be highest. This provides a potential initial patient target and can facilitate trial and ongoing use. ***Think about it, the first question most prescribers ask themselves about a new product is which of my patients would be the best candidates?*** The success of a new product can depend on the answer. If it does not work in the patient they pick, they will very likely be reluctant to use the new product again. Having an initial target defined by a robust analytic process will help them identify the ideal initial patient and maximize the chances of initial success, which provides the best opportunity for long term success.



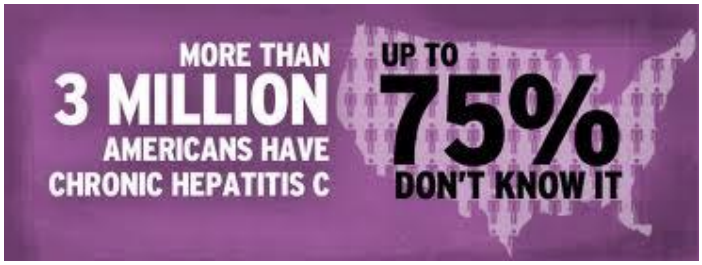
CUSTOM SOLUTIONS DRIVE OUR INNOVATION

Our practice leverages the best available survey programming and marketing science to provide a custom solution for each client and situation. Across our extensive experience with this approach we have developed a number of solutions that we are now component parts that we can easily modify and apply as needed in any given context. The list below is not comprehensive, but provides good perspective on the specific analytical solutions we provide:

User Adjusted Volume Weighted Patient Totals	Using volume estimates for individual patient characteristics, calculated dynamic weighted totals across any combination of patients, including a grand total; Weights are installed in stimulator to be user adjusted
User Adjustable Order of Entry Effects	Allows user to apply a penalty or bonus market entry sequence; Application is additional and independent of estimates from choice task and model
Explicit Test of Warehousing	Treats availability as an attributes in choice task and model; Allows explicit estimation of treating right away versus waiting to treat, and for how long
Product Specific Adjustment	Typically used to control for overstatement; the effect of a product in the market can be mitigated with an adjustment control
Product Specific Adjustment Lock	Simulator feature that allows the user to lock adjusted shares while making adjustments to other products in the model
Warning Master /Circuit Breakers	Prohibiting output for illogical scenarios or patient profiles
Pop-up Controls	Custom popup control dialogs that allow for more useable / streamlined interface
Scenario Store	The ability to add user created scenarios and store them for future use
Aggregated/ Combined Levels	Ability to combine levels within attributes via weight adjustments
Cycle Level Reports	Automated levels report for all attributes in any model
Concentration Targets	Create designs that match concentration or density targets for attributes within designs
Interpolation and Bootstrapping	Converting scales to continuous values where ever possible using interpolation; and when necessary layering in additions effect using a reference point
Most Likely Choice	Independent models for each alternative, which allows us to assess any aspect of the probability distribution, including which low probability outcome is most likely
Individual Level Estimation	Use HB estimation to generate utilities at the individual level, which best accounts for heterogeneity and provides flexibility for ad-hoc data cuts

Case Study: Hepatitis-C

Situation



Until the summer of 2011, treatment of Hepatitis-C virus (HCV) was primarily limited to the combination of pegylated interferon (PEG-IFN) and ribavirin (RBV), a regimen that posed significant challenges to patients due to the length of therapy, unpleasant side effects, and relatively low rate of success as determined by sustained viral response (SVR). In 2011, the FDA approved two agents in a new class of products, protease inhibitors, Vertex's Incivek (telaprevir) and Merck's Victrelis (boceprevir). These products, when administered in conjunction with PEG-IFN+RBV, nearly double the SVR attainable in treatment naïve patients and more than triple the SVR in treatment experienced patients. However, these products are not without their drawbacks; anemia, rash, and dietary requirements cause significant treatment challenges.

Even with the extremely high expectations around this class of products prior to launch, Vertex's Incivek exceeded its highest initial revenue forecasts. In its first year of launch, over a billion dollars of Incivek were sold, solidifying its position as one of the fastest drugs to reach blockbuster status in pharmaceutical history. This unprecedented uptake of Incivek is clearly threatened by other activity in the HCV market. Within months of Incivek's launch, talk of new and more effective products dampened the excitement and potential future sales of Incivek. This has resulted in a staggering decline in sales of Incivek which presumably has HCV manufacturers taking note and hypothesizing how the Incivek uptake and decline will translate to the opportunity for their new products.

There are several classes of treatment options in development for the treatment of HCV, broadly referred to as direct-acting antivirals, or DAAs. Within the DAAs are second generation protease inhibitors (PIs), nucleotide polymerase inhibitors (nucs), non-nucleoside polymerase inhibitors (non-nucs), and NS5A inhibitors, among others.

Within each of these classes, several agents are drawing significant interest:

Protease Inhibitors

- TMC435 (simeprevir): Being developed by Janssen Pharmaceuticals, this second generation PI is currently in phase III clinical trials in conjunction with PEG-IFN+RBV and is expected to submit its NDA in 2013. Initial data indicates TMC435 will deliver at least 80% SVR with a side effect profile comparable to other protease inhibitors.
- BI-201335: Developed by Boehringer Ingelheim, BI-201335 is now in phase III trials after demonstrating superior efficacy in genotype 1 patients. Studied in a variety of combinations with BI's polymerase 207127, with and without ribavirin, as well as in combination with the legacy backbone PEG-IFN+RBV, 201335 appears to deliver over 80% SVR in treatment naïve patients.
- BMS-650032 (asunaprevir): Being developed by Bristol-Myers Squibb, who have experienced some significant setbacks in their development of other HCV agents, this agent is being studied in both a quad regimen including PEG-IFN+RBV and BMS's non-nuc 790052 as well as a dual, interferon-free regimen also including 790052. Initial data looks promising with SVR rates comparable to those seen with TMC435 and BI-201335.

Nucleotide Polymerase Inhibitors

- GS-7977 / PSI-7977: Acquired by Gilead from Pharmasset, this agent is drawing significant attention for its reported superior efficacy and its potential to reach the market as a component of one of the first all-oral, interferon-free regimens. Recently reported data of GS-7977 in combination with ribavirin indicated nearly 90% SVR in treatment naïve patients. Further clinical studies have been conducted with GS-7977 and BMS's 790052 and indicate this could be a game-changing regimen should they both become approved.

Non-Nucleoside Polymerase Inhibitors

- BI-207127: A second leading product for Boehringer Ingelheim, 207127 is demonstrating efficacy superior to currently available protease inhibitor regimens, when used in combination with BI's protease inhibitor 201335, with and without ribavirin.

- ANA-598 (setrobuvir): Acquired by Roche from Anadys, data from phase IIb clinical studies was positive, demonstrating over 70% SVR attained with ANA-598 in combination with PEG-IFN+RBV. Importantly, ANA-598 delivered equivalent SVR rates in partial responders and relapsed HCV patients as in treatment naïve patients (where partial responders and relapsers have historically had significantly lower SVR rates than naïve).
- GS-9190 (tegobuvir): Discovered and studied by Gilead Sciences, GS-9190 initiated clinical trials in combination with several agents. Its study in combination with PEG-IFN+RBV and one of their protease inhibitors was amended following serious adverse events in patients using that regimen, but its study in combination with Gilead's NS5A 5885 continued and appears to be delivering promising results.
- VX-222: Vertex's experience in this category with Incivek provides an excellent platform for Vertex to continue its leadership in HCV. Vertex's lead polymerase inhibitor VX-222, currently in phase IIb studies in combination with Incivek and PEG-IFN+RBV, delivered initial results of nearly 90% SVR in genotype 1 naïve and relapsed HCV patients.

NS5A Inhibitors

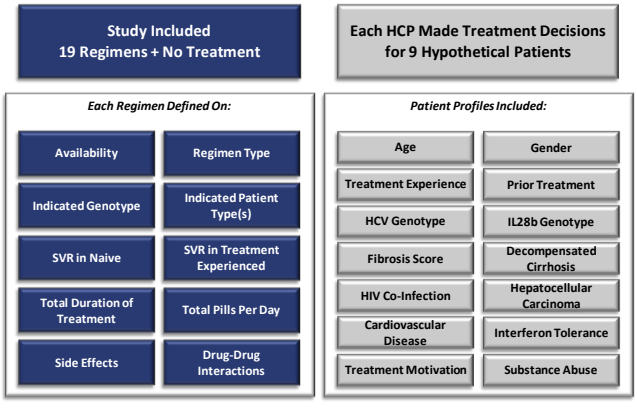
- BMS-790052 (daclatasvir): Despite having to halt their development of BMS-094 (INX-189) due to toxicity issues, Bristol-Myers Squibb remains a prominent player in the HCV market with 790052. Studied in conjunction with both BMS's protease inhibitor 650032 as well as Gilead's nuc 7977, with or without PEG-IFN+RBV, BMS has the opportunity to position this agent as a key component of regimens including or excluding interferon.
- GS-5885: Also being developed by Gilead Sciences, GS-5885 is being studied in a number of combinations including Gilead's non-nuc polymerase GS-9190, with or without its protease inhibitor GS-9451, and with or without ribavirin and/or pegylated interferon. The wide variety of combinations being evaluated sets the stage for this NS5A to play a key role in a variety of potential future treatment regimens.

Future Treatment Regimens & Warehousing

Due to the ongoing upheaval of the HCV market, there is a lot of uncertainty around what the treatment of HCV will look like over the next few years. Which products will be approved, what their efficacy and safety profiles are, and when they will become available are all key factors in how and when they will be used in the treatment algorithm. In the past, the expectation was that regimens would be incremental, with new classes of products being added on to existing treatment regimens as they become available. Now, however, there is the potential for an all-oral, all-DAA, interferon-free and potentially ribavirin-free regimen to become available in the same general timeframe as quadruple therapy with a protease inhibitor, interferon, ribavirin, and a new DAA.

Many physicians treating HCV are aware of these products on the horizon, but may not be willing to wait an extended period of time to treat certain patients. As products progress through clinical trials, and the timeframe to anticipated approval shortens, there could be a dramatic shift toward deferring treatment to wait for more advantageous treatment options. ***How many patients get warehoused and at what point they will begin to warehouse is a topic industry analysts are speculating about every day.*** It is sure to become a key factor in treatment decisions and have significant impact on product adoption and ongoing use.

Methodology: Patient-Based Discrete Choice



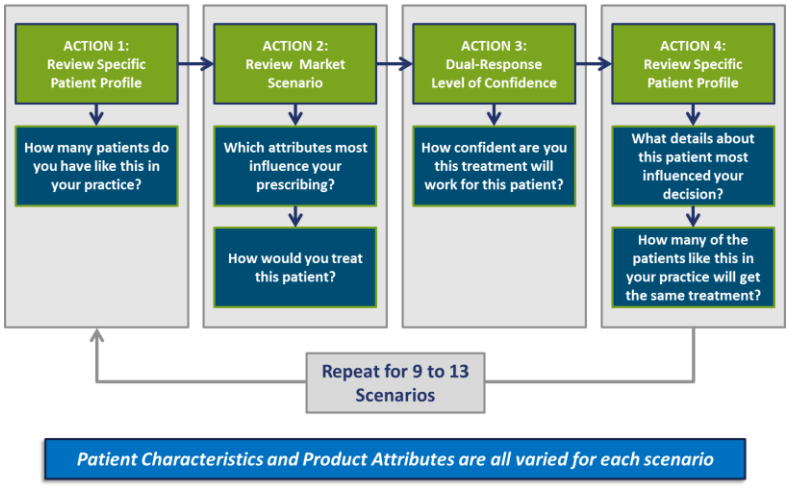
A patient-based discrete choice task was used to systematically test the likely use of a wide range of new HCV products. Each scenario presented both patient and product profiles. The task for participating physicians was simply to specify how they would treat the patient profiled with the treatment options provided. We tested 8 hypothetical patients with each respondent and the key design feature was that both product attributes and patient characteristics vary across scenarios. Prescribers could choose from 19 existing and emerging treatment regimens plus the option not to treat. Each emerging treatment option varied across ten attributes (see figure to left). The details of the patient varied across 14 attributes. Note that each of these details was established in extensive pretest as a critical factor in treatment decisions for HCV.

Task Flow

Our patient-based discrete choice task is customized for each engagement to best address the business issues at hand. In general it proceeds thru four steps.

- First respondents are asked to evaluate an individual hypothetical patient and indicate how many similar patients they have in their practice.
- Then respondents evaluate the treatments available in each scenario and indicate how they would treat the specific patient profiled. This second action is the discrete choice task and is what drives our analysis.
- Respondents are then asked to indicate their level on confidence (i.e., how confident are you that the treatment you specified will work for this patient?). This third action allows us to employ a "dual response" method and allows us to better control for overstatement.

Illustration of Patient-Based Discrete-Choice Task



- Finally, respondents are to specify how many of the patients in their practice that are similar to the patient being profiled they would expect to give the same treatment. In addition to providing volume estimates, the first and fourth actions also provide an additional way to control for overstatement.

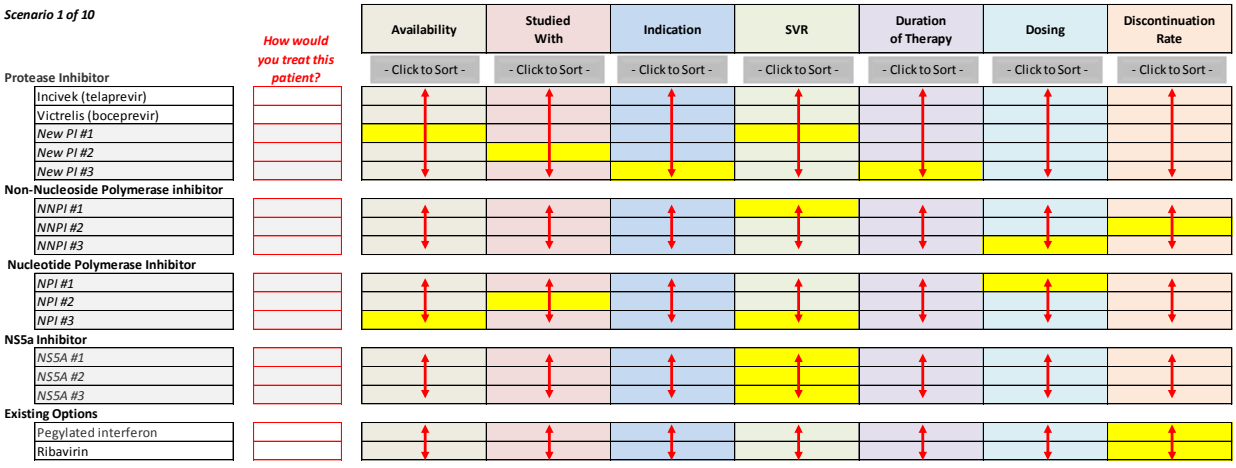
Managing a Significant Number of New Products and Engaging Respondents

The biggest challenge with simultaneously testing a large number of new products is presenting the information we want to test in a way that engages respondents. We have a simple, but effective tactic for meeting this challenge – *we make the information we present interactive and then make the respondent interact with it.*

The figure below illustrated how we tested the array of potential new HCV treatments[5] and the key features include:

- The presentation put products in the rows and attributes in the columns. This orientation is a 90-degree rotation of what is typically done and allowed the functions listed below
- The specific details for each regimen in each row varied from scenario to scenario

Illustration of Recommended Product Profiles for Choice Task



[5] A demonstration of our choice task can be provided.

- Respondents interacted with each scenario in two ways:

  First, they had to click to highlight the most important feature or features for each alternative (illustrated with the yellow cells). This was recorded and used as an indication of stated importance.

  Second, they had to sort each scenario at least once. The sort function moved the best regimen to the top of the grid based on that attribute selected (illustrated with the red arrows). Multiple sorts (i.e., nested) were allowed, making it quick and easy for respondents to find the best regimen based on that attributes that mattered most. This information was also be recorded and used as an indication of stated importance.

- Warehousing was operationalized as availability, which was treated as a product attribute (i.e., currently available, available in 6 months, available in 12 months, or available in 2 years). Warehouse was explicitly incorporated into the task by dividing the discrete choice into two parts:

  The first part of each scenario presented just the regimens with availability equal to "currently available". Respondents had to highlight and sort and then indicate how they would treat the patient profiled. Again, their choices were limited to only regimens defined as currently available in that scenario or no treatment.

  The second part displayed their initial decision (from part 1) at the top of the screen followed by all the future regimens, available at various intervals. Again they had to highlight and sort to find the best alternative. Then they had to decide if they would stick with their initial decision or wait (i.e., warehouse) for a regiment that would be available in the future before treating the patient profiled.

Analytics: Design, Estimation, and Simulation

The essential detail to know about our approach to analytics is that we are transparent. While we are professional with our execution and delivery, there is no black box. Expertise is difficult to appreciate and hard to trust, so we are willing to clarify every aspect of our analytics. To illustrate, here are several example specific to this case study.

Design – A Fundamentally Different Orientation

Fractional factorial designs (FFDs) have been used to systematically study phenomena of interest for more than 200 years and have been the basis of conjoint and discrete choice experiments since their inception. FFDs allow us to test a carefully selected subset combination and then use inferential statistics to estimate effects for all the possible combinations. The conventional orientation to constructing designs is to establish specific number of "cards" (i.e., scenarios) and the collect a specific number of observations for each card, typically 20 to 30. So in a study like this one, the scope of the study might require something like 200 cards. With a sample of 300 prescribers, each seeing 8 cards, we would be able to collect 2400 observation, which would translate into only 12 observations per card. The typical response to this situation is to reduce the scope of the study, thereby reducing the number of cards needed and increasing the number observations possible for each card.

We take a fundamentally different approach that focuses on observations per design points instead observations per card. The estimation process happens for each level of each attribute, where we get a separate utility for each level. We build our designs with that in mind, where we are focused on maximizing the number of observations we have for each level of each attribute. To best accomplish that, we need to pair each level of each attribute as often as possible with every other level of every other attribute. So instead of something like 200 cards, we test as many cards as possible. With a sample of 300, each seeing 8 scenarios, we test 2400 unique cards. So for any one attribute with 3 levels, for example, we collect 800 observations, which is a robust sample by any standard.

We do have a limit to what we can test. Instead of limiting the number of attributes to test, we limit the number of levels. The reason for this limit is quite specific. Since we are trying to cross every level of every attribute with every level of every other attribute, we minimally want each participant to see each level of each attribute at least twice. Since we know we can typically only test eight scenarios in a 45 minute survey, we need to limit each attribute to no more than four levels (i.e., 8/4=2). An attribute with five levels requires 10 scenarios, six levels requires 12 scenarios.

Estimation – The War is Over, the Bayesian Won

Over the last 20 years a heated debate has transpired over the best way to estimate utilities for statistical models. The debate has had two fronts. The first is Frequentist vs. Bayesian, where classic statistical thinking about probability has been challenged by the fundament contribution of Bayes Rule and the notion of conditional probabilities (i.e., priors). ***The extensive debate boils down to Frequentists saying, "That's cheating." While Bayesians say, "Why wouldn't you?"*** Despite the academic argument[6], Bayesian estimation has won out in practice because it simply does a better job. Utilities derived with Bayesian methods, specifically hierarchal Bayes (HB), typically generate substantially better fit statistics. This is critically important because before we make any inferences, we want to make sure the utilities we have derived do the best possible job of accounting for the patterns in the data we have collected.

The second front of the debate stems from the first, but is equally important. Generally speaking, there are two ways to estimate utilities, either at the ***aggregate-level***, where one set of utilities is estimated across an entire sample, or at the ***individual-level***, where a separate set of utilities is estimated for each person in the sample. Like with taking a Bayesian orientation, it is well established the most practical approach to estimating utilities is at the individual-level because it does the best job of accounting for the patterns in data (i.e., heterogeneity).

In addition, individual-level HB estimation provides several additional benefits that add real value to the analysis. First, separate utilities for each participant make it very easy to create ad hoc groups. No re-estimation is needed, we can combine individuals as needed into any groups we find useful. Second, at the individual-level we have a distribution of estimates. We can take an average as the overall predicted estimate, but we can also examine the distribution for patterns to determine if it is skewed, or multi-modal, or if there is something unique about estimates at each end of the distribution. Third, because we have a distribution we can estimate confidence interval, which is by no means a trivial point. We always stress that estimates from a model are just that and need to be considered carefully. It is always best to put confidence limits around estimates so we can demonstrate a level of uncertainty.

Simulation – Two Steps to Success

All of our simulators are delivered in Excel so they are in a format that is easily incorporated into other activity streams, most notably a broader forecast. We divide our simulators into two conceptual pieces, the backend and the frontend and our process (see below) includes a separate step to review the details of each piece.

The ***backend*** review starts with a review of the effects in the raw data before the estimation. These are simply average effects for each level of each attribute. We then compare those directly to the estimated effects from our models to see how well we are accounting for the patterns in the raw data. We then review how each model is set up in terms of both inputs and outputs, decide if calibration is needed, and determine the level of adjustment for overstatement needed. This backend review is a critical step to make the analysis transparent and provide an opportunity to make modification. All models are based on assumptions and assumptions change.

The ***frontend*** review is about making the model functional and maximally usable. Again we are focused on both inputs and outputs, but this time it is about making sure the simulation tool is set up to be most compatible with each client's needs. We plan in detail how each simulator will function. We share the plan with clients in advance and then allow for changes and enhancements once clients have had the opportunity to use tool and discover way to make it even more useful[7].

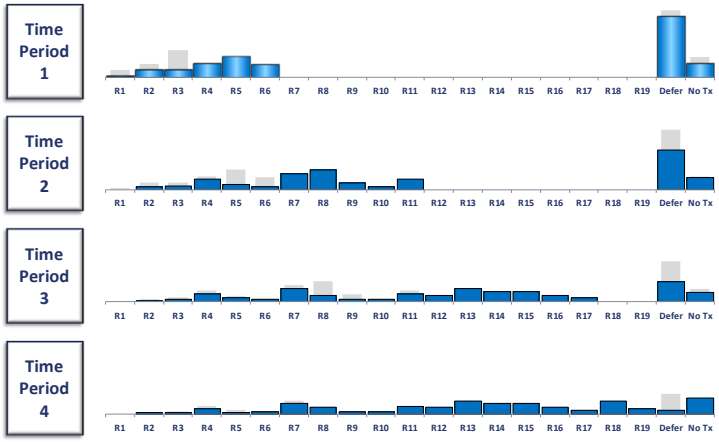
Analysis & Reporting

Sophisticated analytics and simulation amount to very little if we fail to answer the business questions under consideration. The central focus of this case was an assessment of warehousing. We also wanted to understand drivers of adoption from both a stated and a derived perspective. Finally, we followed thru on adding the perspective of identifying the optimal patient for key regimens. For each set of finding our reporting was focused on establishing concrete conclusion and articulating clear implications.

[6] This statement vastly over simplifies the debate to make the contrast salient.
[7] A demonstration simulator can be provided.

Warehouse

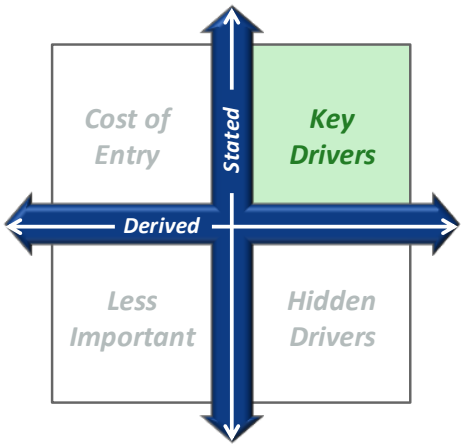
The structure of our task, analysis, and simulation translated directly into our findings. Using specific time periods we model a range of scenarios to demonstrate how deferment (i.e., warehousing) would change over time[8].



Several regimens entering the market in Time Periods 1 and 2 were of particular interest. The chart to the right clearly shows the impact of later entries on both earlier entries and deferment, where the most salient features of Time Period 4 is a very low deferment rate and share distributed towards later entries.

The implications of this were clear cut. Regimens entering in Time Periods 1 and 2 should expect an experience similar to Incivek, a meaningful, but short-lived, success. The launch strategy was set up to reflect this accelerated product life cycle.

Stated vs. Derived Importance



Primary market research in our industry has a long history of demonstrating that what prescribers say does not necessarily reflect what they do. As a result we have always been interested in a comparing stated and derived importance. Our approach provides very robust data for this assessment[9]. We have the truest possible measure of ***derived importance*** based on an experimental design that isolates the independent effect of each attribute. Our measure of ***stated importance*** is simply and unobtrusive. It is the highlighting and sort data collect from our tasks that we used to engage participants. This assessment was done for both specific product by product attribute and for patient characteristic.

The implications of this analysis are very meaningful. Key Drivers (high on both stated and derived) and Hidden Drivers (high on derived but low on stated) were of particular interest because they provide the starting point for positioning and messaging.

Finding an Initial Patient Target

In our experience, when considering a new treatment option nothing helps a prescriber more than establishing exactly which of their patients are the best candidates. Without help they are uncertain and then typically push a new treatment to a later line of therapy, leaving it an option of last resort.

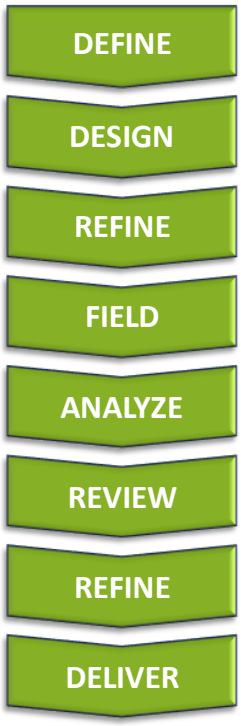
Ideal initial patient for Regimen 5 clearly emerges
Estimated share is 55% relative to a TPP share of 12%

	Category 1		Category 2			Category 3						Category 4	
	ATT 1	ATT 2	ATT 3	ATT 4	ATT 5	ATT 6	ATT 7	ATT 8	ATT 9	ATT 10	ATT 11	ATT 12	ATT 13
Ideal Patient	Level 2	Level 1	Level 2	Level 4	?	Level 1	Level 1	Level 1	Level 2	Level 1	Level 3	Level 1	Level 3
Level 1	5%	57%	22%	6%	28%	68%	92%	98%	41%	67%	22%	90%	17%
Level 2	85%	26%	78%	15%	31%	32%	8%	2%	59%	22%	21%	9%	34%
Level 3	1%	13%	0%	22%	21%	0%	0%	0%	0%	4%	57%	1%	48%
Level 4	9%	5%	0%	56%	20%	0%	0%	0%	0%	7%	0%	0%	0%

Our approach allows us to systematically explore which combination of patient characteristics prompts the most use for any specific treatment. Demonstrating that share for a patient with a specific constellation of characteristics is two or three or five times greater provides a concrete and compelling reference point that can be used to help prescribers understand where to start. While a product's label may limit what can actually be said, identifying the ideal patient is an extremely valuable exercise that informs sales planning and tactics.

[8] Note that we could also attribute the deferment to specific regimens.
[9] See Tim O'Rourke's 2009 Presentation on this topic at the AMA: Advanced Research Technique Forum.

LOGISTICS & TIMING



A sophisticated approach is only as good as its execution and there is no substitute for experience when it comes to execution. The Difference Engine™ has been at the center of our practice since 2008. We have literally executed dozens and dozens of these projects. We have refined our process to the point where we can be both proactive and flexible with respect to timing and deliverables.

Starting with an in-person kickoff we define the unique scope of each project, establish hypotheses, and align on key deliverables. We then design study materials, establish how product and patient profiles will be defined (attributes and levels), and create a custom task and survey to functionality to address the study's scope. Working from a programmed survey, we conduct extensive pretesting, either in-person or via a web-based meeting, to literally watch how participants answer. This refinement process amounts to an efficient pilot test. Once we have established the best possible survey, we field quickly and efficiently, recruiting target HCPs via wide array of trusted partnerships. The analysis and final deliverables are facilitated by an initial review process that allows for refinement. The final deliverables consist of both an Excel-based simulator and detailed report that both thoroughly documents the study and makes key findings accessible with clear conclusions and implications.

The typical timing of a project like this is 12 weeks, we spend 3 to 4 weeks preparing for fielding, 2 to 4 weeks fielding, and 3 to 4 weeks analyzing and reporting. The process can be accelerated as needed[10], but timing is often dependent on client access and availability.

Our process relies on partnership and collaboration. No one can know our client's business better than our client. We need your help to succeed.

CONCLUSIONS

Our philosophy regarding predicting new product adoption can be summarized in one word – parsimonious. We keep it a simple as possible, but no simpler. Unfortunately our industry has matured to the point that every new product, even legitimate improvements to the standard of care, faces substantial challenges. Any assessment that fails to account for the scope of these challenges is risking an error of omission. We are also strongly oriented to the fundamental nature of decision making emerging being a dual-process (i.e., System 1 and System 2) and believe that any assessment of decision making must have as its foundation a careful evaluation of deliberate decisions. We believe this is particularly relevant when the decisions under consideration are treatment decisions.

To accomplish a necessary scope we rely on realism and engagement, along with an orientation to developing study designs that provide substantially greater statistical power. In the process we put a patient-based discrete choice task at the center of our studies. Our method delivers on estimating both product adoption and key drivers. It also provides an important additional benefit. Since we also include hypothetical patients in our assessment, we can provide the additional value identifying initial and ideal patient targets.

Over years we have developed a host of custom solutions, the latest of which is a clear and compelling approach to modeling the impact of warehousing in hyper-competitive categories such HCV. Most of all, our expertise and experience allow us to work quickly, efficiently and transparently to provide business insights that prompt meaningful action.

[10] Notably, in 2010 we executed an 11 country study using this method in 9 weeks.

HEALOGIX

Healogix is a global, research-based strategic consultancy specializing in the healthcare industry. Built on a business model leveraging deep, diverse senior executive experience, Healogix delivers comprehensive insights and recommendations to clients that go beyond simply reporting results.

We execute both qualitative and quantitative engagements in highly specialized therapeutic areas, pulling insights together into a cohesive story. Each project is staffed with high-level research and industry professionals, utilizing the optimal methodology to derive the answers needed within budget.

Difference Engine™ from Healogix helps you understand how and for whom physicians will prescribe your product, enabling you to accelerate adoption and correct mistakes before the band positioning is solidified.

We have a proven track record of delivering mission-critical results and recommendations that help our clients develop strategies and achieve business objectives.

For further information about Healogix or Difference Engine ™, please contact:

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