Anticipation in Medicine and Healthcare: Implications for Improving Safety and Quality

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Introduction

Healthcare is often acknowledged to be among the most complex human activities. Despite substantial efforts, problems with safety and quality in healthcare continue.[1] Concepts from systems sciences, high reliability industries, and from system and complexity sciences are increasingly being applied in attempts to improve safety and quality.[1,2] The absence of a common definition of complexity and of a shared understanding of the features of a complex system can be a barrier to using an understanding of complex systems to improve safety and quality in healthcare.[3]

The theoretical biologist, Robert Rosen, identified anticipation as a fundamental characteristic of living complex systems in a seminal work, *Anticipatory Systems: Philosophic, Mathematic, and Methodological Foundations.*[4] Rosen subsequently provided a relational model of living complex systems In *Life Itself: A Comprehensive Inquiry Into the Nature, Origin, and Fabrication of Life*.[5] An improved understanding and application of anticipatory models in healthcare could improve safety, quality, and financial outcomes. Healthcare organizations are complex data-rich environments that offer unique opportunities for learning how to apply anticipatory principles to improve outcomes.

This chapter provides a brief overview of Rosen's anticipatory theory of complex systems and discusses the implication of these concepts for the physician-patient relationship, for clinical teams, and for the clinical team-patient/family relationship. It includes an overview of the current state of predictive analytics in healthcare and provides examples of healthcare organizations employing a combination of predictive analytic and anticipatory models in efforts to improve outcomes. Potential educational and research opportunities from an anticipatory approach to healthcare are also discussed.

Anticipatory Systems

In *Anticipatory Systems: Philosophic, Mathematic, and Methodological Foundations*, Robert Rosen defined an anticipatory system as a system that contains "a predictive model of itself and/or its environment, which allows it to change state at an instant in accord with the model's prediction pertaining to a later instant." [4, p.313]. (For a more detailed description of Rosen's ideas than is provided here, see Chapters XXX in the Handbook of Anticipation.) In an anticipatory system, models of the future influence how the system changes. Changes in an anticipatory system can occur at the scale of the molecular level, such as increased activation of regulatory enzymes, or at a macroscopic level as changes in individual or organizational behavior based on anticipated future conditions.

In Rosen's conceptual framework, anticipatory systems are complex systems that fundamentally differ from recursive (simple) systems. In a recursive/simple system, change occurs only due to the effects of forces acting on the present state of the system. An anticipatory system differs in that it can change due to the effect of forces acting on the system as well as from the influence of the system's anticipatory models.

Modeling relations are central to Rosen's descriptions of simple, complex, and anticipatory systems and to understanding how organisms represent and anticipate their internal and external environments. Rosen provides a detailed discussion of the modeling relationship and of formal models, a specific type of model, in a third seminal publication, *Fundamentals of Measurement and Representation of Natural Systems.*[6] Common-usage definitions of a model, such as "a simplified description put forward as a basis for theoretical understanding" or "a conceptual or mental representation of a thing" are useful ways of describing a model, however these descriptions do not fully capture the essence and utility of a formal modeling relationship.[7]

The mathematical biologist, A.H. Louie, a student of Rosen's, described the formal modeling relationship as follows (Figure 1):

> Roughly, the essence of a modeling relation consists of specifying an encoding and a corresponding decoding of particular system characteristics into corresponding characteristics of another system, in such a way that implication in the model corresponds to causality in the system. Thus in a precise mathematical sense a theorem about the model becomes a prediction about the system.[7]

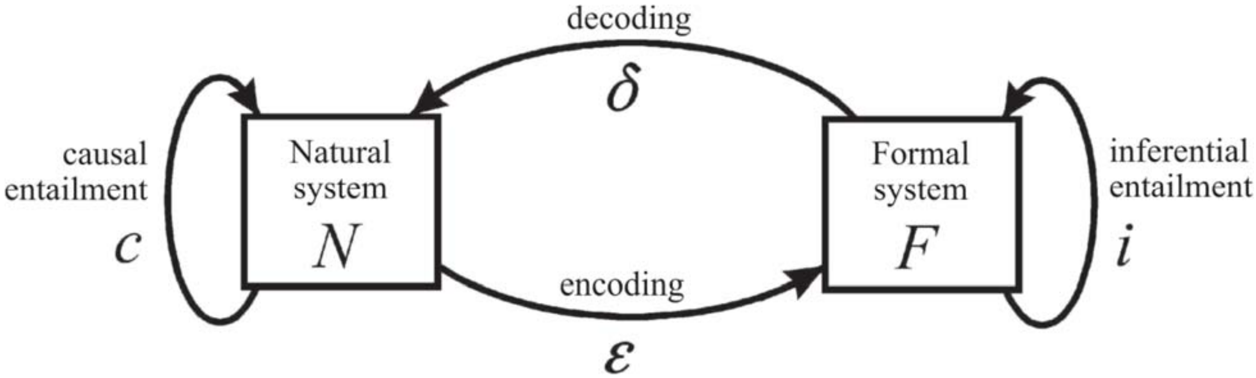

Fig. 1. The protypical modeling relationship

Formal models have transformed our understanding of the natural world and our ability to manipulate the natural world. The most recognizable, and arguably most influential, examples of formal models are the models of classical and modern physics.

One of Newton's key discoveries was that change in physical systems is recursive. Recursion in the context of Newtonian mechanics means that what is occurring in a system at a given instant in time (i.e., the positions, velocities, and forces acting on a set of particles) determines what occurs at the next instant in time. As Rosen wrote, "the heart of recursion is the conversion of the present to the future, or the entailment of the future by the present." This discovery led to the "effective introduction of recursion as the basic underpinning of science itself." [5, p.90] In describing the Newtonian paradigm and its impact on scientific thought, Rosen said:

> The essential feature of that paradigm is the employment of a mathematical language with a built-in duality which we may express as the distinction between internal states and dynamical laws. In Newtonian mechanics the internal states are represented by points in some appropriate manifold of phases, and the dynamical laws represent the internal or impressed forces. The resulting mathematical image is what is now called a dynamical system […] Through the work of people like Poincare, Birkhoff, Lotka, and many others over the years, however, this dynamical systems paradigm or its numerous variants, has come to be regarded as the universal vehicle for representation of systems which could not be technically described mathematically; systems of interacting chemicals, organisms, ecosystems, and many others. Even the most radical changes occurring within physics itself, like relativity and quantum mechanics, manifest this framework […] This, then, is our inherited mechanical paradigm, which in its many technical variants or interpretations has been regarded as a universal paradigm for systems and what they do. These variants take many forms: automata theory, control theory, and the like, but they all conform to the same basic framework first exhibited in the Principia. [4, p. 376-7]

Newton's discovery of recursion in nature continues to shape how scientific models are formulated and our basic understanding of causation in the natural world. As Joslyn wrote in a review of *Life Itself*, "...three hundred years of science has been dedicated to the idea that the special class of simulable systems is in fact a universal paradigm for explanation of natural phenomena"[8]

The recursive framework for change in systems is also present in most currently accepted approaches to understanding complex systems. For example, a fundamental principle of complexity, according to Paley is that:

> …a complexity account always takes the same form…successive states of the system, globally defined, are determined by previous states, locally defined. The function which links the state at t1 to the state at t2 is defined as a set of stimulus-response rules ('If…then…') applying to individual units (whether cells, ants, termites, birds, or drivers) whose behavior conforms to this function. Normally future global states are unpredictable, given only initial conditions future and the state transition functions; however the systems states are still completely explained by the starting conditions and the rules governing local behavior.[9]

According to Roberto Poli:

> In fact, all human and social sciences have accepted, to varying extents, what is possibly Newton's most important implicit assumption, what Rosen called the Zeroth Commandment: "Thou shalt not allow the future to affect the present." [5, p 49] The Zeroth Commandment implies that all information comes from the past and no information comes from the future. The idea that at least some information can be understood as if it derives from the future is the source of the theory of anticipatory systems. [10]

Rosen's anticipatory theory of complex systems is a framework for understanding complex natural systems. It helps explain how complex systems change in ways that are not recursive. Although anticipatory systems (i.e., organisms) are systems in which change does occur recursively, anticipatory systems can also change due to the system's capacity to respond to anticipatory models. In "Robert Rosen's anticipatory systems," an excellent concise summary of the key concepts related to anticipatory systems, Louie states:

> Note, in contrast, that a reactive system can only react, in the present, to changes that have already occurred in the causal chain, while an anticipatory system's present behavior involves aspects of past, present, and future. The presence of a predictive model serves precisely to pull the future into the present; a system with a "good" model thus behaves in many ways as if it can anticipate the future. Model-based behavior requires an entirely new paradigm, an "anticipatory paradigm", to accommodate it. This paradigm extends—but does not replace—the "reactive paradigm" which has hitherto dominated the study of natural systems. The "anticipatory paradigm" allows us a glimpse of new and important aspects of system behavior. [11]

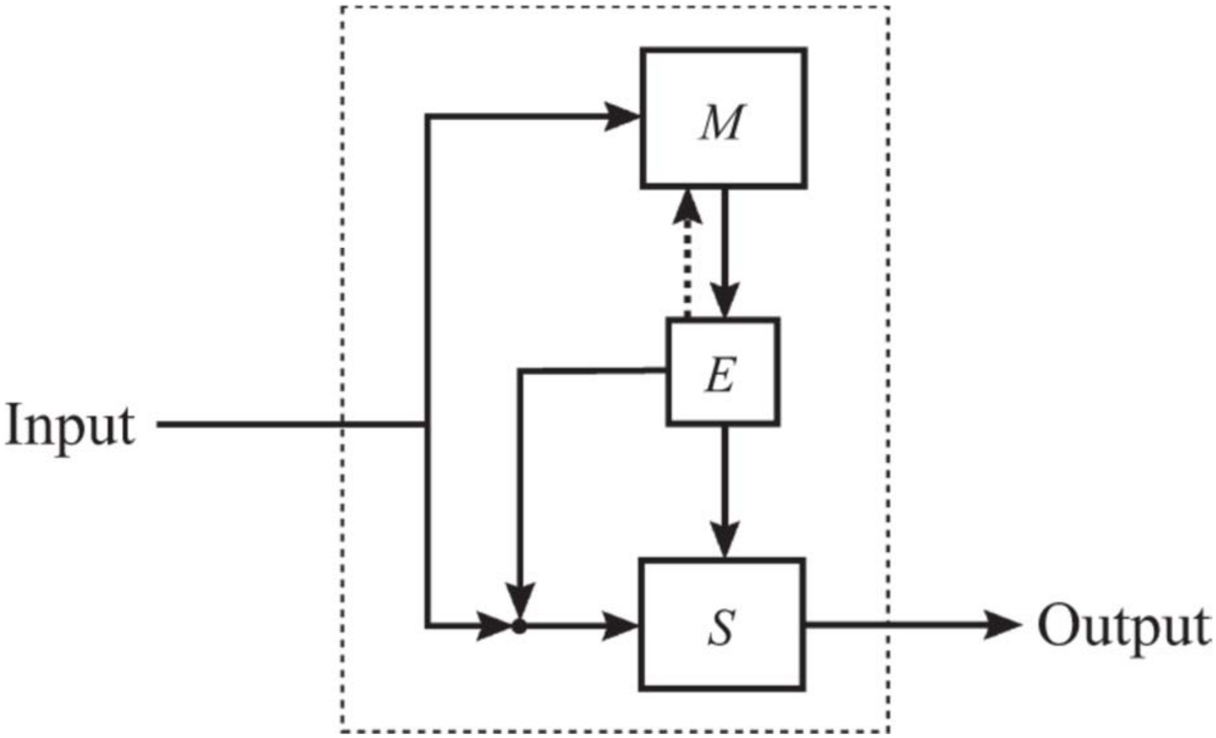

Fig. 2 Anticipatory System

Figure 2 depicts an anticipatory system. The system enclosed in the dotted box could represent a metabolic pathway, an organism, or an organization. S, M, and E are components of the system. M is a predictive model of S for which the time variables in M run faster than real time. As a result, any observable (measurable characteristic) of M serves as a predictor of a corresponding observable of S at a later instant. The "system M is equipped with a set E of effectors that operate either on S itself or on the environmental inputs to S" [11]. Louie describes how this system functions as follows:

> We shall now allow M and S to be coupled; i.e., allow them to interact in specific ways. For the simplest model, we may simply allow the output of an observable on M to be an input to the system S. This then creates a situation in which a future state of S is controlling the present state transition in S. But this is precisely what we have characterized above as anticipatory behavior. It is clear that the above construction does not violate causality; indeed, we have invoked causality in an essential way in the concept of a predictive model, and hence in the characterization of the system M. Although the composite system (M + S) is completely causal, it nevertheless will behave in an anticipatory fashion. [11].

Feedforward and Feedback

Anticipatory systems often employ feedforward processes. Louie has described the role of feedforward in anticipatory systems as follows:

> Anticipatory behavior involves the concept of feedforward, rather than feedback. The distinction between feedforward and feedback is important, and is as follows. The essence of

> feedback control is that it is error-actuated; in other words, the stimulus to corrective action is the discrepancy between the system's actual present state and the state the system should be in. Stated otherwise, a feedback control system must already be departing from its nominal behavior before control begins to be exercised.
>
> In a feedforward system, on the other hand, system behavior is preset, according to some model relating present inputs to their predicted outcomes. The essence of a feedforward system, then, is that the present change of state is determined by an anticipated future state, derived in accordance with some internal model of the world.
>
> We know from introspection that many, if not most, of our own conscious activities are generated in a feedforward fashion. We typically decide what to do now in terms of what we perceive will be the consequences of our action at some later time. The vehicle by which we anticipate is in fact a model, which enables us to pull the future into the present. We change our present course of action in accordance with our model's prediction. The stimulus for our action is not simply the present percepts; it is the prediction under these conditions. I emphasize again that "prediction" is not prescience, but simply "output of an anticipatory model". Stated otherwise, our present behavior is not just reactive; it is also anticipatory [11].

In biochemistry feedforward has been defined as: the anticipatory effect that one intermediate in a metabolic or endocrine control system exerts on another intermediate further along in the pathway; such effect may be positive or negative.[12]

One description of feedforward regulation includes this example from the glycolysis pathway:

Control of a metabolic pathway by a metabolite of the pathway that acts in the same direction as the metabolic flux, i.e., downstream or "later" in the pathway, e.g., the activation of pyruvate kinase by fructose 1,6 bisphosphate. [13]

If glycolysis is represented as an anticipatory system as in Fig. 3, E (Effector)=pyruvate kinase, M (Predictive Model of S)= Fructose 1,6 bisphosphate, and S (Subsystem subject to anticipatory effects)= phosphoenolpyruvate, a substrate catalyzed by pyruvate kinase. The level of Fructose 1,6 bisphosphate serves as predictor of subsequent levels of phosphoenolpyruvate. Increased Fructose 1,6 bisphosphate levels upregulate the effector, pyruvate kinase. Pyruvate kinase then catalyzes the transfer of a phosphate group from phosphoenolpyruvate to adenosine diphosphate (ADP).

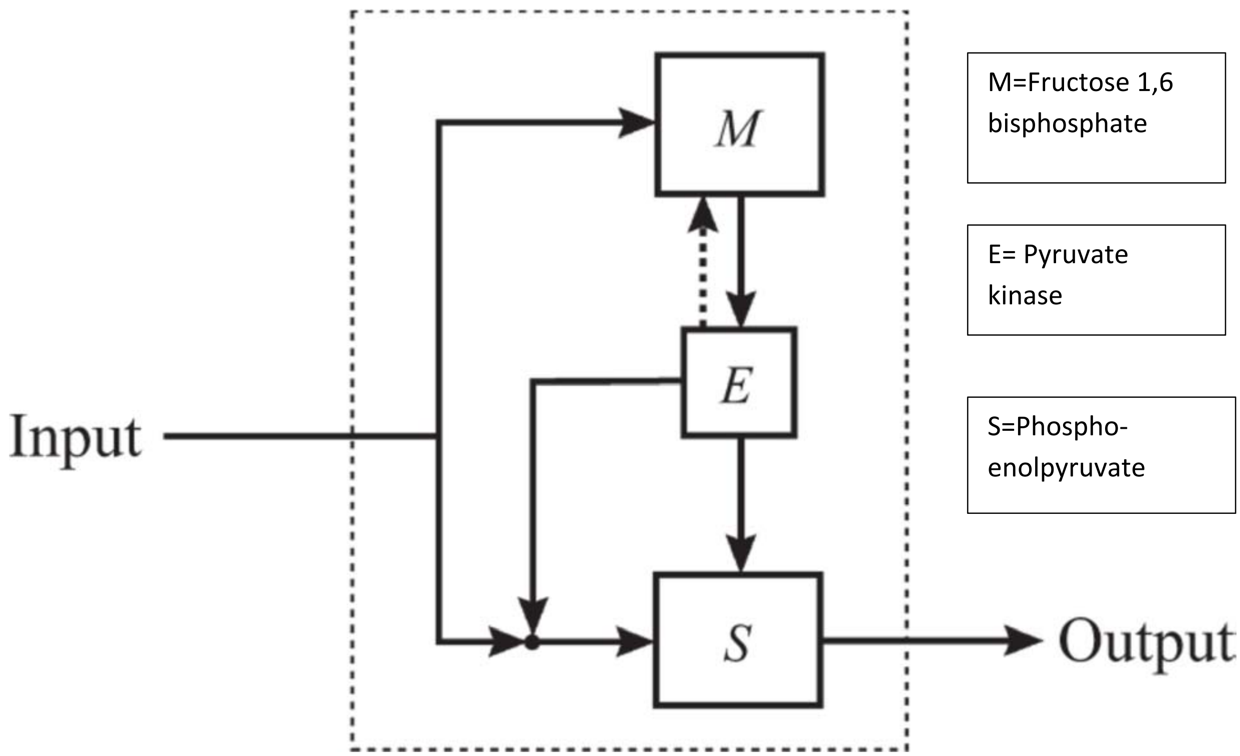

Fig. 3 Glycolysis pathway represented as an anticipatory system

A number of feedforward processes are recognized to occur within the endocrine system. For example, insulin acts directly on beta cells to enhance insulin production in an autocrine feedforward loop. [14]

Simple and Complex Systems

Generally accepted features of a complex system are that the components (parts with a function) of a complex system are interrelated and that fragmentation or decomposition of these components causes a loss of information regarding the system. [3,15] *In Life Itself: A Comprehensive Inquiry into the Nature, Origin, and Fabrication of Life*, Rosen proposed a definition of complex systems that is consistent with these characteristics, but adds greater detail.[5] Rosen defined a simple system as one in which all of the information can be captured in a single formal model and complex systems as those in which it is not possible to represent all of the system's information with any single formal model or any finite sets of formal models.

A brief summary of Rosen's conceptual approach to simple and complex systems is as follows [16]

I. Simple systems

  a. Are non-living.

  b. All of the information about the system can be captured in a single model of the system.

c. The system can be fractionated (broken into parts) and reassembled without loss of information about the system.

d. A system may be complicated and composed of many parts (i.e., an aircraft carrier) and still be “simple”.

e. All change is recursive.

II. Complex systems

a. All living systems are complex systems.

b. No finite set of models can capture all of the information about the system.

c. A complex system can’t be fractionated without destroying information about the relationship of the components of the system.

d. A fundamental and necessary characteristic of complex living systems is a capacity to adapt to a changing environment.

e. Complex living systems are anticipatory, meaning they have a capacity for change based on inputs from their anticipatory models.

Stability and failure modes in simple and anticipatory complex systems

There are fundamental differences in how simple and anticipatory complex systems malfunction. To paraphrase Rosen, in a simple system every global failure results from local failures in the component subsystems, however in a complex system a global failure is not necessarily associated with a local subsystem failure.[17] Like a simple system, it is possible for an anticipatory complex system to malfunction when a component in the system fails. In contrast to a simple system, the stability of an anticipatory complex system is partially dependent on the accuracy of its models of its present environment and of its anticipatory models of its future environments. A complex system cannot, by definition, have a perfectly accurate and comprehensive model of its internal environment and future environments, but more accurate models of the states of its present and future environments are associated with a greater likelihood of the ongoing stability of the system. Similarly, the greater the divergence between the actual present and future environments and the system’s models of those environments, the greater the likelihood of maladaptive responses to the present and future environments, and the greater the likelihood of an anticipatory complex system malfunctioning.

Implications and Applications of an Anticipatory Theory of Complex Systems to Improving Safety, Quality, and Efficiency in Healthcare

If Rosen’s anticipatory theory of complex systems is substantially correct, what are some of the implications for healthcare providers, administrators, and patients?

1) Guiding principles [18]

    a. No clinician's mental model of a complex system, such as the health status of a patient, can ever be complete.
    b. It is impossible for a team of clinicians, or a team of clinicians, patient, and family, to ever have a fully congruent "shared mental model" of a patient's complex clinical situation.
    c. Greater congruence between the models of the current situation and anticipatory models of future states among clinical team members, and among the clinical team, patient, and family increases the likelihood of attaining preferred outcomes.
    d. Inputs from the anticipatory models of clinical team members, patients, and families may be useful for identification and real time mitigation of some clinical situations in which there is an increased risk of a future serious adverse outcome.
    e. Clinicians, patients, or family members who believe, even if based only on intuition, judgement, or a "gut sense" that the diagnosis or plan for a patient is wrong or that a patient is at high risk for an adverse outcome, should be encouraged to speak up.
    f. Significantly discrepant present-state or anticipatory mental models between clinical team members or between team and patients/families may indicate an increased risk for an adverse outcome.
    g. Clinical teams that recognize disagreements regarding appropriate care may indicate increased risk of an adverse outcome, may be able to create better shared present-state and anticipatory mental modes and thereby help mitigate some future risks.
    h. Optimal team functioning should encourage anticipatory inputs from all clinical team members and identification of significantly discrepant current state and anticipatory models among clinical team members and between clinical team and patients/families, especially in high-risk situations.

Anticipation in Physician-Patient Relationships

Physicians are typically taught to make a diagnosis based on the history, exam findings, additional studies such as laboratory and imaging tests, and consultations with other clinicians, as needed. Physicians are not generally taught that there is value in acting on a sense they may have or the patient/family may convey that something adverse could occur. The concepts above derived from an anticipatory theory of complex systems suggest that both physicians and patients could benefit if physicians and other care providers were educated that we are all continuously generating anticipatory models and that heeding these anticipatory models, which can sometimes be experienced as an intuition or a gut sense, can help reduce the risk of certain adverse outcomes.

A study of serious infections in children provides evidence that this approach can be beneficial. 3890 patients (ranging from 0 to 16 years of age) who presented with an acute illness were evaluated by clinicians in a primary care setting.[19] The clinicians who provided an overall clinical impression of severity were asked if their "gut-feeling" was that the patient had something more serious than what the history and exam suggested. "Intuition that something was wrong despite the clinical assessment of non-severe illness substantially increased the risk of serious illness (likelihood ratio 25.5, 95% confidence interval 7.9 to 82.0)."[19]

Physicians and their patients are both continuously generating models that provide partial and generally imperfect explanations for what is occurring with a patient and are also generating imperfect anticipatory models of the future course of a patient's illness and/or health status. Greater concordance between the present state and anticipatory models of physicians and their patients, while not guaranteeing that something important has not been missed, increases the likelihood of the accuracy of the explanatory or anticipatory models. For example, it has been shown that "Agreement between physicians and patients regarding diagnosis, diagnostic plan, and treatment plan is associated with higher patient satisfaction and better health status outcomes in patients with back pain."[20] Similarly, if physicians are alert for the possibility that significant discrepancies between their and their patients' explanatory and anticipatory models may indicate that something important is missing from those models, they may be able to modify their own and/or the patient's explanation of what is going on or what is likely to occur in a way that will improve future outcomes.

Anticipation within Clinical Teams

Anticipation is essential for a clinical team to function at its best. Each member of the healthcare team has a unique role, but it is through communication and collaboration that the most effective patient care occurs.

Rapid response team (RRT) triggers is a good example of how anticipation is incorporated into the care of hospitalized patients. Rapid response teams are usually comprised of a physician, a nurse, and a respiratory therapist who respond to calls when a patient seems to be at high risk for clinical deterioration. The goal of this response is to intervene early enough to avoid decompensations including cardiac arrest, respiratory arrest, or transfer to the intensive care unit. Ideally, this occurs through anticipation of these events and prompt interventions.

RRTs are triggered by a variety of events. The majority of these are changes in vital signs (e.g., elevated heart rate, low blood pressure), changes in clinical picture (e.g., increasing oxygen requirement), or new laboratory values such as a fall in hematocrit. Through analysis of data, these parameters have been determined to help predict, or anticipate, clinical decline. Essential to the success of a rapid response system, however, is the inclusion of the bedside nurse's clinical sense that something is wrong, even if all the numeric parameters are unchanged.

The most effective rapid response systems are the ones that support and encourage the nurse to use this intuitive sense of concern.[21] Creating a culture where this is expected and valued is essential.[22] While there has been some effort to emphasize analytic thinking in nursing decision-making, the field has valued and emphasized intuition more than what is seen in medical training.[23,24] Embracing and supporting the value of intuition is essential for full anticipation of clinical decline.[25]

Anticipation in Clinical Team-Patient/Family Relationships

In many healthcare settings, one of the less represented voices on the healthcare team is that of the patient and the patient's family. While it is obvious that the patient is at the center of the care being delivered, care is often care delivered *to* the patient as opposed to care determined *with* the patient and their family. Engaging the patient's perspective and input in clinical decision-making is essential and the role of this voice in anticipation is crucial.[26]

The phrase "patients know their bodies best" is often repeated, but perhaps not listened to as often as it should be. While there are clearly some who worry excessively or create maladies that don't exist, many sick patients have an intuitive sense that something is not right. Listening to this voice, allowing the vagueness of the complaint not to deter the healthcare team is essential. While it is common that a patient might not be able to explain exactly what is causing the sense that something is not right, the message is correct and it is essential that the team works to figure out what is driving that sense.

It has become more common for medically complex patients to have prolonged inpatient stays. In this setting, patient's family members often become quite in tune to the flows of the hospital. With this increasingly nuanced sense, this voice becomes crucial to anticipation. A clinical example highlights this role.

A patient who had undergone liver transplantation was receiving care in the intensive care unit (ICU). His course had been complicated with infection and recurrent bleeding from his gastrointestinal tract. In this ICU, the patient and family are intentionally included in daily rounds, with the goal of including their perspectives both for decision-making and for patient safety. On this day, the clinical team discussed the most recent events and determined that the patient had stabilized significantly and was ready to transition from the ICU to an acute care bed (i.e., less intense monitoring). As had been the case for many days, the patient's wife participated in rounds and when this aspect of the plan was discussed, she expressed her concern about transfer out of the ICU. When asked by the clinical team, what was causing her hesitation, she could not identify a specific issue, but she reported that she had a sense of something being off with her husband that morning. The team reassured her that his blood pressure, heart rate, laboratory values, and other key indicators all demonstrated that he was stable. In subsequent discussion, the decision was made to watch him in the ICU until late afternoon, valuing the anticipatory sense of the patient's wife, but also hoping to progress care if he remained stable. About three hours later, while still in the ICU, the patient's blood pressure dropped and it became clear he was again bleeding quite profusely. While this had not been apparent on rounds, the anticipatory sense was correct and the clinical decision to incorporate anticipation into decision-making allowed for quick response to the patient's critical event.

Predictive Analytics in Healthcare

Role of Predictive Analytics

The fundamental goal of medical decision making at the patient level is to integrate information specifically about the patient with a corpus of medical knowledge in order to make optimal decisions about screening, prevention, diagnosis, and treatment.[27] Implicit in this process is that given a set of input variables (i.e., patient characteristics and one or more interventions), one can predict a future state and use this to optimize decision making. The area of predictive analytics in healthcare is that of developing, using, and refining predictive models to guide interventions. Heterogeneity in genetic background, environmental exposures, social milieu, compliance with therapy, and other factors result in different outcomes for the same disease and differing responses to the same treatment across patients. This heterogeneity presents challenges to healthcare providers trying to optimize decision making and predict future states for a particular patient as, for example, a given preventive measure or therapeutic intervention may or may not work as well for that patient as on average for a group of patients.

At a relatively coarse grained level, healthcare providers already factor in patient characteristics in medical decision making. Thus, an active elderly patient with normal weight and no family history of heart disease is treated differently than an overweight elderly patient with a strong history of heart disease. At a finer grained level, biomarkers, ranging from blood cholesterol to genetic markers, are used to more precisely guide medical decision making. With this in mind, the screening, preventive measures, and therapy differ for a woman with the BRCA1 mutation associated with breast cancer. The concept of personalized medicine, a superset of the concept of genomic medicine, is predicated on the idea that with increasingly sophisticated models, leveraging increasingly large amounts of medical data (e.g., the exome of a patient and their complete electronic health record) will increase the accuracy of our predictions of future state and subsequently the optimization of medical decision making. An elegant articulation of the core precepts of precision medicine is “predictive, preventive, personalized and participatory medicine”, which captures the key elements of predictive and personalized while adding the elements of prevention (generally being more effective than treatment) and the important concept of patient engagement and activation (“participatory”). [28] There is thus a fundamental and ever growing appreciation of the importance and need for more accurate predictive models to guide interventions at the individual patient level.

At the population level (i.e., healthcare system, county, country), there is also a need for predictive analytics to guide medical decision making. These models can differ from those at the individual level, as the parameters that society seeks to optimize at the population level may or may not be the same as those at the individual level. The goals of healthcare systems are captured in what are frequently referred to as Berwick’s triple aims of a) improving the experience of care, b) improving the health of populations, and c) reducing per capita costs. [29] In principle, predictive analytic models that optimize the care of individual patients do optimize the health of population. However, patient level predictive models do not necessarily include per capita costs as a factor. When per capita costs are introduced into models, high-cost interventions with diminishing return (e.g., less cost effectiveness, lower return on investment) are not favored as much even if they may optimize individual patient outcome. This has the potential to create a conflict at the healthcare provider level between maximizing outcomes for a given patient vs. maximizing population outcomes while keeping per capita costs low.

Opportunities and Challenges for Predictive Analytics

For both individual and population level predictive analytic models in actual use today, there is a challenge around the lack of a sufficient evidence base. The practice of evidence based medicine is hampered by this.[27] Put another way, our predictive models in healthcare do not perform nearly as well as we would hope. More and/or better quality data are needed for these models. Data collected by the British Medical Journal Clinical Evidence resource illustrate the scope of the problem.[30] As of September 2016, the data on the "effectiveness of 3000 treatments as reported in randomized controlled trials" selected by the resource showed: 11% "beneficial," 24% "likely to be beneficial," 7% "with a tradeoff between benefits and harms," 5% "unlikely to be beneficial," 3% "likely to be ineffective or harmful," and 50% of "unknown effectiveness." In other words, for 50% of treatments examined, the predictive model could not determine whether the treatment intervention was effective.

The Clinical Evidence Project and related evidence based medicine projects such as the Cochrane Collaboration seek to synthesize the evidence in the published peer reviewed literature, generally focusing on randomized controlled studies using statistical techniques such as meta-analysis. Challenges to these approaches include the lack of clinical studies of sufficient quality in a given domain, relatively small percentages of affected population sampled in these studies, questions about the degree that the study populations reflect the population at large, and lack of granular detail on genetic, environmental, social milieu, and other factors that can influence outcomes.

Approaches to Advance Predictive Analytics

A potential paradigm shift drawing on the concept of predictive analytics, data science, and the concept of "big data" is emerging and may address the lack of evidence base. The concept of a learning healthcare system posits that by using all data acquired as part of the healthcare process (including the rapidly growing data in electronic health records and patient reported outcomes), one can learn what does and does not work for a given type of patient as a by-product of the healthcare process.[31] In an iterative process, interventions that appear to work for a particular group are adopted and then the performance of these interventions for that group can be validated or refuted by data from the healthcare system. The concept of predictive analytic models emerging from the learning healthcare system is typically applied at the population level factoring in cost effectiveness, but could equally be applied at the individual patient level. Given our sparse evidence base, population level predictive analytics has the appeal of allowing us to look, for example, for interventions that drive up per capita costs without improving outcomes. The fact that there is no clear correlation between healthcare expenditures and outcomes can be seen by looking at per capita healthcare expenditures and population level health outcomes across countries and subgroups within a country.

The bulk of predictive analytics in healthcare to date focuses on forecast employing quantitative models (e.g., the concept of the learning healthcare system) rather than foresight, in which an analytic exploration of possible futures (qualitative modeling) is conducted. Much as in other domains, large amounts of data are used along with powerful mathematical and machine learning approaches to derive models to predict future outcomes based on past experience. A good overview of forecasting type predictive analytics approaches is provided by Steverberg, who discusses some of the challenges of adapting general approaches to predictive analytics from computer science and biostatistics to the complexities of healthcare.[32] A broad range of approaches have been used for predictive (forecast) models including causal inference [33], logistic regression, neural networks [34], survival analysis [35], and process mining. [36] Similar to the limitations of forecasting in other domains, healthcare forecasting models cannot account for the emergence of unforeseen (e.g., new diseases such as Zika), emergent (e.g., new diagnostic tests such as whole exome sequencing), or changing external factors (e.g., rising global temperatures and associated health impacts).

As noted earlier, in the currently available electronic health data (e.g., social support networks), many factors influencing healthcare outcomes are captured either not at all or not in quantitative ways. As is the case with clinical trials, forecasting models can be very sensitive to factors such as data sources, cohort selection, and outcome definitions.[37] There are efforts to automate the machine learning process inherent in building many forecasting models to allow for using larger and multiple data sets to overcome the limitations of models sensitivity to these factors.[38,39]

Another approach to improving models is to incorporate data outside the health system (e.g., social media or analysis of web search patterns), such as that reviewed in Al-Garadi.[40] When good predictive models are developed in healthcare, a challenge remains in their adoption due to their complexity and opacity. There is ongoing work developing automated ways to explain these models' prediction results to healthcare providers.[41]

Some foresight or modeling of future scenarios does occur. Two common areas are: a) disease outbreak modeling for emerging infectious diseases (e.g., Zika and Ebola) to guide which interventions to use when and where, and b) economic modeling on the costs and outcomes of various approaches. Foresight is generally applied when looking at novel situations for which there are little direct precedent and data that can be used for a forecasting type approach. Examples of research that combines elements of forecasting and foresight include inferring infectious disease transmission using network inference [42] and outbreak detection. [43]

Institutional Support to Promote Anticipation within Healthcare Organizations

Leaders of healthcare organizations who understand the value of anticipation in improving patient care can provide support in a number of ways.[16] They can encourage team members to voice any concerns about the current understanding of a patient's clinical situation, the risk of future adverse events, and/or the plan for care. Team STEPPS is one example of a program that can be employed to provide evidence-based tools to train staff to improve communication and willingness to voice safety concerns.[44] Leaders can promote a culture in which hierarchy and power gradients do not inhibit clinical team members from voicing anticipatory predictions. They can provide support for systems that capture the clinical team's anticipatory predictions of risk of deterioration and encourage planning based on these predications. One example of this approach is the I-PASS handoff tool, which encourages identification of patients requiring additional monitoring and contingency planning and conveying this information to the team assuming the care of the patient.[45] Leaders can provide support for structured clinical rounding, including patients and family members, to create opportunities to refine shared mental models and to better identify situations in which divergent models may suggest an increased risk for an adverse outcome. They can also support increased availability of predictive analytic tools for clinical decision making, such as dashboards or reports to use during rounding that would incorporate real-time results of risk stratification models.

An innovative example in which both anticipatory and analytic/forecasting models are being employed to anticipate patient deterioration is being undertaken at the Mayo Clinic.[46] The Mayo team is mining data to identify covariates that predict deterioration and is iteratively testing the sensitivity and specificity of predictive algorithms. Information from an anticipatory nurse "worry" score is being included in their predictive model, based on a study finding that nurses with more than one year of experience were significantly more accurate in identifying patients at risk for physiologic deterioration than those with less than one year of experience (72% vs 53%, $p<0.05$).[47] A nurse's suspicion/anticipation of sepsis is being evaluated at Harborview Medical Center in Seattle to determine if it will improve the prediction accuracy (specificity) of an alert system derived from a predictive analytic model.[48] There are likely many other areas in healthcare in which synergies between anticipatory and analytic/forecasting models could be employed (e.g., combining forecasting and clinician's anticipations of readmission risks to allow earlier targeted intervention in patients at high risk, combining an analytic approach to predicting a patient's length of stay with clinician's anticipation of day of discharge to better coordinate care.)

Research Opportunities

Healthcare settings offer numerous opportunities for research in anticipation. Studies using designs similar to the predictive role of a "gut feeling" of physicians or the nurse "worry factor" could further define and elucidate the role of predictive intuition in identifying high risk situations. [19, 47]   It would be helpful to have an improved understanding of the factors associated with better anticipation in individual members of healthcare teams and whether interventions with coaching or feedback could promote improved anticipation.

Studies of clinical team function and of the factors that contribute to better team understanding of complex clinical situations and better anticipation of future clinical states would also be useful. Such studies would benefit from the availability of instruments to assess the quality of anticipatory functioning of clinical teams. One option for studying aspects of the theory of anticipation in healthcare settings would be to employ an agreement instrument, such as the one developed to assess a patient's agreement with his/her physician about the diagnosis (current state), and the diagnostic and treatment plans (future states). [20] This could be used in a variety of settings, including the following: [16]

i. Tracking incidence of significant disagreement on an ICU or inpatient unit, providing an alert to clinical team members and assessing the frequency in which identification of significant disagreement resulted in a clinically important change in management.

ii. To determine if a correlation exists between care coordination sensitive outcomes (i.e. length of stay, patient satisfaction, follow-up appointment show rates) and clinical teams with higher agreement scores.

iii. If a correlation between better agreement and care-coordination sensitive clinical outcomes exists, feedback to teams about aggregated patient/family agreement scores could be provided to determine if this resulted in improved agreement scores and in improved care-coordination sensitive clinical outcomes (i.e., an iterative model test).

iv. A modified agreement instrument (“do you agree with the team’s diagnosis, diagnostic plan, and treatment plan”) could be administered to interdisciplinary clinical team members to determine if a correlation exists between teams with higher agreement scores and improved care coordination sensitive outcomes (e,g., length of stay, patient satisfaction). An agreement instrument could be employed in an outpatient setting to determine if better agreement is associated with outcomes such as intention to adhere to treatment, patient satisfaction, or symptom resolution.

Educational Opportunities

How do we teach anticipation and the incorporation of an anticipatory voice into clinical care? It seems two key elements are needed. The first is to acknowledge the extent of uncertainty that exists in clinical decision-making. While the last few decades in medical education have emphasized evidence based medicine, it is clear, as has been discussed, that many patients do not fit nicely into care pathways dictated by randomized controlled clinical trials. While we strive for predictive analytics to guide decision-making, many aspects of patient care are appropriately driven by clinical sense and previous experience. It is in this space where anticipation is essential. Education of healthcare providers should include encouragement of listening to one’s intuitive sense about a patient. Nursing education does this better than medical education, as nurses, from early in their training, are encouraged to speak up if they have a “bad sense” about a patient. In many ways, physician training minimizes this important aspect of care with emphasis instead on numbers, data, and tangible details. While we want to train to appreciate the potential power of data and prediction, we also want to encourage this anticipatory sense.

The second aspect of education required is training to empower the myriad of voices on the healthcare team who may have an anticipatory sense of clinical change. Teamwork is essential to successful delivery of healthcare; from the outpatient medical home to the intensive care unit, interdisciplinary care is the model. Teaching all members of the healthcare team, particularly physicians, the importance of teamwork is the first step. For the team to function at its maximal capacity, we also need to teach the leaders of the team how to encourage, solicit, and hear all members’ perspectives. This is particularly important when working to incorporate intuitive anticipation that may be less valued in a traditional medical model.

One strategy to encouraging this collaborative sense is through interprofessional training early in nursing and medical education. There is an emerging body of literature showing that individuals perform better on teams when they learn together as part of their training. [49]

There may also be opportunities to refine concepts currently utilized in situational awareness training to include a greater emphasis on anticipation. Training in situational awareness is commonly employed in efforts to promote better team functioning to improve safety in healthcare and other high-risk domains. Situational awareness:

> involves being aware of what is happening in the vicinity, in order to understand how information, events, and one's own actions will impact goals and objectives, both immediately and in the near future. One with an adept sense of situation awareness generally has a high degree of knowledge with respect to inputs and outputs of a system, i.e., an innate "feel" for situations, people, and events that play out due to variables the subject can control. Lacking or inadequate situation awareness has been identified as one of the primary factors in accidents attributed to human error. Thus, situation awareness is especially important in work domains where the information flow can be quite high and poor decisions may lead to serious consequences (e.g., piloting an airplane, functioning as a soldier, or treating critically ill or injured patients).[50]

An understanding of anticipatory systems and of the failure modes of complex systems might help healthcare teams being trained in situational awareness better achieve an understanding of how to anticipate and plan for future changes in the course of a patient's treatment.

Conclusions

Healthcare occurs in complex systems, for which improving safety and quality is an ongoing challenge and imperative. The anticipatory theory of complex systems provides a framework for understanding complex natural systems and an explanation for how they can change based on the system's anticipatory models. An enhanced understanding of the characteristics and failure modes of anticipatory systems could enhance existing safety practices and help organizations further reduce the risk of serious adverse events by reducing communications failures that are the most common root cause of these events and by promoting an improved openness to change when concerns about the plan of care are raised by clinicians, patients, or families.

Educating clinicians, patients, and families on how anticipatory complex systems function and contribute to safety in clinical environments would be valuable. Research directed at an improved understanding of factors associated with better anticipation in individuals and of the factors that contribute to better team anticipation of future clinical states would be useful. There may be substantial opportunities in healthcare to improve the accuracy and utility of certain models by including anticipatory inputs into some of the growing number of predictive analytic models. Leaders of healthcare organizations who understand anticipatory systems have an opportunity to promote anticipation as an important aspect of a learning healthcare organization.

A broader understanding of anticipatory systems could have great benefit, in and outside of healthcare. As Rosen said in closing *Anticipatory Systems*:

> The study of anticipatory systems thus involves in an essential way the subjective notions of good and ill, as they manifest themselves in the models which shape our behavior. For in a profound sense, the study of models is the study of man; and if we can agree about our models, we can agree about everything else. [4, p. 370]

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