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Systems science approaches to cardiovascular disease prevention and management in the era of COVID-19: A Humpty-Dumpty dilemma?

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ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic necessitated the implementation and prioritizing of strict public health strategies to mitigate COVID-19 transmission and infection over all else. As we enter a 'recovery' phase in which the impact of the virus recedes (but does not relent), we ask, "*How do we develop a game plan that considers prevention over management of public health threats of a more chronic nature, including cardiovascular disease?*" We frame this choice point as a "Humpty-Dumpty" moment for public health with enduring and potentially irreversible consequences. Citing clear examples of other public health successes and failures, we outline in detail how sustaining cardiovascular population health under complex post-pandemic conditions will necessitate decision-making to be informed with a systems science approach, in which interventions, goals, outcomes and features of complex systems are carefully aligned.

Contents

Abbreviations: CBPR, community-based participatory research; COVID-19, Coronavirus disease 2019; CRC, Colorectal cancer; CVD, Cardiovascular disease; DSM, dynamic simulation model; GMB, Group model building; HEDIS, Healthcare Effectiveness Data Information Set; PA, Physical activity; SARS-CoV-2, Coronavirus disease.

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Cardiovascular diseases (CVD) are a group of interacting disorders that produce a disease state that affects the heart and blood vessels and is currently the leading cause of morbidity and mortality worldwide, currently responsible for 18 million deaths and 366 million disability-adjusted life years lost each year.[1] The established cause-effect relationship between modifiable lifestyle behaviours and the risk for the premature onset of chronic diseases predisposes physical inactivity and poor diets as two of the most pertinent unhealthy living risk factors for CVD,[2,3] both of which are preventable and reversible. Whilst evidence of an established relationship between lifestyle choices and chronic disease exists, there is a dynamic and complex set of factors that interact to produce a disease state and affect disease progression, sequelae and long-term health outcomes.[4] The complexity and interactive nature of chronic disease is an important consideration in the design, development and implementation of prevention and optimal management efforts to ensure broad efficacy and effectiveness.[5] This remains true in the global response to coronavirus disease 2019 (COVID-19) which is equally, if not more, complex in its pathophysiology and epidemiology.[6] Since the start of the COVID-19 pandemic, various lifestyle factors (i.e., physical activity, alcohol consumption, obesity, smoking and sleep quality) have been associated with disease severity, patient outcomes and even mortality[3,7] but as with other chronic diseases, there are multi-dimensional factors that affect patient outcomes with ethnic minority groups disproportionately affected by COVID-19,[8] highlighting potential racial and economic inequalities[9] and social justice considerations.[10]

Whereas modifiable lifestyle behaviours are important in the prevention and management of chronic diseases, the main response to COVID-19 came in the form of broad global efforts to curb rates of transmission and infection. Governments globally enforced social distancing and national and local lockdowns halted international travel and introduced the use of personal protective equipment (e.g., masking, eye protection and sanitisation). Engineering (e.g., ventilation, filtration), and administrative controls (e.g., contact tracing, vaccinations, and testing) were also introduced. Despite the importance of COVID-19 transmission prevention efforts, as the pandemic undoubtedly posed the greatest threat to public health in recent history, it may have inadvertently presented a major risk factor for chronic diseases, including CVD, as, for example, reduced social mobility and the closing of leisure facilities, negatively impacted physical activity[11] and physical wellbeing.[12] Alongside societal challenges, routine clinical appointments and procedures were curtailed to prioritize the burden of the pandemic,[13] prompting a global backlog in routine procedures and treatments in clinical areas[14] that could take years and even decades to address. Whereas clinical services are largely re-established, the time and resources required to address the backlog highlight the importance of healthy living behaviours as a strategy to prevent the increased incidence of diagnosis, disease progression, and mortality. There is a likelihood that the population returning to the clinical setting have a higher prevalence of unhealthy living behaviours compared to the pre-COVID-19 era, creating an even greater need for healthy living medicine.[15]

As communities globally begin to prepare for 'living with COVID-19,' which coincides with effective vaccination programmes and the removal of all restrictions and mass testing, annual peaks of a new infection and emerging variants will likely provide societal challenges for years to come. Whilst acute infections appear to be on a trajectory towards endemic status, the burden of Long COVID, defined as a condition that occurs in people with a history of SARS-CoV-2 infection; usually within three months from the onset of COVID-19, with symptoms and effects that last for at least two months and that cannot be explained by an alternative diagnosis,[16] will present a long-standing risk to population health and wellbeing. A recent scoping review highlighted over 100 common patient complaints that are cyclical and prone to exacerbation.[17] These symptoms significantly impact functional status, exercise capacity, and quality of life as well as pose a significant burden for healthcare services and economic entities globally. With reports suggesting more than 100 million confirmed cases worldwide, Long COVID may arguably be the next global health crisis that will persist due to a lengthy disease course, lack of effective treatments, ongoing transmission, and additional co-morbid conditions along with their toll on physical, behavioral, cognitive, social, and economic burdens.[18]

Considering the enormity and sustained challenges of COVID-19 and Long COVID on population health and wellbeing, the authors postulate that COVID-19 should be recognized as a contributing and attributable risk factor for CVD. The burden of CVD is increasingly placing priority on addressing gaps in access to diagnostic, preventive, and curative services at a population level with an aim of incidence reduction. Preventative approaches will have a significant impact on patient-reported outcomes, disease burden, and morbidity, which equates to 366 million disability-adjusted life years lost each year.[1] With lifestyle factors such as physical inactivity, alcohol consumption, and poor dietary habits being among the prominent reversible risk factors for both CVD and COVID-19,[19] the question to ask becomes: "*Is the priority to mend CVD once it occurs or to prevent CVD from occurring?*" Indeed, a Humpty-Dumpty dilemma. This question demands the consideration of the opportunity and needs to develop effective preventative strategies (see Fig. 1) to alleviate the global burden. Taking proactive steps to address the growing burden of disease will broadly impact population health and alleviate the growing burden upon healthcare systems which are not just limited to acute conditions but also chronic conditions that have been neglected and/or accelerated because of the COVID-19 pandemic.

Acknowledging the complexity of global health challenges, CVD and COVID-19 interact at the population level and may be considered a syndemic with a set of unique interactions. Considering the magnitude of the challenges posed by either CVD and COVID-19 independently or in combination, the need to prevent severe outcomes of a proposed syndemic is paramount to prevent unprecedented challenges to population health. This is imperative at a time where global healthcare systems are recovering from the pandemic and historically under-resourced and underfunded, and economic ramifications that affect the health, well-being, and prosperity of people. We propose taking a proactive approach where the knowledge derived by reductionistic approaches can be complemented with systems science methods that allow for studying whole systems and unique interactions which can yield improved understanding and development of effective preventative approaches.[20] To give context via the use of an analogy (see Text Box), prevention of Humpty-Dumpty's fall would avoid moving from order to disorder or chaos, and thereby eschew our inability to put him back together again. The amount of energy necessary to optimally manage CVD far exceeds that of general maintenance of good health in the absence of CVD. Humpty-Dumpty, once fallen and broken, does not reconstitute; rather, Humpty enters a zone of chaos from which he never returns as a demonstration of the second law of thermodynamics and an illustration of the Levinthal paradox.[21] This inability to fully reconstitute what is broken argues for CVD prevention prioritization, yet the reality of high CVD prevalence also argues for the need to provide for optimally effective management of CVD. (See Fig. 2). In effect, a continuum of cardiovascular health interacts with multiple factors at multiple levels [from individual behaviours (e.g., PA) to upstream determinants (e.g., education)] in a complex and dynamic manner over time. This dynamic complexity invites the application of systems science approaches to gain a better understanding of the "whole" and for the development of interventions that may operate effectively within complex systems that represent the real world.

Fig. 1. The question to ponder: *"Prioritize prevention or management?"* A Humpty-Dumpty dilemma.

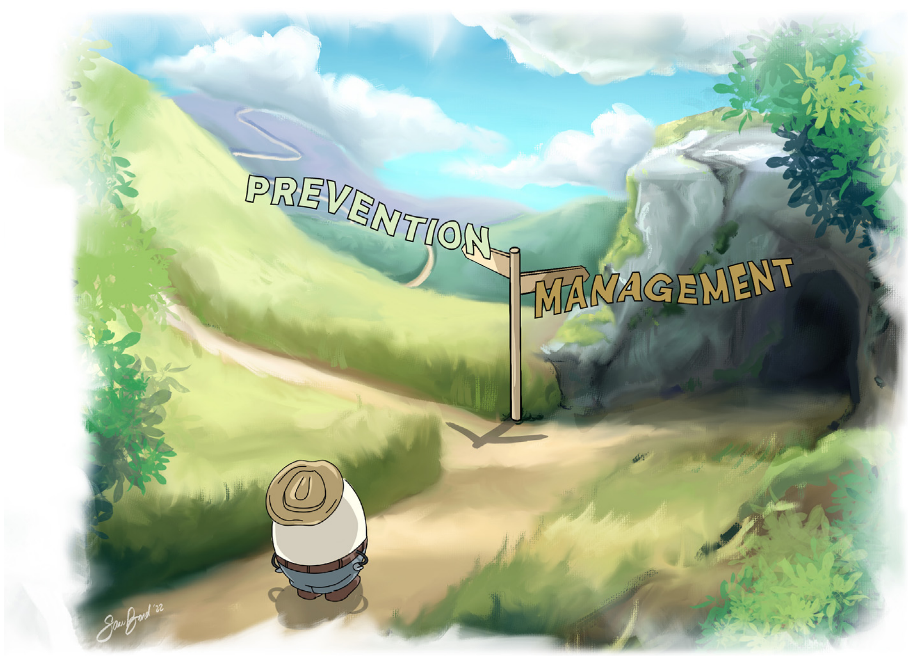
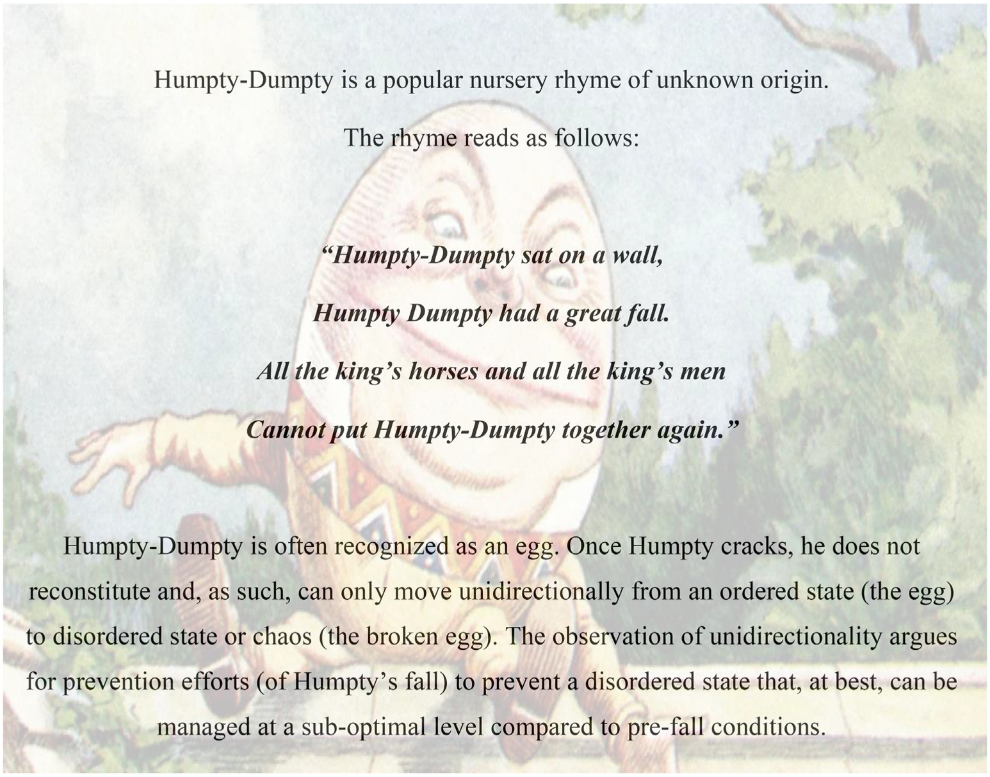


Fig. 2. A path that diverts, with prevention one way and management the other. Prevention is preferred and should be prioritized because with management, we are not able to completely restore or put back together properly that which has been broken, we can merely attempt to optimally manage.



Systems science and complexity

Systems science methods can help illuminate the underlying dynamics of the disease course that are otherwise opaque. Failure to understand the dynamic complexity and broader context for CVD, COVID-19, and their interactions can lead to policy decisions with poor outcomes or even adverse unintended consequences. Therefore, the application of systems science methods can play an important role in improving outcomes in the prevention and management of CVD.

Research in CVD and cardiometabolic disease has mostly progressed along the lines of reductionism methods that deconstruct the problem into its component parts, investigate the parts separate and independently to understand associations and cause-effect relationships and aggregate the learnings to understand the whole. This approach to research and science has persisted in public health and population health for over a century and during that time generated much progress in health outcomes.[22] However, under the prevailing paradigm of Newtonian science (e.g., reductionism, linearity, homogeneity of component parts, and proximal causation), there remains an inability to uncover the underlying dynamic complexity of CVD that plays out over time. The need to examine the dynamic and complex interactions among multiple factors and components over time (including behavioral, physical, biological, social, economic, political, etc.) cannot be met through the application of reductionistic methods alone. There is a need to appreciate the dynamic complexity of the major public health problems of our time (e.g., CVD, COVID-19, low prevalence of healthy living behaviours) and to address the chronic challenges of uneven distribution of disease and illness burden.[23,24] To do so, recognition of CVD and COVID-19, along with all other major public and population health challenges, should be studied using methods that appreciate the complex systems they represent. Hence, the time has come to recognize the paradigm shift underway towards seeking to understand, appreciate and respect complexity and systems science approaches when searching for solutions to the most pressing public and population health problems of our time. This paradigm shift reflects the intention to pursue evidence of effectiveness in the context of whole systems. Alongside more traditional reductionistic approaches, systems science should be considered as being synergistically iterative and can enhance the alignment between knowing what works to improve population health and implementing solutions within the context of the dynamic complexity of problems in the real world.

Solution thinking

Systems science approaches can be both qualitative and quantitative and both approaches are important and encouraged. A qualitative approach, such as the building of a systems map, includes the creation of graphical representations of the system in question, its components, and their relationships, to present a picture of the whole.[25] Quantitative approaches include mathematical modelling of the many interdependent factors of a system so relationships may be presented in dynamic simulation models. Regardless of the method taken, systems mapping approaches are a useful tool that can help researchers, clinicians, and other decision-makers to better understand complex systems and address these systems at many levels, ranging from cellular to a societal scale. A recent article by Mabry and colleagues noted the underutilisation of such approaches in respect of cancer research.[24] The authors highlight that systems epidemiology has the potential to expand cancer research to help in the development of effective prevention, treatment, and control strategies through increased understanding of the nuances of cancer epidemiology, an approach that can be applied to all disease areas, including CVD. When implementing systems science approaches, critical thinking about models is vital, otherwise, the most valuable pieces of information may be missed. Learning from a complex system is iterative. Initial models may be constructed in a simple, static manner based solely on qualitative inputs; yet, following early understanding of the basic workings of such a system, further iterations may introduce dynamic simulations that increasingly reflect the realities of stakeholder perspectives over time. A vivid example includes the need for prevention of diabetes as a risk factor for CVD. Healthy People 2010 objectives called for a 29% reduction of new cases of diabetes in the U.S. by the year 2010. For this objective to be achieved, a 38% reduction in the prevalence of diagnosed diabetes mellitus, type 1 and type 2, would need to be generated by the year 2010.[26] This conclusion was obtained through the application of a dynamic simulation model for diabetes prevalence in the wake of rising levels of obesity in the U.S. population. The simulation model explored versions of diabetes population dynamics to track the rates at which people developed diabetes, were diagnosed with the disease, died, and assessed the effects of various preventive-care interventions. The results of this modelling exercise showed that even a 29% reduction in the number of new cases (the Healthy People 2010 objective) would only slow the growth, not reverse it. Considering the rates at which people develop, are diagnosed with, and die from diabetes, the analysis indicated that because the annual number of new diabetes cases far exceeds deaths, it would take at least a 50% reduction in newly diagnosed cases of diabetes to stop the increase in diagnosed diabetes prevalence. Hence, given the societal health trends, especially the obesity trends, this study showed that the Healthy People 2010 objective, as stated, of reducing diabetes prevalence would be unattainable. This example conveys the importance of considering the multifactorial and interactive nature of actions influencing factors that either separately or in combination affect the incidence or prevalence of disease-specific outcomes. Fig. 3 depicts the causal loop diagram to which the system dynamics model was applied.[27]

Another illustration of dynamic complexity reflected in clinical preventive screening is the consideration of the importance of time as a factor in reaching desired outcomes based on simulation modelling for colorectal cancer (CRC) screening for disease detection, and early treatment when appropriate. Mabry and colleagues built a hybrid dynamic simulation model (DSM) to estimate long-term colorectal cancer outcomes for a number of strategies designed to promote colorectal cancer screening among HealthPartners members.[24] The DSM modelled the HealthPartners screening-eligible member population over a 30-year time horizon, including a natural history of the within-person occurrence and evolution of polyps from precancerous to cancerous.[28] Key insights from HealthPartners colorectal cancer DSM included: 1) Recognition that the use of the Healthcare Effectiveness Data Information Set (HEDIS) CRC screening measure to assess year-to-year organizational performance was problematic. While health plans routinely use the HEDIS measure to assess annual CRC screening performance, the measure's utility is limited to a static measure of performance at a single point in time and cannot be used to meaningfully assess a given organization's performance across multiple years; 2) To estimate downstream CRC outcomes (e.g., incidence, mortality) attributable to upstream screening strategies requires detailed data on longitudinal participation in screening within individuals over a number of years. The insufficient length of time for which data on within-person longitudinal screening participation was captured (i.e., ~3 years for most members) caused the range of uncertainty in the model outputs to be very large. So large, in fact, that for a majority of strategy scenarios intending to be explored, it could not be concluded with any confidence that a given intervention would lead to an improvement vs. a worsening in CRC outcomes, even when assumed that outreach was effective in increasing screening participation rates in the year in which it was introduced. It may seem counterintuitive that increasing screening participation rates would not be accompanied by downstream reductions in CRC burden. The reason, however, is because there is no way to estimate individual screening participation for each year across the full 30-year screening eligibility period, including which screening modality they might choose and whether or not they would also participate in follow up colonoscopies, given their pattern of screening to date and previous test results; and 3) The period for evaluating the downstream impacts must be of sufficient duration for the downstream outcome to manifest itself. Taken together, these findings have inspired a line of work to understand the real-world longitudinal within-person patterns of screening participation that exist and how variations in these patterns impact downstream colorectal cancer burden. Additionally, there are implications for best practices for evaluation of CRC screening outreach programs, including the length of the evaluation period, adequacy of data that should be captured on screening participation in screening studies and programs, and for a review of the use of the existing HEDIS CRC screening measure and the need for additional measures to more accurately reflect organizations' effectiveness in preventing downstream colorectal cancer burden over time.

The insights and learnings derived from the systems science examples described above can be applied to the prevention and management of CVD in the COVID-19 era and beyond. Prevention efforts need to account for influences coming from the macro-system levels that represent the broader upstream determinants of CVD risk across society and consider them over time and space. In addition, attention needs to be paid to leveraging the intersections of multiple chronic conditions, infectious diseases, and healthy living factors that are likely to generate effective treatments and optimal outcomes. Since prevention is not always possible, management of CVD and COVID-19 as well as their sequelae is important. More specifically, Table 1 lists examples of steps to consider when applying systems science approaches to the prevention and management of CVD and COVID-19.

Outcome considerations

Problems may be defined as discrepancies between performance and goals. To define a problem, therefore, goals need to be identified which will in turn allow for an assessment of performance against efforts to reach the stated goals. Hence, meaningful outcomes and indicators of progress are important to consider in quantifying goals

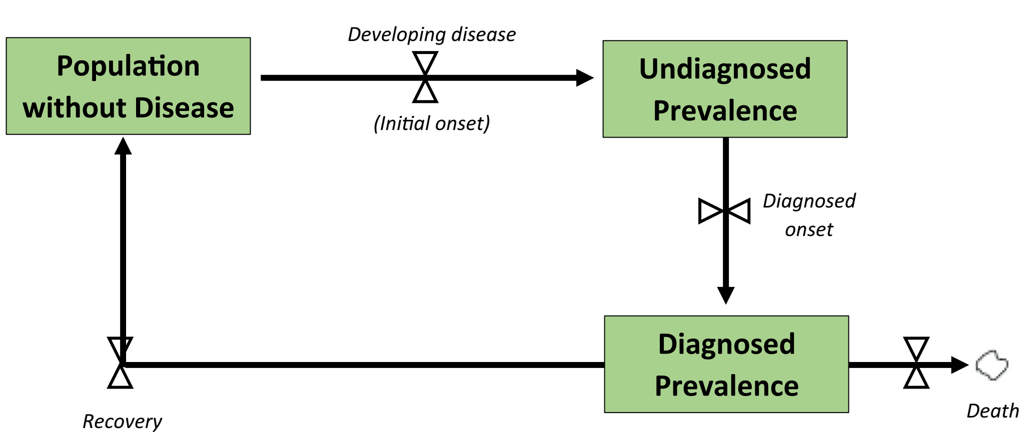


Fig. 3. Basic Stock-and-Flow Structure for Diagnosed Prevalence of a Disease. Adapted from Milstein, et al[26]

Table 1
Examples of qualitative and quantitative steps in the application of systems science approaches to the prevention and management of CVD and COVID-19.

1. Build a causal loop diagram or systems map based on qualitative perspectives gathered using dialogue and facilitated discussions that reflect the mental models of stakeholders involved. An initial map can often support the development of a shared understanding of the system and approach to the use of the map.[24,37]
2. Use dialogue to explore the model and deliberate the content, consider enhancement or refinements, delineate critical elements, discuss implications for prevention and management actions, and explore the potential ramifications of intervening upon one or more factors.
3. Consider how and where to intervene in the system. The "Meadows 12 places to act in a system" framework,[38] is a useful model to consider. However, this model was originally positioned within an engineering context and described as tentative and has been critiqued for its technical language and difficulty of interpretation,[39] and subsequently "translated" to other fields.[39,40] More recently, a specific translation of the Meadows framework was created for public health: the Public Health 12 Framework.[35]
4. Apply data and iteratively develop, refine, or improve upon initial, more simplified versions.
5. Do not limit simulations to a single model. Consider various models and versions all related to similar questions asked about the system. Comparative modelling is useful and different simulations consider the same problem from various perspectives. When many of such simulations begin to converge, confidence in the results increases.
6. Ensure that model outputs are scrutinized by important key stakeholders before reporting and implementation.
7. Report the results in a manner that allows for open dialogue and interpretation. Considerations of ethical, political, resource or other contextual issues need to be noted and judged based on their relationship to real-world application.
8. Follow steps to ensure that continued improvements and adaptations to model output can occur to optimize value to stakeholders.

Table 2
Examples of outcomes aligned with complex adaptive systems properties.

Complex adaptive systems properties examples	Examples of outcomes of interest and their context
Nonlinearity	
▪ Results not proportional to the stimulus ▪ A causal action does not produce a proportional effect	▪ *Cost*: Total health care expense in the U.S. is not proportional to the gains in population health in the U.S. ▪ *Weight change*: (loss or gain) might not be linearly related to the net balance of daily energy intake and expenditure
Emergence	
▪ A response to a self-organizing system property that generates structures, patterns, and properties different from the effect of individual elements ▪ Occurs when multiple agents form more complex behaviours and/or structure as a collective	▪ *The net result* of all relationships, connections, interdependencies, and feedback loops among and between all levels of the system is a certain level of blood pressure, cholesterol, and medication used to manage CVD at a specific time for a given individual patient diagnosed with CVD ▪ Observation of a *Prevention paradox*—the seemingly contradictory situation where many cases of a disease come from a population at low or moderate risk of that disease, and only a minority of cases come from the high-risk population (of the same disease). This is because the number of people at high risk is small.[41]
Adaptive (a temporal property)	
▪ The system changes its behaviour in response to its environment	▪ *Incidence/New cases of CVD, COVID-19:* Feedback loops determine the adaptive response of a system. In an unhealthy environmental context, some people will adapt and will be able to maintain healthy behaviours that prevent CVD or COVID-19, whereas others may not
Openness	
▪ A system continuously interacts with its environment (a larger system level)	▪ *Attraction and Retention of Talent*: Training and health professionals for the future health care workforce need to consider competing individual, organizational, social, and economic factors to maintain sufficient participation in the pipeline
Bounded rationality (information limited)	
▪ In decision-making, individuals are limited by imperfect knowledge, cognitive limitations, and a finite amount of time	▪ *Shared Decision-Making/Clinical Decision-Making and weight change*: Imperfect knowledge about CVD, COVID-19, lifestyle strategies that prevent the conditions, or clinical treatment that help manage exacerbations over time, will limit people's ability to make sound decisions that relate to their weight and weight change over time

and should be aligned with the systems methods applied. Health, well-being, and disease as well as both the identifiable pathologies and the related experiences are complex, dynamic, and adaptive states. These states may be considered from both a subjective and objective measurement perspective. Selecting outcomes of interest may be aligned with characteristics of complex adaptive systems, such as nonlinearity, self-organization and emergence, and openness, among others.[29–31] To provide examples, Table 2 outlines several characteristics of complex systems, an explanation of the characteristics, and aligned examples of outcomes to consider in the context of CVD, COVID-19, and other systems.[30,31] Outcomes to monitor the progress that reflect the interests of all stakeholders involved are important to identify (e.g., health, well-being, illness-burden, equity) and will contribute to research translation efforts into applied programs, practices, and policies.

Future research

Progress in knowledge generation for prevention and management of CVD, COVID-19, and related health and well-being concerns may benefit from exploring, integrating, and leveraging both qualitative and quantitative systems science approaches and adding these to the more traditional research methods. Qualitatively, the use of dialogue as a systems thinking approach to creating shared perspectives may be applied to bring multiple stakeholders together and align their respective interests to pursue action. Applications of Group Model Building (GMB) will allow for the creation of systems maps to reflect the thinking of stakeholder groups and be positioned as a starting point in the identification of intervention options.[25,32,33] These proposed research efforts should be aligned with quantitative efforts to apply data, such as system dynamics modelling and other simulations.

More specifically, future research should use systems science methods to address questions that address specific goals related to CVD and COVID-19 prevention and management that express the needs and interests of society-at-large and communities in general while focusing on: 1) Observed events and the actions that trigger them; 2) Identification of problems (and associated goals and performance gaps) and their underlying patterns; 3) Underlying systems structures that produce observed patterns of events; and 4) Stakeholders' mental models, beliefs and goals.[24,25] Due to the multi-stakeholder and multi-disciplinary nature of systems projects, community-based participatory research (CBPR) should be leveraged whenever community partners are part of the activity. CBPR is designed to improve partnerships between research entities (e.g., universities, health systems, etc.) and community partners while properly accounting for real-world factors and ensuring that the research conducted will benefit and strengthen the community.[34]

Conclusions

COVID-19 and other pandemics (e.g., physical inactivity, obesity) have a close relationship with CVD that will continue to negatively impact and burden the public health and health care delivery systems globally. As a result, we postulate that prevention efforts must be prioritized over the need for ongoing management of chronic disease to mitigate the projected near-and-long-term consequences of these pandemics and syndemics and their related physical, social, and economic environmental effects. The argument to prioritize prevention (i.e., proactive approach) over management (i.e., reactionary approach) may be framed as a "Humpty-Dumpty" dilemma since failure to prevent will have catastrophic consequences due to the disease-related burdens as well as the proportions of the populations affected.[35,36] Sustaining cardiovascular population health under complex post-pandemic conditions will necessitate decision-making to be informed with a systems science approach, in which interventions, goals, outcomes and features of complex systems are carefully aligned.

Declaration of Competing Interest

None.

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