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Beyond multimorbidity: what can we learn from complexity science?

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58 Beyond multimorbidity: what can we learn from complexity science?

59 Abstract

60 Multimorbidity – the occurrence of two or more long-term conditions in an individual – is a major
61 global concern, placing a huge burden on healthcare systems, physicians, and patients. It challenges
62 the current biomedical paradigm, in particular conventional evidence-based medicine’s dominant
63 focus on single-conditions. Patients’ heterogeneous range of clinical presentations tend to escape
64 characterization by traditional means of classification, and optimal management cannot be deduced
65 from clinical practice guidelines.

66 In this article, we argue that person-focused care based in complexity science may be a
67 transformational lens through which to view multimorbidity, to complement the specialism focus on
68 each particular disease. The approach offers an integrated and coherent perspective on the person’s
69 living environment, relationships, somatic, emotional and cognitive experiences and physiological
70 function. The underlying principles include non-linearity, tipping points, emergence, importance of
71 initial conditions, contextual factors and co-evolution, and the presence of patterned outcomes.

72 From a clinical perspective, complexity science has important implications at the theoretical,
73 practice and policy levels. Three essential questions emerge: (1) What matters to patients? (2) How
74 can we integrate, personalise and prioritise care for whole people, given the constraints of their
75 socio-ecological circumstances? (3) What needs to change at the practice and policy levels to deliver
76 what matters to patients?

77 These questions have no simple answers, but complexity science principles suggest a way to
78 integrate understanding of biological, biographical and contextual factors, to guide an integrated
79 approach to the care of people with multimorbidity.

80 **Word Count:** 237

81 Keywords

82
83 Multimorbidity, Complexity Science, Health, Person-Centered Care

84

85 Introduction

86 It can be complicated enough to care for patients with a single disease. But most patients
87 presenting to primary care or to hospital are living with multiple chronic conditions – also known as
88 multimorbidity.¹ Such multimorbidity is not well-addressed by current one-disease-at-a-time
89 scientific evidence and clinical practice guidelines.²

90 Complexity science focuses on understanding, as a contextualized whole, the many parts of
91 multifaceted phenomena.³ Principles from complexity science can be useful in understanding the
92 many interacting processes in multimorbidity, and in integrating care for whole people. Providing
93 this integration is an essential task of the generalist,⁴ but is something that all clinicians need to be
94 able to do when managing patients with multimorbidity.

95 Relevant complexity science principles for understanding and managing multimorbidity include: non-
96 linearity, tipping points, emergence, co-evolution, the importance of contextual factors and initial
97 conditions, and the presence of patterned outcomes.

98 In this paper we articulate these principles and show how they can be used in both diagnostic and
99 therapeutic processes for patients with multimorbidity. We illustrate the application of these
100 principles to a specific case, in order to explicate how complexity science can make explicit the often
101 tacit processes that astute clinicians use to provide patient-centred care.⁵ The composite case
102 vignette of Jennifer's story, based on the clinical experience of the authors, and presented in Box 1,

103 shows a cascade of inter-related medical and social problems, and their less familiar resolution
104 through the application of complex science principles.

105 Multimorbidity – a Manifestation of Complex Causality

106 As human beings (though not always as busy doctors), we can intuitively see the multiple strands in
107 Jennifer’s story. We sense that individual biomedical diagnoses might be related in both their
108 causation and potential resolution, and yet, individual diagnoses paint only fragments of the picture.
109 We comprehend how loss and grief in various intertwined ways negatively affect her life. All of this is
110 compounded by socioeconomic deprivation and the social determinants of health, which Dr. Patel
111 clearly understands and which shape her responses to Jennifer’s predicament as-a-whole.

112 This is what complexity is all about — as Alexander von Humboldt at the end of the 18th century
113 stated: natural phenomena can only be ‘fully understood’ through the frame of a holistic web. In a
114 web “*everything is interconnected*” — a change in one part of the web affects all parts of the web.
115 He saw, as do astute clinicians, that “*In this great chain of causes and effects, no single fact can be*
116 *considered in isolation.*”⁶

117 Through a complexity science lens, multimorbidity is not the sum of discrete diseases. Rather, it is
118 an *emergent state* arising from the interactions between a multitude of factors in a person’s socio-
119 ecological environment and inherited biology.⁷⁻¹³ Jennifer’s health trajectory shows the all-important
120 interconnected, interdependent and dynamically interacting strands of her experience across many
121 scales of aggregation (external environment to internal biological building blocks).¹⁴ A broad,
122 ecological frame enhances understanding of the complexities of her health experiences and her
123 disease manifestations.^{4, 9, 13, 15, 16}

124 Jennifer's health trajectory highlights the well-established associations between social disadvantage
125 and the premature onset of multimorbidity,¹⁷ but more importantly shows the complexities of the
126 lack of strong social support networks,¹⁸ the impact of increasing allostatic load on physiological
127 dysregulation leading to diagnosable and disabling diseases,^{19, 20} the association with social and
128 emotional well-being, and the spiralling utilisation of health service and health system resources.²¹
129 Hence one inevitably has to ask: is there a better way to understand multimorbidity than just two or
130 more chronic conditions?^{22 23} And how might a complex adaptive understanding help patients,
131 health professionals, and their interactions?

132 Understanding & Managing Multimorbidity through a Complexity Lens

133 Box 2 depicts how complexity science principles — knowing the properties of complex systems —
134 can be used to understand and manage multimorbidity. Box 2 also shows how each principle applies
135 to Jennifer's story.

136 The **non-linearity** of complex systems creates **tipping points** in which small interventions can have
137 large effects (or lack of intervention can lead to rapid deterioration). Being open to these tipping
138 points is an opportunity for novel understanding and harm-reducing, efficient, and effective
139 interventions to improve the lives of people living with multimorbidity.

140 The property of **emergence** arises from intricate causal relations across different scales and
141 feedback mechanisms. It provides an opportunity for astute clinicians to search for, and to act on,
142 teachable moments that arise because of the complex causality underlying multimorbidity.

143 Recognizing the **co-evolution** of the many systems affecting people living with multimorbidity
144 provides an opportunity for patients and their clinicians to change together in their shared
145 understanding of the patient's related illnesses and their integrated opportunities for healing.

146 Understanding that **context and initial conditions are important** in multimorbidity can help
147 clinicians and patients to work together to improve the biology underlying multiple diseases, and the
148 social and environmental factors that influence the experience of illness and health.

149 The **patterned outcomes** that are a feature of complex systems allows clinicians to identify
150 phenotypes that include but transcend individual disease labels, and to use therapeutic trials and
151 observation of changes over time to help patients improve.

152 The emergence of multimorbidity is the outcome of ongoing integrated and interconnected
153 processes whose dynamics impact on all parts — the person's living environment, their
154 relationships, their somatic, emotional, social and cognitive experiences, and their internal
155 physiological function. These give rise to a vast and heterogeneous range of clinical presentations,
156 many of which escape characterization by traditional means of clinical classification, and whose
157 management is not captured in clinical practice guidelines.

158 Whole-person multimorbidity management, rather than being focused on the treatment of multiple
159 disease manifestations, requires a systemic person-in-context perspective. Health professionals
160 using complexity science principles are better able to work effectively with non-medical sectors to
161 address the community-level social and environmental conditions²⁴ affecting their patients' health.

162 This is the domain of *complexity-based care*, an approach that consciously takes into account the
163 real-life complex-adaptive dynamics of a person's inter-related illnesses and potential healing
164 trajectories.^{25, 26} This goes beyond the traditional patient-centered approach focused on making the
165 patient a partner in their care²⁷ to consider the complex adaptive systems affecting healing and
166 health.

167 *Complexity Principles Help Clinicians to Focus on the Whole Person in Context*

168 Health problems and treatments tend to *interact in ways* that increase the danger of a narrow,
169 conventional biomedical/EBM focus. Compounded by measuring and rewarding clinicians for their
170 *quality of care*, one disease at a time, even primary care clinicians — whose focus is on the whole
171 person, and in whose practices multimorbidity is the norm — can lose sight of the whole and ignore
172 the fact that improving human health requires different approaches than just treating *the sum of*
173 *diseases*.^{15, 28}

174 Starting with the person in their family and community context, rather than starting with the
175 disease, enables the doctor to focus on what is most important to the patient. Doing that over time,
176 with empathy, develops trusting relationships that allows care to be integrated — such as choosing
177 with the patient a single behavioural or pharmacological intervention that may not be the narrowly-
178 evidence-based treatment for any single condition, but that has beneficial effects for multiple
179 conditions, or that conveys preventive benefits and avoids harmful interactions among therapies —
180 it addresses the *system of the person as-a-whole*.

181 As made explicit by Jennifer's story, almost all of her deteriorating and subsequently improving
182 disease manifestations are related to important initial conditions and occur in an interdependent
183 fashion. It was the shared understanding of her personal circumstances and perceptions that
184 allowed the formulation of a management plan that comprehensively addressed her multiple —
185 somatic, emotional, social and cognitive — care needs. Her illness trajectory also demonstrates the
186 nonlinear responses of the effects of complexity-centred consultations²⁶ — targeted small
187 interventions at the right point in time enabled her to implement changes that modulated — as yet
188 not fully understood — physiological pathways which allowed her health to re-emerge.

189 *The Challenge and Promise for Health Professionals*

190 Managing patients with multimorbidity as *whole-people*, while highly beneficial to those patients,
191 simultaneously has significant effects on health professionals — it can challenge their reductionist
192 basic training, individual clinical and interpersonal competence, practice organisation,
193 interdisciplinary working styles, and last but not least, stress and burnout, especially when working
194 with persistent chronic disadvantaged communities.²⁹

195 The co-occurrence and interactions among multiple diseases in the same person create unique
196 challenges, as EBM-guideline based interventions which focus on each individual disease may not be
197 valid since people with multiple conditions are commonly excluded from the RCTs that inform such
198 clinical guidelines.³⁰ Well-studied single organ diseases behave rather differently in the context of
199 other diseases (e.g. heart disease).³¹ Patients, and especially elderly patients, strictly managed to
200 each disease guideline experience more adverse events, can have poorer quality of life and higher
201 overall mortality rates.³²

202 Patients with multimorbidity benefit from investment of time.³² Continuity of care is an important
203 element of the effective and efficient management of this patient group and is associated with
204 better health outcomes and savings of limited health system resources.^{32, 33} However
205 operationalising continuity of care within increasingly complex care delivered by multidisciplinary
206 teams remains a challenge.

207 *Practice Infrastructure*

208 Effective and efficient multimorbidity care, besides of person-centred clinical approaches, depends
209 on having a practice-based support team connected to the local practice environment and patient
210 population. This allows every health professional to readily tap into the resources and skill of

211 colleagues to seamlessly address a patient's *most pressing issues at this point in time*.³⁴ A local
212 practice-based support team ensures adaptive care responses to enhance a person's road to
213 recovery.³⁴ Information systems are needed that use artificial intelligence to present prioritized
214 information,³⁵ rather than current electronic medical records that typically support one-disease-at-a-
215 time care.

216 *Social Justice*

217 For Jennifer, a holistic approach by a dedicated doctor she knew and trusted, and who knew only too
218 well how the blight of deprivation affected her patients' lives, was transformational. But Dr Patel,
219 like all doctors who work in deprived areas, knows many 'Jennifers' whose life trajectories and
220 outcomes are not so positive. The problems that patients of low socioeconomic status face reflect
221 the wide inequalities in wealth and power that most countries have, and the social determinants
222 that underpin those inequalities.³⁶ The impact of deprivation has been recently shown into sharp
223 focus during the COVID-19 pandemic.³⁶⁻³⁸ Changing the fundamental causes of health inequalities
224 requires political commitment to social justice and social change. Although this is beyond the control
225 of any single individual, doctors (like Dr Patel) can play an important role through advocacy and
226 'social medicine'³⁹ (see Box 3). Whether complexity science can also be helpful in politics and policy
227 making is contested, but in principal it can provide the basis of a collaborative approach based
228 around systems thinking.⁴⁰

229 *Conclusions*

230 The emergence of multimorbidity is a systemic phenomenon that requires systemic approaches at
231 the theoretical, practice and policy levels. Implementing complexity-focused care is facilitated by
232 looking at three key domains: (1) What matters to patients? (2) How can we integrate, personalise

233 and prioritise care for whole people given the constraints of their socio-ecological circumstances?

234 (3) What needs to change at the practice and policy levels to deliver what matters to patients?

235 Systemic care delivered in primary care with its focus on the person complements the specialism

236 focus on each individual disease.²⁸ For people living with multiple chronic conditions, that systemic

237 care can be greatly enhanced by understanding and applying the complexity science principles of

238 non-linearity, tipping points, emergence, co-evolution, the importance of contextual factors and

239 initial conditions, and the presence of patterned outcomes.

240

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- 345
- 346

347 **Box 1 – Case Vignette**

Jennifer, a woman in her 50s, became low spirited and isolated after the death of her spouse. She consulted her GP practice frequently, seeing numerous different doctors and nurses that she didn't know well. The consultations were short and rushed and she generally couldn't make sense of their explanations which often included medical jargon. Over the course of the two years since her husband's death, her diagnoses included depression, anxiety, agoraphobia, obesity, hypertension, and type 2 diabetes. She was on repeat prescriptions for six different drugs. Over the following year, she continued to gain weight, and developed low back pain and indigestion, which resulted in additional prescriptions.

Around this time, the practice was conducting an audit of patients on more than 5 repeat prescriptions, and the senior partner, Dr Patel, recognised her name – she and the district nurse had helped provide terminal care for Jennifer's husband. Dr Patel – who was part of an advocacy group of GPs working in very deprived areas who lobbied for better social conditions and services on behalf of their patients – decided to start afresh and booked an extended consultation with Jennifer (which was only possible because the practice was part of a Government-funded pilot study).

Taking a 'what matters to you' rather than 'what is the matter with you' approach, Dr Patel listened empathically to her patients' story and together they began to unpack the sequence of events following her bereavement, something no-one had done before. It became apparent to both of them how unresolved grief, financial problems, and isolation had affected Jennifer's life; sadness and loneliness fuelled depression and comfort eating of cheap junk food; weight gain led to hypertension and diabetes; all contributed to her chronic pain. This was a painful realisation for both – for Jennifer who felt ashamed that things had got so bad, and for Dr Patel who felt ashamed at the lack of continuity and the polypharmacy and likely over-medicalisation that had occurred. What Jennifer appreciated most was that the GP who had cared for her husband had taken the time to listen to her, and seemed also to understand the 'bigger picture' of the struggles of living in a poor area. Jennifer didn't feel judged.

With Jennifer's agreement, Dr Patel referred her to the practice welfare rights officer, who helped her fill in the correct forms to claim benefits she was entitled to. She also referred her to the community links practitioner (as part of social prescribing and community development) who discussed the things Jennifer used to enjoy doing and the local community resources she might contact. Over time, Jennifer plucked up the courage to contact a suggested mental health charity, and over the course of the next 6 months she had made new friends and taken up her old passion for cooking – something she had stopped doing after her husband died. She also took up walking with her new friends, lost weight and gained fitness. Her blood pressure and diabetes improved, and the back pain reduced. Her depression resolved and several of her medications were reduced or stopped by Dr Patel, who continued to see her every 3-6 months. In Jennifer's own words, she got her life back.

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350 **Box 2 – Making explicit complexity science principles relevant to caring for multimorbidity**

Complexity Science Principle	Use to understand multimorbidity (Diagnosis)	Use to manage & reduce the impact of multimorbidity (Therapy)
Non-linearity / Tipping points <ul style="list-style-type: none"> Results often are not proportional to stimulus Events – often unforeseen – cross a threshold and ‘suddenly’ change the structure and/or behaviour into a new direction 	<ul style="list-style-type: none"> Modelling & stories can be helpful. Statistics are less helpful than in single disease states. Learn from non-proportionate results to interventions. 	<ul style="list-style-type: none"> Look for small interventions that may have a big effect by working across multiple parts of the system. Reduce polypharmacy Don’t get in the way when patients become unstuck. Provide hope and tie hope into small changes that patients can observe.
Case application	<i>Jennifer entered a vortex of unhealthy behaviours, illness and despair after the death of her husband. Lack of being known, and being rushed in consultations, led to over-medicalisation.</i>	<i>An extended consultation with Jennifer (not possible in many settings) and taking a ‘what matters to you’ rather than ‘what is the matter with you’ approach, lead to a major turn-around.</i>
Emergence <ul style="list-style-type: none"> Occurs when entities form complex behaviours as a collective Arises from intricate causal relations across different scales & feedback Cannot be easily predicted or deduced from behaviour of the parts 	<ul style="list-style-type: none"> Look for underlying complex causality. Be open to unexpected effects. Approach understanding and interventions with humility. Listen to paradoxical observations that patients or family members may bring. 	<ul style="list-style-type: none"> Watch for and act on teachable moments. Stay in relationship to allow time for emergence Explore unexpected change, both positive and negative.
Case application	<i>Jennifer became low spirited and isolated after the death of her spouse and multiple declines in connection. Unresolved grief, financial problems, and isolation had affected Jennifer’s life; sadness and loneliness fuelled depression and comfort eating of cheap junk food; weight gain led to hypertension and diabetes; all contributed to her chronic pain.</i>	<i>Jennifer took up walking with her new friends, lost weight and gained fitness. Her blood pressure and diabetes improved, and the back pain disappeared.</i>
Co-evolution <ul style="list-style-type: none"> Each agent is changed Parallel development of a sub-system with new characteristics and dynamics 	<ul style="list-style-type: none"> Observe changes in the patient and environment. Be open to changing your opinion of the patient. 	<ul style="list-style-type: none"> Assess individual risk factors and treatment as they interact in the whole person. Be open to trying new approaches as the patient changes. Look at helping to change the patients social or physical environment.
Case application	<i>There was a painful realisation for both – for Jennifer who felt ashamed that things had gotten so bad, and for Dr Patil who felt ashamed at the lack of continuity and the polypharmacy and likely over-medicalisation.</i>	<i>Her depression waned and many of her medications were reduced or stopped by Dr Patil, who continued to see her every few months.</i>
Context & initial conditions are important <ul style="list-style-type: none"> External conditions impact the behaviour of the system-as-a-whole 	<ul style="list-style-type: none"> Pay attention to family history. Consider social & environmental determinants. Knowing the patient who has the disease is as important as knowing each individual disease. 	<ul style="list-style-type: none"> Consider family interventions. Link to social services. Avoid medicalising social problems such as loneliness and grief. Work on community and public health changes in addition to working with individual patients.
Case application	<i>We wonder about her family history of self-effacing approaches to stress, adverse childhood events, and depression. We wonder how early work accommodations to her losses might have helped to avert the downhill spiral.</i>	<i>It was very helpful to unpack the sequence of events following her bereavement. What Jennifer appreciated most was that the GP who had cared for her husband had taken the time to listen and seemed also to understand the ‘bigger picture’ of the struggles of living in a poor area. She didn’t feel judged.</i>
Patterned Outcomes <ul style="list-style-type: none"> Emergent processes, dependent on initial conditions, evolve in a limited number of possible ways resulting in recognisable patterns of outcomes 	<ul style="list-style-type: none"> Look for patterns across clusters of disease labels. Look for patterns across multiple levels of the person’s biological, social and environmental systems. Look for family/community patterns. Learn from commonalities & differences across multiple patients over time. 	<ul style="list-style-type: none"> Consider off-label treatments that could work across the common pathways underlying multiple diseases. Try therapeutic trials and observe the pattern of results across multiple conditions.
Case application	<i>Around this time, the practice was conducting an audit of patients on more than 5 repeat prescriptions, and the senior partner, Dr Patel, recognised her name – she and the district nurse had helped provide terminal care for Jennifer’s husband.</i>	<i>Dr. Patel tried both medical and non-medical interventions and encouraged Jennifer’s experimentation with things that previously had brought her joy.</i>

352 **Box 3 – Social Medicine**

Rudolph Virchow the father of social medicine said;

“Medicine is a social science, and politics is nothing else but medicine on a large scale. Medicine, as a social science, as the science of human beings, has the obligation to point out problems and to attempt their theoretical solution: the politician, the practical anthropologist, must find the means for their actual solution... Science for its own sake usually means nothing more than science for the sake of the people who happen to be pursuing it. Knowledge which is unable to support action is not genuine – and how unsure is activity without understanding... If medicine is to fulfill her great task, then she must enter the political and social life... The physicians are the natural attorneys of the poor, and the social problems should largely be solved by them.”

Wittern-Sterzel, R (2003). "Politics is nothing else than large scale medicine"--Rudolf Virchow and his role in the development of social medicine". *Verhandlungen der Deutschen Gesellschaft Fur Pathologie*. 87: 150–157. PMID 16888907

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