

An Engineering Systems Approach to Benefit / Risk Decision-Making



Center for Biomedical Innovation

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The objective of this session was to get feedback to help shape a specific collaborative research pilot project focused on some aspect of benefit/risk decision-making to be sponsored by the Center for Biomedical Innovation (CBI). The meeting started with a presentation from Dr. Nancy Leveson (Professor of Aeronautics and Astronautics and Professor of Engineering Systems (MIT); Director, Complex System Research Center, Engineering Systems Division (MIT)) on the work she has been leading in the past few years on engineering systems approaches to safety. This was followed by a round table discussion with the goal of eliciting the modeling needs of the stakeholders present.

Presentation by Dr. Leveson

Dr. Leveson presented the research she has been working on with Prof. John Carroll, Dr. Stan Finkelstein, Dr. Meghan Dirks and Dr. Joel Hoffman. She defined system safety engineering as a sub-discipline of system engineering, focused on eliminating or reducing hazards (in the case of the Pharmaceutical industry, adverse safety events).

The goal of the current research in safety engineering is to model and proactively analyze potential risks with the goal of limiting accidents and understanding unintended consequences of systems designs. However, there are major differences between standard engineering problems and the case of the healthcare industry. For example the healthcare system is extremely complex, and the approach to risk is very different: it is risky to treat someone with a drug, but it is also risky to not treat someone. Engineering Systems cannot address some of the technical and scientific issues associated with drug safety, but it can provide assistance with issues within the social structure, strategies, and organizational design.

By using a new systems approach and treating safety as a dynamic control problem, we can consider the entire socio-technical system and the underlying social dynamics. We can evaluate policies, design of controls, strategic planning and we can also deal with much greater complexity. If we treat risk and systems as dynamic and changing, we can study how different pressures make those systems migrate toward hazardous states. The traditional models for safety analysis are based on linear chains of directly related failure events, which cannot account for multiple and non-linear causes and do not adequately incorporate social and organizational aspect of safety and safety culture. Dr. Leveson instead proposed an expanded model of causality - System-Theoretic Accident Model and Processes, or STAMP - which can help solve those issues. The STAMP model is currently being applied in the healthcare realm with Dr. Meghan Dierks using as a testbed the Ambulatory/outpatient surgical care at the Beth Israel Deaconess Medical Center. The goal here is to develop a realistic model of healthcare risk that captures the complex interactions among production pressures, historical experience, the inherent risk tolerance of the stakeholders and the confidence and compliance in the existing safety controls.

A New Systems Approach to Safety

- Treat as a dynamic control problem
 - Expanded causality model
 - Considers entire socio-technical system and social dynamics (can evaluate policies, design of controls, strategic planning)
 - Allows handling much greater complexity
- Treats risk and systems as dynamic and changing
 - Systems and organizations migrate toward accidents (states of high risk) under cost and productivity pressures in an aggressive, competitive environment
 - Model and try to understand the impact of these pressures



Differences and Difficulties in Applying to Healthcare

- Complexity and social factors
 - "Even small health care institutions are complex, barely manageable places. ...large health care institutions may be the most complex organizations in human history."
P.F. Drucker
- Risk/Risk
- Only potentially applies to engineered (designed) aspects of healthcare

System Safety Engineering

- A subdiscipline of system engineering
- Focus is on eliminating or reducing hazards (adverse events)
 - Emphasis on modeling and analysis
 - Proactive: while do investigate accidents (losses), emphasis is on building safety into the original system design
 - Investigate an accident before it happens (hazard analysis)
 - Understand unintended consequences of system designs




Three slides from Dr. Nancy Leveson's presentation.

Other research has been conducted on the preliminary drug development flow using PAREXCEL data for validation of the system.

One potential focus for the proposed pilot project would be to take a holistic view of how to optimize clinical outcomes for patients through improving the benefit/risk decision-making process by doctors and patients. It could focus on the generation of new information (e.g., information coming from the Sentinel Initiative or from new comparative effectiveness research), the communication of that information, or the impact on doctors and patients.

Research Project Under Design

- Holistic (systems) view of how to optimize clinical outcomes for patients through improving benefit/risk decision-making by MDs/patients.
 - Generation of information
 - Communication of information
 - Impact on doctors and patients
 - How will change as info and info flows change (rapid learning cycles/adaptive trial designs, Sentinel, comparative effectiveness, etc.)
- Discussion: what hypotheses most important to explore?



Additional slide from Dr. Nancy Leveson's presentation.

Round Table Discussion

At this point, the floor was opened to questions. The goal of the discussion was to help CBI refine the focus and approach of the pilot project (comments in italics were made by audience members):

Are we focusing here on communicating information or on the whole of the approach?

Both are important. We would want to focus on communication of information, but also on the generation of that information, for example with the Sentinel Project.

Are the models mostly parametric and do they take into account random events (either positive or negative)?

The models are based on non-linear systems using differential equations and probabilistic analysis and are capable of doing sensitivity analysis.

Often the negative outcomes are completely unexpected and new. Can they be predicted using this kind of model?

System dynamic models are a wonderful tool to model unintended consequences. By finding something we did not expect, we can make two conclusions: Either the model is wrong or the model is right and then we want to study what happened and why it happened.

There is a problem with studying this as a single process. First we need to generate relevant risk/benefit information. Second we need to get that information to the patients and the doctors.

We know we cannot tackle all of those problems at once. We want to understand what would be the most efficient pilot study with the objective of proving that this approach can be useful.

A lot of research is currently being done on risk benefit analysis. However, we have not found a good way to efficiently and promptly communicate that information to the patients. This presents a risk for the patients.

This is the kind of thing we can model in the system and see if our model matches reality. It is a problem we can work on. *There are several problems at stake here. First there is the issue of defining the risk and benefits. Then there is the issue of balancing the risks and benefits and agreeing on how to balance them.*

This model might not be able to help with that. However, it can help with planning risk mitigation and studying what happened when things do go wrong.

The models can be used to see what the benefits are and how do you measure the benefits for a population. The model can also help differentiating between the types of risk (applied to the wrong population, wrong dosages, unwanted effects and so on). For off-label prescriptions, the model can help in predicting what kind of populations the drugs are going to be used for.

The problem is that the systems are based on what benefits and risks are. However, the way those are valued depends on the stakeholders. How then do we weight them? It is the stakeholder's job to make that decision. We have to make sure that we get the proper information to the patients and the physicians. The risks have to be communicated to both of them, especially nowadays, in a world where the patients are self informed through the Internet. It would be interesting to study the controls and the effects of the Internet on prescriptions and how effective our current communication systems are.

Different actors see the risks and benefits differently. How is this represented in the models?

The models are broken down into different components. We model the patients, the FDA, the doctors, the pharmaceutical companies and so on. Once all of those are independently modeled, we study the interactions between them, running all the models at the same time. This is when you see the unexpected results.

Another interesting question is to study the different risk management systems that are in place, and in the case when they do not work, study why they failed.

There are a lot of issues with the implementation of REMS for pharmaceutical companies. The 120 day timeline prevents a real discourse on the effectiveness of the information that is communicated. REMS puts a large pressure on the physicians and the pharmaceutical companies. What happens when you extend this to all the types of drugs?

Using system dynamics, we can study the feedback loops existing in the environment. This means that we can study the effects of changing one aspect of the system and following the repercussion of that change throughout the whole structure.

How do we tell legislators that REMS is not optimally designed? Do we wait until after the fact? What happens to us [the pharmaceutical companies] when we realize that the information is not good enough and we decide to redo it? Are we going to be viewed negatively for that or are we going to be rewarded for acting proactively? How do we predict how this is going to be received?

It would be great to have published documents that show how the intrusion of Congress has changed the feedback loops and the impacts it has on the system.

We can do that. We have done a similar study with NASA where we studied the effects of Congress on both the success of the program and the effects on the deadlines.

There are two types of risk: Some are avoidable risks, some are not. We should focus first on truly avoidable risk instead of inherent risk where the issue has more to do with the fact that the patients have to be fully informed. We should focus on prescribing errors (drugs sounding alike or wrong doses being prescribed). Furthermore, we do not know where the real risks are. Are we using our resources where they can be the most efficient? An idea would be to only allow doctors to prescribe drugs they have been shown to be able to prescribe properly. An existing example is computerized systems that check that doctor's prescriptions fit the patient's disease. If not, the doctors need to justify themselves.

Another important part of the system is the clinical pharmacists who can pre-process the information for the doctors. How do we get that knowledge to doctors who cannot afford clinical pharmacists? Electronic records and electronic prescription guides could be a first step towards solving that problem. Could we measure the effects of those systems? What is the most affordable way to get the information to the doctors?

A few other important key points to keep in mind when working on the models are:

- 1) Do not forget the pharmacist. They play a key role;*
- 2) Focus on preventable and avoidable events: They can make a huge difference in the outcomes; and*
- 3) Information and communication: We need to shift from*

information communication to education. The information is there but physicians are not using that information. We need to find a way to change behavior and prevent what is preventable.

Next Steps

The following next steps were outlined through a follow up meeting that the research team held on October 30 to debrief from the discussion on October 23, and to synthesize the feedback we have received from a number of you since then.

- 1) The research team, led by Nancy as Principal Investigator, will begin immediately by doing a causal analysis of a particular case (Vioxx) in order to understand the dynamics and controls that operate in the pharma arena. This will entail several levels of analysis using the STAMP model, starting with a hazard, stakeholder and a controls analysis. A first crude model is expected by December.
- 2) In parallel to #1, a small cross-disciplinary Advisory Group of experts will be established to provide ongoing feedback to the research team throughout the project.
- 3) The team will solicit feedback on the preliminary model from the Advisory Group in mid-December. The objective will be to refine the causal analysis.
- 4) The team will then do a comparative causal analysis on Tysabri in order to try to generalize and extend the preliminary model. The team will then solicit additional feedback from the Advisory Group in preparation for a working session that CBI will host for the research team, the Advisory Group, and other CBI members/collaborators in early February. The objective of this meeting will be to provide an opportunity for an in-depth discussion of the model and next steps.

Longer term goals are to examine risk/benefit communication and develop decision-support tools to facilitate improved communication and evaluation of risk/benefits.

The Center for Biomedical Innovation (CBI) focussed on improving global health by overcoming critical roadblocks to the development and implementation of biomedical innovation. CBI is a collaborative effort across the Schools of Science, Engineering, and Management of the Massachusetts Institute of Technology (MIT); and the Harvard-MIT Division of Health Sciences and Technology (HST). For additional information, visit: <http://web.mit.edu/cbi>

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