Adaptive Models in Quantitative Research

Presented to:

QWAFAFEW – NYC Chapter

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A quant's journey into the pharma sector

Areas of exploration

- Drug-approval processes
- Formulary
- SMC (Scottish Medicines Consortium)
- HTA (Health technology assessment)
- OR/EMB
- QUALYs (Quality-adjusted life years)

Purpose

- Collect non-typical data
- Model committee-based decision-making
- Interpret findings and determine how, when and where to use it

Background: Original presentation of research

An Exploration of the Use of Risk Management in HTA

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President, ETC Inc. and Director, CIBC World Markets

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Country Manager for Scotland & Northern Ireland, Pfizer UK

‘Decision guidance’

- Motivation for quantitative work on the topic
- Overview of the drug approval process
- Collecting the data
- The ‘Decision Guidance’ Model
- The results
- The potential uses of the model

And last, but not least . . .

- Is there anything that can be utilized in finance?

Pharma: A sector facing many challenges

- Regulatory demands

  Both approval requirements (clinical & HTA) have become tougher in the past

- Clinical trials

  The costs of trials is skyrocketing

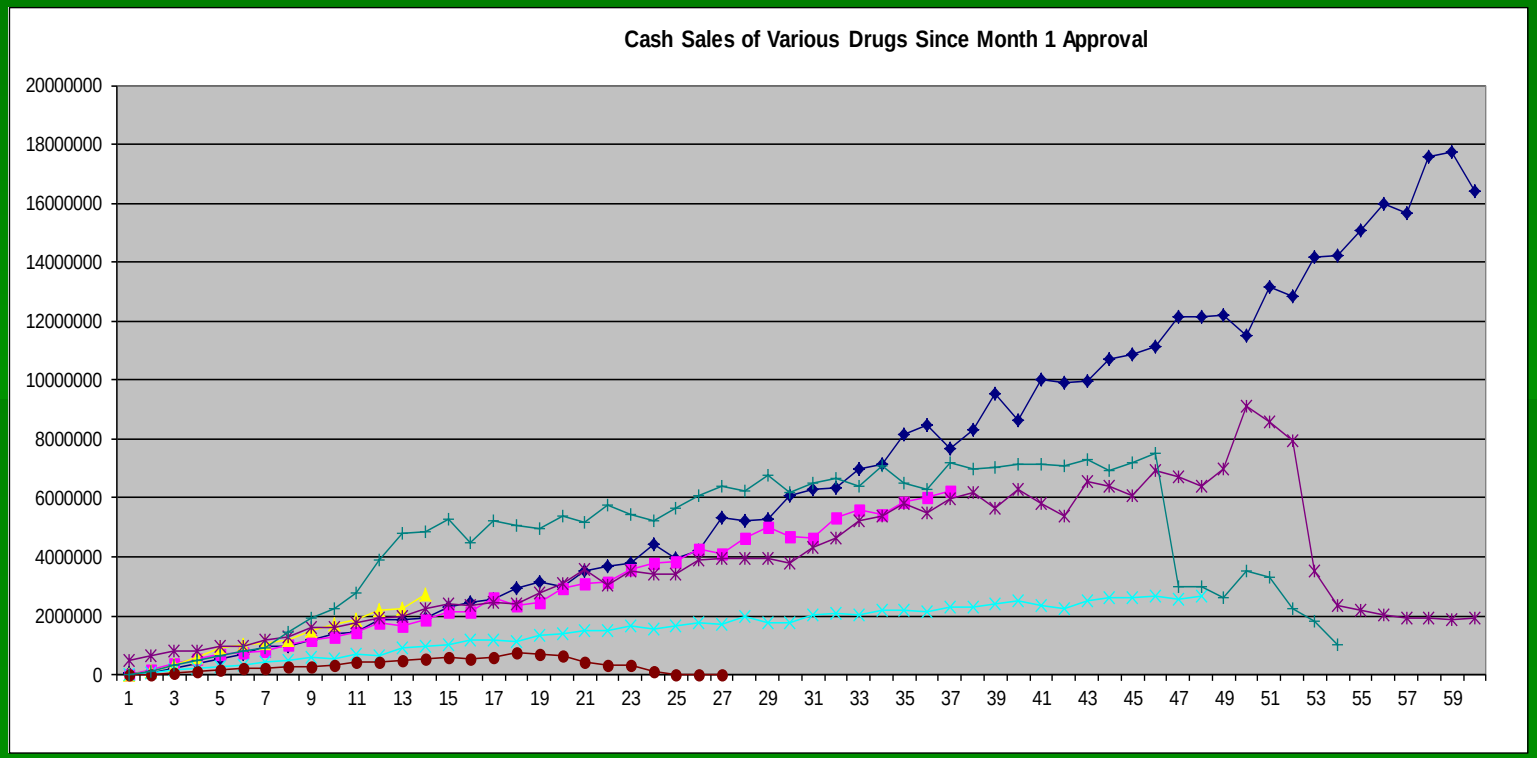
- Budgetary pressures

  The need for fiscal reform conflicts with the growing need for spending on new drugs

➡ Quant analysis can uncover solutions for these challenges!

New drugs: The economic challenge

Revenues don't start until ALL approvals are done!



➡ Better management of approval process can improve $$!

Decision guidance: Improving the odds

- Goal

  Develop an analytical method with the potential to increase a product's lifecycle revenue by ensuring the optimum chance of a successful *Scottish Medicines Consortium* submission outcome

- Methodology

  Advanced modeling techniques are used to capitalize on the informational value offered by quantitative and qualitative data and to ensure that relevant influential data is collected in a consistent, comprehensive and objective manner

- Benefit

  Indirectly identify value-added trade-offs between elements of the submission, facilitating effective direction and allocation of resources

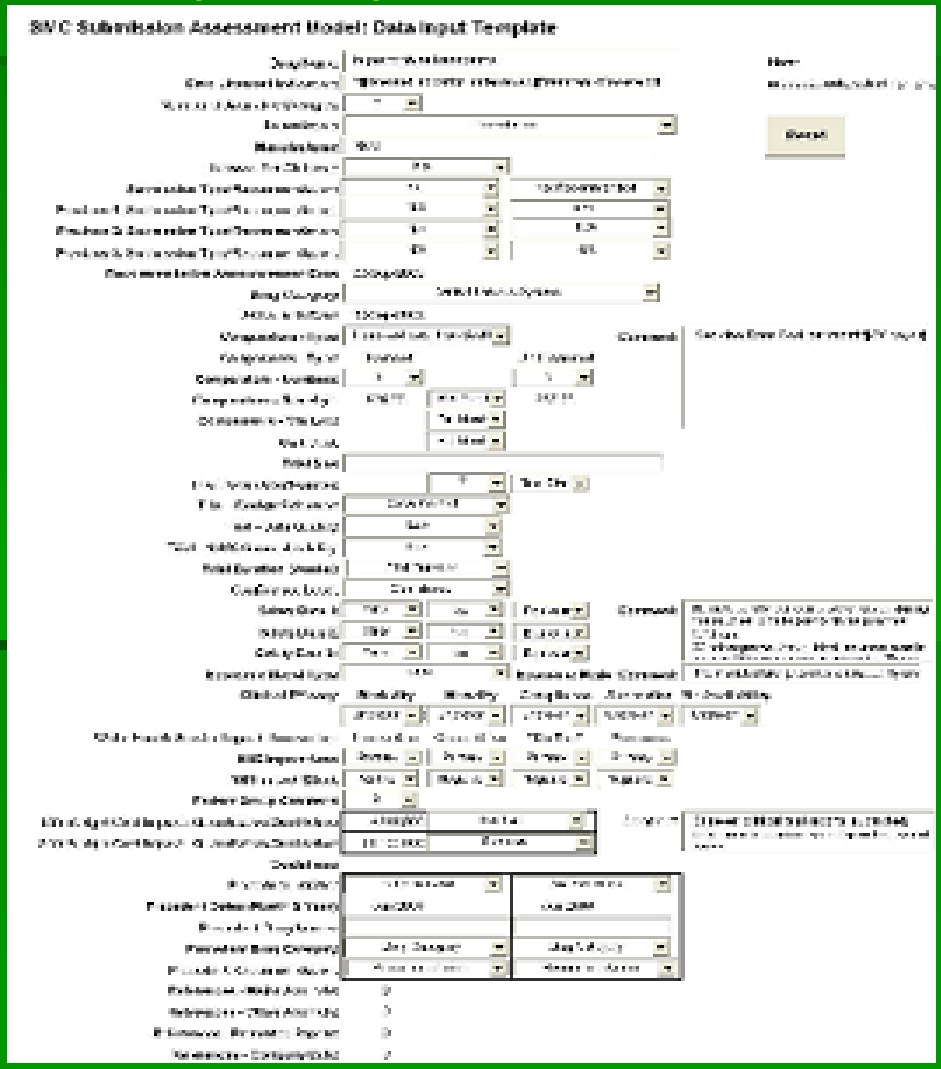
Decision guidance: Unique features

- Top-to-bottom design to minimize ‘entropy’/uncertainty
- Simultaneous modeling of all 12 drug categories
- Qualitatively-based input template for input consistency
- Both demand and supply factors are included
- Two-dimensional ensemble structure for both input factors and output decision outcomes
- Flagging of inconsistencies – i.e., the model tells you when it’s confused!
-

Data collection: Template design is crucial

- 75 input variables
  Most are discrete and either ordinal (high/med/low) or categorical (drug type, manufacturer)
- 225 resulting variables
  via combinations (before applying dimension reduction techniques)
- Expertise required for input
  We tested >12 people with varying degrees of domain expertise and found < 1% variation in input values

Data input template



Data analysis: Collection methodology

Variables defined according to SMC decision criteria

- Hard data – comparators, formulations, budgets
- Soft data – wider health service impact, trials

Subjective variables defined in terms of attributes

- E.g., innovative, competitive, ‘me too’, resources attributes within wider health service impact

Attributes defined in terms of qualitative categories

- E.g., positive/neutral/negative, high/moderate/low

An easy-to-use, pre-defined template

providing comprehensive, consistent and objective data

Data analysis: Approval factors

Conventional hard data

- Formulations
- clinical efficiency
- Safety
- Price (absolute and relative to comparators)
- Results versus competitor trials
- Full or abbreviated submission
- Budgets/political agendas

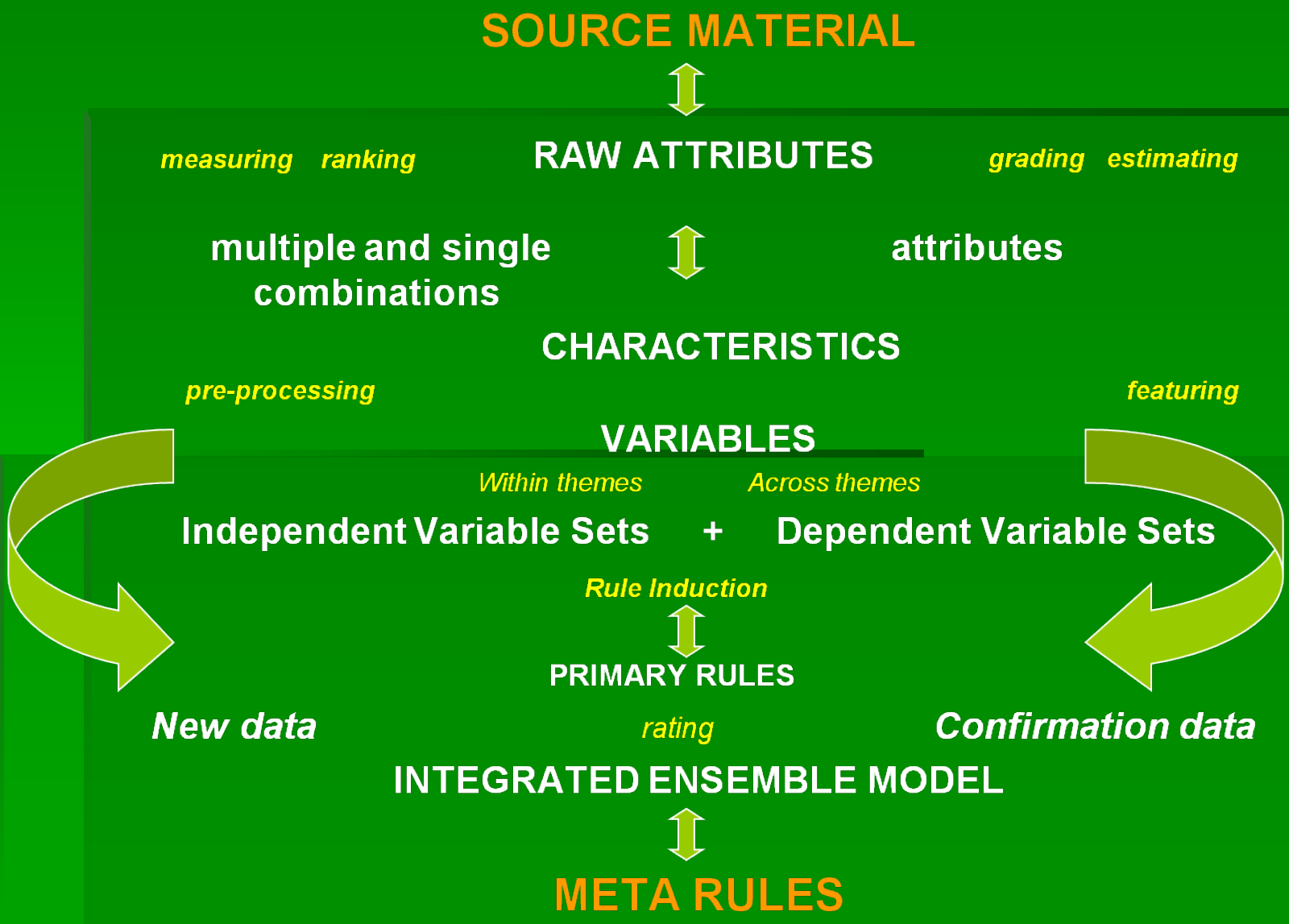
Unconventional soft data

- Disease area
- Patient group pressure
- Political imperative / media pressure
- Innovation
- Company credibility / litigation experience
- Assessor panel makeup
- Workload

Data analysis: Modeling methodology

- Based on a 40-year old economic theory that decomposes variables into their attributes
- Utilizes advances in classification, in combination with math from information theory
- Replaces classical linear approaches with ones based on non-linear dynamical systems
- Uses not one, but three techniques based on different machine learning / computational intelligence
- Results are excellent: Hybrid method maps complex input spaces to classified outcomes, such as the ‘Yes/No’ of Health Technology Assessment (HTA) decisions

Overview of the model



Data analysis: Modeling methodology

Two sets of models are constructed

- Baseline model utilizes only annually updated data set
- Contemporaneous model utilizes additional data as available

Model design replicates expected production process

- Each month's new data serves as out-of-sample test forecast against existing baseline and contemporaneous models
- Contemporaneous model re-estimated each month

Reconciliation of results variances

- Baseline model results to forecasts
- Contemporaneous model results to forecasts
- Baseline to contemporaneous models

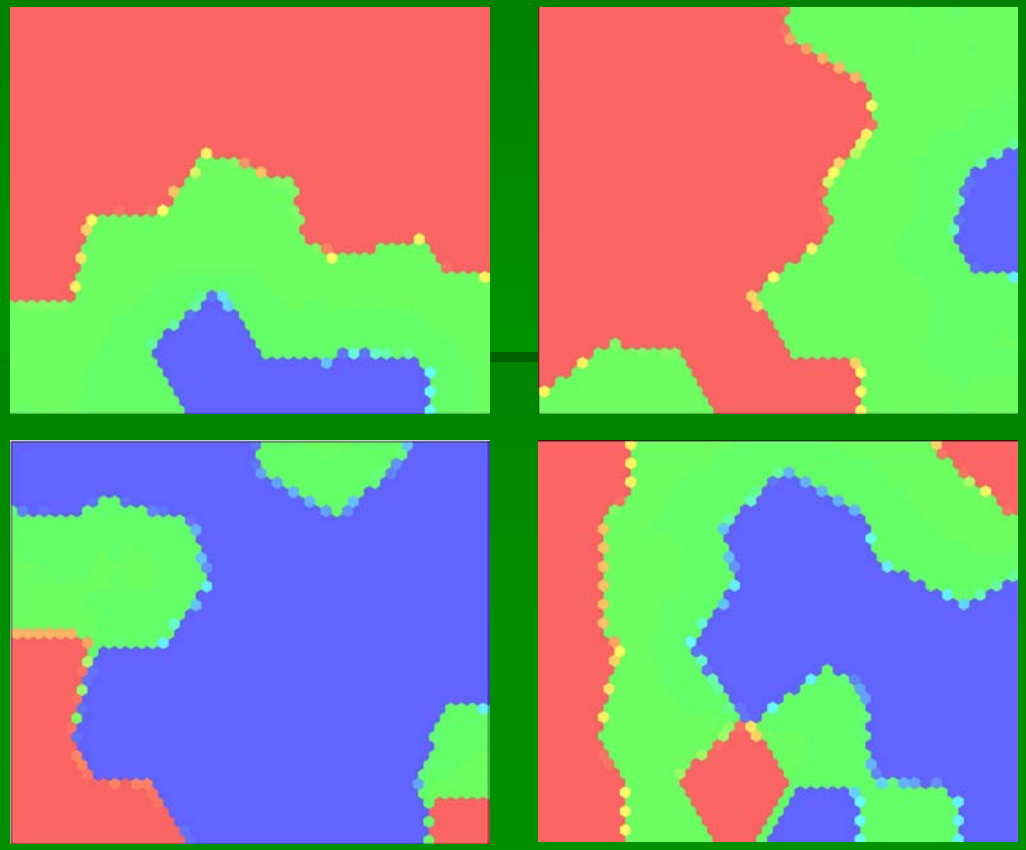
Data analysis: An illustration

Goal: Determine whether the raw data was consistent with our theory

- We examined just one variable and its four attributes
- We *did not* manipulate the data to maximize the information extracted
- We *did* stratify the outcomes to model ‘least’, ‘medium’ and ‘most’ successful outcomes

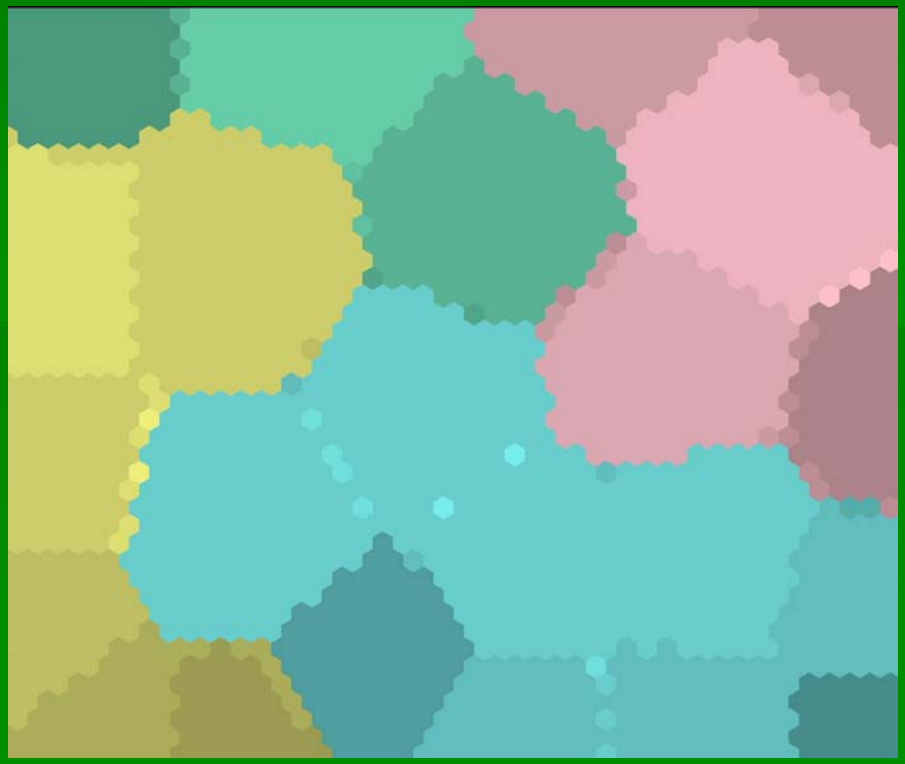
Data analysis: Four variable attributes

Four attributes of a variable are presented in the same space



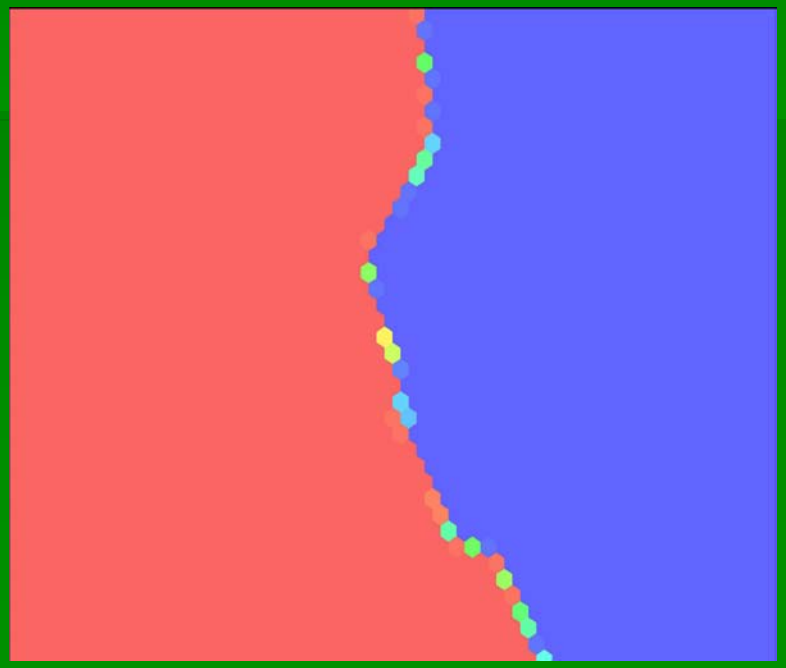
Data analysis: One very complex space!

The result is complex



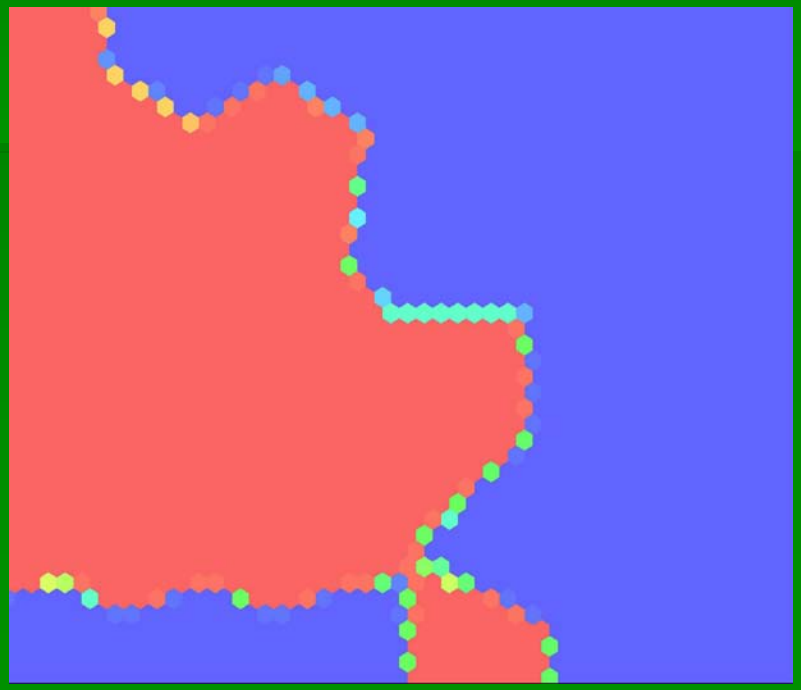
Data analysis: An example that's apparent

Can this least successful outcome space be explained? Fairly apparent!



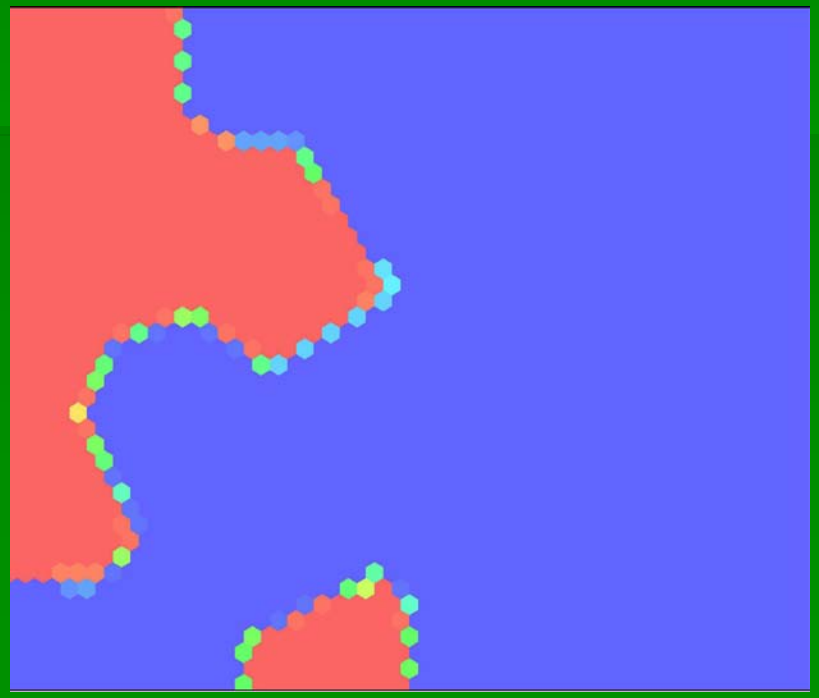
Data analysis: A not-so-apparent example

Can this medium successful outcome space be explained? - Not apparent!

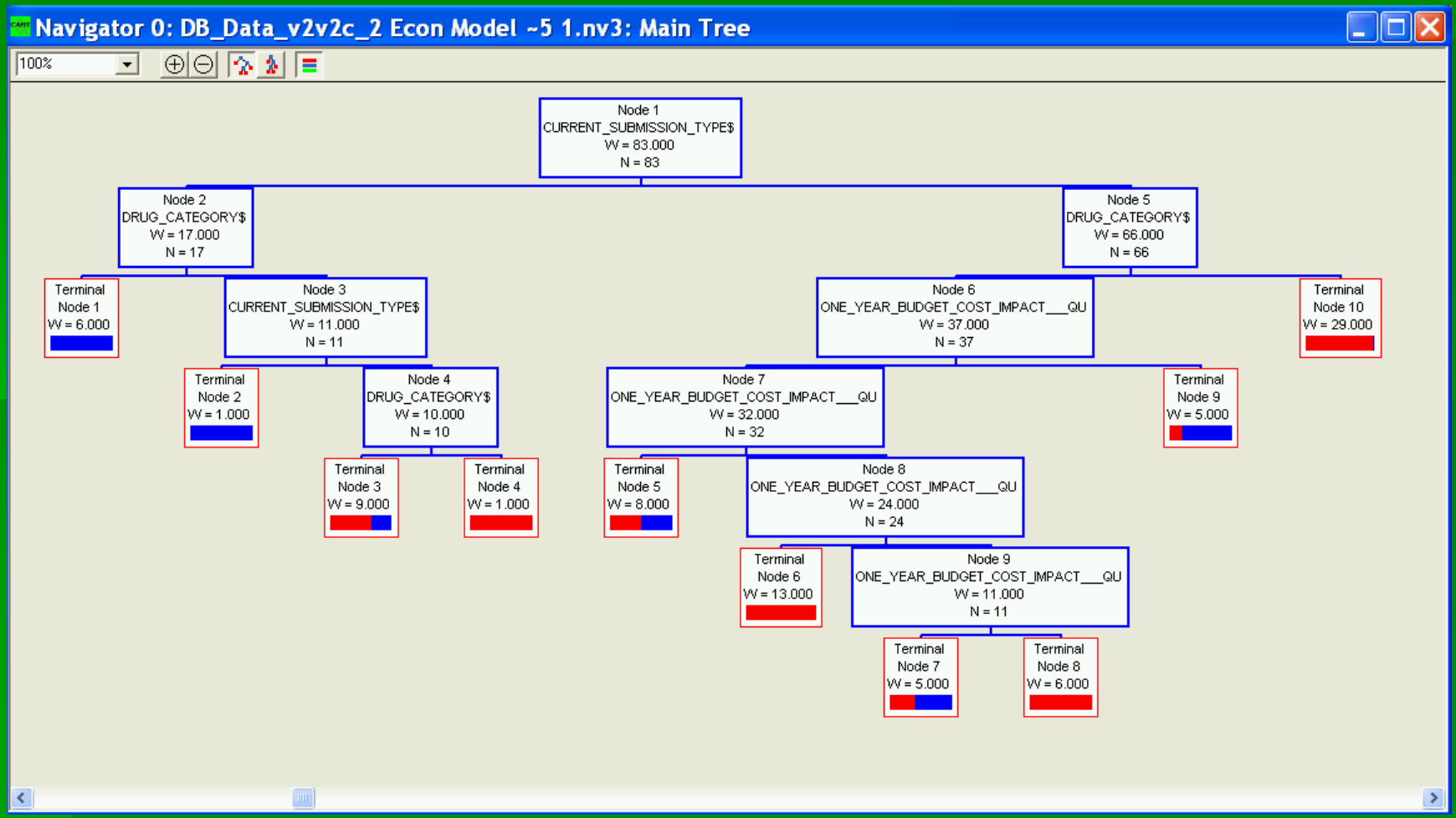


Data analysis: Not at all apparent!

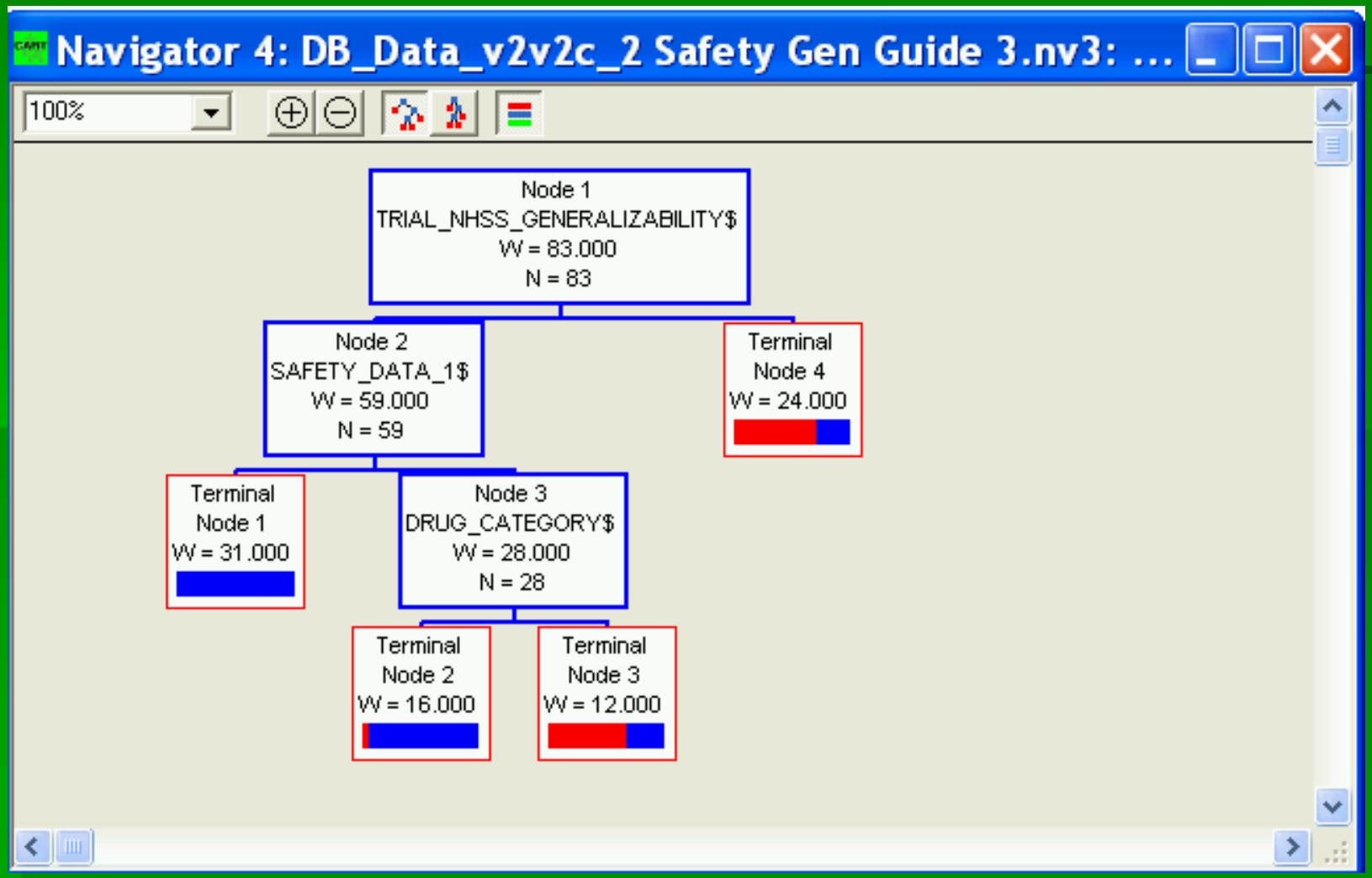
Can this most successful outcome space be explained? - Not apparent at all!



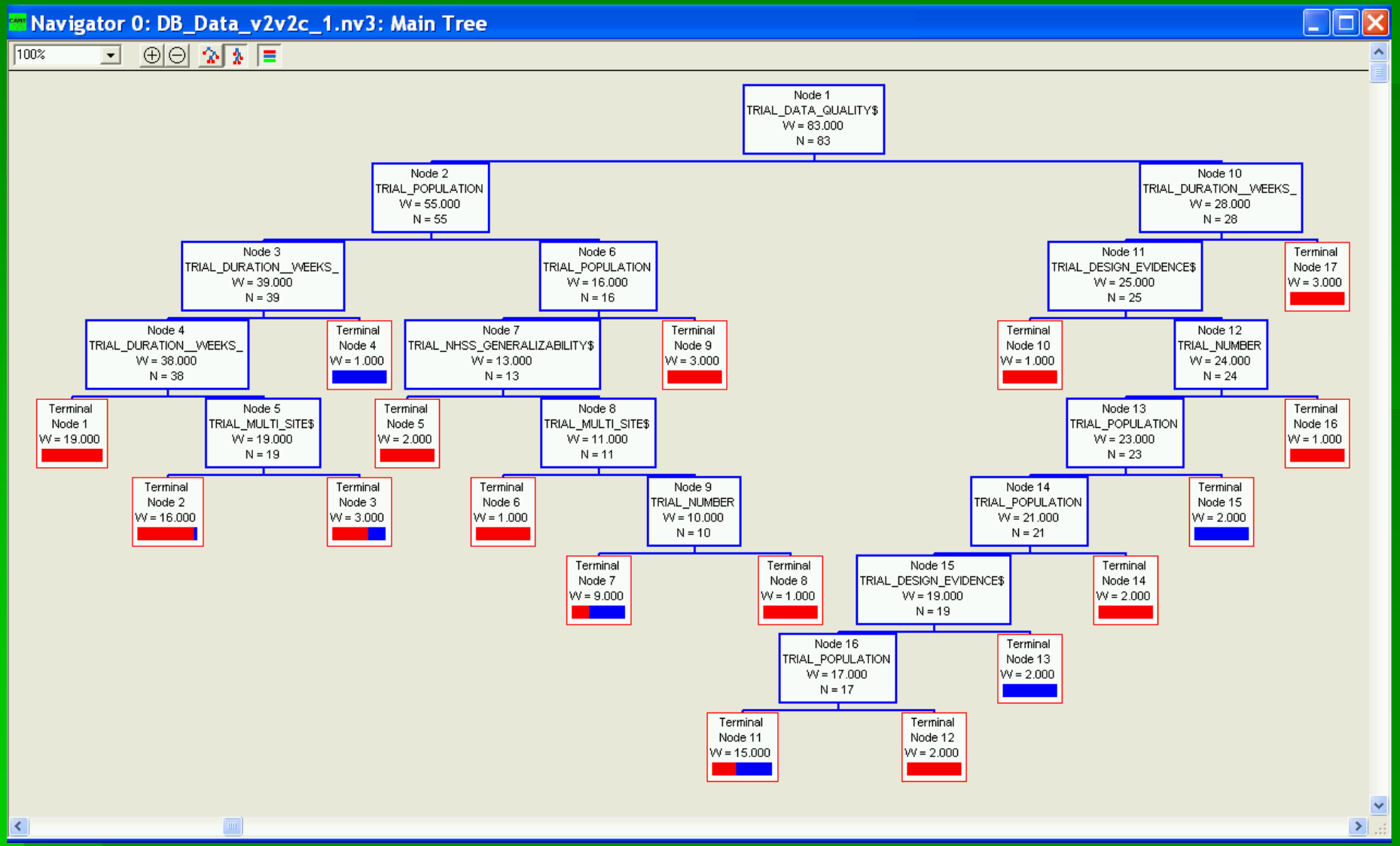
‘Economic Model’ theme decision tree



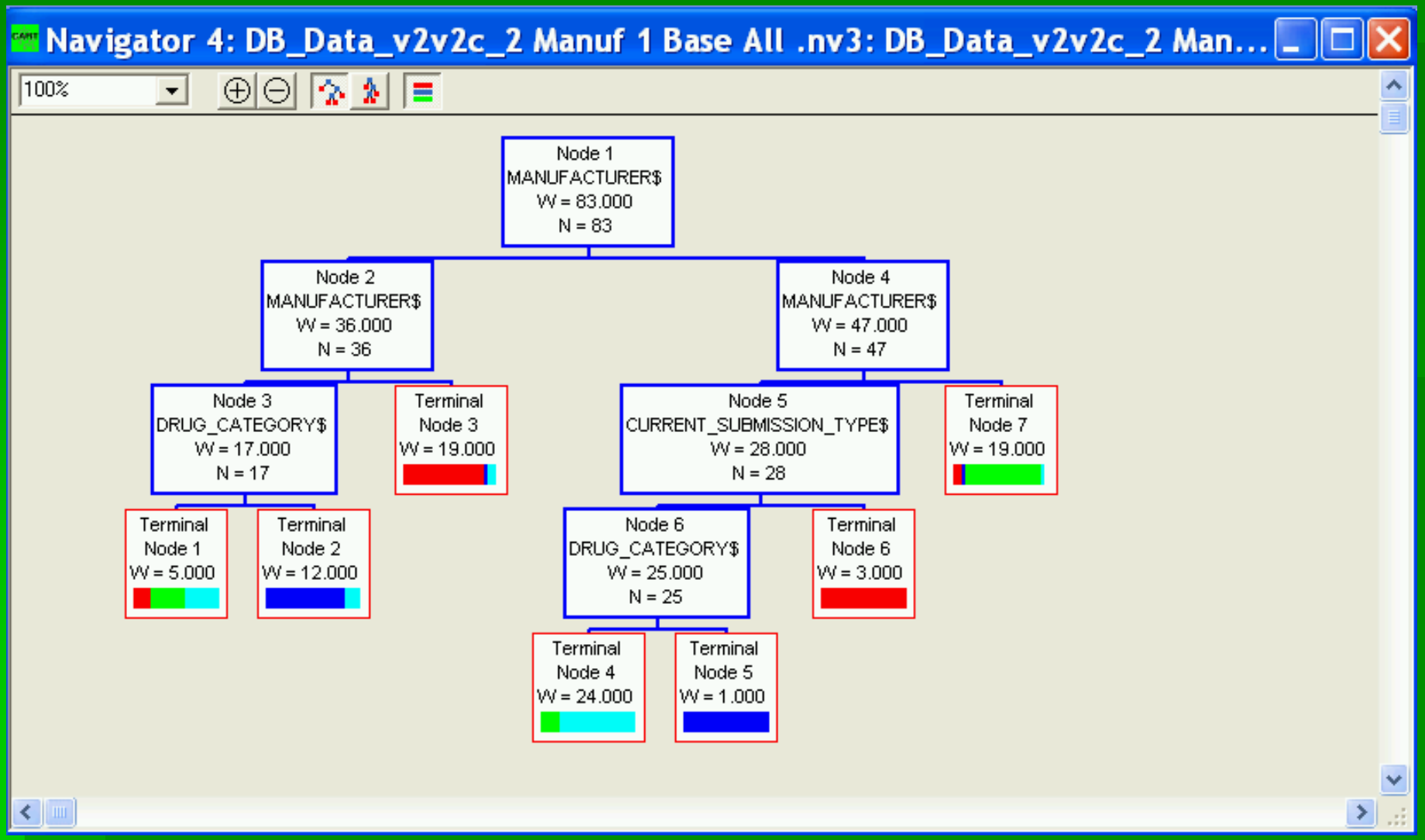
‘Safety’ theme decision tree



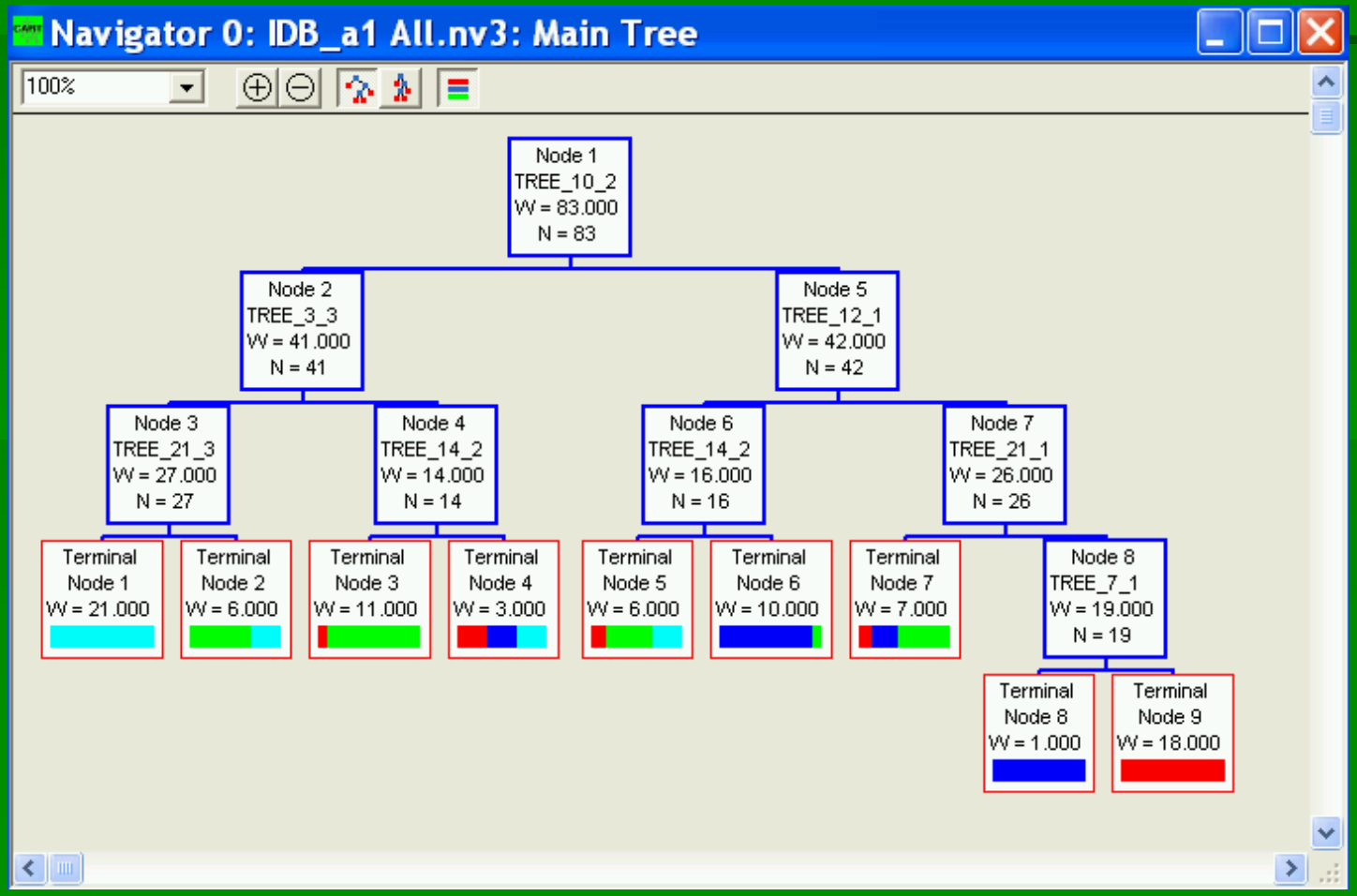
‘Trials’ theme decision tree



‘Manufacturers’ theme decision tree



‘Cross-Theme/Ensemble’ decision tree



HTA ‘Decision Guidance’: The results

	In-sample		Out-of-sample	
Exactly correct	57	69%	17	59%
Partially correct	11	3%	5	17%
Not correct	6	7%	5	17%
Inconsistent	9	11%	2	7%
Totals	83		29	

Micro-level inferences

Improves submission tactics

Must do's:

- Non-'elite' drugs must include a favourable cost model plus a demonstrable cost saving
- If not an 'elite' drug, trial sites must include Scotland, UK and/or North America
- To minimize chance of failure, European trials must include at least 4 sites
- To maximize chance of success, NHSS Generalizability must be at a high level

Micro-level inferences

Improves submission tactics

Can do's:

- Influencing SMC meeting agenda can improve chances of success
- Decision boundaries can be pushed by including Scottish data, RCT economic cost model, favourable cost comparators, or high trial population
- Success can be improved by including any element of high trial quality data
- Submitting 'Elite' indications first can improve the chances for success of the non-'elite' indications

Micro-level inferences

Improves submission tactics

Don’t do’s:

- Don’t use low- or moderate-quality trial data if mortality is unproven
- Don’t use trials of less than 1,000
- Don’t make submissions later than 4 months post-launch
- Don’t expect external endorsement – i.e., patient interest group or SIGN – to improve chances of a weak submission
- Don’t assume cost is primary driver as trial data, mortality and NHSS generalizability are key influencers

Macro-level inferences

Model leads to better overall decisions

- Data requirements
- Trial design
- Trial location
- Submission strategy
- Launch decisions
- Marketing strategy

‘Decision Guidance’: The epilogue

The sponsor of the ‘Decision Guidance’ project and the recognized expert on SMC said this at the end of the project:

“After being involved with and part of the SMC for over 20 years, this program can predict the Committee’s decisions as good, and in many ways, better than I can.

➡ Furthermore, this program does not have a bad day, does not go on vacations or get sick, and can actually be in more than one place at the same time.”

‘Decision Guidance’: Post-epilogue

- Expectations exceeded

  We exceeded the expectations of the project’s objectives…significantly

- Global applicability

  The potential of this applying this framework on a global basis were also proven

- Ultimately . . .

  . . . the dollar value of the decisions being influenced was too high and the faith in this new ‘black box’ was too low. This pharma’s decision was to ‘moth-ball’ the model!

‘Decision Guidance’: Post Epilogue

Is there a place for the ‘Decision Guidance’ style of model in finance?

HTA ‘Decision Guidance’

Additional Notes:

Conceptual Learning Paradigm

How could we streamline our response?

Raw Data

Information

Interpretation

Application

Implementation

Evaluation

Replication

Extrapolation

How could we streamline our response?

Raw Data **Learn**

Information

Interpretation

Application

Implementation

Evaluation

Replication

Extrapolation

How could we streamline our response?

Raw Data

Information

Interpretation

Application

Implementation

Evaluation

Replication

Extrapolation

Learn

How could we streamline our response?

Raw Data

Information

Interpretation

Application

Implementation

Evaluation

Replication

Extrapolation

Experience

How could we streamline our response?

Raw Data

Information

Interpretation

Application

Implementation

Wisdom

Evaluation

Replication

Extrapolation

'Where is the wisdom we have lost in knowledge?
Where is the knowledge we have lost in information?'
– T.S. Eliot