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What Comes First, the Behavior or the Condition? In the COVID-19 Era, It May Go Both Ways

Ross Arena^{a,b,*}, Carl J. Lavie^{b,d}, and
Mark A. Faghy^{a,b,c}, On Behalf of the HL-PIVOT Network

From the ^a Department of Physical Therapy, College of Applied Sciences, University of Illinois at Chicago, Chicago, IL, ^b Healthy Living for Pandemic Event Protection (HL-PIVOT) Network, Chicago, IL, ^c Human Sciences Research Centre, University of Derby, Derby, United Kingdom and ^d Department of Cardiovascular Diseases, John Ochsner Heart and Vascular Institute, Ochsner Clinical School-University of Queensland School of Medicine, New Orleans, LA.

Abstract: Which came first, the chicken or the egg? This causality dilemma was first proposed by the Greek biographer Plutarch in the 1st century CE. While the *cause-effect relationship* between lifestyle behaviors and chronic disease is not always a certainty, and genetic predisposition can independently lead to premature chronic disease, the likelihood of developing one or more chronic conditions is significantly higher in those who: (1) lead sedentary lifestyles; (2) consume unhealthy diets; (3) smoke; or (4) have excess body mass. Recently, the Royal College of General Practitioners issued an apology for the title of an online event that suggested the coronavirus disease 2019 (COVID-19) is a lifestyle disease. We feel that this was the correct course of action as leading an unhealthy lifestyle is certainly not the *cause* for an individual contracting COVID-19 (ie, *effect*). However, a body of evidence has demonstrated that unhealthy lifestyle behaviors and characteristics as well as being diagnosed with one or more chronic diseases does significantly increase the risk for a complicated medical course in individuals infected with COVID-19.

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Moreover, the cause-effect relationship between lifestyle behaviors and characteristics and COVID-19 may eventually prove to go both ways, as the pandemic may lead to a higher prevalence of unhealthy lifestyle behaviors and characteristics over the long term that eventually leads to a higher prevalence of chronic disease. As such, health living medicine must be widely practiced and prescribed to all individuals globally. (Curr Probl Cardiol 2022;47:100963.)

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hich came first, the chicken or the egg? This causality dilemma was first proposed by the Greek biographer Plutarch in the first century CE.¹ This question has been used in numerous causality dilemmas over the centuries and holds relevance to the cause-effect relationship between lifestyle behaviors and the risk for the premature onset of one or more chronic diseases, including cardiovascular disease (CVD), diabetes, and certain forms of cancer.²⁻⁴ The phrase ‘Exercise is Medicine’⁵ is well known in medical and physical activity domains but while the cause-effect relationship between lifestyle behaviors and chronic disease is not always a certainty, and genetic predisposition can independently lead to premature chronic disease, the likelihood of developing one or more chronic conditions is significantly higher in those who: (1) lead sedentary lifestyles; (2) consume unhealthy diets; (3) smoke; or (4) have excess body mass.⁶ Put another way, unhealthy lifestyle behaviors (ie, sedentary lifestyle, poor nutrition and smoking) and characteristics (ie, excess body mass) is a common, leading *cause* for premature chronic disease (ie, *effect*). In a cohort of more than 110,000 individuals, Nyberg et al⁷ recently found males with the healthiest lifestyle behaviors and characteristics lived 9.9 (95% confidence interval [CI] 6.7-13.1) more years free of chronic diseases, while women with the same characteristics lived 9.4 (95% CI 5.4-13.3) more years free of chronic diseases compared to those individuals with the unhealthiest lifestyle behaviors and characteristics. Given these and other findings, several chronic diseases have also been characterized as *lifestyle-related* diseases.⁸⁻¹⁰ It is important to note that, even in individuals who are genetically predisposed to developing premature chronic disease, leading a healthy lifestyle significantly mitigates against this risk,^{11,12} further supporting the oftentimes cause-effect relationship between lifestyle and chronic disease. Lastly, while not a lifestyle behavior per-se, maintaining a high cardiorespiratory fitness (CRF), which is often the result of leading a healthy lifestyle (ie,

being physically active), is a proven independent prognostic marker and now designated as a vital sign.¹³⁻¹⁶

Recently, the Royal College of General Practitioners issued an apology for the title of an online event that suggested the coronavirus disease 2019 (COVID-19) is a lifestyle disease.¹⁷ We feel that this was the correct course of action as leading an unhealthy lifestyle is certainly not the *cause* for an individual contracting COVID-19 (ie, *effect*). To date, there have been more than 190 million cases of COVID-19,¹⁸ certainly, millions of healthy individuals who lead a healthy lifestyle (ie, exercise, consume a healthy diet, maintain a normal body weight and not smoking) and have no chronic disease diagnoses have contracted COVID-19. In fact, Rodriguez et al¹⁹ recently reported lifestyle habits and chronic disease diagnoses were not predictive of contracting COVID-19, rather, the rate of transmission is exacerbated by increased exposure to other individuals in public settings, not following disinfection recommendations, and living with someone with COVID-19 were all significant predictors on becoming infected. In this context, there is no *cause* and *effect* between unhealthy lifestyle behaviors and characteristics and contracting COVID-19 and, as such, issuing an apology was appropriate. However, a body of evidence has demonstrated that unhealthy lifestyle behaviors and characteristics as well as being diagnosed with one or more chronic diseases does significantly increase the risk for a complicated medical course in individuals infected with COVID-19. In 48,440 individuals diagnosed with COVID-19, Sallis et al²⁰ found those who reported being inactive were at greater risk for hospitalization [odds ratio (OR) 2.26; 95% CI 1.81-2.83], ICU admission (OR 1.73; 95% CI 1.18-2.55) and death (OR 2.49; 95% CI 1.33-4.67) compared to those reporting meeting current physical activity (PA) guidelines. Moreover, inactive individuals continued to have a greater risk of hospitalization (OR 1.20; 95% CI 1.10-1.32), ICU admission (OR 1.10; 95% CI 0.93-1.29) and death (OR 1.32; 95% CI 1.09-1.60) compared to individuals reporting some PA but not meeting current PA guidelines. In a UK cohort of 387,109 individuals, Hamer et al²¹ found those who reported being physical inactive [Relative risk (RR) = 1.32, 95% CI = 1.10-1.58], smoking (RR = 1.42, 95% CI = 1.12-1.79) and obese (RR = 2.05, 95% CI = 1.68-2.49) were all associated with risk of hospitalization due to COVID-19 infection. Moreover, there was a dose-dependent association where those individuals with all the aforementioned unhealthy lifestyle behaviors and characteristics were more than 4 times more likely (RR = 4.41, 95% CI = 2.52-7.71) to be hospitalized due to COVID-19 infection compared to individuals who had ideal lifestyle behaviors and characteristics (ie, physically active, not smoking

and normal body weight). In 568 confirmed COVID-19 cases (138 moderate-severe and 430 very mild-mild), Kim et al²² found individuals who reported adhering to ‘plant-based diets’ had a 73% (OR 0.27, 95% CI 0.10-0.81) lower odds of moderate-severe COVID-19 symptoms while individuals who reported adhering to ‘plant-based diets or pescatarian diets’ had a 59% (OR 0.41, 95% CI 0.17-0.99) lower odds of moderate-severe COVID-19 symptoms, when compared to individuals who did not report adhering to these diets. In a search of literature assessing risks for poor outcomes with COVID-19 infection, Harrison et al²³ performed a comprehensive review of medical databases and pre-print servers, identifying 31 reviews of moderate quality and one of high-quality. Obesity, smoking, hypertension, diabetes, and CVD were all associated with poorer outcomes following COVID-19 infection. Other analyses have also reported unhealthy lifestyle behaviors and characteristics and chronic disease diagnoses are clearly and significantly linked to an increased risk for increased symptom severity and poor outcomes with COVID-19 infection.^{21,24-34} In fact, the evidence demonstrating the increased risk for severe outcomes with COVID-19 infection in those with unhealthy lifestyle behaviors and characteristics and/or one or more chronic disease diagnoses may already be to a point where the link is irrefutable. In addition, evidence has emerged demonstrating a higher CRF, now considered a vital sign, provides protection against increased COVID-19 severity and may be a more important indicator of risk than obesity.³⁵⁻³⁹

To reiterate, COVID-19 is not a lifestyle disease and the apology issued by the Royal College of General Practitioners for suggesting the converse was appropriate. However, it is readily apparent that lifestyle behaviors and characteristics play a significant role in determining health status, resiliency in the event of an untoward health event (eg, COVID-19 infection), and the risk for premature chronic disease.⁴⁰ Moreover, it is also readily apparent that, in individuals who are infected with COVID-19, lifestyle behaviors and characteristics and the presence or absence of pre-existing chronic conditions significantly influence the severity of the viral infection. In this context, [Table](#) lists 4 scenarios asking the classic causality dilemma question. Clearly, an individual’s lifestyle behaviors and characteristics and the presence or absence of pre-existing chronic conditions *comes first*, an individual infected with COVID-19 comes into the infection (ie, what comes next) with one of the health phenotypes listed in [Table](#). In this sense, there is truly no causality dilemma; what *comes first* and what *comes next* is clear and beyond dispute. The outcomes of three of the four scenarios, in the context of COVID-19

Table. Proposed causality scenarios for lifestyle behaviors and characteristics, chronic disease and COVID-19

What comes first?	What comes next?	Outcome
Causality scenarios supported by scientific evidence		
Healthy lifestyle behaviors and characteristics No chronic disease diagnoses	COVID-19 infection	Decreased likelihood for more severe course with viral infection and hospitalization
Unhealthy lifestyle behaviors and characteristics No chronic disease diagnoses		Increased likelihood for more severe course with viral infection and hospitalization
Unhealthy lifestyle behaviors and characteristics. One or more chronic disease diagnoses.		Increased likelihood for more severe course with viral infection and hospitalization
Causality scenario requiring further investigation		
Healthy lifestyle behaviors and characteristics. One or more chronic disease diagnoses.	COVID-19 infection	More research is needed to determine the protection from a more severe course with viral infection and hospitalization healthy lifestyle behaviors and characteristics afford in those genetically predisposed to chronic disease or adopt healthy lifestyle behaviors and characteristics following a chronic disease diagnosis.

severity, is, however, influenced by lifestyle behaviors and characteristics, both independently (eg, unhealthy lifestyle and no chronic disease diagnoses) and secondary to their link to chronic disease risk (eg, unhealthy lifestyle significantly increases risk for chronic disease). There is a fourth scenario in [Table](#) that has not extensively investigated to this point and does warrant further investigation. This involves individuals with healthy lifestyle behaviors and characteristics who are genetically predisposed and have developed a chronic disease as well as individuals who, once diagnosed with a chronic disease, made a significant, long-term shift toward healthy lifestyle behaviors and characteristics. As previously mentioned, individuals who are genetically predisposed to developing premature chronic disease but who lead a healthy lifestyle have a significantly reduced risk for developing a chronic disease.¹¹ Moreover, there are individuals who lead an unhealthy lifestyle, are diagnosed with a chronic disease, and then make dramatic changes that emulate healthy lifestyle behaviors and characteristics. In both instances, there would be justification to posit there is a level of protection afforded to individuals

with chronic disease who are infected with COVID-19 but lead a healthy lifestyle. Interestingly, Hamer et al²¹ reported individuals with healthy lifestyle behaviors and characteristics continued to have a lower risk for hospitalization due to COVID-19 infection after adjustment for chronic conditions (ie, diabetes, hypertension and CVD), indicating leading a healthy lifestyle offers a level of protection even if you have been previously diagnosed with a chronic disease. In addition, Sallis et al²⁰ found the risk of adverse outcomes associated with COVID-19 infection in those who were physically inactive exceeded the risk associated with being diagnosed with a chronic disease, indicating the importance of this lifestyle behavior. These findings are in line with cardiac rehabilitation literature, consistently indicated far better outcomes in those individuals diagnosed with CVD who attend cardiac rehabilitation and adopt a healthier lifestyle compared to those who do not participate.⁴¹ Inquiry into the importance of healthy lifestyle behaviors and characteristics in those already diagnosed with a chronic disease should be investigated further moving forward. In the *cause-effect-outcome* model presented herein, the authors affirm COVID-19 infection is not *caused* by lifestyle behaviors and characteristics or chronic disease. However, the severity of symptoms and risk for hospitalization in those infected with COVID-19 is significantly *influenced* by both lifestyle behaviors and characteristics and chronic disease diagnoses.

There is another troubling future *cause-effect-outcome* scenario to consider as we emerge from the COVID-19 pandemic. Evidence continues to demonstrate measures taken to mitigate viral spread (ie, social distancing and lockdowns) have led to individuals, irrespective of viral infection status, leading unhealthier lifestyles (eg, less physically active, poorer nutrition, etc.).⁴²⁻⁴⁶ Over the long-term, there is justifiable concern that the international response to the COVID-19 pandemic in an attempt to curtail transmission, commonly referred to as the ‘new norm’, will *cause* a larger percentage of the global population to lead an unhealthy lifestyle permanently, leading to a higher incidence of chronic disease and exacerbating pressures on healthcare systems globally. In this scenario, the COVID-19 pandemic *came first*, an increased prevalence of unhealthy lifestyle behaviors and characteristics *came next*, and the outcome over the long term may be an even higher risk for chronic disease on a population level. This be truly troubling given physical inactivity and chronic diseases were already being characterized as pandemics prior to COVID-19.⁴⁷

In conclusion, as indicated in the title, the *cause-effect relationship* between lifestyle behaviors and characteristics and COVID-19 may eventually prove to go both ways. We recently proposed that the combination

of unhealthy lifestyle behaviors and characteristics – chronic disease – COVID-19 should be considered a syndemic, as it is clear these three conditions “adversely interact with and negatively affect the outcomes of one another.”⁴⁸ Perhaps it would be best to view these conditions from the syndemic perspective as opposed to *cause-and-effect*. However, irrespective of the perspective adopted, these conditions are inextricably linked now and potentially for many years to come. Moreover, adopting healthy lifestyle behaviors and characteristics is vital to *uncoupling* this syndemic. As such, health living medicine must be widely practiced and prescribed to all individuals globally.^{49,50}

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