

## Returning to Holism — An Imperative for the 21st Century

Joachim Sturmberg

jp.sturmberg@gmail.com

**Abstract.** *The success of 20th century medicine, grounded in a reductionist research paradigm, has had a profound impact on morbidity, mortality and quality of life. These successes have shaped our understanding of diseases as having specific causes and at the same time led to the fragmentation of clinical care. What we have gained in a greater understanding of minute aspects of disease, we have lost in the appreciation of its consequences on the person, family and their environment. Medicine for the 21st century must broaden its understanding and appreciation of health and disease while extending its practices to embrace the dynamics of complex adaptive systems integral to much of the disease processes and for patients' adaptive responses to their disease and its management. These understandings and practices have profound implications for the reorganization and financing of health systems.*

# Foundations of Systems Medicine

## Chair: Mark Smith

**Howard Federoff** - Systems Neuromedicine and Alzheimer's Disease: Detecting Preclinical Disease

**Henrik Vogt** - Systems Medicine - holistic and personalized in a humanistic sense?

**S. Lee Hong** - Complicated vs. Complex, Disease vs. Illness: Rethinking Diagnosis, Therapy, and Restoring Health

**Abdulrahman El-Sayed** - A system for systems epidemiology. The example of inference from agent-based models

**Martin Kornitzer** - Complexity and Risk in Family Medicine's Epidemiology. An Interdisciplinary Approach

**Sonali Vaid** - Complexity Science and Rabies Control. Applying complexity science to understand the spread and mitigation of a public health problem

**James C. Palmer** - The Human Processual Interdependent Phenotype: A Complexity Sciences contribution to the Theoretical Foundations of Systems based Medicine

**Tom Staiger** - The theoretical biologist, Robert Rosen, proposed that a capacity for anticipatory change is a fundamental characteristic of complex adaptive systems

**Moderator of Panel Discussion: Howard Federoff**

## **Systems Neuromedicine and Alzheimer's Disease: Detecting Preclinical Disease**

**Howard Federoff**

hjf8@georgetown.edu

**Abstract.** Alzheimer's disease is becoming the scourge of this century. There is no cure and all clinical trials intended to modify the disease have failed. The economic and social burdens of Alzheimer's disease are unacceptable. A systems approach to identify cognitively normal older individuals who will progress to Alzheimer's disease will be described. Efforts to fully characterize the underlying pathophysiology and implications for secondary prevention will be presented.

## **Systems Medicine - holistic and personalized in a humanistic sense?**

**Henrik Vogt**

vogt.henrik@gmail.com

Physicians, especially in primary care, face the full complexity of human function and dysfunction. Therefore, a fundamental challenge for medicine, is the development of a comprehensive conceptual account of and approach to the patient as an entity. Systems medicine is an emerging development in biomedicine, which is promised as a holistic, personalized and humanistic framework for medicine that will tackle all components of disease complexity. We analyse to what extent systems medicine is – and can be expected to become – holistic and personalized in a humanistic sense. In this, we take as our point of departure a comparative analysis of the theories of humanistic physician-philosopher Eric Cassell and systems biologist Denis Noble, where Cassell represents the view of persons found in humanistic medicine. We find that, while much of systems medicine currently has a reductive and mechanistic approach to, there are conceptual developments in systems medicine that can contribute significantly to a holistic and personalizing theory of medicine. Important examples are a process view of living entities, Noble's Theory of biological relativity and downward causation. However, these concepts notwithstanding, systems biologists do not as yet know how to conceptualize living wholes and systems medicine accentuates the need for a genuine theory of life that can also account for include phenomena like agency, goal-directedness, consciousness, meaning and values. On a methodological level, the gap between systems medicine and humanistic medicine is also significant. Systems medicine is envisioned as a quantitative science that seeks to quantify disease and health. If human agency, values and defining characteristics of human biology, such as symbolic interaction and development of narratives, are important constraints on human health, and cannot be meaningfully parameterized, it is difficult to see how systems medicine – as a quantitative-only science – can become holistic and personalized in a humanistic sense or account for all components of disease complexity.

# **Complicated vs. Complex, Disease vs. Illness: Rethinking Diagnosis, Therapy, and Restoring Health**

**S. Lee Hong and Simeon J. Hain**

hongs@ohio.edu

Medical physiology is generally studied as a static and complicated system where dynamic processes are captured as flow charts. From this perspective, when 'X' increases, 'Y' decreases, captured as feedback loops and cascades, or, after 'A' happens, then 'B' takes place. Such a static and sequential view on human physiology lends itself well to the biomarker approach to diagnosis, therapy, and maintenance of health. Here, "abnormal" levels of biomarkers are indicators of disease to specific physiological systems and health would be defined by the absence of aberrant biomarker levels. However, the human body is a complex system where "the whole is greater than the sum of its parts." The human body has processes that occur simultaneously and fluctuate consistently over time. Complexity affords human physiology the capacity for compensatory adaptive patterns and creates a distinction between illness and disease, where one does not necessitate the other. This conceptual talk will discuss the concepts of complexity and degeneracy, providing a theoretical framework of the relationship between the whole and parts. The primacy of complex, interacting dynamic physiological patterns will be presented in contrast to the biomarker approach. This talk will present a challenge to the idea that the absence of visible, "meaningful" structural or functional disruption alone cannot be used as an indicator of health. The absence of disease is not the absence of illness, and the presence of disease does not reflect illness. Clinically relevant outcomes from the complex dynamics perspective will be provided, where alternative views of the detection and management of disease and illness will be presented. A critical outcome of this talk will be an emphasis on the importance of rediscovering the pathway to health that goes beyond the normalization of physiological biomarkers.

## **A system for systems epidemiology. The example of inference from agent-based models**

**Abdulrahman El-Sayed**

ame2145@columbia.edu

The past 10 years have seen a growth in interest in systems approaches in non-infectious disease epidemiology. A fair body of literature in the field has discussed how these methods, in theory, can capture non-linearity, dynamic feedback loops, and emergence in policy-relevant epidemiologic research. However, while calls for these approaches have grown, empiric research that has effectively used these approaches to yield new insight regarding the etiology of high-burden diseases lags behind. Systems epidemiology is hampered by a paucity of guidelines, best practices, and illustrative applications of systems tools to epidemiologic questions. Agent-based modeling is one such systems tool with promise for meaningful applications, yet lacking with respect to a methodologic framework for valid implementation. Here, I establish a conceptual paradigm to designing, parameterizing, and implementing agent-based models in epidemiology. Using this conceptual paradigm, I compare and contrast differing approaches to the parameterization and validation of agent-based models via the design and implementation of two agent-based epidemiologic models, one exploring the role of social networks in obesity, and the other exploring the relationship between collective efficacy and community violence. With robust methodologic frameworks, systems epidemiology has the potential to expand our toolkit with respect to understanding the causes and consequences of chronic disease.

# Complexity and Risk in Family Medicine's Epidemiology. An Interdisciplinary Approach

**Martin Kornitzer**

m-konitzer@t-online.de

**Background, Objectives and Aim.** This presentation links up with the debate on natural and social inverse power law networks in medicine (West 2010, 2013). The objective is to describe the complex distribution of family medicine's diagnoses by sociological and linguistic tools (Pareto 1909, Zipf 1949) and to focus on the distribution's risk problem referring to complexity in economics (Keynes 1921, Mandelbrot 2004). The aim is to reduce the complexity of diagnoses' distribution by mathematical principles and to minimize diagnostic risks by apt heuristics.

**Methodology, Material.** CONTENT's (Kühlein 2008), SESAM's (Voigd 2002) and Braunian grid's (Fink 2007) results of consultations are processed mathematically to verify inverse power law properties and generate graphs and formulas in case of a power law fit.

**Results.** Inverse power law properties. CONTENT's, SESAM's and Braunian grid's results of consultations share inverse power law properties as can be demonstrated by graphs and formulas.

Diagnostic risks. Diagnoses' inverse power law distribution owns a limited predictability concerning potentially dangerous conditions. The fat tail of the diagnoses' distribution consists of 80 % results of consultations labeled by 20% most frequent but least hardened diagnoses and the thin tail of hardened but less frequent ones. In terms of Keynes' probability (Keynes 1921, Skidelsky 2009) the thin tail's risk is „ordinal“ (known unknowns) because of its low frequency, the fat tail's risk is „uncertain“ (unknown unknowns) because of its poor hardening. Bayesian strategy – to be based on certain prevalences - is not an apt tool to handle limited predictability of inverse power law distributions as shown (Keynes 1921, Mandelbrot 2004, Taleb 2007) in economics.

**Conclusions.** Family medicine's distribution of diagnoses is an inverse power law network which can be interpreted as social as well as natural one. A social one it is by the linguistic properties of the diagnoses, a natural one by diagnoses' biological quality. The latter implies the problem of limited predictability of potentially dangerous conditions under power law circumstances. To solve this problem non-Bayesian heuristics as diagnostic protocols (Braun, Mader 2005) and Sadegh-Zadeh's set theory approach (2012) are finally discussed.

# **Complexity Science and Rabies Control. Applying complexity science to understand the spread and mitigation of a public health problem**

**Sonali Vaid**

Svaid@post.harvard.edu

Rabies transmission is dependent on an entire gamut of factors which operate at multiple levels – human (host), agent(dog), social level, environmental factors, policy etc. These elements interact with each other in various ways and these interactions can lead to unpredictable results which occur because the system reorganizes itself in response to external factors. This behavior can be characterized as a 'complex adaptive system'.

We will focus on some of the characteristics of a complex adaptive system and how they apply to rabies control. These concepts include nested systems, feedback loops, internalized rules, fuzzy boundaries, tension and paradox, self-adaptation, simple rules and dispersed control.

This thesis will explain how the attributes of the rabies control problem can be viewed through a complexity lens. Using rabies control as an example, this thesis will demonstrate that complexity science can help contribute to our conceptual understanding of public health problems and provide us with better insights on addressing them"



# **The Human Processual Interdependent Phenotype: A Complexity Sciences contribution to the Theoretical Foundations of Systems based Medicine**

**James C. Palmer**

caldwellpalmer@aol.com

This presentation introduces the human Processual Interdependent Phenotype (PIP) as an applied research framework and its unifying contribution to the theoretical foundations of Systems based medicine. The Processual Phenotype takes as its starting point the emergent multitudinous and multidimensional points of interdependent interactions with self, others and environments – natural and built. It is a unifying physiological – psychological complexity sciences and commensurable theories perspective of the human organism. The core proposition of PIP is that variability is the inseparable fraternal twin of viability. PIP informs integrated variability analysis of the intrinsic nature of disease and health complexities. Dynamic and continuous variability is taken as the given nature of existence in the universe for the human organism -- with the implication being “Never Quite at Equilibrium”. The processual phenotype provides enabling processual capacities and qualities to survive, reproduce and thrive interdependently.

PIP will be explained with examples and applications related to: 1) COPD (Chronic Obstructive Pulmonary Disease) for improved pheno-typing and actionable biomarkers; 2) tBI (traumatic brain injury) regarding risk assessment and prognosis; 3) Earlier detection and diagnosis of sepsis. For COPD an example clinical processual phenotype template and uses will be described. A pilot data study will be described that applies PIP to COPD to develop a remotely-monitored prognostic biomarker for COPD exacerbations. The pilot uses wireless biosensors and smart phones.

For tBI and associated complications a possible risk index of non-linear variability measures will be shared.

The earlier detection and diagnosis of sepsis in post-transplant Bone Marrow Patients will be described.

Fractal analysis of processes as structure and as function will be described with the above examples. Currently untapped contributions of fractals as temporal/scaling symmetries will be mentioned. The unifying ubiquity of fractals across the body and its significance for systems based medicine will be discussed.

The widely ramified and potentially significant implications of PIP for Systems based medicine will be briefly summarized.

# Anticipation in Complex Systems: Potential Implications for Improving Safety and Quality in Healthcare

Tom Staiger  
staiger@uw.edu

The theoretical biologist, Robert Rosen, proposed that a capacity for anticipatory change is a fundamental characteristic most complex systems, including all living complex systems. As defined in his *Anticipatory Systems: Philosophic, Mathematic, and Methodological Foundations*, an anticipatory system 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.” In Rosen’s view, two key features which differentiate most complex systems from “simple” mechanistic systems are: 1) living complex systems have a capacity for anticipatory change and 2) no single model or finite set of models are capable of capturing all of the information in a complex system (while a mechanistic system always has a model which can capture all of the information about the system). Consequently, change in mechanistic systems occurs only due to forces acting iteratively on the system’s current state, while change in living complex systems occurs through both iterative state transitions and from anticipatory feedback loops.

Healthcare organizations are complex adaptive systems composed of multiple micro systems. If Rosen’s anticipatory systems hypothesis is correct, implications for improving safety in healthcare organizations include the following:

1. Anticipatory inputs can be useful for identifying and mitigating some clinical situations for which there is an increased risk of a serious adverse event.
2. Optimal team functioning should include encourage identifying discrepant current state and anticipatory assessments from clinical team members and from patients and families, especially in high-risk situations.
3. 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 event.
  - a. Teams that recognize that disagreements/conflicts regarding the appropriate care of a patient may indicate an increased risk of an adverse event may be able to mitigate this risk in real time.
4. Healthcare organizations may be able to reduce certain adverse events by promoting an awareness of the role of anticipation and of recognizing discrepant present-state or anticipatory models in reducing risk and by promoting ongoing assessments of the degree of agreement between team members and patients/families regarding a patient’s plan of care.

# **Disease Complexity - Physiology**

## **Chair: Frances Griffith**

**Bruce West** - Thinking About Complexity for Medicine

**Andrew Seely** - Monitoring Variability and Complexity at the Bedside

**Henry Heng** - Heterogeneity mediated system complexity: the ultimate challenge for studying common and complex diseases

**Martin Piccard** - A bioenergetic origin of disease complexity

**Moderator of Panel Discussion: Brian Castellani**

## Thinking About Complexity for Medicine

**Bruce West**

The theory of medicine is intended to explain the workings of the large number of mutually interdependent, complex, physiologic networks in the human body and to apply that understanding toward maintaining the functions for which nature designed them. The same ideas can be used to describe healthcare organizations. However, when what had originally been made as a simplifying assumption or a working hypothesis becomes foundational to understanding the operation of physiologic (healthcare) networks, it is in the best interests of medicine (healthcare organizations) to replace that assumption and to determine how the new hypothesis affects understanding of medical organizational science. Normal statistics is an arcane assumption in complex systems. We explore some implications of its replacement with fractal statistics and examine the difference between black swans and dragon kings. One implication of the difference is how to relate disease to the loss of complexity rather than to the loss of variability.

## **Monitoring Variability and Complexity at the Bedside**

**Andrew Seely**

aseely@Ottawahospital.on.ca

Continuous monitoring patterns of variations of heart rate and respiratory rate has proven to be life-saving in fetal and neonatal medicine. Evidence demonstrates reduced a degree and complexity of heart and respiratory rate variability in association with the presence and severity of critical illness. Monitoring variability promises to assist bedside clinical decision-making in such areas as deciding when to liberate an individual patient from a ventilator, and others. The physiologic understanding of complex variation remains under investigation with theories being debated even as this technology bridges to the bedside.

## **Heterogeneity mediated system complexity: the ultimate challenge for studying common and complex diseases**

**Henry Heng , JB Stevens, BY Abdallah, SD Horne, G Liu, KJ Ye, SK Chowdhury, SW Bremer and CJ Ye**

hheng@med.wayne.edu

Influenced by the gene-centric conceptual framework, current studies of disease mainly focus on the characterization of gene mutations or other molecular mechanisms. It is generally accepted that genes are the drivers of diseases. However, it has been very hard to identify these common drivers for most common and complex diseases, despite extensive efforts spanning decades. Furthermore, various –omics based studies have illustrated that the common feature of most common diseases is genetic and non-genetic heterogeneity at multiple levels!

Heterogeneity is traditionally considered to be insignificant “noise”, and good research strategies are needed to reduce or eliminate the noise in order to determine the pattern of the signal. However, if heterogeneity represents a key feature of disease, such approaches are fundamentally limited. It is challenging to translate this “noise free” knowledge back into “noise rich” systems. This paradoxical situation is reflective of the current status of disease research. On one hand, we know much about genes linked to these common diseases, yet, it is extremely difficult to apply this gene knowledge to effectively treat these diseases.

The key to solving this dilemma is to directly study system heterogeneity, the key contributor to biological complexity. For example, without heterogeneity, cancer would be incapable of existing in the first place. It is only when the degree of heterogeneity is used as an index of system instability or evolutionary potential that cancer evolution can be realistically studied. In fact, monitoring system behaviors such as stability often result in better prediction power than focusing on lower level of component, as most disease systems are highly dynamic by nature.

Here we use cancer, Gulf War Illness and chronic fatigue syndrome as examples to illustrate these concepts. We will discuss how system inheritance and inherited heterogeneity contribute to diseases more strongly than individual genes, and why the time factor must be incorporated within the multiple levels landscape model in order to explain the stochastic behavior of disease progression and response to treatment. Stress-induced heterogeneity not only serves as a tool of cellular adaptation, but as a trade-off it also contributes to diseases.

## **A bioenergetic origin of disease complexity**

**Martin Picard**

[martinpicard@mac.com](mailto:martinpicard@mac.com)

Life and health processes depend on the flow of energy through the system. At the cellular level, energy flow occurs mainly within organelles known as mitochondria – the seat of cellular bioenergetics. In concert with their role in energy production, mitochondria produce critical signals of adaptation that influence epigenetic regulation and gene expression in complex ways. When mitochondria become increasingly dysfunctional, rather than causing progressive (linear) alterations in gene expression, they can induce phase-like opposite transitions in the cellular transcriptome. Disruption of a single biological processes (i.e., bioenergetics) can thus yield multiple co-morbid states. Because mitochondria are present in every cell of the body and dynamically respond to a variety of neuroendocrine factors, “mitochondrial retrograde signaling” represents a potential mechanism by which biological and psychosocial factors are integrated and transduced to impact disease complexity.

# **Disease Complexity - Clinical**

**Chair: Hakima Amri**

**Carmel Martin** - Multimorbidity – Through a Glass Darkly

**Brian Castellani** - Modeling the Temporal Dynamics/Trajectories of Depression. A Case-Based Density Approach

**David Katerndahl** - Viewing mental health through the lens of complexity science

**David Katerndahl** - Quantitatively demonstrating the complex nature of partner violence

**Jeanette Bennett** - Depression: Not just a top-down phenomenon

**Moderator of Panel Discussion: Joachim Sturmborg**



## **Multimorbidity – Through a Glass Darkly**

**Carmel Martin**

carmelmarymartin@gmail.com

Multimorbidity is a maladaptive network phenomenon. Diseases, syndromes and symptoms are emergent phenomena of the intricate interactions between complex genomic, proteomic and metabolomics networks within the complex dynamic environmental context and the individual's intimate and wider social networks. These network interactions 'stress' the immune function resulting in the modulation of inflammatory responses that may ultimately lead to distress and disease. Tackling stress, immune function and biopsychosocial root causes of underlying processes is a disruptive shift from managing an individual's care according to narrowly based disease guidelines and traditional practice.

## **Modeling the Temporal Dynamics/Trajectories of Depression. A Case-Based Density Approach**

**Brian Castellani, Rajeev Rajaram, Frances Griffiths, Emma Uprichard and Jane Gunn**  
bcastel3@kent.edu

This study is fourth in a series of papers outlining a new method – case-based complexity – for modeling the temporal and spatial complexity of complex longitudinal data. It is also second in a series of papers exploring depression trajectories. The specific procedure we employ is called a case-based density approach. This approach is unique in two important ways. First, it conceptualizes complex systems as a set of cases, where each case is a  $k$ -dimensional vector; and where the velocity vector for each case is computed according to its particular measurements on some set of empirically defined variables. Second, it takes a mixed-methods approach to modeling these case-based trajectories and their velocities, primarily by employing ordinary differential equations and the linear advection partial differential equation; which treats macroscopic, dynamical change as a transport issue of aggregate cases across continuous time/space. The three main strengths of this approach are its ability to: (1) translate the data driven, nonlinear trajectories of microscopic constituents (cases) into the linear movement of macroscopic trajectories, which take the form of densities; (2) detect the presence of multiple, complex steady state behaviors, including sinks, spiraling sources, saddles, periodic orbits, and attractor points; and (3) predict the motion of novel cases and time instances. To demonstrate the utility of this approach, we applied it to an existing longitudinal depression study – which has already been studied using growth modeling. Our goal was to see if our approach could lead to similar but also new/novel insights into the data. Results confirmed and extended the insights of our original study.

## Viewing mental health through the lens of complexity science

**David Katerndahl**

Katerndahl@uthscsa.edu

A nonlinear perspective may be relevant to understanding mental disorders, particularly in primary care settings. There is growing evidence that variability in heart rate and mood over time, that nonlinearity of a variety of parameters (from heart rate to mood), and that the degree of covariability of anxiety and depression may be relevant to our understanding of what constitutes mental health and illness as well as their outcomes. In a small study (n=15) of adult primary care patients with major depressive disorder, panic disorder or neither disorder, patients recorded hourly levels of anxiety and depression while awake for four weeks. Analysis of data employed measures of nonlinearity as well as state space grid analysis. Eleven subjects completing the mood diary had missing data rates of 0-2.4%. Results showed that all three groups differed in their patterns of mood variability and anxiety-depression covariability. These results suggest that healthy mood variability includes both linear and nonlinear components, and that mental illness may represent a disturbance in either of these components or in the coupling between different moods. Such a proposed model is based upon the linear-nonlinear relationships between symptoms of anxiety and depression, and how these dynamics change as illness severity increases. If true, then nonlinear dynamics may have important clinical implications for classification of mental disorders (necessitating revision in diagnostic approaches and the classification of mental disorders), identification of novel treatments (small but well-timed, pulse interventions or multifaceted, whole patient approaches), and monitoring of dynamics (i.e. cardiac monitoring) and response. For this reason, a dynamical systems approach has been advocated for psychiatrists and psychologists alike, but such advice may be of particular importance to primary care physicians. However, these implications are based upon preliminary evidence that a nonlinear, dynamical basis for classification and treatment of mental disorders is more parsimonious than the current linear, symptom level model. Further investigations are needed to assess whether a nonlinear, dynamical framework may provide us with a new, yet rewarding, perspective for understanding the emergence and evolution of mental illness.

## Quantitatively demonstrating the complex nature of partner violence

**David Katerndahl**

Katerndahl@uthscsa.edu

**Background, Aims & Objectives.** While the criticism that the use of complexity science concepts in qualitative medical research merely represents the application of a novel metaphor, prior quantitative research does suggest that intimate partner violence (IPV) is nonlinear in its dynamics, its decision-making, and effects of community interventions. The purpose of this study was to quantitatively demonstrate that characteristics seen in complex adaptive systems are present in violent relationships.

**Methodology.** 200 women in violent relationships were recruited from primary care settings and asked to report daily on the presence of violence and the household environment for 12 weeks using a telephone-based, interactive verbal response method. Attitudinal, behavioral and clinical outcomes were assessed at the end-of-study interview. Analysis employed three nonlinearity measurements as well as assign dynamic pattern when possible, vector autoregression using multiple concurrent time series to develop models explaining other variables' time series, orbital decomposition (based on symbolic dynamics) using categorical time series to identify recurrent patterns of strings, and staged multiple regression.

**Results.** The 200 participants provided 9,618 daily assessments; women reported experiencing abuse on 39% of days, while perpetrating violence themselves on 23% of days. First, based on nonlinearity assessments of daily violence, IPV generally displayed nonlinearity with only a few relationships exhibited periodic dynamics. Second, using vector autoregression, relationship violence involved multiple, interdependent factors, circular causality, and feedforward dynamics as expected in complex systems. Third, using orbital decomposition, recurrent multi-day, alcohol-violence patterns suggesting attractors were observed within dynamic patterns. Fourth, after controlling for demographics and violence frequency and severity, measures of violence nonlinearity predicted three of five attitudinal/behavioral outcomes and two of four clinical outcomes.

**Conclusions.** IPV is a complex phenomenon, quantitatively demonstrating many of the features expected in complex systems. As this study shows, IPV is nonlinear, noncausal and attractor-laden, and violence dynamics contributes to relevant outcomes. Complexity science is not just a metaphor applied a posteriori in a vain attempt to explain unexplainable findings; it is a paradigm whose time has come.

## **Depression: Not just a top-down phenomenon**

**Jeanette Bennett and Joachim Sturmberg**

jeanette.m.bennett@gmail.com

Depression is the 2nd leading cause of disability world-wide with prevalence ranging from 2.5-20% of the population dependent on the country. It can present as a single condition, but often it is comorbid with chronic diseases such as cardiovascular disease, type II diabetes, osteoarthritis, and cancer. Depressive symptoms are universal across communities including sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep and/or appetite, feelings of tiredness, and poor concentration. Medical professionals commonly treat depression as a neurotransmitter imbalance; yet, many effects ascribed to anti-depressant medication, such as selective serotonin reuptake inhibitors, have also been explained by the placebo effect in patients with mild to moderate depression.

So far largely ignored research indicates that depression is caused by highly complex interactions of neuroendocrine and inflammatory mechanism. This presentation outlines some of the key findings of this research and its implication for clinical practice.

(1) Endocrinologists have found that over activation of the hypothalamic-pituitary-adrenal (HPA) axis can lead to depressive symptoms including overproduction of corticotropin releasing hormone leading to dysregulated levels of cortisol.

(2) Psychoneuroimmunologists have shown that systemic inflammation may play a critical role in depression. Immune cells produce excessive levels of inflammation due to reductions in sensitivity to the anti-inflammatory effects of cortisol and suppression of parasympathetic activity. Recent findings indicate that inflammation is especially important in treatment-resistant forms of depression.

(3) In addition, culture/stigma, access to mental health services, and social instability play significant roles in perpetuating HPA and inflammatory pathways to maintain the disease and treatment resistance.

The presented evidence highlights the need to appreciate depression through a multi-disciplinary lens to properly treat it and successfully reduce the debilitating effects on quality of life, comorbidity and mortality, especially from suicide.

# **Ethics and Education – the Challenges for Systems-based Medicine**

## **Chair: Beverley Ellis**

**Kevin FitzGerald** - Ethical Complexities Issues in Systems Medicine: What Care and for Whom?

**Fred Hafferty** - Reconceptualizing Medical Education as a Complex Adaptive Environment: An Institutional Imperative

**Stewart Mennin** - Uncertainty and Praxis in Medical Education

**Stewart Mennin** - Integration in Health Professions Education as Emergence

**Eric Valdes** - Complexity and Bioethics in the 21st Century

**Damjana Rozman** - Systems medicine of multifactorial disorders: the approaches of CASyM, the Coordinated Actions Systems Medicine in Europe

**Frances Griffiths** - Systematic literature reviews – beyond Cochrane to complexity

**Moderator of Panel Discussion: Rene Crichlow**

## **Ethical Complexities Issues in Systems Medicine: What Care and for Whom?**

**Kevin FitzGerald**  
Ktf3@georgetown.edu

The ascendance of a systems approach in 21st century medicine promises revolutionary rather than merely evolutionary advances in medical care. Change involves uncertainty which can be expressed as confusion and contention regarding the trajectories and goals to be pursued in medical research and care. This presentation will explore some of the major ethical challenges arising from the shift to a systems science approach in medicine. It will present a possible way to navigate through this complex ethical terrain toward healthcare that benefits all.

## **Reconceptualizing Medical Education as a Complex Adaptive Environment: An Institutional Imperative**

**Fred Hafferty**

fredhafferty@mac.com

This presentation will examine how complexity thinking, and more specifically medical education as a complex adaptive system can be used to improve the education of future physicians. To this end, I will use complexity as an analytic lens to examine (1) how medical education actually functions in the here and now and with particular attention to analytic frameworks heavily used in medical education such as the hidden curriculum, and (2) how future researchers might use the tools of complexity to critically examine, and improve, medical education of the future.



## Uncertainty and Praxis in Medical Education

**Stewart Mennin**

menninsp@gmail.com

The practices of health care, the health professions themselves and the education and preparation for those professions are grounded in observation, sense making and action. All involve a continuous flow of information, collecting and sorting through data, and looking for patterns. We experience and understand the world as patterns made up of "... similarities, differences, and connections that have meaning across space and time." How we think about patterns gives agency to teaching, learning and practicing as a professional. Three types of conditions for pattern formation can be discerned and illustrated in a landscape diagram: certain, variable and emergent. Certainty and variability occupy a limited area in the landscape diagram and a corresponding portion of medical education. Emergent patterns, formed through self-organization, are prominent in living systems, medical education and practice.

Paradoxically, many teachers and learners try to linearize nonlinear situations in order to know what to do and to avoid the uncertainty of appearing to not know. Not knowing is culturally uncomfortable in the practice of medicine and in medical education. Experience teaches us otherwise. Learning to recognize and differentiate certainty and uncertainty and matching the dimensionality of teaching, learning and health care environments with the predisposition of the learners and patients enhances the effectiveness of both learning and patient care.

The essence of learning is experience and the sense and meaning we make from it. Learning to become a physician requires a tolerance for uncertainty because most of what you are learning is new to you. We can begin to improve learning effectiveness in medical education as we move away from the concept of linear sequences of topics, learning as "banking information" and storage and retrieval models of cognition and reasoning toward models that recognize the dynamical and complex adaptive nature of thinking as a relational process dependent on the learners life history and highly sensitive to the conditions and context of the moment learning.

## Integration in Health Professions Education as Emergence

**Stewart Mennin**

menninsp@gmail.com

Integration in health professions education is a much sought after condition yet has remained elusive and difficult to achieve; and near impossible to sustain. The argument is put forward that integration in health professions education is misunderstood and miscast as proximity that is additive. Putting things together in time and space is necessary but not sufficient for integration in a curriculum or in learning. The present work examines this problem from the perspective of learning and integration as emergent properties of a complex adaptive system. The process of self-organization in which a group of agents within a shared boundary or container exchange differences under far from equilibrium conditions leading to system-wide changes as new dissipative structures. In the moment of emergence the new structure/pattern is fully integrated and fit for purpose. Subsequent interaction with the environment leads to the build-up of tension and the process is iterative. This view of change in complex adaptive systems suggests that frequent small changes in a dynamical curriculum setting can sustain integration. The conditions supportive of self-organization must be considered, the container, the differences within the container and the exchange of differences, all affect self-organization. Integration of learning is an emergent process that is fit for purpose. As that conditions change, a continuous self-organization is necessary to sustain a viable and integrated curriculum. Given that learning is an emergent property of a self-organizing complex adaptive process, the conditions that promote learning and integration will be discussed. Examples will be drawn from medical education.

## Complexity and Bioethics in the 21st Century

**Erick Valdes Meza**

erv7@georgetown.edu

Theories of complexity critically impact scientific reductionism in the context of sciences in general and healthcare in particular. One of the key features of these new theories is their ability to integrate, connect and, at the same time, respect and foster diversity inside healthcare systems as well as to recognize that scientific knowledge has limits, and phenomena are not predictable but preventable. One of the axioms of complexity is the impossibility of reaching new knowledge fractionally, so that scientific disciplines should work in a transdisciplinary way, namely to address and study problems jointly from diverse but complementary perspectives.

Complexity does not deny the value of simplifier thought prevalent in sciences. However, healthcare is an ever-changing field, which needs a multidisciplinary approach to identify, address and resolve its problems and correct its deficiencies. This can be justified in the light of globalization and technological empowerment, which are two intrinsic categories of contemporary existence. The emergence of new epidemics and pandemics as well as new types of bacterial and viral pathogens as a consequence of ecological and environmental changes, increases instability, insecurity and inefficiency of healthcare systems.

These transformations cannot be explained or resolved scientifically, in a holistic way, if fragmented and fractionated thought prevails between scientific, political, economic, cultural, religious, ethical and social components of healthcare. In this scenario, bioethics, jointly with complexity sciences, may play a significant role in identifying, clarifying and resolving healthcare's problems. Bioethics is not merely a neutral discipline in the context of current technological world. Despite the impossibility of achieving full consensus about what bioethics' proper task should be, today more than ever before, the need for moral regulations to provide deliberative procedures to reduce pernicious effects and consequences of techno-scientific empowerment inside healthcare systems has become an unavoidable call for bioethicists.

In this paper, I explore the relationships between bioethics and complexity and propose a deliberative and procedural transdisciplinary platform to think about eventual consequences for practice, research and public policy regarding healthcare in the 21<sup>st</sup> century.

## **Systems medicine of multifactorial disorders: the approaches of CASyM, the Coordinated Actions Systems Medicine in Europe**

**Damjana Rozman**

damjana.rozman@mf.uni-lj.si

Human diseases can be viewed as dynamic perturbations of complex, integrated genetic, molecular and cellular networks sensing and responding to the environment. Such a perspective emerges from Systems Biology (SB) and fuels a paradigm shift in classical medicine which re-defines clinical phenotypes. CASyM aims at bridging the current gap between SB and medicine by implementing a multidisciplinary, inter-institutional doctoral training scheme in Systems Medicine across Europe. We aim to supplement the existing doctoral programmes at individual training sites with the new educational concepts proposed by stakeholders including Systems Medicine Centres, major Clinical Centres in Europe and Life Sciences industries. Training will address the clinical needs with a translational focus on personalized (P4) medicine, discovery of effective diagnostics and biomarkers and rational design of combinatorial and chronotherapies encompassing biological clocks. The CASyM concerted training effort represents a template for sustainable interdisciplinary Systems Medicine education programmes, and is a show-case of European training implementation actions. It will broaden the pool of biomedical researchers that combine quantitative techniques and systems approaches in translational and clinical medicine settings and integrate them with health applications of Information and Communication Technologies. By such systems training of the next generation biomedical researchers, CASyM aims to contribute towards reduction of chronic disease-related healthcare costs. In addition to educational procedures we develop research projects that highlight the added value of interdisciplinarity for pending clinical issues. System medicine research within CASyM acknowledges the rapidly increasing number of -omics, and other quantitative and temporal biomedical data. Importantly, the approaches undertaken are not disease-specific, but are relevant for studying any complex disease. The examples within CASyM are malignant, autoimmune and metabolic chronic disorders. Approaches towards understanding the appearance and progression of multifactorial liver diseases will be presented in more details in the talk, by describing the role of hepatic cholesterol synthesis, and the SteatoNet as the first integrated human metabolic model with multi-layered regulation to assess liver-associated pathologies.

## **Systematic literature reviews – beyond Cochrane to complexity**

**Frances Griffiths**

f.e.griffiths@warwick.ac.uk

From the perspective of complexity science the deterministic approach of Cochrane systematic reviews appears restricted, seemingly missing the complex interaction between social and environmental context, individuals and social groups, health care providers and specific health interventions. However, the Cochrane Collaboration has established a rigour for evidence review of the effect of interventions and there is guidance for rigorous reporting. This rigour can be applied to other types of research questions that use peer reviewed published empirical evidence as their data source. Drawing on published literature, this paper considers the role of Cochrane style reviews for our complex world and compares this with a realist approach to the review of research literature. The latter seeks to understand how an intervention works in particular contexts. Both recognise complexity, both include the identification of key components – what the intervention is intended to do, both recognise the importance of context, and rigour is equally important in both. However, Cochrane reviews limit the reach of the review to specific contexts where-as realist reviews seek to understand how mechanisms work in differing contexts. Cochrane reviews seek to include studies of interventions with similar components. These components are context specific manifestations of the theory on which the intervention is based. Realist reviews seek to understand how theoretical mechanisms are manifest in different contexts. For collaborative international research a Cochrane reviews may need to be undertaken separately for contexts that are very different such as high and low income countries. However, the theoretical mechanisms of an intervention, which are identified as part of the review process in a realist review, are likely to be similar internationally. The realist review itself seeks to understand how context makes a difference to outcome. Cochrane style and realist reviews can be complimentary in advancing understanding of our complex world and how complex interventions have their effect. Further development of theory about mechanisms of action/non-action of complex interventions may be more fruitful when undertaken collaboratively with very different contexts in mind.

# Change in an Adaptive Organization

## Chair: Aviad Haramati

**Shimon Waldfogel** - Public Reporting: Potential for healing the US healthcare system

**Russell S. Gonnering** - Agent-Based Modeling of Organizational Performance

**Sergio Camorlinga** - Leading the Healthcare Organization as a Complex Adaptive System

**Beverley Ellis** - The value of systems and complexity thinking to enable change in adaptive healthcare organisations, supported by informatics

**Andrew S. Valeras** - Addressing avoidable ED utilization and rehospitalizations as symptoms of complexity through a quality improvement methodology

Lunch

## Chair: Paul Plsek

**Carmel Martin** - Access to Primary Care: a Complex Adaptive Systems perspective

**Yaneer Bar-Yam** - Complex Systems Science and Healthcare Improvement

**Joachim Sturmberg** - "If the theory don't fit the facts, change the theory." Implications for Health System Reform

**Lucy Leykum** - Manifestations and implications of uncertainty for improving healthcare systems: an analysis of observational and interventional studies grounded in complexity science

**Curt Lindberg & Elizabeth Ciemins** - Embracing Uncertainty: Complexity-inspired Innovations at Billings Clinic

**Moderator of Panel Discussion: Stewart Mennin**

## **Public Reporting: Potential for healing the US healthcare system**

**Shimon Waldfogel**

Shimonw@comcast.net

Transparent data about function and outcomes is essential for learning about and “treating” complex evolving systems. This presentation will explore the role of public reporting of healthcare outcomes and related performance information about hospitals and other healthcare systems. In particular we will focus on our work that tests the proposition that reliable, timely actionable data about healthcare organization’s performance can inform citizens about their healthcare system and motivate them to play a role in improving healthcare outcomes.

It is well recognized that improving the performance of the US healthcare system has been severely hampered by a lack of reliable and meaningful data about the performance of the many healthcare organizations serving the US public. Currently, where data does exist, its value is inaccessible due to poor transparency. We seek to change that by leveraging advances in digital technology, recent legal pronouncements, and cultural expectations for public reporting of healthcare outcomes.

Building on an understanding of information flow in complex systems, we provide meaningful data in an assessable way to citizens and give them tools to interact with other stakeholders. In our presentation we share a number of “case reports “ from our work to highlight ways that maximize citizen oriented public reporting of healthcare outcomes and relevant performance by healthcare organizations. Our discussion will address the potential for as well as pitfalls of meaningful public reporting within the emerging healthcare system.

# Agent-Based Modeling of Organizational Performance

Russell S. Gonnering and David Logan

rsgonnering1@me.com

**Background.** In a Complex Adaptive System such as healthcare, co-evolution of the agents and the system produces emergent order. Investigations into drivers of organizational performance reveal the importance of coherent group effort (Organizational Culture) as well as strategy. Nonlinear improvements in performance result as organizational culture advances. These advances are heavily dependent upon starting point and exhibit path dependency.

**Aims & Objectives.** When faced with a desire to improve performance, an organization may have difficulty in planning and prioritizing first steps. Where should one begin? How should resources be allocated? Agent-based modeling can be used to allow an organization to experiment with multiple “What if?” scenarios and do so rapidly and with minimal resource expenditure.

**Methodology.** We developed a NetLogo™ agent-based model showing the evolution of Organizational culture based upon selected starting points of Organizational Culture, Values, Purpose, Intellectual Capital and Perspective. Parameters change in accordance with interactions of the agents in time and space as well as the impact of both planned and stochastic external variables on the parameters. We used the biologic allometric scaling equation,  $y = k x^\alpha$ , reasoning that Organizational Productivity behaves in the organization like biologic variables behave in the organism. In this model,  $k$  is a dynamic constant reflecting changes in Organizational Culture, Values, Purpose and Innovation,  $x$  is the Intellectual Capital of the organization (analogous to mass in the organism) and  $\alpha$  is .75.

**Results.** At baseline, the model consistently mirrors a 10-year empiric study of real-world organizations. Without intervention, Organizational Culture reaches an asymptotic maximum with minimal, linear improvement in performance over time. By altering the starting point, or by closing “structural holes” in the organization, Organizational Culture passes through phase-transitions with resulting non-linear increase in Organizational Performance.

**Conclusions.** We concur with George Box that “all models are wrong but some are useful”. This model, though incomplete, offers an insight into the interactions of factors influencing performance in an organization. An important corollary is the need for healthcare professionals to include agent-based modeling in their capability quiver.



# Leading the Healthcare Organization as a Complex Adaptive System

**Sergio Camorlinga**

s.camorlinga@uwinnipeg.ca

**Background.** Healthcare is a convoluted system with a large number of opportunities and challenges. No matter what administrative task is performed, interdependencies of people, resources and processes are everywhere. Many times services provided are not achievable as originally expected. Due to the business complexity it is difficult if not possible to identify what is the cause of the inefficiency. Performance metrics can be defined and measured without having a good understanding of the factors that generated those metrics. This has an impact on the value of health systems interventions because no clear cause of benefit or costs can be associated to the intervention outcomes. Another instance are initiatives to integrate healthcare, which are faced with limited success to reduce costs and bring substantial improvements in healthcare delivery. These are some of many examples where health systems' complexity requires of a different perspective in its administration and leadership. Complex adaptive systems (CAS) is an interdisciplinary field that brings a different perspective to lead healthcare organizations. CAS concepts of non-linearity, interdependencies, adaptability and emergence are applicable to health system administration and provide a relatively novel approach to manage healthcare organizations.

**Objectives.** To have an understanding of essential CAS concepts and discuss how healthcare administrators can use the CAS concepts in their organizations. Several cases for healthcare administration will be examined to illustrate how the CAS concepts can be applied in their institution and the benefits that they potentially introduce.

**Methodology.** CAS concepts are demonstrated with simple simulations to facilitate their understanding. Then health system cases where CAS theory is applied are reviewed, including cases for health systems interventions and health care integration. The scenarios exemplify challenges in healthcare administration and how CAS brings an alternative perspective to manage and lead.

**Conclusions.** The proposed approach facilitates comprehension of existing healthcare organization contexts from a CAS perspective and shows how simple steps can lead the organizations to other desired scenarios. The CAS principles offer administrators and leaders a framework that will help understand the organization complexity and get insight to potentially achieve better outcomes when health interventions are done

# The value of systems and complexity thinking to enable change in adaptive healthcare organisations, supported by informatics

**Beverley Ellis**

BSEllis@uclan.ac.uk

**Background.** This paper provides an overview of complex adaptive systems (CAS) theories and value in enabling change in an adaptive organisation. A CAS approach is interpreted here as a framework that assists thinking about the nature of quality improvement programmes with a focus on the people involved.

**Objective.** To identify key elements and characteristics of complex adaptive systems, drawing on examples from primary care informatics and clinical governance programmes.

**Method.** The research strategy is built on longitudinal case studies of the implementation of clinical governance arrangements in two United Kingdom (UK) Primary Care Organisations (PCOs) and includes a literature review to develop theoretical models relevant to the governance of quality improvement.

**Results.** The findings show that CAS theories are a valuable tool to help make sense of natural phenomena, which include human responses to problem solving. Approaches incorporate professional self-regulation that builds on the skills and strengths of the clinicians. There is considerable variation in the way in which consultation data is captured, recorded and organised, which includes free text, coded data and structured data collected using templates. An emphasis on incentivised information sharing led to local consensus on standard coding policies and models of data recording before any national contractual requirement. Informatics is acknowledged as a mechanism to link electronic health record outputs, quality improvement and resources. Investment in informatics, education and training are identified as development priorities in order to embed clinical governance principles in practice.

**Conclusions.** This study suggests that a CAS approach is useful in describing evolutionary change processes in semi-autonomous, networked PCOs. The adoption of new forms of governance do not necessarily neutralise previous models, but add further dimensions to them. For instance, clinical governance models have moved from deterministic and 'objective' factors, to incorporate cultural aspects and the exploitation of the potential offered by networks, interactions and feedback mechanisms enabled by developments in primary care informatics.

## **Addressing avoidable ED utilization and rehospitalizations as symptoms of complexity through a quality improvement methodology**

**Jacqueline Morse, Andrew S. Valeras, Dominic Geffken, Aimee Valeras,  
Dan Eubank and Travis Harker**

[jmorse@crhc.org](mailto:jmorse@crhc.org)

This presentation will describe two quality improvement (QI) projects in our Family Medicine Residency / community health center practice. These projects sought to understand and reduce a) high utilization of the Emergency Department (ED) and b) hospital readmissions. Patients who have high ED utilization and patients who are rehospitalized within 30 days of discharge often have complex medical needs and challenging psychosocial concerns and barriers in navigating the healthcare system. We created two registries of patients from our EMR data, a) patients who had high ED utilization and b) patients who had hospital readmissions within 30 days. To address avoidable ED utilization, two targeted interventions were implemented: a Patient Advisory Committee (PAC) and an Urgent Plan of Care (UPOC). To address avoidable rehospitalization, three interventions were implemented: improving the quality of discharge summaries through the use of electronic reminders in order to capture key information, having an outpatient nurse place a follow-up call within 48-hours post discharge, and a weekly team-based group visit. We measured significant reductions in ED utilization and hospital readmissions. These concurrent QI projects included both population-based and person-centered approaches to better manage complexity in healthcare. The mainstream focus on avoidable ED utilization and re-hospitalization used primarily problem-focused methodologies. Reframing these two forms of utilization as symptoms of a complex system and using complex adaptive systems principles to better understand the relationships inherent in these processes allowed for a meaningful and valuable understanding of both topics. With these new understandings, cultural change was enabled, allowing and supporting different and novel ways to address such complex outcomes.

## Access to Primary Care: a Complex Adaptive Systems perspective

Carmel Martin and David Emanuel Surate Solaligue

carmelmarymartin@gmail.com

**Aims and objectives.** This paper analyses access to primary care/general practice (PC) through a complex adaptive systems (CAS) lens. The driver for this analysis is the current policy and operational push to deliver improved access to PC to avert pressure on emergency departments, without necessarily improving supply of PC services.

**Methods.** The 2002 – 2014 literature was scoped using major mesh heading general practice; access to healthcare was the mesh subheading with key words primary care, appointments and or scheduling. The study reviewed 75 papers (240 identified) and categorised them using thematic analysis within a CAS framework.

**Findings.** Primary care, internationally, aims to provide timely access and continuity of care to a comprehensive range of services for most personal health needs. Interdependent PC dimensions of access, continuity, case-mix, preventive care, convenience and social needs do not fall into static linear categories. Current research focuses on provider organisations and intensity of need according to population risk. Practices are heterogeneous and operate diverse access accommodation practices. While studies focus on intensity of need according to population risk, little research is conducted on individual patient journeys of the very high risk 5% with potential for chaotic deteriorations. Studies focus on emergency department access and risk of readmission, but not on the nature of access for this subgroup who require unpredictable urgent attention. Historical lessons indicate that imposed constraints linked to pay for performance type incentives on processes, often do not deliver the intended outcomes, with unintended and unwanted consequences.

The diversity of patient types and needs, the number of actors involved in primary care – doctors, nurses, receptionists and a wider network of providers outside of the practice all make for multiple interactions in a CAS. A CAS framework for access to PC would focus on the access acuity needs of heterogeneous individuals, prioritising those with a risk of acute or sub-acute deterioration for prompt access. Modelling the dynamics of access-accommodation is possible for most patients who fit case mix type categories, but the timing of chaotic or sub-acute deteriorations is unpredictable. All practices will need to pay attention to the acuity of presentations, and make adjustments with receptionists and or nurse and doctor triage. Balancing needs and demands in accordance with supply of appointments will always require continual adaptation in complex PC systems.

**Conclusion.** In order to improve accommodation of potentially urgent presentations to PC, a CAS framework provides for a whole systems dynamic picture of competing priorities, emergence and unintended consequences. Modelling the complex dynamics of access accommodation together local organizational sense-making processes will likely provide the best outcomes.

## **Complex Systems Science and Healthcare Improvement**

**Yaneer Bar-Yam**

yaneer@necsi.edu

We provide eight complex systems science based steps for improving the healthcare system. The core of the approach is promoting the best use of resources by matching the people and organization to the tasks they are good at, and providing the right incentive structure. High quality service and low costs can be achieved by making sure the right people and the right organizations deliver services. Effective management must not interfere with the performance of care. Otherwise, cost control only makes care more cumbersome, increasing rather than decreasing costs and reducing quality. The eight steps we propose are designed to dramatically improve the effectiveness of the healthcare system, both for those who receive services and those who provide them. In brief: 1. Separate simple care from complex care. 2. Empower workgroup competition as an incentive, and avoid regulating costs or quality. 3. Create superdoctor teams to rapidly diagnose and treat highly complex conditions. 4. Accelerate intake routing to rapidly identify the right provider. 5. Add redundancy to improve communication to prevent prescription errors. 6. Create disinfection gateways at spatial boundaries to reduce hospital-based infections. 7. Use e-records for research to supplement clinical studies. 8. Promote “First Day” celebrations to encourage healthy behavior.

## **“If the theory don't fit the facts, change the theory.” Implications for Health System Reform**

**Joachim Sturmberg**

jp.sturmberg@gmail.com

Health systems have all the hallmarks of complex adaptive systems, they respond to changing demands in multiple different ways depending on local situations or national constraints. Mostly these constraints are based on economic/industrial considerations and essentially apply universally around the globe.

The economic/industrial considerations are measured and communicated in terms of access to care, waiting times, distribution of funding, staying on budget, maximising service output, effective use of resources, safety of care, meeting incentivised service provision targets, satisfaction, mortality and other public health statistics.

However, besides of the economic/industrial perspective the system needs to respond to the patient's considerations/expectations of achieving quality of life, managing when living with disability and being supported when self-management alone is no longer sufficient.

The facts are: the predominant economic/industrial focus has resulted in every increasing healthcare costs and slowly decreasing patient-focused health outcomes. So what needs to change? As complex adaptive system behaviour is driven by the systems core focus, the current focus has to change from an economic/industrial to a person-centered one. This talk outlines how a change towards a person-centered focus will result in the emergence of a health system that is both more effective and more efficient for both, patients and economic sustainability.

# Manifestations and implications of uncertainty for improving healthcare systems: an analysis of observational and interventional studies grounded in complexity science

Lucy Leykum, Holly J. Lanham, Jacqueline A. Pugh, Michael Parchman, Ruth A. Anderson, Benjamin F. Crabtree, Paul A. Nutting, William L. Miller, Kurt C. Stange and Reuben R. McDaniel, Jr.  
Leykum@uthscsa.edu

**Background.** Results of efforts to improve healthcare systems remain mixed. Complexity science suggests that paying attention to the relationships between individuals in healthcare systems could be an important strategy for improving outcomes. However, results of our observational and interventional studies focusing on relationships to understand or improve outcomes have also been inconsistent. We sought to better understand and explain these inconsistencies, using complexity science as a framework to analyze our findings and build new theory.

**Methods.** We used the eight observational and interventional studies in which at least 2 members of the author team were involved as the basis of our analysis. The author team held 16 meetings over 11 months using an approach guided by set theory. We iteratively analyzed our studies by dividing them into subsets based on their sharing similar attributes, and then examining differences in outcomes to assess whether the subset attributes could explain our outcomes. Insights from each subset analysis informed the next set of subsets identified and analyzed in a constant comparative manner. We initially focused on differences in setting, but these did not explain our findings. We then turned to differences in patient care activities and tasks being studied, and the attributes of the disease being treated. Finally, we examined the interdependence between task and disease. We utilized system-level uncertainty as a defining characteristic of complex systems through which we interpreted our results.

**Results.** We identified several characteristics of healthcare tasks and diseases that impact the ways uncertainty is manifest across diverse care delivery activities. These include disease-related uncertainty (pace of evolution of disease and patient control over outcomes), and task-related uncertainty (standardized versus customized, routine versus non-routine, and interdependencies required for task completion).

**Conclusions.** Uncertainty is an important aspect of clinical systems that must be considered in designing approaches to improve healthcare system function. The uncertainty inherent in tasks and diseases, and how they come together in specific clinical settings, will influence the type of improvement strategies that are most likely to be successful. Process-based efforts appear best-suited for low-uncertainty contexts, while relationship-based approaches may be most effective for high-uncertainty situations.

## **Embracing Uncertainty: Complexity-inspired Innovations at Billings Clinic**

**Curt Lindberg, Elizabeth Ciemins**

complexitypartners@gmail.com

Listen in on a conversation as two staff members explore Billings Clinic's journey with complexity science. Learn how the science inspired innovative approaches to improvement like Positive Deviance and Relational Coordination, new understanding about change, involvement in predictive monitoring research, and development of leaders at all levels. Learn about strategies employed to spread understanding and use of complex systems concepts and factors that impacted the expanding complexity-inspired agenda. In this dialogue, a surprise or two may emerge. You know how conversations go.

Joining in the discussion will be two leaders who are guiding the complexity initiative: Elizabeth Ciemins, Director, Center for Clinical Translational Research and Curt Lindberg, Director, Partnership for Complex Systems and Healthcare Innovation.



## **Poster Session**

**Chair: Rene Crichlow**

# **The Complex Nature of Health (NH)**

## **Chair & Moderator: Lee Hong**

**NH 1. Robert Eyre** - Social Networks and Health: Spreading of depressive symptoms over adolescent friendship networks

**NH 2. William M. Taylor** - A Complexity Definition of Health

**NH 3. Krithika Bhuvaneshwar** - G-DOC Plus – the next generation systems medicine platform for precision Medicine

**NH 4. Carmel M Martin** - Taxonomic 'Complexity'! Complex versus Complex adaptive/nonlinear concepts in evaluative primary care research

**NH 5. Henry White** - Mapping Complex Co-morbidities

## **NH 1. Social Networks and Health: Spreading of depressive symptoms over adolescent friendship networks**

**Robert Eyre, Frances Griffiths and Thomas House**

r.w.eyre@warwick.ac.uk

**Background.** Depression forms a major contribution to the global disease burden, playing a debilitating part in the lives of millions of people across the world. It affects a significant percentage of adolescents. Depression is characterised by a set of symptoms affected by social networks. Previous work, utilising the Add Health data set, used a binary model of “depressed” versus “not depressed”, and demonstrated that being “not depressed” can transmit over a friendship network.

**Aims and Objectives.** We aim to consider greater layers of complexity to the transmission of depressive symptoms.

**Methodology.** We do this by applying two changes to the previous work. First, we consider whether people change in their level of depression at all, and in what direction, i.e. getting worse or getting better over time. Second, we consider individual symptoms. We use data from 2194 young people aged 12-19 from the Add Health dataset. We examine changes in symptom levels and the dependency of the probabilities of worsening and improving of symptoms on the number of better off and worse off friends. We achieve this with empirical data analysis and parametric inference.

**Results and Conclusions.** We find that, for almost all symptoms, having more worse off friends makes it more likely for an individual to get worse, and less likely for them to improve, and vice versa for better off friends. This suggests that whether having more friends will make you emotionally healthier is dependent on the emotional state of the friends. We also find that individuals are more likely to change in symptoms than not at all, and no bias exists towards improving or worsening. Evidence also suggests that the change in symptom level follows an exponential distribution. This suggests that the change in symptom levels between time points occurs in one direction only, i.e. people keep getting worse or keep getting better between time points, instead of following a random walk. Therefore, the effects of the friendship network happen progressively.

## NH 2. A Complexity Definition of Health

**William M. Taylor**

wtaylo27@jhmi.edu

Despite the lack of a common definition, the terms health and healthy are understood and used in a wide range of circumstances by both professionals and the general public. We know what we mean when we say healthy tissue, healthy heart or environment. The current definition of health written by the World Health Organization in 1946 satisfies no one and attempts to craft a new one have not gained wide acceptance. The scale-free nature of complexity science may provide the conceptual and mathematical tools that can be used to develop a definition of health that is applicable in a variety of settings. The concept of “free energy minimization” first developed by British neuroscientist Karl Friston has shown success at modeling behavior in the brain as a minimization of predictive error. It will be demonstrated that the free energy principle can be extended in a scale-free manner to the concept of health; where health is seen as a nested network predictive hierarchy with the system as a whole seeking to minimize predictive error. From this a complexity definition of health is derived.

### **NH 3. G-DOC *Plus* – the next generation systems medicine platform for precision Medicine**

**Krithika Bhuvaneshwar, Anas Belouali, Varun Singh, Robert M Johnson, Lei Song, Shruti Rao, Adil Alaoui, Michael A. Harris, Yuriy Gusev and Subha Madhavan**  
sm696@georgetown.edu

G-DOC *Plus* is an enhanced web platform that uses cloud computing and other advanced computational tools to handle NGS and medical images so that they can be analyzed in the full context of other omics and clinical information. It allows translational science researchers to explore data one sample at a time, as a sub-cohort of samples; or as a population as a whole, providing the user with a 360-degree view of the data. G-DOC *Plus* tools have been leveraged in the cancer and non-cancer realms for hypothesis generation; biomarker detection and multi-omic analysis, in-silico and population genetics analysis; and to explore somatic mutation and breast cancer MRI images. The long-term vision of G-DOC *Plus* is to extend this systems medicine platform to hospital networks to provide clinical decision support using multi-omics and relevant clinical information to support personalized patient care.

## NH 4. Taxonomic ‘Complexity’! Complex versus Complex adaptive/nonlinear concepts in evaluative primary care research

**Carmel M Martin**

carmelmarymartin@gmail.com

**Context.** There is significant variation in the use of the term complexity in the primary care research and practice evaluative literature. Greater clarity with respect to the terms complexity, complex interventions, complex adaptive systems theory and non-linear dynamics.

**Objective.** To explore the use of the ‘complex’ terminology in the Medline electronic database in relation to primary care.

**Methods:** Historical Narrative Literature Scoping Review. Literature searches scoped each term: ‘complexity’; ‘complex interventions’; ‘complex adaptive systems’ (CAS) and non-linear dynamics (NLD) and the term ‘primary care’ from 2000 to 2013 in primary care research and academic articles. Analysis included descriptive categorization and identification of key themes in relevant articles using grounded theory methodology

**Results.** Literature scoping yielded the following English language article counts: complexity and primary care 1446; complex adaptive systems and primary care 226; complex adaptive systems and non-linear dynamics and primary care 154; and complex interventions and primary care 904. The major themes identified were: complex - ‘difficult’ to implement or control and unclear; complexity - ‘multi-faceted’ or ‘complicated’ such as multi-morbidity, multiple steps, polypharmacy; ‘complex intervention’ - ‘black box’ of multiple interventions in a trial requiring detailed process evaluation to interpret attribution; and complex adaptive systems – all systems have dynamics, feedback loops, non-linearity, adaptability. Non-linear dynamics refer to modelling of data and explores theoretical complexity and chaos and other dynamic theories, to be understood in retrospect when underlying adaptive rules became evident and could be described by mathematics and/or sociological theory Multi-morbidity, as an emergent theme over time constructing multiple diagnosis or problems as complex, complexity, complex-intervention and less commonly complex adaptive system phenomenon.

**Conclusions.** The most common use of the term complexity relates to the lay definition of multifaceted and complicated. A complex intervention refers to a type of trial with multifaceted interventions with difficulty determining the effect of discrete components of the interventions on trial outcomes (as opposed to trials of discrete, static and linear interventions). In contrast, complex adaptive systems and/or non-linearity denoted understanding agents, actions or interventions in the dynamics of an individual, groups, practice, organization and/or health systems.

## **NH 5. Mapping Complex Co-morbidities**

**Henry White**

henrywhite@brooklinecenter.org

One of the top challenges facing the health system today is finding effective strategies for treating patients with complex comorbidities - who represent about 5% of the population, but generate about 40% of the healthcare costs. Our siloed system of care reinforces a fragmented view: each provider has a limited understanding of the patient based on their particular specialty, role and interaction leading to inefficient and uncoordinated practice, high costs and poor outcomes. Disorganized and isolated, such patients' large set of medical, behavior, social, and environmental problems hinder traditional efforts at care coordination and engagement in primary care. Over the past, three years, we have developed Healthy Lives, an intensive, community-based intervention for adults with serious mental illness and two or more chronic medical conditions that increases access to primary care, helps patients engage with providers, and fosters adherence to prescribed treatments. Patients' clinical presentations are a complex system that represents the interaction of medical, behavioral, social, environmental and systemic factors. Using open source software, we have developed a straightforward method to create a small world network graph to represent the interaction of these manifold problems facing an individual (between 10 and 20) as well as the set of providers and interventions that are in place (averaging 8 providers and more than 10 medications). This visual representation has become an invaluable tool for treatment planning, for communication with providers and patients, and ultimately for predictive modeling.

# Technology (TH)

## Chair & Moderator: Martin Picard

**TH 1. Frances Griffiths** - The potential for digital communication to improve access to UK National Health Service (NHS) General Practice by marginalised groups: a realist review

**TH 2. Naiem T Issa** - Net-TMFS: Novel Computational Platform for Drug Discovery and Repurposing that Integrates Systems Pharmacology and Metabolite Signatures

**TH 3. Abhishek Pandey** - Reducing the Complexity of Clinical -Omics Reporting Using the Syapse Semantic Data Platform

**TH 4. Francis Griffiths** - Improving health outcomes for young people with long term conditions: the role of digital communication in current and future patient-clinician communication for UK National Health Service (NHS) providers of specialist clinical services: The LYNC study



## **TH 1. The potential for digital communication to improve access to UK National Health Service (NHS) General Practice by marginalised groups: a realist review**

**Frances Griffiths**

f.e.griffiths@warwick.ac.uk

**Background.** Digital communication technologies such as text messages and email are in widespread use but clinicians in the UK NHS are hesitant to use them with patients as confidentiality and security issues have not been resolved. However, this is changing. Communication technology has the potential to increase the channels through which patients can communicate with General Practitioners (GPs), and this may particularly benefit groups traditionally considered to be marginalised.

**Method.** Realist synthesis focuses on how interventions operate in particular contexts. A theoretical framework on health care access was identified. This suggested those having difficulty accessing health care included refugees, homeless people, gypsy travellers, carers, and people with mental illness. We searched for empirical research on the barriers to access for these groups and undertook a thematic analysis of identified evidence until we reached data saturation. We then systematically searched for all relevant theory and empirical research on the potential for the use of digital communication to overcome each of the identified barriers and summarised the evidence.

**Results.** Nine different barriers were identified ranging from cultural to practical issues. As digital communication removes the need for face-to-face interaction with clinicians, barriers related to embarrassment and fear of negative reactions from others (stigma and discrimination) would be ameliorated. Practical access issues would also be improved, as there would be reduced need to travel to and wait for the consultation. Digital communication is unlikely to impact issues relating to lack of candidacy for healthcare and lack of knowledge about health services, and it is unclear how this technology would affect cultural and language-related access barriers.

**Conclusion.** Digital communication can offer some improvement of access to GP services for marginalised groups, but cannot remove all barriers to care and may create new barriers.

## **TH 2. Net-TMFS: Novel Computational Platform for Drug Discovery and Repurposing that Integrates Systems Pharmacology and Metabolite Signatures**

**Naiem T Issa, Jordan Kruger, Rajarajan Raja, Stephen W Byers, and Sivanesan Dakshanamurthy**

nti@georgetown.edu

Identification and targeting of disease-related protein targets are important for targeted drug discovery and repurposing. Two significant bottlenecks in the target-based drug discovery process involve: (1) establishing biologically valid drug-target associations, and (2) assessing the physiologic effect of those drug-target interactions at the systems level. Network pharmacology of drugs and metabolites can help overcome these bottlenecks to reduce failures at the early-phase clinical trial level and to further reveal new disease targets and biomarkers through systems biology analytics. Here we present Net-TMFS, a computational drug discovery platform that accurately predicts empirical drug- and metabolite-target (DT/MT) interactions and integrates them into a multi-tiered network analysis. Net-TMFS incorporates information from disease-associated targets, cell signaling pathways, protein molecular functions and protein-protein interactions to enrich predicted DT effects on overall disease pathophysiology. We apply Net-TMFS to cancers and rare diseases to provide examples of the platform's utility. Furthermore, we use Net-TMFS for the novel prediction of MT interactions for cancer-associated metabolites to hypothesize new links between diseases and metabolites. Many Net-TMFS-generated predictions were also validated using existing literature and experimental evidence. In summary, Net-TMFS is a powerful method for sampling a large chemical and protein target space to predict biologically plausible interactions and contextualizing those interactions in systems biology through network analysis for enriched pharmacological and clinical success.

### **TH 3. Reducing the Complexity of Clinical -Omics Reporting Using the Syapse Semantic Data Platform**

**Abhishek Pandey**  
abhi@synapse.com

Generating, delivering, and updating a clinical genomic sequencing report for routine clinical use has proven to be a challenge in the implementation of Systems Medicine. To maximize the impact of omics-based testing at the point of care, labs and clinics must be able to handle complex medical & clinical data, high-volume genomics data, and an evolving biomedical knowledge. This talk will present a software solution, based on semantic computing principles, that enables the integration of these very different data types for the purposes of clinical reporting. We will present the results of clinical pilots focused on the maintenance of an evolving variant interpretation knowledge base; the sharing of variant interpretation across institutions; and the coupling of knowledgebase revisions to automated updates of clinical reports. We will also present the results of physician adoption of a web-based, interactive clinical genome report format that incorporates clinical care guidelines with genomic report data.

## **TH 4. Improving health outcomes for young people with long term conditions: the role of digital communication in current and future patient-clinician communication for UK National Health Service (NHS) providers of specialist clinical services: The LYNC study**

**Francis Griffiths**

f.e.griffiths@warwick.ac.uk

**Background.** Young people with long term conditions who require specialist health care for their condition, often disengage from health services endangering their long term adult health. In the UK digital communication with patients is currently out-with NHS Information Governance although new NHS systems are being introduced to enable encrypted communication with patients. Unofficially, many NHS clinicians and young people are already communicating through digital media. This project will learn from these innovators.

**Aims.** (1) To evaluate the impacts of digital clinical communications for young people living with long term conditions  
(2) To analyse critically the provision and use of digital clinical communications by UK NHS specialist care providers.

**Method.** We will study digital clinical communication between NHS clinicians and young people (age 16-24 years): what works for whom, where, when and why, how much does it cost, what is the impact and what are the ethical and safety issues? Examples of clinical communication include: adjustment of medication, monitoring health conditions and providing test results. We do not specify digital communication technologies as these are rapidly changing and we will study what is in use. Current examples are email, Voice over Internet Protocol (e.g. Skype), text messages, patient portals and social media. The project includes case studies of approximately 20 specialist clinics/teams from across the UK. Data will be collected through observation, interviews with staff, patients and carers, and examination of clinic policy and guidelines. Clinics will provide summary data on health outcomes such as emergency admissions and cost data. Data will be analysed using multiple perspectives: realist evaluation, ethics, patient safety, health economics, health outcome.

**Results.** Results will be presented from the initial six case studies of this ongoing two year project funded by the UK National Institute of Health Research.

**Conclusion.** The challenge is to synthesis these results to inform both NHS policy and clinician use of digital communication with patients to improve patient health.

# Organizational Learning (OL)

## Chair & Moderator: Paul Plsek

**OL 1. Rick Botelho** - Design Health Movements: Creating Catalytic Innovation for Transformational Leadership Development

**OL 2. Andrew S. Valeras** - A Family Medicine curriculum to teach the role of complexity science in healthcare

**OL 3. Nneka Mokwunye** - Ethically Complicated Patients: Moving Clinical Ethics Beyond Informed Consent Forms to Full Systemic Integration at a Tertiary Care Hospital (presented by Evan G. DeRenzo)

**OL 4. Alan E Zuckerman** - Opportunities to Use the New Sub-Specialty of Clinical Informatics to Improve the Management of Complexity in Healthcare

**OL 5. Gaetano R. Lotrecchiano** - Measuring Culture Change Preference in an Academic Medicinal Center Steering Team for Education

**OL 6. Kathrine Skinner** - Responding to the complexity of a nested system of new paradigms to support the emergence of a new palliative care service in New South Wales (Australia) providing last-days-of-life home support primary healthcare

## OL 1. Design Health Movements: Creating Catalytic Innovation for Transformational Leadership Development

**Rick Botelho**

rbotelho@me.com

**Background.** Catalytic innovations are complex socio-behavioral learning interventions to improve the health and well-being of the overall population. These disruptive innovations are designed to raise the performance floor of evidence-based guidelines and mobilize communities to break through the ceiling of organizational performance. The digital learning revolution can make these dynamic, adaptive, iterative, convenient and inexpensive interventions widely available. The vision for Health Coaching Buddies (HCB) is to reverse the rising tides of unhealthy habits and reduce the mounting burdens of chronic diseases.

**Objectives.** The HCB system is designed to inspire, motivate and sustain healthy habits for all. Proactive dissemination of the HCB program involves creating a cascade of leadership, professional and social movements to galvanize the momentum needed to launch the HCB movement. This movement fosters the development of self-organizing learning communities at all levels.

**Methods.** This HCB program makes peer health coaching skills accessible for every day life: any time, anywhere and any place within a social network of peers for lifelong learning. This program helps peers set up self-organizing learning communities at three levels:

- Leaders and their change management teams (leadership)
- Health care workers and students (professional)
- Patients and their families (social)

This is like layers of Alcoholic Anonymous programs, except the program development, evaluation and improvement are under the stewardship of educational, health care, community, work and religious organizations. Together, these organizations can create an abundance of coaching services that are for the people and led by the people. Synergy between these vertical and horizontal approaches amplifies the positive impacts on improving the health habits of the overall population.

**Conclusions.** Healthcare leaders, change management teams and trainers can cultivate social networks of transformational leadership movements to proactively disseminate the HCB program. Transformational leadership begins within oneself. “Be the change that you wish to see in the world”. Healthcare teams, practitioners, coaches, staff and students can develop learning organizations and professional movements. Couples, family members, friends and colleagues can create learning communities and social movements. Program evaluation of catalytic innovations requires multi-modal, multi-method approaches to assess the ecological dynamics (linear and non-linear) of population health improvement at the macro-, meso- and micro-levels.

## **OL 2. A Family Medicine curriculum to teach the role of complexity science in healthcare**

**Andrew S. Valeras, Dominic Geffken, Rocco Ricci, Douglas Dreffer, Aimee Valeras, Martha Seery, Mary Danca, Angela Yerdon McLeod, Tina Kenyon, William Gunn and Joni Haley**

asvalera@crhc.org

This presentation describes a curriculum designed for Family Medicine Residents over 8 weeks of protected time throughout the three years of Residency. The [Systems] curriculum introduces the skills and knowledge necessary to understand and manage the complexity inherent within a family physician's work. Incorporating adult learning theory into our teaching, we utilize narrative based reflection, information mastery, and system thinking techniques to encourage residents to recognize their role in achieving the tenets of the Patient Centered Medical Home. The experience aims to expand mental models of a) patient care, b) team, and c) change management while incorporating Senge's Learning Organization process skills of 1) personal mastery, 2) interpersonal communication, 3) collaboration, 4) systems thinking, and 5) change management. These skills are re-enforced throughout residency in clinical rotations which combine excellent medical training with skills that allow for increased efficiency, effectiveness, empathy, and enjoyment in the provision of primary care.

### **OL 3. Ethically Complicated Patients: Moving Clinical Ethics Beyond Informed Consent Forms to Full Systemic Integration at a Tertiary Care Hospital**

**Nneka Mokwunye**

nneka.o.mokwunye@medstar.net

As technology becomes more sophisticated and pharmaceuticals specialized, the care of the patients has become more complex. New multidisciplinary and transdisciplinary models have emerged to help address these new levels of complexity and the integration of clinical ethics in patient care upstream is one way to address the system issues. The Clinical Ethicists at the Center for Ethics at MedStar Washington Hospital Center have revolutionized the concept of preventative ethics through daily ethics assessment rounds on patients in the ICU for more than 5 days, and joining multiple rounding sessions with the clinicians. These new models of ethics integration have moved the practice of clinical ethics squarely into the systemic fabric of the hospital. This talk will discuss best practices and outcomes of preventative ethics integration at a tertiary care hospital.



## **OL 4. Opportunities to Use the New Sub-Specialty of Clinical Informatics to Improve the Management of Complexity in Healthcare**

**Alan E Zuckerman**  
aez@georgetown.edu

**Introduction.** The American Board of Preventive Medicine created the new ABMS sub-specialty of Clinical Informatics (CI), gave the first board exam November 2013, and certified the first group of diplomates in January 2014. ACGME fellowships in Clinical Informatics will begin soon and will be required for new candidates in 2020.

**Methods.** The American Medical Informatics Association (AMIA) defined the core content and curriculum of the board exam and fellowships. We reviewed the core content to identify topics that can support the needs of systems medicine and also to identify topics where emerging needs of managing complexity will require new tools.

**Results.** The curriculum is organized into four main topic areas each with abundant relevance and opportunities for systems medicine. Fundamentals of Clinical Informatics identifies relevant resources in the field of informatics and focuses on healthcare system organization, economic, legal, regulatory, and ethical issues shaping the role of informatics in healthcare delivery. Clinical Decision Support and Care Process Improvement will be the main area to support systems medicine and where CI needs to integrate new models and approaches. Health Information Systems includes many areas where new approaches and extensions to existing systems are needed to meet emerging needs and integrate molecular and research data into routine clinical care. Leading and Managing Change is a critical feature of CI training that uses theories, models, and tools from other disciplines to guide effective change in healthcare.

**Key Question.** A key issue for the new clinical sub-special will be defining who will be the patients of a clinical informatics sub-specialist and what are the indications for referrals and direct patient care beyond leading organizations that are implementing or evaluating clinical information systems and quality improvement programs.

**Conclusions.** The creation of a new sub-specialty of Clinical Informatics provides abundant opportunities to assist the development of systems medicine. The emerging needs of managing complex diseases and systems create a need for the new sub-specialty to develop new tools and rethink existing approaches to electronic medical records and clinical decision support to meet changing healthcare needs.

## **OL 5. Measuring Culture Change Preference in an Academic Medicinal Center Steering Team for Education**

**Gaetano R. Lotrecchiano, Paige McDonald, David R. Livingston, and Robin W. Newman**

glotrecc@gwu.edu

**Purpose.** This study measures culture and change preferences in an academic medical center steering for education amidst episodic and strategic change by utilizing an organizational diagnosis model to measure preference for culture change in a disparate team striving for a unified organizational strategy.

**Design/methodology/approach.** By administering a modified Organizational Culture Assessment Instrument (OCAI) and asking structured open answer response questions data about now and preferred group culture was obtained and analyzed by mapping individual culture preferences and comparing them against group composites, providing thematic mapping of written responses with Pearson  $r$  correlations of culture quadrant strengths.

**Findings.** Preference for culture change calling for a move from a market-based culture to one that is more clan-oriented shown strong. Key team functions were mapped and assigned to different sectors of the cultural framework used. An analysis of frequency of framework quadrant responses shows no significant relationship between group values and retention in a process of change. However, there is a strong negative correlation shown between clan and hierarchical orientations, and between clan and market value orientations.

**Research implications.** Analysis of collected data provides a description of group self-perception in the context of cultural outlook and planning.

**Practical Implications.** The diagnosis process shows how groups can desire directional change amidst a diversity of sectoral goals.

**Originality/value.** This paper uses a well-tested organizational diagnosis tool to investigate a group level academic hospital education team amidst episodic change. It provides insights for this unique sample and uses novel analytics not usually applied to this type of data set.

## **OL 6. Responding to the complexity of a nested system of new paradigms to support the emergence of a new palliative care service in New South Wales (Australia) providing last-days-of-life home support primary healthcare.**

**Skinner, K.A., et al.**

Kath.Skinner@Silverchain.org.au

In New South Wales (NSW) more than 70% of people facing the end of their life want to die at home, but less than 16% achieve that goal (1). In December 2013, Silver Chain Group (SCG) commenced a new palliative care service in NSW focusing entirely on the last-days-of-life and aimed specifically at increasing the death at home rate for those who desire this outcome.

The program is funded by the NSW Ministry of Health and essentially incorporates a nested system of new paradigms: a new paradigm for healthcare in NSW in that it involves contracting and sub-contracting arrangements to outsource clinical service delivery to a not-for-profit (NFP) organization; a new paradigm for eight public health care providers to embrace a shared-care service model; and a new paradigm for SCG, a NFP organization with over 120 years of experience providing healthcare and wellbeing programs primarily across Western Australia and South Australia, now heavily engaged in developing a national mindset requiring new skills to operate effectively in new geographies with new partners and in new political landscapes, whilst at the same time investing heavily in technology based service delivery enablers in support of its strategic goal to extend organizational reach.

This presentation features a short video narrative documenting the establishment of the service, and proposes that the key to successes to date have been as a result of approaching the challenges with an increasing appreciation for working effectively in complex adaptive systems. This approach included:

- Trained approach to start up applying reflexis and incorporating iterative learnings
- Unorthodox approach to recruitment and selection of emotionally intelligent managers and front line staff
- Facilitated 'dialogue' to fast track the development of a group social identity and establish an authentic and inspiring organizational sub-culture
- Novel approaches to up-skilling front line staff to manage the dissonance encountered working within the new paradigms and focused entirely on end-of-life care
- Overt attention to effective self-care enablers in order to build a responsive and resilient workforce
- Developing new corporate strengths to respond effectively to the technological and political challenges of new geographies, working with multiple partners and within complex variations of medical and funding governance structures.

# Disease Complexity (DC)

## Chair & Moderator: Marcus Thygeson

**DC 1. Hakima Amri** - Parsimony Phylogenetics: A Systems Biology Solution to Cancer Data Heterogeneity and Complexity

**DC 2. Mary R. Talen** - Tackling Complexity Care: An Empanelment Process using EHR variables for identifying and Medical, System, and Patient Engagement Complexity

**DC 3. Amrita Cheema** - Role of TGF- $\beta$  induced Epithelial Mesenchymal Transition (EMT) and Metabolism in Pancreatic Ductal Adenocarcinoma

**DC 4. Vivian Rambihar** - 25 years experience with chaos and complexity in medicine and healthcare

## DC 1. Parsimony Phylogenetics: A Systems Biology Solution to Cancer Data Heterogeneity and Complexity

Hakima Amri, Mones Abu-Asab, Simeng Suy, Zhang P, Sinem Nalbantoglu, Cheema A and Sean Collins

amrih@georgetown.edu

**Background.** Despite the latest advances in bioinformatics and biomedical research, disease modeling remains a challenge. This is due to disease and patients' heterogeneity as well as the high dimensionality of Data. This is found as inter- and intra-specimen diversity, a high rate of variability, and multiple pathways of disease development, such as in cancer, which pose the challenge of whether such a process can be modeled by a bio-informatics paradigm.

**Aim & Objectives.** The aim is to apply a biologically compatible computational tool that accounts for heterogeneity and high dimensionality, which cannot be resolved with statistical approaches. Thus, we applied parsimony phylogenetics to metabolomics prostate cancer data to map groups of patients into clades that share clonal aberrations, and stratifies them based on their response to treatment onto a predictive tree-like diagram: cladogram.

**Methodology.** Phylogenetics has been applied in other fields (botany, microbiology, and zoology); but unfortunately ignored in biomedicine. The classification is produced by polarizing data values into derived and ancestral states, using UNIPAL (USPTO Patent to Amri et al. 2014) followed by a parsimony analysis of the polarized matrix with the parsimony algorithm, MIX. It constructs the most parsimonious hierarchical classification of the specimens onto a cladogram that permits the mining of the shared derived states (synapomorphies: potential biomarkers).

**Results.** Serum from prostate cancer patients (n=54) was collected before and after radiotherapy at the LCCC, and subjected to UPLC-MS-Q-TOF within a scan range of 50-850 m/z for a total of 4497 metabolites. The demographics included 34 White, 18 Black, and 3 Others, at low (n=14), intermediate (n=34), and high (n=7) risk. The cladogram grouped patients into 5 subclades with 71 synapomorphies characterizing the cancer metabolome before treatment, and 5 subclades with 72 different synapomorphies 24 hours after radiotherapy. The patients were stratified into groups that share common molecular traits, which might explain their response to treatment. The clinical correlations will be determined in our ongoing studies.

**Conclusion.** Parsimony offers an analytical paradigm that brings the high throughput data, the disease phenotypes, evolutionary approach, and a bioinformatics tool together to achieve novel multidimensional systems biology synthesis without traditional overdependence on statistical methods.

## **DC 2. Tackling Complexity Care: An Empanelment Process using EHR variables for identifying and Medical, System, and Patient Engagement Complexity**

**Mary R. Talen, Paul Ravenna, Anuj Shah and Jessica Reader**  
mary.talen@gmail.com

How do we go define and untangle complexity care beyond medical diagnoses? Healthcare providers have struggled to define what makes complex care complex. Healthcare teams lack a systematic model for identifying complex elements of patient care that is more robust than medical diagnoses or a “gut feeling”. The purpose of this presentation is to describe a population-based empanelment process using EMR data to stratify patients’ levels and types of complexity care. While bio-medical markers have been the hallmark for identifying complex care, it is woefully inadequate. The Minnesota Complexity Assessment Method—MCAM, is a more robust model that is clinically and theoretically sound model and includes medical diagnoses, system-fragmentation, and patient engagement factors. We will describe the process to develop a reliable process using EHR variables to build our registry of patients with these complexity care risk factors in the domains of medical, system fragmentation and patient engagement. We will describe how our team of QI staff, faculty, residents, and support staff were involved in developing and validating this empanelment process. We will outline how the empanelment of patients was initially reviewed by the healthcare team to validate the accuracy of the EMR stratification of complex patient care. The comparison between the team’s assessment and EMR stratification has been used to revise and modify the patient panels. The descriptive data from this empanelment process will be shared to demonstrate the outcomes of this empanelment process. The goal of this empanelment process will be reviewed and the team-based care protocols that align with stratified levels and types of complex care will described.

### **DC 3. Role of TGF- $\beta$ induced Epithelial Mesenchymal Transition (EMT) and Metabolism in Pancreatic Ductal Adenocarcinoma**

**Amrita K Cheema, Talgat Nurkas, Prabhjit Kaur and Bridgette Clarke**  
akc27@georgetown.edu

Pancreatic cancer is an aggressive disease in large part due to the lack of diagnostic and prognostic biomarkers. According to the American Cancer Society, the survival rate for pancreatic cancer patients five years after diagnosis is 4%. The malignancy of cancer cells has been attributed to a phenomenon called EMT, inducible by Transforming growth factor (TGF- $\beta$ ). TGF- $\beta$  has been known to profoundly augment metastasis and chemoresistance in many tumor epithelial cells by inducing epithelial to mesenchymal transition (EMT). However, the concomitant metabolic changes remain unexplored. The goal of this study was to identify and characterize metabolic changes associated with EMT in pancreatic cancer. PANC-1 and BxPC-3 cell lines were treated with TGF- $\beta$ , which resulted in the reduction of epithelial marker E-cadherin and an increase in N-cadherin and Vimentin, the markers of the mesenchymal phenotype. Phase contrast microscopy revealed changes in cell morphology indicative of EMT in PANC-1 cells. We subsequently performed untargeted metabolomic profiling in the pancreatic cell lines before and after treatment with TGF- $\beta$  using UPLC-ESI-QTOF-MS (Ultra performance Liquid Chromatography – Electrospray Ionization – Quadrupole - Time of Flight Mass Spectrometry). Feature extraction was performed using XCMS followed by multivariate analysis for selection of significant features ( $p \leq 0.05$ ). Functional pathway analysis revealed the induction of pathways associated with oxidative stress and cell differentiation. The investigation of discerning the role of the metabolites in mediating pancreatic cancer progression is ongoing.

## **25 years experience with chaos and complexity in medicine and healthcare**

**V Rambihar, S Rambihar and Vanessa Rambihar**

Vivian.rambihar@utoronto.ca

**Background and purpose.** Complexity, considered the science for the 21st century by Stephen Hawking, emerges from systems and chaos science, and describes the nature of complex dynamic social, economic, biologic, behavioural and other interactions, central to health and healthcare. These exhibit specific features of - nonlinearity, sensitive dependence, feedback, adaptation, uncertainty, self-organization and emergence, suggesting a different approach for change and practice, as adaptive, dynamic, coevolving and co-learning multiple approaches. This paper describes a 25 year experience with chaos and complexity in healthcare.

**Methodology.** Review of the author's experience and the literature.

**Results.** A 25 year experience with complexity in medicine and healthcare will be described, including advocacy, CME, lectures, book-writing, global networking, education and proposals for a complexity based medicine (bmj eletter). Complexity ideas were explored to reduce disparities in health, in a Diversity and Health project, and in seeking to reduce excess and premature diabetes and heart disease across the Indian diaspora, considered a "wicked problem" requiring new approaches. Complexity was proposed as a translation factor for evidence to the individual and to reality, restoring lost complexity and context. Complexity science was seen as a means to rethink and transform medical education and healthcare for the 21st century, with the major 20th century reforms in health education recognized as 1) science based 2) McMaster problem based, which we consider as illustrating complexity (bmj eletter), and 3) systems based, which includes complex systems and complexity.

**Discussion and Conclusions.** Chaos and complexity, the science for the 21st century, has been used by us for 25 years in various aspects of healthcare, medicine, and medical and health education. Increasing complexity of 21st century healthcare and society suggests that complexity should be an important part of 21st century healthcare.



## **Clinical Care (CC)**

### **Chair & Moderator: Martin Kornitzer**

**CC 1.**

**CC 2. Abduhrahman M El-Sayed** - Stigma and the Etiology of Depression among the Obese: Insights from an Agent-Based Social Network Model

**CC 3. Sister Grace Miriam (Rachel) Usala** - Hyponatremia is Associated with Increased Osteoporosis and Bone Fractures in a Large Health System Population

**CC 4. Jenna Nicole Ray** - Disentangling Irritable Bowel Syndrome

**CC 5. Carmel Martin** - Assessing Primary Care: Patterns in Individuals with High Risk Health Journeys

## CC 1. Lack of Utility of Head CT in Concussive Head Injury Amongst Non-Geriatric Patients

Jeremiah Altman, Sarada Rao, Leena Ramadanl, Zach Hatoum, Jack Sava and Dave Milzman

Jra73@georgetown.edu

**Background.** The use of imaging studies in patients post-concussion has been a developing subject of debate. In the past decade there have been a number of publications detailing criteria for CT imaging of a brain following trauma. Currently, the two major standards are the New Orleans Rules and the Canadian Head Ct Rules, which have high sensitivity, but lack specificity. This has combined lead to the overuse of head Ct due to the efforts of practitioners trying to avoid missed injury with little acknowledgement of evidence-based practice outcomes.

**Objectives.** This study sought to evaluate the results of current metrics in CT ordering and report on the accuracy of head Ct in concussive injury

**Methods.** Retrospective data was collected for three years on all head CT performed in the Emergency Department and Trauma Center at a Level One Trauma Center with 100,000 annual Emergency Department visits and 4,500 annual trauma visits. Patients were included if they were diagnosed with a concussive injury, had a Glasgow Coma Scale score of greater than 13, and a loss of consciousness of less than 5 minutes.

**Results.** 1,198 patients met the inclusion criteria with a mean age of 48.4 year (SD 2.8). Additionally 55.4% were female and 28% were over 65 years of age. The overall admit rate was 2.9% with 97% of the admitted being greater than 65 years old. 1.5% of non-geriatric patients were admitted for non-operative observation compared to increased rates for geriatric concussion patients, 23% of whom were admitted for observation. The accuracy of Head Ct in patients less than 65 and low to moderate mechanism of the concussive injury was 0.7%. By comparison the finding of TBI in those greater than 65 years was 10.5 % ( $p < 0.01$ ). The overall mortality in patients under 65 was 0.0%, while it was 1.9% in those over 65 for all cause 30 day mortality. MRIs were performed in 3.1% of patients with an increase in TBI findings that were not seen on Ct. Only 1/36 of these patients found a neurosurgically amenable lesion.

**Conclusion.** The routine use of Head CT in concussive injury in patients younger than 65 was found to have almost no utility and only a single patient of the 928 had any lesion that required neuro ICU admission and that patient did not require any neurosurgical intervention. In the geriatric patients subset (those older than 65) 11% of patients had TBI findings with 62% of these patients being on medication which increased risk of bleeding. The results suggest that non-geriatric use of Ct in concussion patients is an extremely low yield procedure, and the indication for head CT is not warranted in minor TI in adults less than 65. There are limitations to this study as it is retrospective, focused on a single center, and only included those that underwent scanning so false negatives were missed.

## **CC 2. Stigma and the Etiology of Depression among the Obese: Insights from an Agent-Based Social Network Model**

**Abduhrahman M El-Sayed**

ame2145@columbia.edu

Obesity and depression are comorbid more often than chance predicts. However, depression among the obese is more common where obesity is less common. This suggests that stigmatization of the obese in contexts where obesity is less normative may contribute to depression in this group. We developed an agent-based social network model to explore mechanisms by which obesity norms may shape depression in the obese. At each of 120 simulated months, each agent updated its body mass index (BMI) based on previous BMI and environmental and stochastic factors. The risk of social ostracization was a function of the difference between the agent's BMI relative to its peers, its peers' peers, and the global mean. If ostracization occurred, agents became depressed with an increased probability proportional to the number of ostracization incidents. We ran simulations comparing a 'high-obesity' context to a 'low-obesity' context. Over 1000 simulations in each context, 41% (95%CI: 36%, 47%) of obese agents in the low-obesity context were ever-depressed as compared to 25% (95%CI: 22%, 28%) percent in the high-obesity context, while 16% of non-obese agents were ever-depressed in each setting. These findings were robust to sensitivity analyses. Our findings demonstrate that social stigma and ostracization that occurs due to deviance from body image norms are a plausible mechanism by which obesity norms may influence depression. The findings suggest that public health messaging around obesity as deviation from norms may have deleterious implications for depression among the obese.

### CC 3. Hyponatremia is Associated with Increased Osteoporosis and Bone Fractures in a Large Health System Population

Sister Grace Miriam (Rachel) Usala, Stephen J. Fernandez, Mihriye Mete, Laura Cowen, Nawar M. Shara, Juliana Barsony, and Joseph G. Verbalis

rlu4@georgetown.edu

**Background.** Several independent studies have shown increased bone fracture rates in patients with hyponatremia (serum  $[Na^+] < 135 \text{ mmol/L}$ ). Likely major contributors to this finding are gait instability and increased falls in hyponatremic patients. Studies in experimental animals have also demonstrated hyponatremia-induced bone loss, and analysis of human subjects in the National Health and Nutrition Examination Survey (NHANES III) showed increased odds ratio for osteoporosis by hip DXA in the hyponatremic subjects. Furthermore, a recent case report demonstrated significant partial improvement of severe osteoporosis in a chronically hyponatremic patient after correction of serum sodium abnormalities.

**Aim.** We sought to assess the potential clinical significance of these findings from a systems perspective.

**Methodology.** We identified osteoporosis and fragility fracture cases by querying the clinical database of the MedStar Health system with the Explorys electronic health record (EHR) tool. We matched osteoporosis ( $n=30,517$ ) and fragility fracture ( $n=46,256$ ) cases separately on age at first encounter, sex, race, and duration of the patient record in the database with controls without osteoporosis ( $n=30,517$ ) and without fragility fracture ( $n=46,256$ ), respectively. After extracting laboratory measurements and relevant clinical coded variables for both cases and controls, we utilized multivariate conditional logistic regression models to analyze the association of prior, chronic, and recent hyponatremia and multiple other clinical variables with risk for either osteoporosis or fragility fracture.

**Results.** The multivariate logistic regression models demonstrated that many previously reported clinical variables were independently associated with both osteoporosis and/or fragility fracture, including prior hyponatremia (osteoporosis OR 1.084, CI 1.054-1.114; fragility fracture OR 1.359, CI 1.329-1.389). Greatest independent risk for both osteoporosis and fragility fracture was demonstrated among patients with chronic hyponatremia (osteoporosis OR 3.987, CI 3.787-3.989; fracture OR 4.712, CI 4.462-4.962) and recent hyponatremia (osteoporosis OR 3.076, CI 2.946-3.206; fracture OR 3.079, CI 2.959-3.199).

**Conclusions.** Using a systems and research informatics approach, our analyses of a large clinical database support the integrative hypothesis that hyponatremia is an important clinical risk factor for osteoporosis and fracture by two related, but mechanistically separate, processes: chronic hyponatremia contributes to loss of bone mass and integrity, while acute hyponatremia compromises gait stability and leads to increased falls.

## **CC 4. Disentangling Irritable Bowel Syndrome Interventions: Social Care, Breath Training, and Mindfulness**

**Jenna Nicole Ray**

jray51@uncc.edu

Irritable bowel syndrome (IBS) has made a striking impact on western health systems (Andrews et al., 2005). It is a costly illness psychologically, socially, physiologically, and economically. The need to augment or replace the traditional biomedical attempts at treatment for IBS is evident in the increased number of patients who seek complementary and alternative medicine for relief of their symptoms, as well as the large number who do not seek conventional treatment at all (van Tilburg et al., 2008). One such complementary treatment is the practice of mindfulness: a meditation technique to increase cognitive awareness and acceptance (Zernicke et al., 2013). This study is searching for a way to add the important components of low cost and effectiveness to treatment options for IBS individuals through natural ways of activating a balance between the Sympathetic Nervous System and Parasympathetic Nervous System and increasing emotional and cognitive health. It is also seeking to dissect mindfulness meditation's effects by measuring the effect sizes of each component of the biopsychosocial model, to reveal what component is most helping IBS sufferers.

## CC 5. Assessing Primary Care: Patterns in Individuals with High Risk Health Journeys

Carmel Martin, David Emanuel Surate Solaligue and Lucy Hederman  
carmelmarymartin@gmail.com

**Aims and objectives.** The Patient Journey Record System (PaJR) provides a biopsychosocial week-day monitoring and support service to chronically ill and older people over 65 who are at risk of an avoidable hospital admission. This study describes reported profiles associated with planned and unplanned Primary Care (PC) visits during the week in the PaJR database of regular outbound phone calls made by Care Guides (community health workers) to multi-morbid older patients.

**Methods.** One hundred and ninety eight consecutive patients with one or more chronic condition (including chronic obstructive pulmonary disease, heart/vascular disease, heart failure and/or diabetes), one or more hospital admission in previous year, and consecutively recruited from hospital discharge, out-of-hour care and PC practices comprised the study sample. Using a semi-structured online conversational guide, Care Guides telephoned the patients approximately every 3 week days, and entered call data into the PaJR database in 2011-13. The PaJR project identified and prompted unplanned primary care visits according to its algorithms. Modelling identified significant predictors of planned and unplanned visits and patterns of PC visits on weekdays reported in calls.

**Results.** In 11255 telephone calls, unplanned versus planned PC visits were predicted by change in health state, significant symptom concerns, poor self-rated health, bodily pain and concerns about caregiver or intimates. Calls not reporting visits had significantly fewer of these features. Planned visits were associated with general and medication concerns, reduced social participation and feeling down. Planned visits were highest on Monday and trended downwards to Fridays. Unplanned visits were reported at the same rate each weekday and more frequently when the interval between calls was  $\leq 3$  days. The PaJR project Care Guides advised patients to make unplanned visits in 6.3% of calls and advised planned visits in 2.5% of calls.

**Conclusion.** Unplanned PC visits consistently indicated a significant change to worse health with planned visits presenting less acuity in this study of older multi-morbid patients in general practice, when monitored by regular calls at about every 3 days. The PaJR study actively prompted primary care team visits according to its algorithms. Assessing and predicting acuity in older multi-morbid patients appears to be a promising strategy to improve access to primary care, and thus to reducing avoidable hospital utilization. Further research is needed to investigate the topic on a wider scale.

# Health System Development (HD)

## Chair & Moderator: Holly Lanham

**HD 1. Sreenivas Rangan Sukumar** - Long-Tails, Power-laws and Complexity: What it means to our healthcare system?

**HD 2. Samuel McAleese** - Understanding System Variation to Improve Sepsis Care at Medstar Health

**HD 3. Syed Azizur Rahman** - Unqualified Health Care Providers in Rural Health Care System in Bangladesh: Quality of services and effects on Maternal and Child Health

**HD 4. Mallikarjun Shankar** - Complementing RCTs: In Silico Analytics, Modeling, and Simulation of Healthcare

**HD 5. Rutger Ijntema** - Success factors within business models for primary health care businesses physical therapy in the Netherlands; Systematic review with critical interpretative synthesis

## **HD 1. Long-Tails, Power-laws and Complexity: What it means to our healthcare system?**

**Sreenivas R Sukumar and James Sorace**

sukumarsr@ornl.gov

Long-tails (also popularly known as the 80-20 rule) are the norm while observing interactions in our complex healthcare system. Several papers in literature expose the long-tailed behavior across different facets of the healthcare system - provider-cost, beneficiary-cost, beneficiary-chronic illness, etc. In this paper, we survey the state-of-the-art in the emerging role of power-law science in markets outside of healthcare such as financial markets, internet, economics, ecology, city planning, etc. and observe how the generating models (such as preferential attachment, scale-freeness, sick becoming sicker, Bak-Sneppen species-environments interaction, etc.) from those domains manifest in the healthcare system. We support our claims based on analysis of claims-data from the Centers of Medicare and Medicaid Services and argue that risk-management solutions developed in domains outside of healthcare are very relevant to our healthcare system. We present data-driven case studies, based on which we are able to make the following recommendations for decision makers: (i) focus more on the niche of really sick beneficiaries in the long tails and not the average beneficiary, (ii) identify opportunities where beneficiaries, providers and payers can all succeed in a healthy environment (in economic equilibrium), and (iii) emulate the internet-like personalization for outreach and delivery of health services for patients to adopt healthy behaviors.



## **HD 2. Understanding System Variation to Improve Sepsis Care at Medstar Health**

**Samuel McAleese**

sm2859@georgetown.edu

According to the Agency for Healthcare Research and Quality, sepsis affected over 1.6million patients in 2009 including over 250,000 deaths. Moreover, in 2011, over \$20billion in healthcare costs were attributable to sepsis care. Despite years of clinical research on how to diagnose and treat sepsis, and large scale efforts aimed at implementing best practices, progress is slow and evidence for how to improve is often weak and conflicting. The recent ProCESS trial illustrates the complexity of treating sepsis regardless of clinical protocol.

Clinicians and leaders at MedStar Health want to improve sepsis care and outcomes. This 10 hospital, not for profit system serves a diverse geographic and patient population and has nearly 6,000 physician affiliates and 30,000 employees.

Viewing healthcare as a complex adaptive system is integral to the sepsis project. Studies of why quality improvement efforts fail, or why improvements are not sustained, increasingly acknowledge the need to understand that change processes operate at individual, collective/professional, organizational, and cultural levels.

Developing clinical enthusiasm for a new sepsis initiative required exploring how different processes, priorities, and pressures create variability across MedStar Health. Preliminary work involved review of the empirical literature and assessing current status through qualitative (clinician and administrator interviews at each hospital) and quantitative data (review of publically reported and internal comparative outcome data).

Results demonstrate wide variation in awareness and agreement regarding existing structures and processes to support sepsis care as well as concern about validity of existing data.

System-wide quality improvement research, informed by these preliminary findings, will begin in October. The study employs a modified "clinical communities" construct and robust interrupted time series study design. Clinical communities have been shown effective in change efforts and are characterized by the inclusion of bottom-up, participatory and informal social processes. Attributes of clinical communities include clinician driven interventions, centralized coordination of efforts and knowledge translation via social networks.

This effort has the potential to improve sepsis outcomes. If successful, MedStar Health may eschew the mechanistic approaches that have impeded progress and strengthen what Paul Plsek calls the 'receptive context for change' within the entire organization.

### **HD 3. Unqualified Health Care Providers in Rural Health Care System in Bangladesh: Quality of services and effects on Maternal and Child Health**

**Syed Azizur Rahman, Ahmed Mustafa and Mustak Hassan Md Iftekhar**  
syrahman@sharjah.ac.ae

**Objectives.** To assess the quality and extent of maternal and child health services provided by Unqualified Health Care Providers (UHCPs) in rural Bangladesh and to explore the possibility of integrating their services in public health care system.

**Background.** Unqualified Health Care Providers (UNHCPs) are the gateway for seventy seven percent of the population in rural Bangladesh, prescribing allopathic medicine without or limited training and knowledge. Women and children's health care in rural areas mostly depend on them. Information about the quality of services they deliver and its contributions to maternal and child health in rural areas is inadequate. This study is an attempt to reduce those information gaps.

**Methods.** A combination of qualitative and quantitative approaches has been employed. Ninety-eight UHCPs, twenty-two key informants were interviewed. Twenty-two facilities were surveyed; twenty treatment protocols of UHCPs were reviewed. Study was conducted in the sub-district and below. The quantitative data were gathered from interviews and observation checklists and were analyzed using SPSS. The qualitative information was listed as key concepts, themes and images that generated meaningful answers on the key areas of investigation selected for the study.

**Results.** Half of the UHCPs were found completed 10th grade of schooling and most of them received some sort of medical training. Most common training was village doctor course. Eighty-five percent of the UHCPs provide maternal and child healthcare, majority of them does not have professional medical qualification on these areas. Low-cost, proximity, accessibility and modes of payment were found main factors to use their services. Unnecessary use of antibiotics and antihistamine was detected. For ante-natal and post-natal check-up majority did not follow standard protocol. Wrong prescriptions in serious cases like eclampsia were reported.

**Conclusion.** Unqualified health care providers are deeply rooted in the rural areas in Bangladesh. Health services that are providing by them cannot be ignored. Immediate elimination is also not possible. By providing appropriate training and under professional supervision their services can be integrated in primary healthcare system. Findings may help Bangladesh in taking policy decisions on how to integrate them in the system.

## **HD 4. Complementing RCTs: In Silico Analytics, Modeling, and Simulation of Healthcare**

**Mallikarjun Shankar**

shankarm@ornl.gov

Healthcare R&D or innovation trials are increasingly employing non-randomized studies (NRS) in the form of observational or pragmatic investigations. Rapid translation and patient centeredness using a randomized controlled trial-today's acknowledged "gold standard" for testing in healthcare-may not be practical or desirable when there is a need for flexibility, responsiveness, or timeliness. The challenge facing NRS studies is providing sufficient rigor in evaluation. We describe an approach to address this challenge by presenting an in silico evaluation methodology and framework for healthcare trials. The methodology extends and includes today's practice of rapid cycle evaluation methods, by adding computationally-based big data analysis as well as modeling and simulation components. Our proposed integrated data, analytics, modeling, and simulation approach for the healthcare domain is a scientifically validated methodology currently used in disciplines ranging from climate studies to nuclear science.

## **HD 5. Success factors within business models for primary health care businesses physical therapy in the Netherlands; Systematic review with critical interpretative synthesis**

**Rutger Ijntema, Jurgen Mollema and Hans Duits**

Rutger.Ijntema@hu.nl

**Background.** Because of changing health care market forces in the last 2 decennia, physical therapists in The Netherlands have the need to adjust their business model of their own business to be able to deliver quality and sustainable business. But one does not know exactly in what way it should be adjusted and the impression is that information about this is not readily available.

**Research question.** What are success factors within business models for primary health care businesses physical therapy in the Netherlands?

**Method.** Systematic review with critical interpretative synthesis.

**Study identification and findings.** The aim of this systematic review is to describe success factors within business models for primary health care businesses physical therapy in the Netherlands. In this review business models act on a strategic level and can be the basis for more detailed business process models and business cases. Publications were retrieved through a systematic search in medical and economic databases. The search yielded 2253 articles that were screened on title and abstract. Selection of results was done on: 1. Generalizable information related to business models, 2. Information related to business models in health care, 3. Success factors in business, 4. Quality of health care related to business models. This led to a selection of 42 relevant full text articles. Relevant results were ordered into two frameworks of business model components.

**Conclusions.** The results of this review are promising for further research and application within business models for primary health care businesses physical therapy in The Netherlands. This research can be used for inter-subjectivity testing and qualitative research in physical therapy practices in The Netherlands. Not only isolated business model components need to be considered here, but an integration of more than one component resulting in a theory for the primary health care physical therapy business. Business model definition research is necessary for the near future.