
InSPIRE
Innovating UK clean air policies
to prevent cognitive disorders


Our vision is for everyone in the UK to be able to breathe clean air that promotes a healthy brain and cognitive life regardless of where they live.

Early Life Brian Development, Air Pollution and the Exposome:

A Complexity Perspective

GOV.UK

Cognitive decline, dementia and air pollution

A report by the Committee on the Medical Effects of Air Pollutants

Chairman: Professor Frank Kelly
Chairman of Subgroup on Cognitive Decline and Dementia: Professor Robert L Maynard

Headline News!

U.S. **INTERNATIONAL** CANADA ESPAÑOL 中文

The New York Times

Air Pollution May Damage the Brain

Tiny air pollutants may cause changes in brain structure that resemble those of Alzheimer's disease.

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Air pollution particles in young brains linked to Alzheimer's damage

Exclusive: if discovery is confirmed it will have global implications as 90% of people breathe dirty air

This was one of the landmark studies

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Air pollution, cognitive deficits and brain abnormalities: A pilot study with children and dogs

Lilian Calderón-Garcidueñas [a,b,*], Antonieta Mora-Tiscareño [a], Esperanza Ontiveros [a], Gilberto Gómez-Garza [a], Gerardo Barragán-Mejía [a], James Broadway [c], Susan Chapman [d], Gildardo Valencia-Salazar [a], Valerie Jewells [e], Robert R. Maronpot [f], Carlos Henríquez-Roldán [g], Beatriz Pérez-Guillé [a], Ricardo Torres-Jardón [h], Lou Herrit [b], Diane Brooks [b], Norma Osnaya-Brizuela [a], Maria E. Monroy [a], Angelica González-Maciel [a], Rafael Reynoso-Robles [a], Rafael Villarreal-Calderon [i], Anna C Solt [j], Randall W. Engle [c,1]

Review article

Exposure to air pollution and cognitive functioning across the life course – A systematic literature review

Angela Clifford [a], Linda Lang [a,b], Ruoling Chen [a,b,*], Kaarin J. Anstey [c], Anthony Seaton [d]

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A FEW EXAMPLES

- Attention
- Memory
- Global cognition
- Learning
- Motor coordination and psychomotor stability
- Some intelligence subscales, such as verbal intelligence
- Dose-dependent neurodevelopmental deficits
- Poorer performance – McCarthy Scales of Children's Abilities

Review article

Exposure to air pollution and cognitive functioning across the life course – A systematic literature review

Angela Clifford [a], Linda Lang [a,b], Ruoling Chen [a,b,*], Kaarin J. Anstey [c], Anthony Seaton [d]

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NOTE: These are preliminary studies. This research is in the early stages. Results should be considered but with a degree of doubt and the need for more research.

Overview of talk

- The purpose of this presentation is to explore the intersection between *social determinants* and the *exposome* and their impact on *brain health development* as a function of *place.*
- The theoretical frame for our exploration is complex systems theory.
- The case study is air pollution and brain health in early life and adolescence.

Overview of talk

- OUTLINE
- What is the exposome?
  - Where does air pollution fit into the mix?
  - What are the strengths and limits of an exposome framework?
- The importance of place-based social determinants
  - How social determinants improve our understanding of exposome
  - Complexities of place approach
- Allostatic load as life-course pathways to brain health
  - What is allostatic load?
  - Linking allostatic load across the life-course to brain health
- Why a case-based complex systems approach?
  - What is a complex systems approach?
  - What makes it case-based?
- Throughout, we will apply our framing to early childhood brain health!

What is the exposome?

- Success in mapping the human genome has fostered the complementary concept of the “exposome”.
- The exposome is the **measure** of all the exposures of an individual (or community) in a lifetime and how those exposures relate to health.

What is the exposome?

- An individual's exposure begins before birth and includes insults from environmental and occupational sources.
- Understanding how exposures from our environment, diet, lifestyle, etc. interact with our own unique characteristics such as genetics, physiology, and epigenetics impact our health is how the exposome will be articulated.

Ecosystems

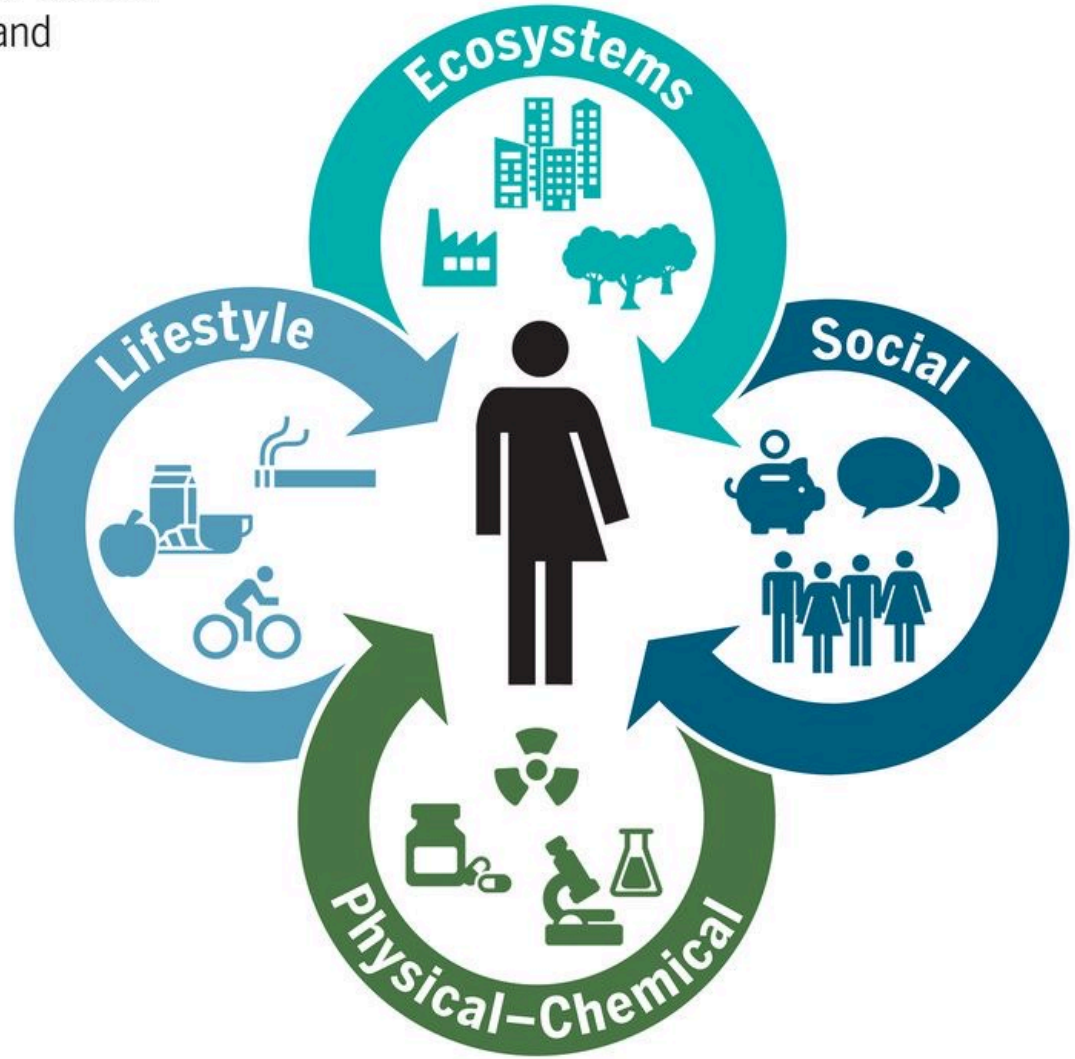
Food outlets, alcohol outlets
Built environment and urban land uses
Population density
Walkability
Green/blue space

Lifestyle

Physical activity
Sleep behavior
Diet
Drug use
Smoking
Alcohol use

Social

Household income
Inequality
Social capital
Social networks
Cultural norms
Cultural capital
Psychological and mental stress



Physical–Chemical

Temperature/humidity
Electromagnetic fields
Ambient light
Odor and noise
Point, line sources, e.g. factories, ports
Outdoor and indoor air pollution
Agricultural activities, livestock
Pollen/mold/fungus
Pesticides
Fragrance products
Flame retardants (PBDEs)
Persistent organic pollutants
Plastic and plasticizers
Food contaminants
Soil contaminants
Drinking water contamination
Groundwater contamination
Surface water contamination
Occupational exposures

What is expsomics?

- Exposomics is the study of the exposome and relies on the application of internal and external exposure assessment methods.
- Internal exposure relies on such fields as genomics, metabonomics, lipidomics, transcriptomics and proteomics.
- External exposure assessment relies on measuring environmental stressors.

What is expsomics?

- Commonalities include:
  - use of biomarkers to determine internal exposure, effect of exposure, disease progression, and susceptibility factors.
  - use of technologies that result in large amounts of data.
  - use of data mining techniques to find complex, nonobvious patterns.
  - The need for interdisciplinary teams working together.

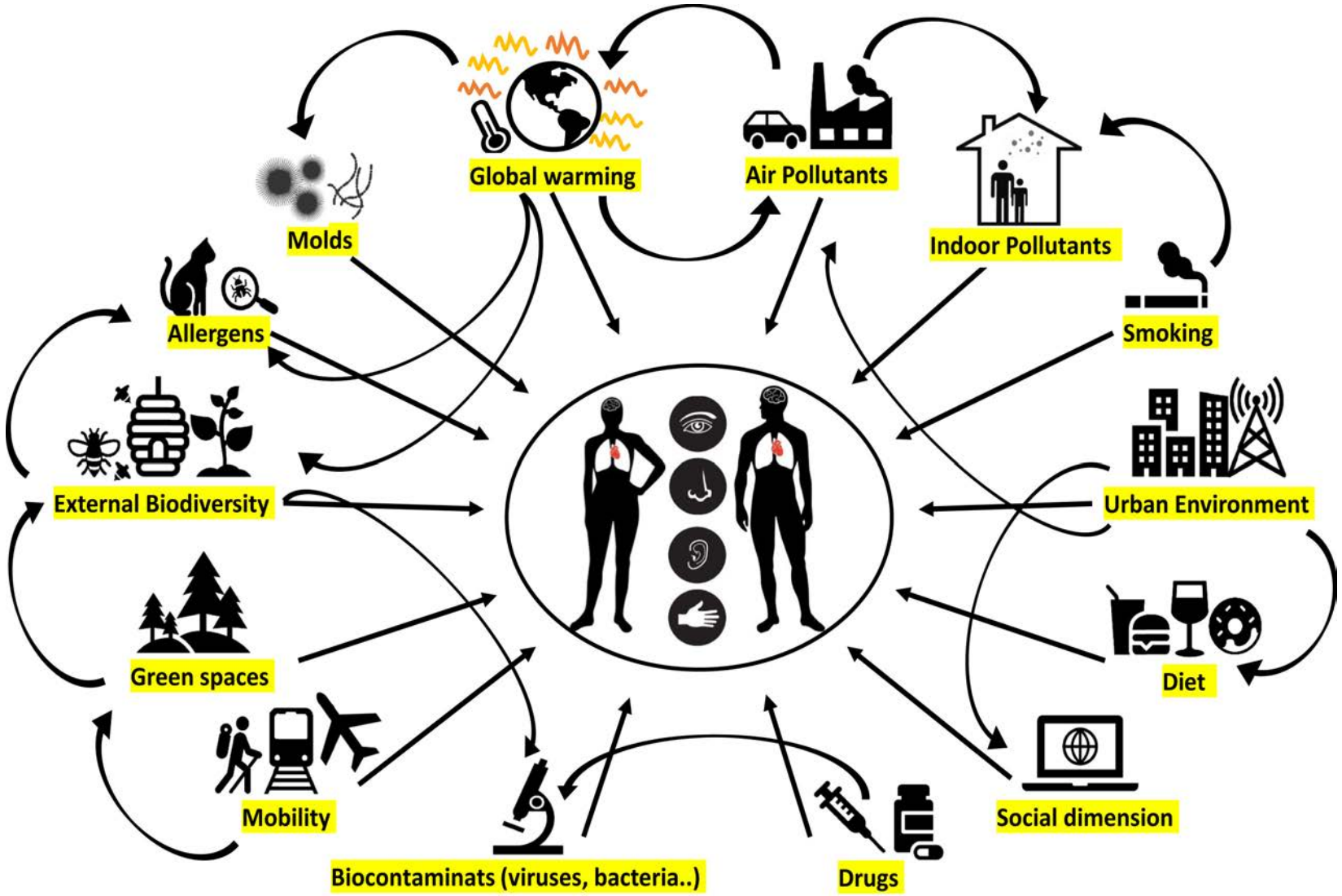
Exposome and air pollution

- The focus is on thinking about air pollution and its more immediate links with other forms of exposure, which can vary by disease and location and social factors.

Exposome and air pollution

- Example publications:
- Annesi-Maesano, et al (2021). **Call to action: air pollution, asthma, and allergy in the exposome era.** *Journal of Allergy and Clinical Immunology*, *148*(1), 70-72.

    - **QUOTE:** To fully explain the increase in the prevalence of asthma and allergy observed worldwide, however, air pollution has to be considered as a part of the exposome, namely, the set of all exposures to the external environment to which a given individual is subjected from preconception onward and the consequences of these exposures at the cellular and organ levels (the internal exposome).



Journal of Allergy and Clinical Immunology 2021 14870-72DOI: (10.1016/j.jaci.2021.05.026)

Archival Report

Biological Psychiatry

Air Pollution Exposure During Fetal Life, Brain Morphology, and Cognitive Function in School-Age Children

Mònica Guxens, Małgorzata J. Lubczyńska, Ryan L. Muetzel, Albert Dalmau-Bueno, Vincent W.V. Jaddoe, Gerard Hoek, Aad van der Lugt, Frank C. Verhulst, Tonya White, Bert Brunekreef, Henning Tiemeier, and Hanan El Marroun

Limits of the exposome

- An individual's exposome is highly variable and dynamic throughout their lifetime.
- The impact of exposures can also vary with the individual's stage of life.
- Exposures during early years may also predispose an individual to certain chronic diseases later in life.
- The impact of environmental or occupational exposures can be different for each individual because of differences in genetic and other personal factors.
- Some people will develop a disease while another person with the same or greater exposure will not.

Limits of the exposome

- Mapping an entire exposome for an individual will be difficult, if not impossible because of the complexity of a life-time of exposure.
- Specific exposures can be difficult to measure due to lack of sensitive methods or not knowing that an exposure has even occurred.
- **The research is very biologically focused and has yet to really engage the brain and psychology.**
- **There is also an absence of engagement with external exposures based on social determinants.**

Overcoming the limits of the exposome

- There are solutions to some of these problems.

- Integrating the exposome with place-based social determinants
- Using allostatic load as life-course pathways to brain health
- Employing a case-based complex systems approach to modelling.

Overcoming the limits of the exposome

ELSEVIER

Environmental Research

Volume 215, Part 2, December 2022, 114362

Review article

Mitigating the impact of air pollution on dementia and brain health: Setting the policy agenda

Brian Castellani [a b c e], Suzanne Bartington [d], Jonathan Wistow [e c], Neil Heckels [f], Amanda Ellison [c g], Martie Van Tongeren [h], Steve R. Arnold [i], Pete Barbrook-Johnson [j b], Martha Bicket [b], Francis D. Pope [k], Tom C. Russ [l m], Charlotte L. Clarke [e n], Monica Pirani [o], Matthias Schwannauer [n], Massimo Vieno [p], Rachel Turnbull [q], Nigel Gilbert [b], Stefan Reis [p r s]

Place-based social determinants

Invited Perspective

A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/EHP12030.

Invited Perspective: The Mysterious Case of Social Determinants of Health

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https://doi.org/10.1289/EHP12030

Refers to https://doi.org/10.1289/EHP11015

Place-based social determinants

- Switching from attributes and behaviours to social context/social determinants
- Attributes: Age, gender, ethnicity, education, occupation.
- Behaviours: smoking, diet, and alcohol consumption, the picture that emerges from recent research[5] is more complex than the traditional one cause–one effect paradigm, where “extraneous” variables—such as SES—were dealt with as confounders.
- Social determinants: inequalities, places, deprivation, job setting, housing.
  - Michael Marmot has written that only 50% of social inequalities in health can be explained by classical risk factors, whereas the rest can be due to “status syndrome”—or social standing—in its manifold manifestations and via multiple mechanisms.
  - This thesis has been partially supported by empirical evidence showing associations between social inequalities and mechanistic pathways investigated with biomarkers.

Where people live matters, particularly for those in deprived places with high health inequalities

First Step in Our Innovative Equation

PLACE = Social Determinants Health Inequalities **<=> Exposome (air quality) =>** **Cognitive/Brain Health Outcomes**

Allostatic load and the life-course

- The concept of allostatic load was introduced by McEwen and Stellar in 1993
- **It refers to the cost of chronic exposure or intense short-term exposure that an individual reacts to as being particularly stressful.**

Allostatic load and the life-course

- It derives from the definition of allostasis as the ability of the organism to achieve stability through change, and the view that healthy functioning requires continual adjustments of the internal physiological milieu.

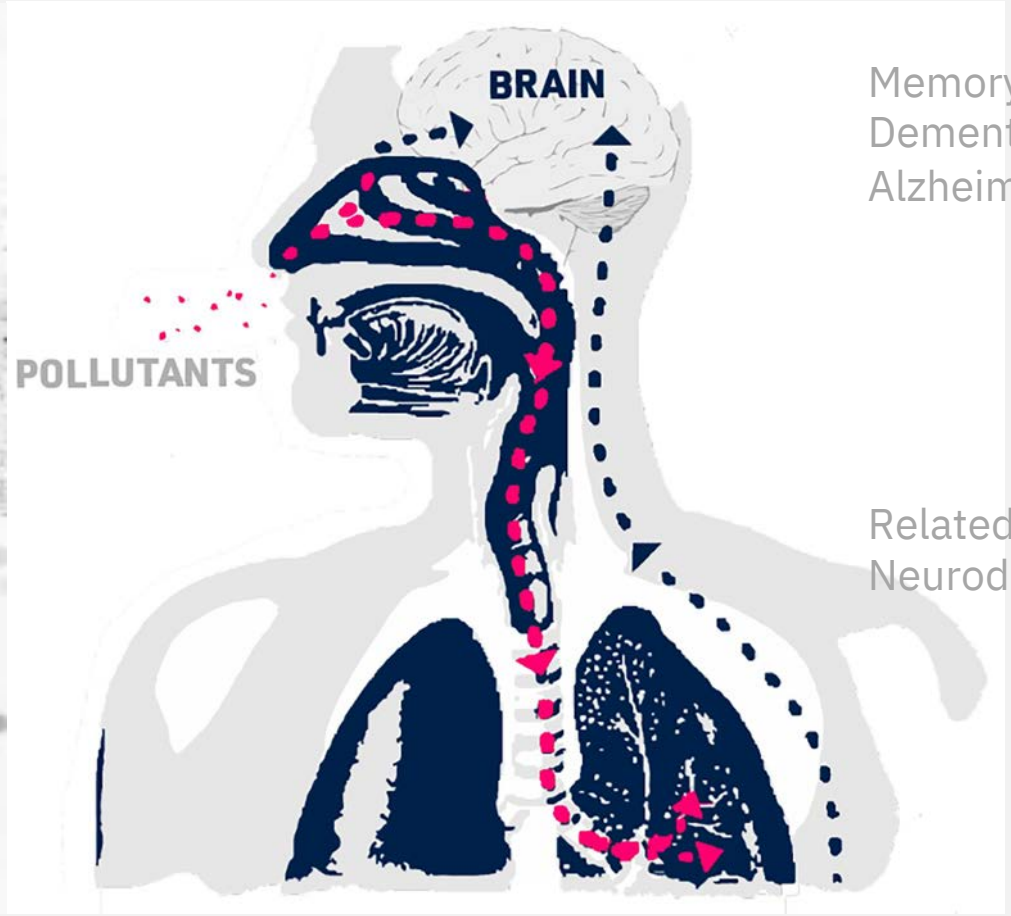
- When environmental challenges exceed the individual ability to cope, then allostatic overload ensues as a transition to an extreme state where stress response systems are repeatedly activated and buffering factors are not adequate.

Allostatic load and the life-course

- Situations that may lead to the development of allostatic load/overload are:
  - (a) exposure to frequent stressors that may determine a status of chronic stress and repeated physiological arousal;
  - (b) lack of adaptation to repeated stressors;
  - (c) inability to shut off the stress response after a stressor is terminated;
  - (d) allostatic response not sufficient to deal with the stressor

Starting point

Birth • Infancy and Early Years • Childhood and Adolescence • Adulthood and Later Life



Memory Impairment
Dementia
Alzheimer's Disease

Depression
Learning Disabilities
ADHD

Related Cardiopulmonary
Neurodegenerative Disorders

Longitudinal association between air pollution exposure at school and cognitive development in school children over a period of 3.5 years

Joan Forns[a,b,c,*], Payam Dadvand[a,b,c], Mikel Esnaola[a,b,c], Mar Alvarez-Pedrerol[a,b,c], Mònica López-Vicente[a,b,c,d], Raquel Garcia-Esteban[a,b,c], Marta Cirach[a,b,c], Xavier Basagaña[a,b,c], Mònica Guxens[a,b,c,d,e], Jordi Sunyer[a,b,c,d]

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[d] *Pompeu Fabra University, Barcelona, Spain*
[e] *Department of Child and Adolescent Psychiatry/Psychology, Erasmus University Medical Centre–Sophia Children's Hospital, Rotterdam, The Netherlands*

Results: We found detrimental associations between all TRAPs (traffic related air pollution) and annual change in 3-back d′ (working memory) (i.e. slower development of working memory in children attending schools with higher levels of air pollution).

The associations (per one interquartile range increase in exposure) were strongest for outdoor NO2 (Coefficient (Coef) = – 4.22, 95% confidence interval (CI), – 6.22, – 2.22) and indoor UFP (Coef = – 4.12, 95%CI, – 5.68, – 1.83). These reductions were equivalent to – 20% (95%CI, – 30.1, – 10.7) and – 19.9% (95%CI,–31.5,–8.4) change in annual working memory development associated with one interquartile range increase in outdoor NO2 and indoor UFP, respectively.

Conclusion: Our findings suggest the persistence of the negative association between TRAPs exposure at school and cognitive trajectory measured by n-back test over a period of 3.5 years.

Early Alzheimer's and Parkinson's Disease Pathology in Urban Children: Friend versus Foe Responses—It Is Time to Face the Evidence

Lilian Calderón-Garcidueñas,[1] Maricela Franco-Lira,[2] Antonieta Mora-Tiscareño,[3] Humberto Medina-Cortina,[3] Ricardo Torres-Jardón,[4] and Michael Kavanaugh[1]

Chronic exposure to particulate matter air pollution is known to cause inflammation leading to respiratory and cardiovascular related sickness and death.

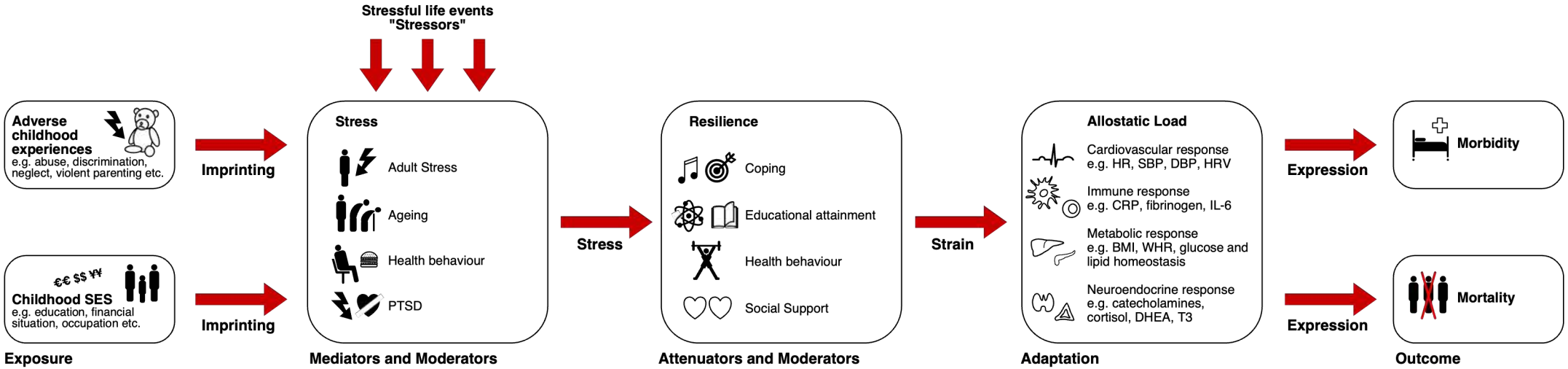
Mexico City Metropolitan Area children exhibit an early brain imbalance in genes involved in oxidative stress, inflammation, and innate and adaptive immune responses. Early dysregulated neuroinflammation, brain microvascular damage, production of potent vasoconstrictors, and perturbations in the integrity of the neurovascular unit likely contribute to progressive neurodegenerative processes.

The accumulation of misfolded proteins coincides with the anatomical distribution observed in the early stages of both Alzheimer's and Parkinson's diseases.

We contend misfolding of hyperphosphorylated tau (HPπ), alpha-synuclein, and beta-amyloid could represent a compensatory early protective response to the sustained systemic and brain inflammation.

However, we favour the view that the chronic systemic and brain dysregulated inflammation and the diffuse vascular damage contribute to the establishment of neurodegenerative processes with childhood clinical manifestations.

Allostatic load and the life-course



Here, we focus on the results of early life exposure and adverse experiences

Putting the next step into the equation

PLACE = Social Determinants Health Inequalities <=> Exposome (air quality) => <=> Allostatic Load => Cognitive/Brain Health Outcomes

Air Pollution, Stress, and Allostatic Load: Linking Systemic and Central Nervous System Impacts

Errol M. Thomson*
Environmental Health Science and Research Bureau, Healthy Environments and Consumer Safety Branch, Health Canada, Ottawa, ON, Canada

Allostatic load and the life-course

The stress pathway posits that those in disadvantaged circumstances are exposed to a higher degree of stressful experiences over time resulting in an accumulated biological burden which subsequently relates to poorer health.

Trajectories of disadvantage, in the form of neighbourhood deprivation and structural social capital, are evaluated in their relation to allostatic load representing the cumulative “wear and tear” of chronic stress.

This paper uses data from the British Household Panel Survey and Understanding Society in a latent class growth analysis. We identify groups of exposure trajectories over time using these classes to predict allostatic load at the final wave.

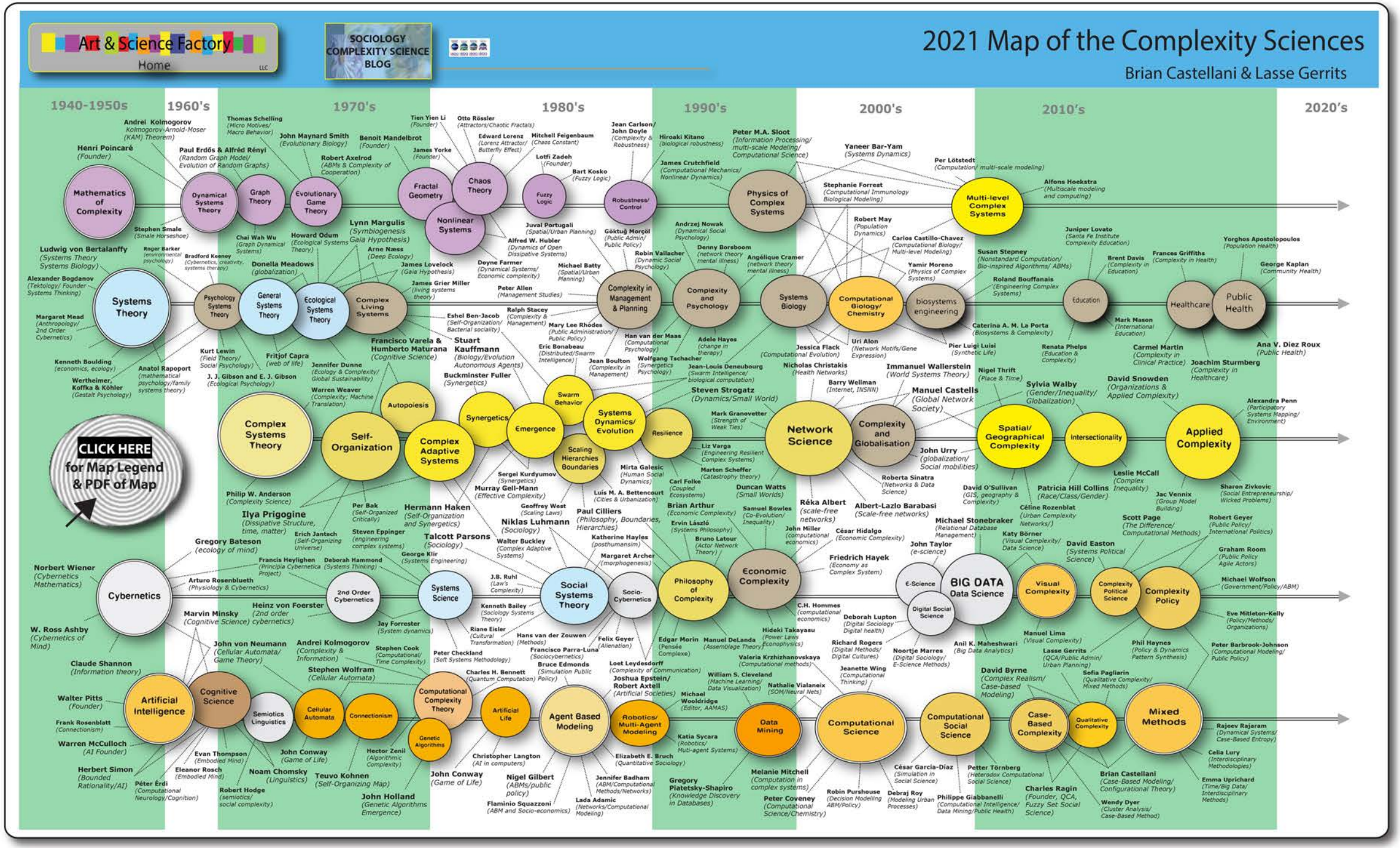
Allostatic load and the life-course

The results show that persistent exposure to higher deprivation is related to worse allostatic load.

By demonstrating a gradient in allostatic load by histories of deprivation, this analysis supports a biological embedding of disadvantage through chronic exposure to stressful environments as an explanation for social health inequalities.

Case-Based Complexity

A new approach to computational modelling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Fractal Geometry
Chaos Theory
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Robustness/ Control
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Multi-level Complex Systems
Systems Theory
Psychology Systems Theory
General Systems Theory
Ecological Systems Theory
Complex Living Systems
Complexity in Management & Planning
Complexity and Psychology
Systems Biology
Computational Biology/ Chemistry
biosystems engineering
Education
Healthcare
Public Health
Complex Systems Theory
Self-Organization
Complex Adaptive Systems
Autopoiesis
Synergetics
Emergence
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2nd Order Cybernetics
Systems Science
Social Systems Theory
Socio-Cybernetics
Philosophy of Complexity
Economic Complexity
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Visual Complexity
Complexity Political Science
Complexity Policy
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Artificial Life
Agent Based Modeling
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Data Mining
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Computational Social Science
Case-Based Complexity
Qualitative Complexity
Mixed Methods
Andrei Kolmogorov (Kolmogorov-Arnold-Moser (KAM) Theorem)
Henri Poincaré (Founder)
Paul Erdős & Alfréd Rényi (Random Graph Model/ Evolution of Random Graphs)
Thomas Schelling (Micro Motives/ Macro Behavior)
John Maynard Smith (Evolutionary Biology)
Benoit Mandelbrot (Founder)
Robert Axelrod (ABMs & Complexity of Cooperation)
James Yorke (Founder)
Tien Yien Li (Founder)
Otto Rössler (Attractors/Chaotic Fractals)
Edward Lorenz (Lorenz Attractor/ Butterfly Effect)
Mitchell Feigenbaum (Chaos Constant)
Lotfi Zadeh (Founder)
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Mark Granovetter (Strength of Weak Ties)
Immanuel Wallerstein (World Systems Theory)
Manuel Castells (Global Network Society)
Nigel Thrift (Place & Time)
Sylvia Walby (Gender/Inequality/ Globalization)
David Snowden (Organizations & Applied Complexity)
Alexandra Penn (Participatory Systems Mapping/ Environment)
Liz Varga (Engineering Resilient Complex Systems)
Marten Scheffer (Catastrophy theory)
Duncan Watts (Small Worlds)
Roberta Sinatra (Networks & Data Science)
John Urry (globalization/ Social mobilities)
David O'Sullivan (GIS, geography & Complexity)
Patricia Hill Collins (Race/Class/Gender)
Céline Rozenblat (Urban Complexity Networks/)
Leslie McCall (Complex Inequality)
Jac Vennix (Group Model Building)
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Stephen Wolfram (Cellular Automata)
Charles H. Bennett (Quantum Computation)
Joshua Epstein/ Robert Axtell (Artificial Societies)
Michael Wooldridge (Editor, AAMAS)
William S. Cleveland (Machine Learning/ Data Visualization)
Nathalie Vialaneix (SOM/Neural Nets)
Jeanette Wing (Computational Thinking)
David Byrne (Complex Realism/ Case-based Modeling)
Sofia Pagliarin (Qualitative Complexity/ Mixed Methods)
Walter Pitts (Founder)
Frank Rosenblatt (Connectionism)
Warren McCulloch (AI Founder)
Herbert Simon (Bounded Rationality/AI)
Péter Érdi (Computational Neurology/Cognition)
Evan Thompson (Embodied Mind)
Eleanor Rosch (Embodied Mind)
Robert Hodge (semiotics/ social complexity)
Noam Chomsky (Linguistics)
John Conway (Game of Life)
Teuvo Kohonen (Self-Organizing Map)
Hector Zenil (Algorithmic Complexity)
John Holland (Genetic Algorithms Emergence)
Christopher Langton (AI in computers)
John Conway (Game of Life)
Nigel Gilbert (ABMs/public policy)
Flaminio Squazzoni (ABM and Socio-economics)
Jennifer Badham (ABM/Computational Methods/Networks)
Lada Adamic (Networks/Computational Modeling)
Elizabeth E. Bruch (Quantitative Sociology)
Katia Sycara (Robotics/ Muti-agent Systems)
Gregory Piatetsky-Shapiro (Knowledge Discovery in Databases)
Melanie Mitchell (Computation in complex systems)
Peter Coveney (Computational Science/Chemistry)
Robin Purshouse (Decision Modelling ABM/Policy)
César García-Díaz (Simulation in Social Science)
Debraj Roy (Modeling Urban Processes)
Petter Törnberg (Heterodox Computational Social Science)
Philippe Giabbanelli (Computational Intelligence/ Data Mining/Public Health)
Charles Ragin (Founder, QCA, Fuzzy Set Social Science)
Brian Castellani (Case-Based Modeling/ Configurational Theory)
Wendy Dyer (Cluster Analysis/ Case-Based Method)

Thinking about complex systems

The need for a complex systems model of evidence for public health

Harry Rutter, Natalie Savona, Ketevan Glonti, Jo Bibby, Steven Cummins, Diane T Finegood, Felix Greaves, Laura Harper, Penelope Hawe, Laurence Moore, Mark Petticrew, Eva Rehfuess, Alan Shiell, James Thomas, Martin White

Thinking about complex systems

Approaches to research that aim to understand single components within systems, or attempt to factor out the system context using randomisation and control, are of limited use for identifying how to influence complex systems.

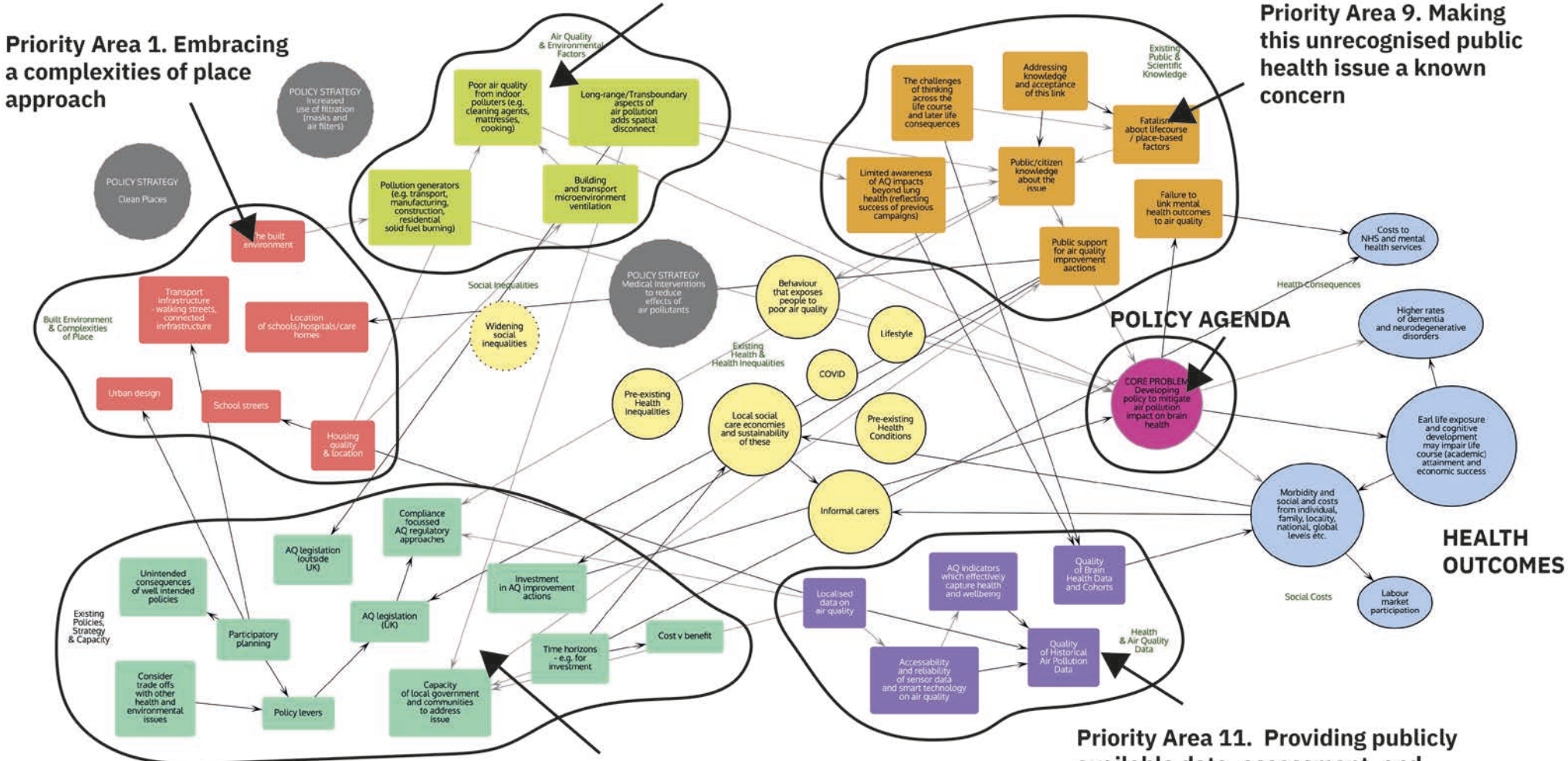
Research funding, research activity, and the published evidence base are all heavily skewed towards studies that attempt to identify simple, often short term, individual-level health outcomes, rather than complex, multiple, upstream, population-level actions and outcomes.

This skew echoes the prioritisation by policy makers of individual-level interventions over system-level responses.

Priority Area 3. Detailing the impact of ambient PM2.5; Priority Area 4: Building high resolution historical exposure models; and Priority Area 5: Studying indoor air pollution

Priority Area 1. Embracing a complexities of place approach

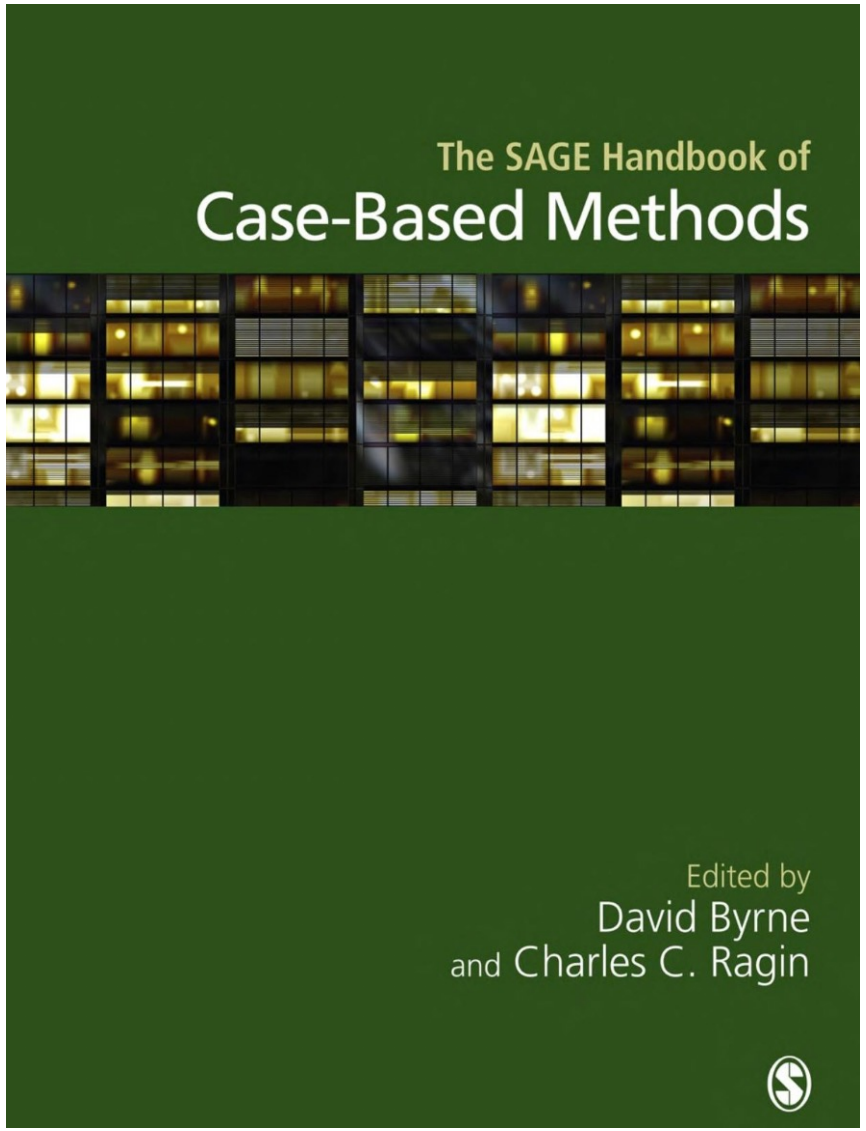
Priority Area 9. Making this unrecognised public health issue a known concern

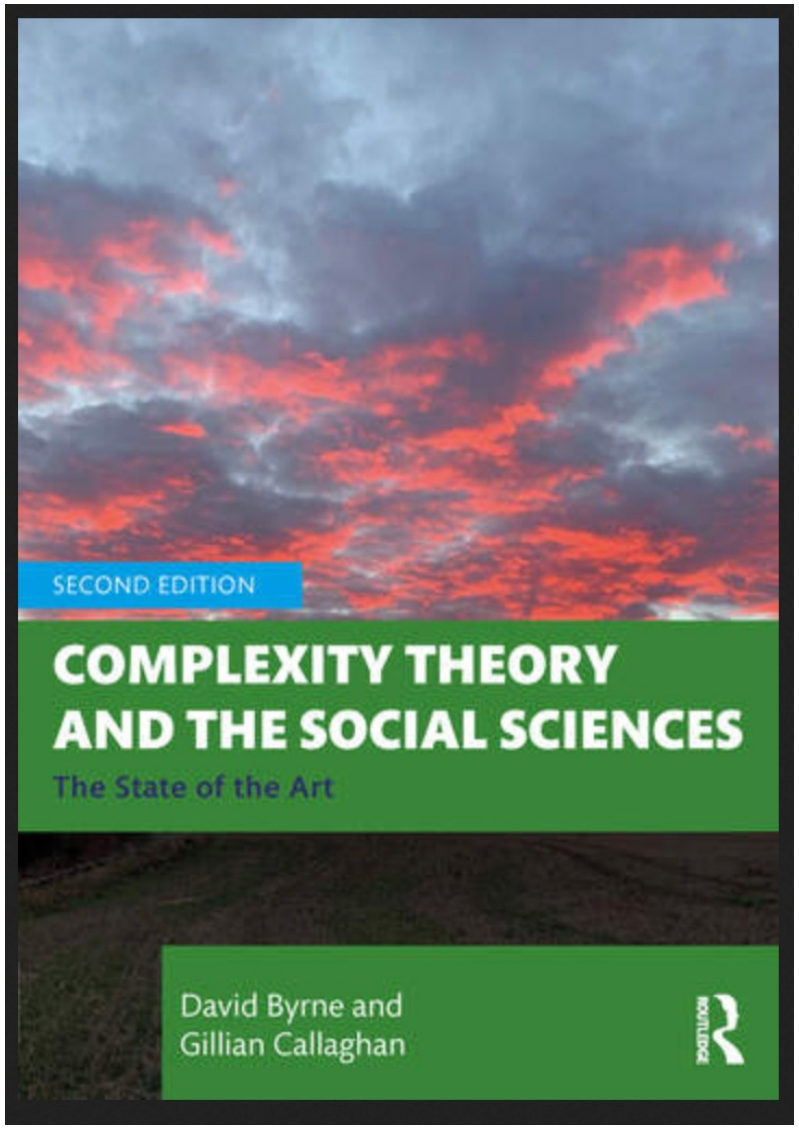


Priority Area 14. Attaching air pollution to existing brain health strategies and campaigns

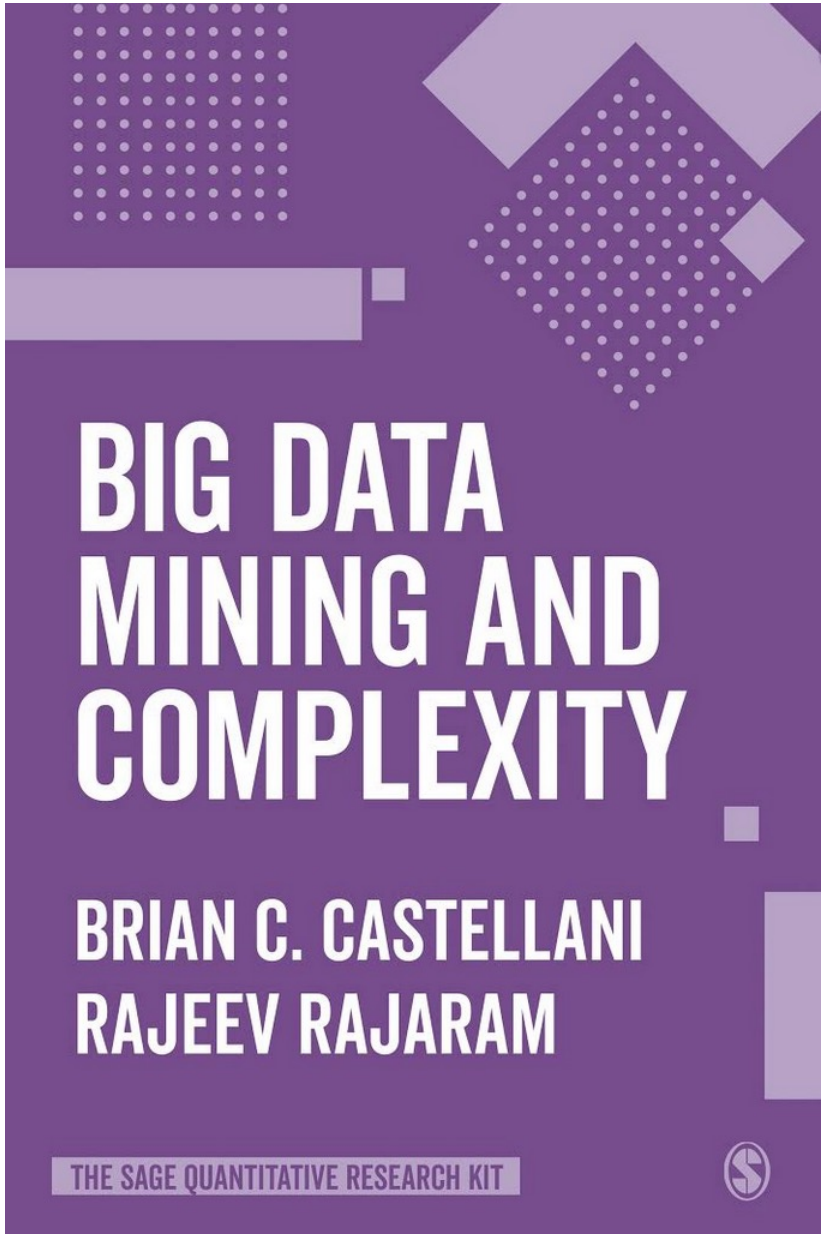
Priority Area 11. Providing publicly available data, assessment, and screening tools

Types of Case-Based Complexity





- **PRIMARY TEXT:** Castellani and Rajaram (2019). *Data Mining Big Data: A Complex and Critical Perspective*. SAGE Quantitative Methods Kit. **READ: Chapters 6 and 7.**
- Jain, A. K. (2010). Data clustering: 50 years beyond K-means. *Pattern recognition letters*, *31*(8), 651-666.



Basic Tenets

1 The case and its trajectory across time/space are the focus of study, not the individual variables or attributes of which it is comprised.
2 Cases and their trajectories are treated as composites (profiles), comprised of an interdependent, interconnected sets of causal conditions, variables, factors or attributes.
3 And, finally, cases and their relationships and trajectories are the methodological equivalent of complex systems – that is, they are emergent, self-organising, non-linear, dynamic, network-like and so on – and therefore should be studied as such.

Basic Tenets

1 Cases and their trajectories are dynamically evolving across time/space and, therefore, should be explored to identify their major and minor trends.
2 In turn, these trends should be explored in the aggregate for key global–temporal patterns, as in the case of spiralling sources and saddles.
3 The social interactions amongst cases are also important, as are the hierarchical social contexts in which these relationships take place.
4 And, finally, the complex set of relationships amongst cases is best examined using the tools of network science and simulation.

ORIGINAL PAPER

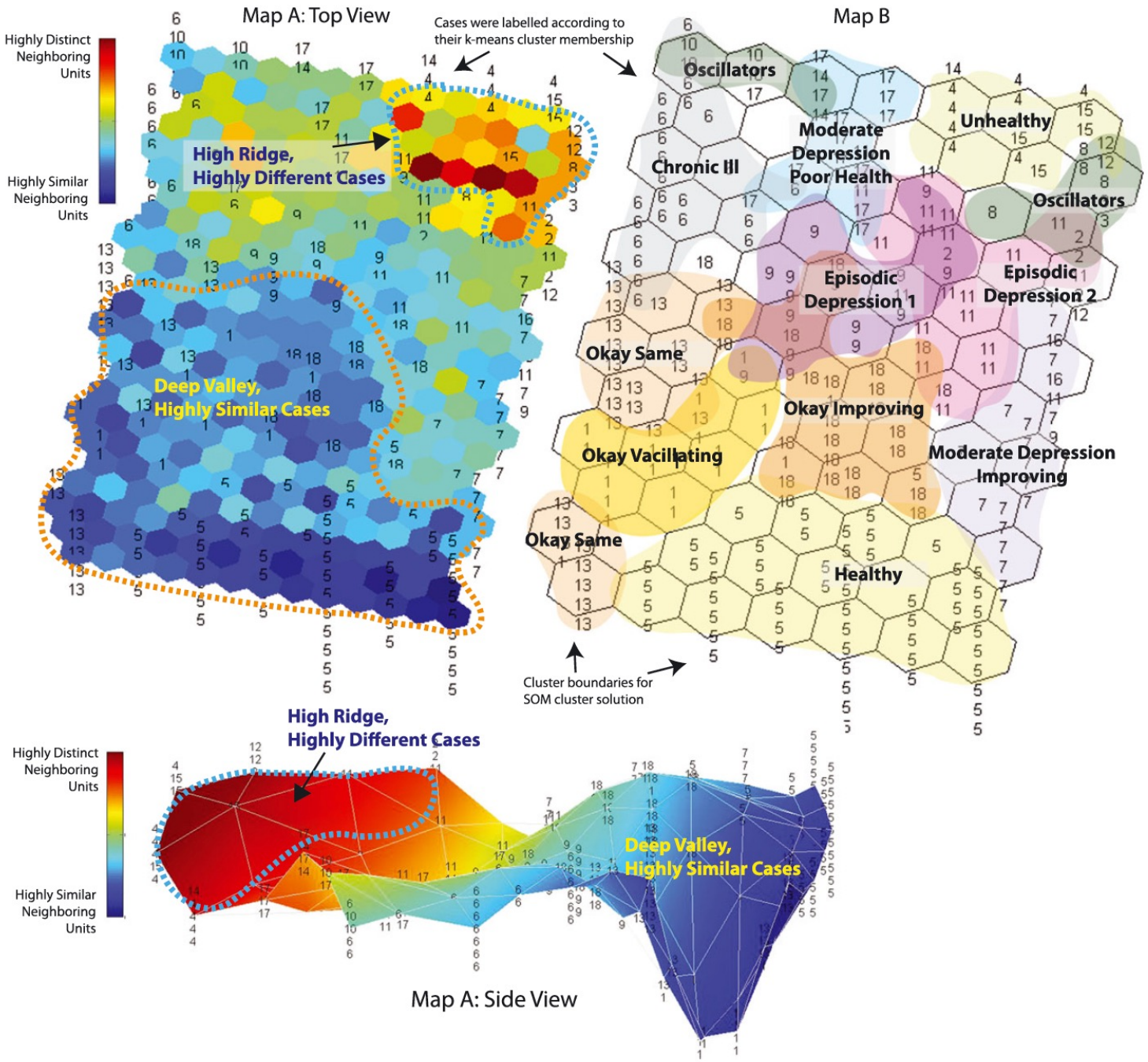
WILEY Journal of Evaluation in Clinical Practice

Exploring comorbid depression and physical health trajectories: A case-based computational modelling approach

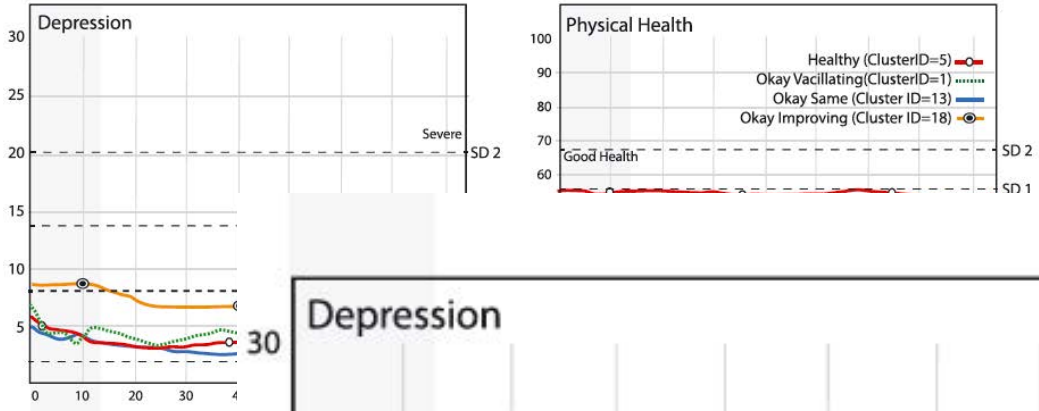
Brian Castellani PhD, Professor of Sociology[1,6] |
Frances Griffiths MD PhD, Professor of Medicine[2,3] |
Rajeev Rajaram PhD, Associate Professor[4] | Jane Gunn MD PhD, Professor of Medicine[5]

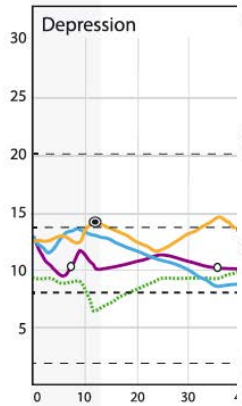
Abstract

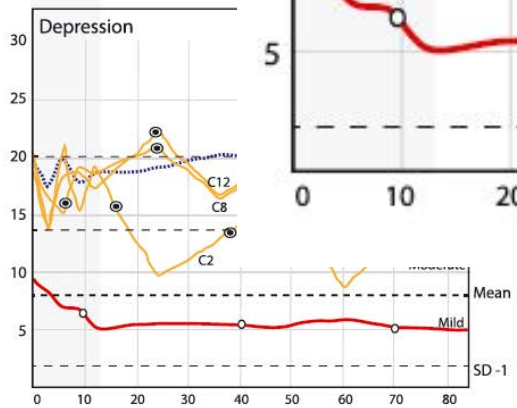
While comorbid depression/physical health is a major clinical concern, the conventional methods of medicine make it difficult to model the complexities of this relationship. Such challenges include cataloguing multiple trends, developing multiple complex aetiological explanations, and modelling the collective large-scale dynamics of these trends. Using a case-based complexity approach, this study engaged in a richly described case study to demonstrate the utility of computational modelling for primary care research. N = 259 people were subsampled from the *Diamond* database, one of the largest primary care depression cohort studies worldwide. A global measure of depressive symptoms (PHQ-9) and physical health (PCS-12) were assessed at 3, 6, 9, and 12 months and then annually for a total of 7 years. Eleven trajectories and 2 large-scale collective dynamics were identified, revealing that while depression is comorbid with poor physical health, chronic illness is often low dynamic and not always linked to depression. Also, some of the cases in the unhealthy and oscillator trends remain ill without much chance of improvement. Finally, childhood abuse, partner violence, and negative life events are greater amongst unhealthy trends. Computational modelling offers a major advance for health researchers to account for the diversity of primary care patients and for developing better prognostic models for team-based interdisciplinary care.

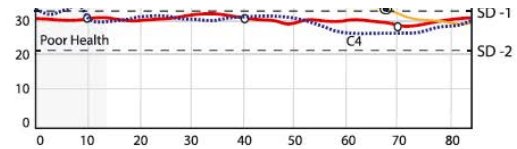


Healthy to Okay Health Group

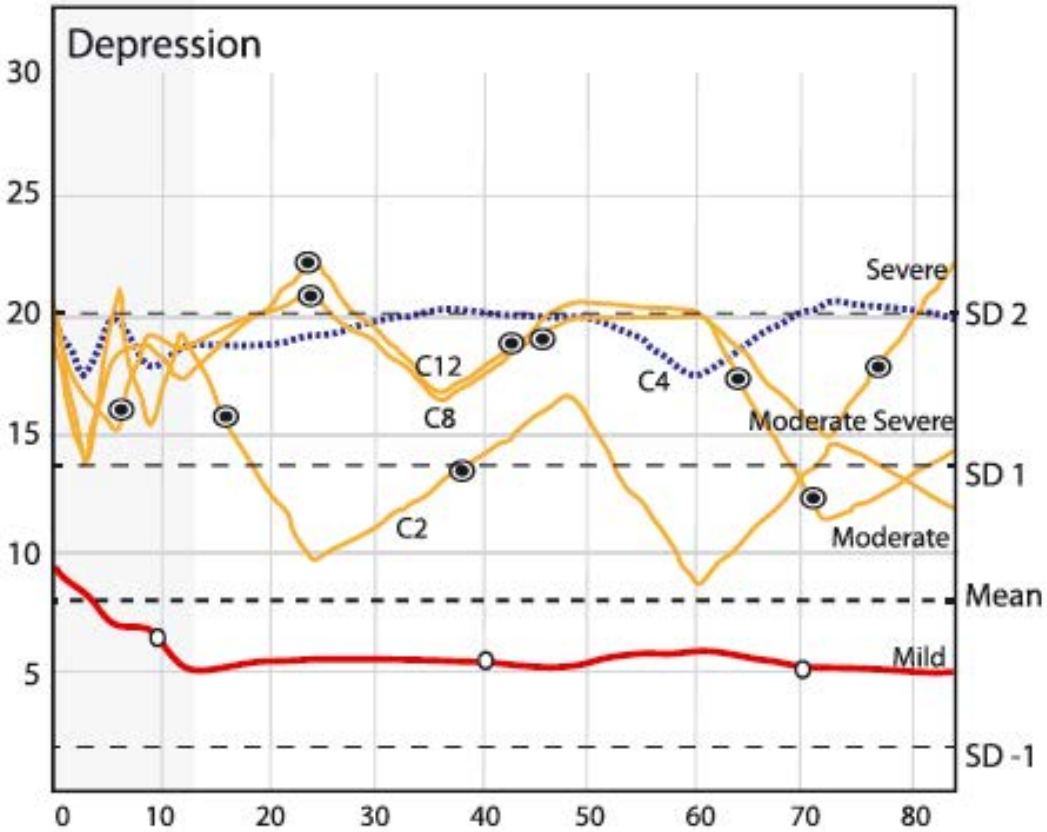


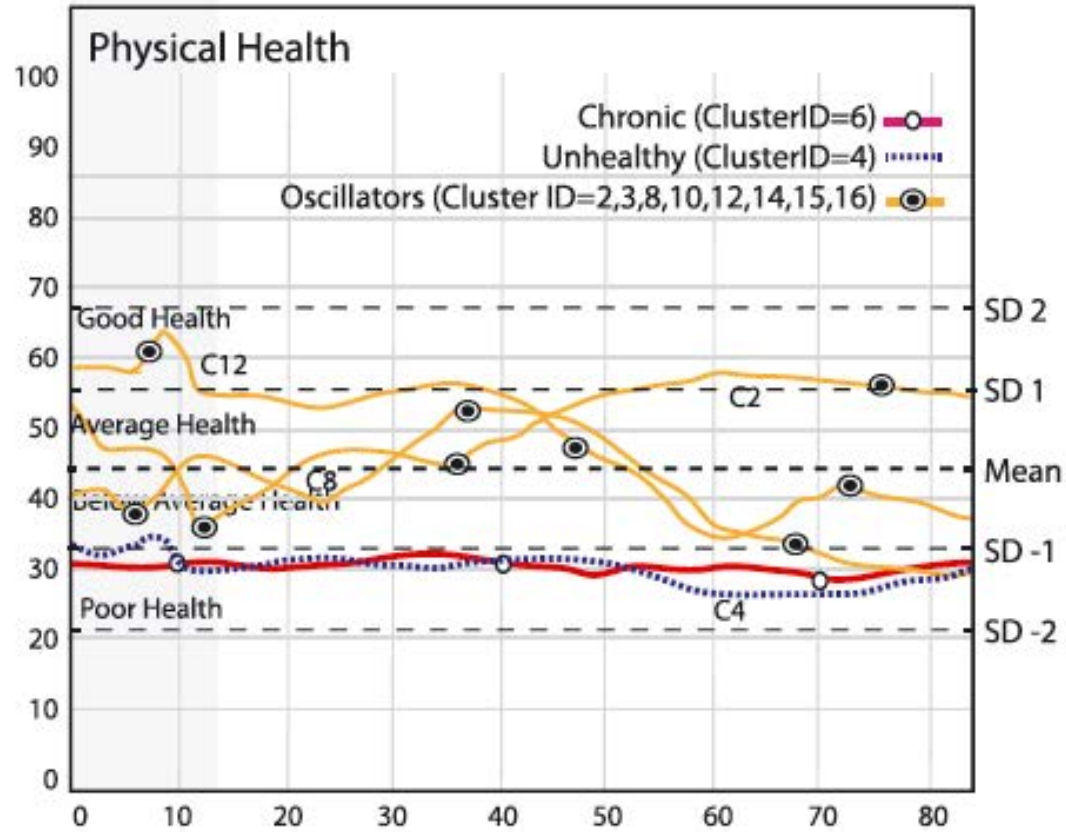


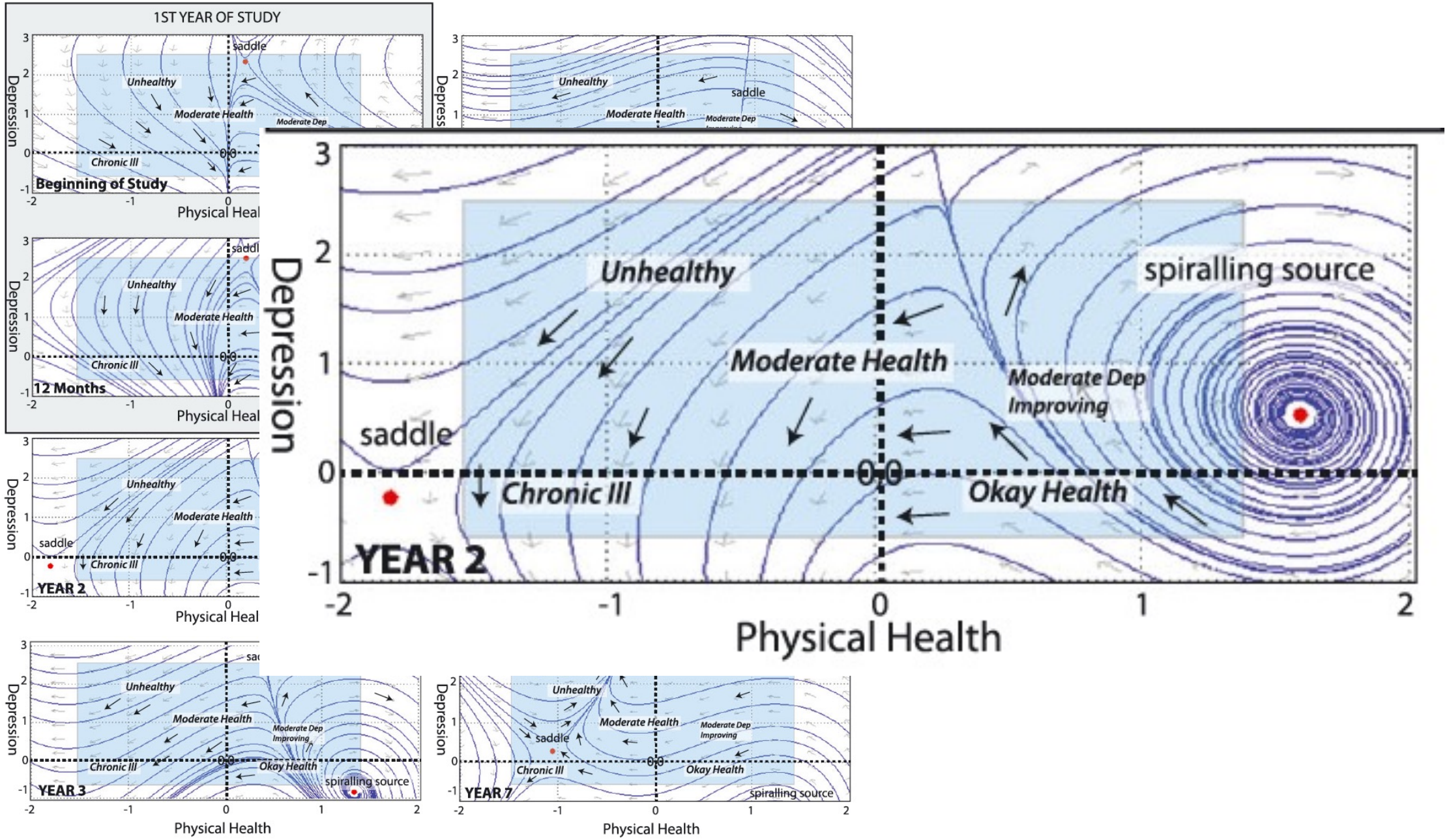




Overall Poor Health Group






1ST YEAR OF STUDY
saddle
Unhealthy
Moderate Health
Moderate Dep
Chronic Ill
0,0
Beginning of Study
Depression
Physical Heal
12 Months
YEAR 2
Okay Health
spiralling source
YEAR 3
YEAR 7
Physical Health

Putting the next step into the equation

PLACE = Social Determinants Health Inequalities <=> Exposome (air quality) => <=> Allostatic Load => Cognitive/Brain Health Outcomes

Complex system of factors (exposome, allostatic load) at multiple levels (biological, psychological, sociological) situated in particular places =>

Clusters and trajectories of different outcomes

Allostatic Load as a Complex Clinical Construct: A Case-Based Computational Modeling Approach

J GALEN BUCKWALTER,[1] BRIAN CASTELLANI,[2] BRUCE MCEWEN,[3] ARUN S KARLAMANGLA,[4] ALBERT A RIZZO,[1] BRUCE JOHN,[1] KYLE O'DONNELL,[1] AND TERESA SEEMAN[4]

[1]Institute for Creative Technologies, University of Southern California, Los Angeles, California 90094; [2]Department of Sociology, Kent State University, Ohio 44240; [3]Laboratory of Neuroendocrinology, Rockefeller University, New York, New York 10065; and [4]Division of Geriatrics, David Geffen School of Medicine, University of California, Los Angeles, CA, United States

Case-Based Complexity Modeling

TABLE 1

Allostatic Load Seven Factor Structure Solution

	Factors/Components[a]						
Biomarkers	Blood Pressure	Metabolic Syndrome	Cholesterol	Pro-Inflammatory Elements	Stress Hormones	Blood Sugar	Stress Antagonists
Systolic BP[b]	**0.880**	0.158	0.060	0.132	0.054	0.130	−0.106
Diastolic BP[b]	**0.883**	0.181	0.120	−0.052	0.141	0.020	0.220
Waist to hip ratio	0.305	**0.700**	−0.090	0.113	0.150	0.308	0.294
HDL[c]	−0.096	**−0.829**	0.103	−0.084	−0.191	−0.129	−0.122
Insulin	0.082	**0.677**	0.030	0.379	0.025	0.411	−0.007
Triglycerides	0.164	**0.786**	0.297	0.113	0.039	0.235	−0.093
Total cholesterol	0.099	−0.005	**0.980**	0.021	−0.033	0.011	−0.011
LDL[d]	0.098	0.095	**0.935**	0.021	0.040	−0.077	0.093
IL6[e]	0.030	0.271	−0.141	**0.786**	0.000	0.169	−0.257
Fibrinogen	0.001	−0.009	0.092	**0.804**	−0.037	0.148	−0.096
C Reactive proteins	0.071	0.249	0.100	**0.816**	0.033	0.185	−0.259
Cortisol	0.094	−0.046	−0.008	−0.119	**0.613**	−0.093	0.264
Norepinephrine	0.124	0.237	0.006	0.124	**0.889**	0.075	−0.001
Epinephrine	0.112	0.077	−0.028	−0.085	**0.855**	−0.016	0.178
Dopamine	0.044	0.190	0.000	0.020	**0.888**	−0.006	0.124
Hemoglobin A1c	0.036	0.208	−0.059	0.238	−0.018	**0.887**	−0.163
Glucose	0.115	0.355	−0.015	0.130	0.006	**0.895**	−0.015
DHEAS[f]	−0.005	0.127	0.110	−0.098	0.226	−0.005	**0.729**
Peak flow	0.208	0.307	−0.089	−0.286	0.111	−0.004	**0.629**
IGF-1[g]	0.031	−0.081	0.020	−0.190	0.026	−0.162	**0.719**

TABLE 2

Allostatic Load Nine Cluster Solution

	Clusters[a]									
	1 Low Cholesterol	2 Healthy	3 High Blood Pressure	4 Low Stress Hormones	5 Metabolic Syndrome	6 High Blood Sugar	7 Low Stress Antagonist	8 High Stress Hormones	9 High Pro-Inflammatory Elements	
Factor/Components[b] Range (min−max)										**ANOVA F-test[c]**
Stress hormones (−3.02 to 3.11)	−0.79[d]	0.33	0.35	−0.92	0.66	−0.22	−.62	1.03	−0.30	118.41e
Metabolic syndrome (−2.81 to 2.90)	−0.55	−1.08	−0.40	0.16	1.22	1.00	−0.74	12	0.95	**177.97**e
Pro-inflammatory (−3.03 to 3.08)	−0.41	−1.19	−0.71	0.29	0.99	0.57	−0.27	0.12	1.08	**154.72**[e]
Cholesterol (−4.69 to 2.75)	−1.12	0.06	0.42	0.73	0.73	−0.01	−0.08	−0.69	−0.82	93.77
Blood sugars (−1.83 to 6.70)	−0.32	−0.48	−0.36	−0.13	0.18	3.71	−0.25	0.08	0.36	**215.42**[e]
Stress antagonists (−3.86 to 2.26)	0.31	0.22	0.58	0.14	0.35	−0.10	−1.7	0.30	−0.73	102.06[e]
Blood pressure (−3.91 to 3.17)	−0.60	−1.10	0.94	−0.06	0.47	0.26	0.15	0.21	−0.52	80.78[e]
	N=96[f]	N = 138	N = 155	N = 169	N = 144	N = 35	N = 109	N = 146	N = 104	

[a]This nine-cluster solution was obtained using k-means, with standard Euclidian distance measures; convergence criterion was set to zero.

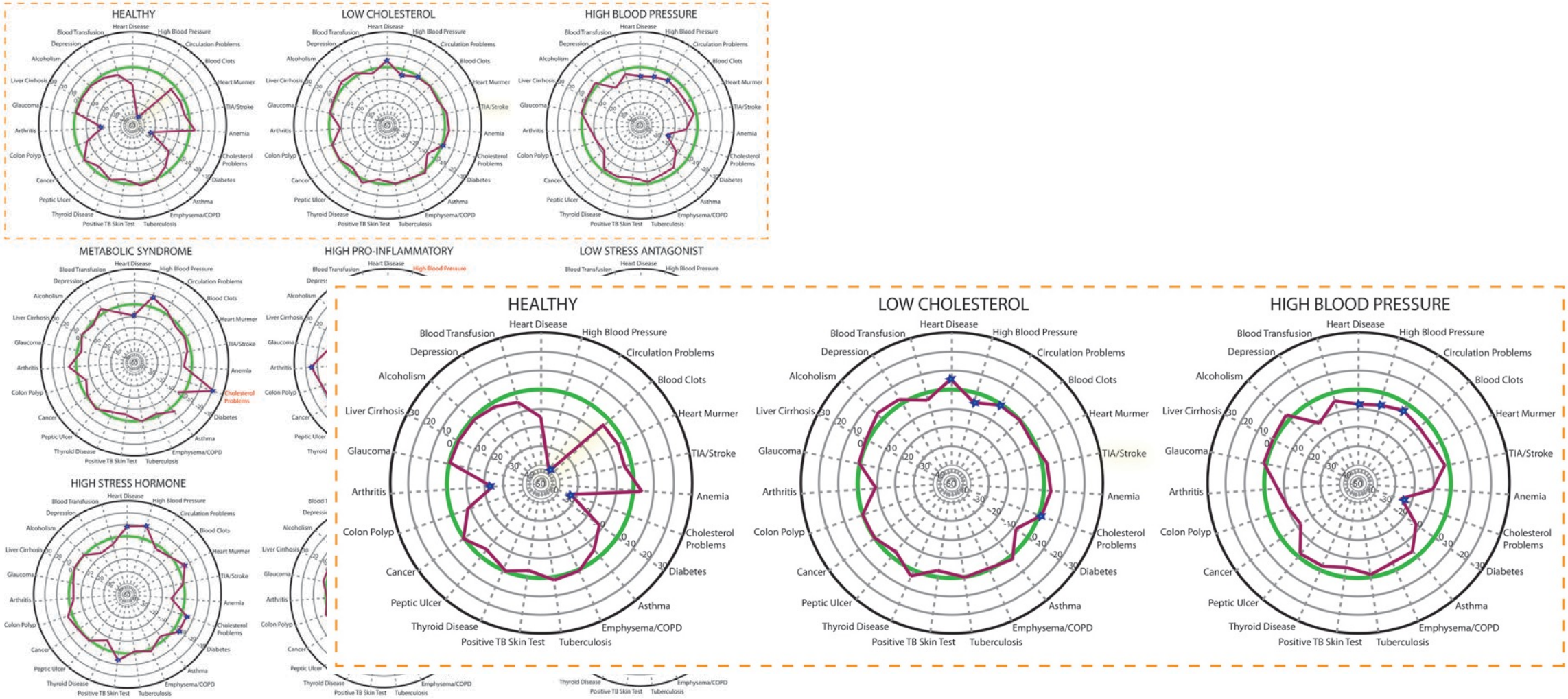
[b]These are the seven factors from Table 1, used to construct the different profiles for the nine clusters. Included below each factor is its min and max score possible, which comes from summing the biomarkers that loaded on it and converting this sum into a z-score.

[c]Unstandardized F scores (ANOVA) demonstrating, for descriptive purposes only, the relative impact the seven factors had in determining cluster membership

[d]The score for each case, for each of the seven factors, was computed (as noted in ***b*** above) by summing each case's scores on the biomarkers for each factor, as shown in Table 1. In turn, these summed factor scores were converted into z-scores to normalize the data.

[e]F test was significant at.000. The factors with the three highest scores are highlighted.

[f]Number of cases in each cluster.



Clinical Health Risk Outcomes for Nine Allostatic Load Profiles. This Figure displays the differences between observed and expected frequencies for each self-reported medical condition. Each of the radii represents a self-reported medical condition, labeled at the top of their respective radius. The case clusters are circumscribed around the 23 points of each circle based on the average frequency on a particular self-reported medical condition. The resulting profile (which constitutes each Cluster's health risk profile) is in red. Score higher than 0 (the green circle) indicate a greater observed value than expected, whereas scores below 0 indicate a smaller than observed value than expected. For those scores higher than 20, the corresponding medical condition is labeled in red. The three healthy to marginally healthy profiles are at the top, outlined in orange.