

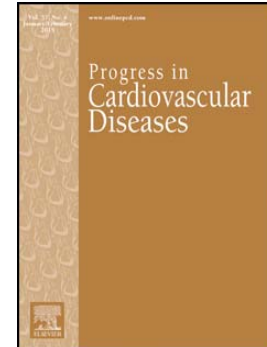
## Accepted Manuscript

Healthy Living: The Universal and Timeless Medicine for Healthspan

Ross Arena, Amy McNeil, Michael Sagner, Carl J. Lavie

PII: S0033-0620(17)30018-X  
DOI: doi: [10.1016/j.pcad.2017.01.007](https://doi.org/10.1016/j.pcad.2017.01.007)  
Reference: YPCAD 787

To appear in: *Progress in Cardiovascular Diseases*



Please cite this article as: Arena Ross, McNeil Amy, Sagner Michael, Lavie Carl J., Healthy Living: The Universal and Timeless Medicine for Healthspan, *Progress in Cardiovascular Diseases* (2017), doi: [10.1016/j.pcad.2017.01.007](https://doi.org/10.1016/j.pcad.2017.01.007)

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

**Healthy Living: The Universal and Timeless Medicine for Healthspan**

Ross Arena, PhD, PT<sup>1</sup>, Amy McNeil, BA<sup>1</sup>, Michael Sagner, MD<sup>1,2</sup>, Carl J. Lavie<sup>3</sup>

<sup>1</sup>College of Applied Health Sciences, University of Illinois at Chicago, Chicago, IL, USA

<sup>2</sup>SARENA P4 Medicine Clinic and Research Center

<sup>3</sup>Department of Cardiovascular Diseases, Ochsner Clinical School-the University of Queensland School of Medicine, New Orleans, LA, USA

**Address for Correspondence**

Ross Arena, PhD, PT  
Department of Physical Therapy  
College of Applied Health Sciences  
University of Illinois at Chicago  
1919 W. Taylor Street, 454 AHSB  
Chicago, IL 60612  
Office: 312.355.3338  
raarena@uic.edu

**Word Count:** 1,508

The Merriam-Webster dictionary defines *medicine* several ways, including: “1) a - substance or preparation used in treating disease, b - something that affects well-being; and 2) a - the science and art dealing with the maintenance of health and the prevention, alleviation, or cure of disease, b - the branch of medicine concerned with the nonsurgical treatment of disease.”<sup>1</sup> Relevant to this editorial and this edition of *Progress in Cardiovascular Diseases*, salient touchstones from the definition of *medicine* include *treating disease*, *affecting well-being*, *maintenance of health*, *prevention and alleviation of disease*, and *non-surgical*. At this juncture, a primary threat to the health and wellbeing of the global population is the incidence and prevalence of chronic diseases as well as future projections, including cardiovascular, pulmonary and metabolic diseases, as well as several forms of cancer are leading concerns.<sup>2-4</sup> To address the chronic disease burden successfully, there is a need to reformulate our approach to *medicine*, including what constitutes *medicine*, optimal therapeutic dosages and by whom and where it is administered.<sup>5</sup>

The rise in chronic disease incidence and prevalence is paralleled by an unrelenting rise in an *unhealthy living* phenotype; central to his phenotype are physical inactivity, poor diet, and, now, to a lesser extent in some countries but continuing to be a significant concern, tobacco use.<sup>6</sup> Excess body weight is intricately related to physical inactivity and poor diet and is thus also a common characteristic of the *unhealthy living* phenotype. In fact, a recent position statement by the American Association of Clinical Endocrinologists and the American College of Endocrinology has proposed new terminology, “adiposity-based chronic disease”, bringing new attention to the detrimental impact to excess body mass to one’s health.<sup>7</sup> There is broad recognition that a lifelong adoption of the *healthy living* phenotype (i.e., primordial prevention) or reversal of the *unhealthy living* phenotype (i.e., primary and secondary prevention), even if the

reversal is only partial, portends profound health (i.e., decreased morbidity and mortality as well as improved function and quality of life) and economic (i.e., decreased utilization of the most costly aspects of health care – hospitalizations, surgical procedures, and prescription medications) benefits.<sup>8-11</sup> Compared to individuals who emulate the poorest lifestyle characteristics, it has been found that those with an ideal *healthy living* phenotype demonstrate a  $\geq 45\%$  reduction in chronic disease risk.<sup>9, 12, 13</sup> Even in individuals genetically predisposed to chronic disease, the ideal *healthy living* phenotype remains highly protective.<sup>13</sup> Truly there is no other drug or surgical procedure that can boast such risk reductions. It is again important to stress that risk reduction is on a continual scale, with any movement away from the *unhealthy living* phenotype toward facets of a *healthy living* phenotype portending significant health benefits. Suffice to say, taking 20 minute walks twice per week is preferable to no leisure time physical activity (PA) as is having 2 servings of fruits and vegetables per day compared to no daily servings.<sup>8, 14</sup> This pragmatic approach should replace the traditional dichotomous, guidelines-based approach (i.e., all or nothing) and is well-suited to optimize the uptake of characteristics of the *healthy living* phenotype in a larger proportion of the global population, particularly those currently emulating the poorest *unhealthy living* phenotype. From a population perspective, minimal movements towards the *healthy living* phenotype are projected to have significant benefits.<sup>15</sup> While we should always strive for an ideal *healthy living* phenotype in all individuals, recognizing the importance of medicinal pragmatism (i.e., a two-way health-related dialogue with the intent of finding practical solutions to a problem and ultimately a common truth) will undoubtedly increase the likelihood of adherence to a healthier lifestyle.

The clear line between *health living* and the profound reduction in the risk for chronic disease is irrefutable.<sup>16, 17</sup> In fact, the best approach to addressing the chronic disease crisis is to promote the adoption of the *healthy living* phenotype. In revisiting the definition of medicine (i.e., treating disease, affecting well-being, maintenance of health, prevention and alleviation of disease, and non-surgical), a clear case is made for the concept of *healthy living medicine* (HLM). The concept of *exercise as medicine* has already been established and promoted for several years.<sup>18, 19</sup> In fact, we have been aware of the medicinal power of exercise for centuries.<sup>20</sup> However, this is a fragmented approach that does not capture the full potential and importance of HLM. The overarching goal of HLM is to optimally prolong the *healthspan*, which can be defined as the number of years an individual is healthy and free from debilitating disease.<sup>5, 21</sup> Being physically active, consuming nutritious and healthy food, not smoking and maintaining an appropriate body weight are all essential to the *healthspan*. This is in sharp contrast to the concept of the *lifespan*, which exclusively speaks to the number of years an individual is alive without necessarily considering functional independence and quality of life. From an economics standpoint, a health system that focusses on promoting the *healthspan* as opposed to the *lifespan* is far more favorable.<sup>22, 23</sup>

The framework for the essential elements of HLM is well-captured by Life's Simple 7 (LS7) put forth by the American Heart Association, consisting of 4 health behaviors (PA, diet, tobacco use, and body weight) and 3 health factors (cholesterol, blood pressure, blood sugar).<sup>8</sup> Moreover, practicing ideal LS7 health behaviors synergizes with more favorable health factors. There is abundant evidence linking a more favorable LS7 score, on a continual scale, and improved health outcome.<sup>24, 25</sup> As such, LS7 serves as both a vital sign and *healthy living* polypill.<sup>26</sup> All individuals should be prescribed this polypill, the ingredients of which are the

foundation of HLM. As mentioned previously, to optimize adherence to HLM, a pragmatic approach to up-titration as well as variable dosages and ingredients that constitute the *healthy living* polypill should be considered. Such an approach aligns with the concept of precision medicine<sup>27</sup>; the *healthy living* polypill can and should consider personal characteristics and likelihood for adherence. Unlike traditional pharmacology, the *healthy living* polypill can be constituted with variable ingredients and dosages while maintaining significant therapeutic efficacy and virtually no side effect profile. For example, a common approach to providing PA recommendations focus on the *ideal* exercise phenotype with little forethought into the PA level from which an individual is beginning their journey toward a *healthy living* phenotype. For an individual who leads a sedentary lifestyle, considering the instantaneous adoption of an exercise program consisting of 150 minutes or more of moderate intensity exercise per week<sup>28</sup> may seem unattainable. Moreover, the literature clearly indicates that movement away from a sedentary lifestyle toward any level of increased PA portends significant health benefits.<sup>24</sup> Thus, with respect to the *healthy living* polypill and HLM moving forward, we should consider a medicinal pragmatism approach; finding a common truth, which in this case being any mutually agreed upon adoption of the *healthy living* phenotype, an achievement that should always be celebrated. Moreover, as the pragmatic two-way communication continues, the health care provider and individual receiving care should continually strive for increased adoption of the *healthy living* phenotype. Literature examining the relationship between the incremental improvement in LS7 scores and improved health outcome aligns with this premise.<sup>25</sup>

In conclusion, to best address the current chronic disease burden and future projections, there is broad recognition and acceptance for the need to reinvent how healthcare is delivered. There must be a shift away from reactionary care, waiting for a diagnosis of one or more chronic

diseases to be highly likely, due to entrenchment of an *unhealthy living* phenotype, or to in fact be diagnosed before care is initiated. Preventing chronic disease and, ideally, associated risk factors (e.g., excess body mass, elevated blood pressure, cholesterol and blood sugar) from ever occurring is of paramount importance. To ideally deliver HLM, what constitutes a “health care” setting must change; parks, schools, and the workplace, for example, should all be considered clinical settings ideal for the delivery of HLM in the context of primordial and primary prevention.<sup>29</sup> The traditional healthcare settings (i.e., hospitals and outpatient clinics) must also embrace the delivery of HLM to all patients receiving care. Essentially, every individual on the planet is eligible for HLM and should receive an individualized *healthy living* polypill prescription. The stakeholders invested in and required for the successful delivery and uptake of HLM and the *healthy living* polypill must also be expanded.<sup>30</sup> For example, a 4<sup>th</sup> grade educator should be invested in HLM, dispensing the *healthy living* polypill to his/her students. Significant consideration must be put into how traditional healthcare professionals (e.g., physicians, nurses, pharmacists, dentists and other allied health professionals) are uniformly trained to deliver HLM and dispense the *healthy living* polypill. The ability to effectively harmonize communication between the health care provider and individual receiving care as well as leverage technology are also key considerations. Lastly, there is a need for a strategic HLM research agenda, focused on continually improving the way HLM is delivered. This edition of *Progress in Cardiovascular Diseases* will provide a blueprint for the new Healthy Living Healthcare System and address key considerations needed to ensure this new system is optimally effective.

## References

1. Definition of Medicine: Merriam-Webster Dictionary. <https://www.merriam-webster.com/dictionary/medicine>. Date Accessed: 1/13/17
2. Barquera S, Pedroza-Tobias A and Medina C. Cardiovascular diseases in mega-countries: the challenges of the nutrition, physical activity and epidemiologic transitions, and the double burden of disease. *Current opinion in lipidology*. 2016;27:329-44.
3. Organization WH. Noncommunicable diseases country profiles 2014. <http://www.who.int/nmh/countries/en/>. Date Accessed: 2/7/2016
4. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, Abraham J, Adair T, Aggarwal R, Ahn SY, Alvarado M, Anderson HR, Anderson LM, Andrews KG, Atkinson C, Baddour LM, Barker-Collo S, Bartels DH, Bell ML, Benjamin EJ, Bennett D, Bhalla K, Bikbov B, Bin Abdulhak A, Birbeck G, Blyth F, Bolliger I, Boufous S, Bucello C, Burch M, Burney P, Carapetis J, Chen H, Chou D, Chugh SS, Coffeng LE, Colan SD, Colquhoun S, Colson KE, Condon J, Connor MD, Cooper LT, Corriere M, Cortinovis M, de Vaccaro KC, Couser W, Cowie BC, Criqui MH, Cross M, Dabhadkar KC, Dahodwala N, De Leo D, Degenhardt L, Delossantos A, Denenberg J, Des Jarlais DC, Dharmaratne SD, Dorsey ER, Driscoll T, Duber H, Ebel B, Erwin PJ, Espindola P, Ezzati M, Feigin V, Flaxman AD, Forouzanfar MH, Fowkes FG, Franklin R, Fransen M, Freeman MK, Gabriel SE, Gakidou E, Gaspari F, Gillum RF, Gonzalez-Medina D, Halasa YA, Haring D, Harrison JE, Havmoeller R, Hay RJ, Hoen B, Hotez PJ, Hoy D, Jacobsen KH, James SL, Jasrasaria R, Jayaraman S, Johns N, Karthikeyan G, Kassebaum N, Keren A, Khoo JP, Knowlton LM, Kobusingye O, Koranteng A, Krishnamurthi R, Lipnick M, Lipshultz SE, Ohno SL, Mabweijano J, MacIntyre MF, Mallinger L, March L, Marks GB, Marks R, Matsumori A, Matzopoulos R, Mayosi BM, McAnulty JH, McDermott MM, McGrath J, Mensah GA, Merriman TR, Michaud C, Miller M, Miller TR, Mock C, Mocumbi AO, Mokdad AA, Moran A, Mulholland K, Nair MN, Naldi L, Narayan KM, Nasser K, Norman P, O'Donnell M, Omer SB, Ortblad K, Osborne R, Ozgediz D, Pahari B, Pandian JD, Rivero AP, Padilla RP, Perez-Ruiz F, Perico N, Phillips D, Pierce K, Pope CA, 3rd, Porrini E, Pourmalek F, Raju M, Ranganathan D, Rehm JT, Rein DB, Remuzzi G, Rivara FP, Roberts T, De Leon FR, Rosenfeld LC, Rushton L, Sacco RL, Salomon JA, Sampson U, Sanman E, Schwebel DC, Segui-Gomez M, Shepard DS, Singh D, Singleton J, Sliwa K, Smith E, Steer A, Taylor JA, Thomas B, Tleyjeh IM, Towbin JA, Truelsen T, Undurraga EA, Venketasubramanian N, Vijayakumar L, Vos T, Wagner GR, Wang M, Wang W, Watt K, Weinstock MA, Weintraub R, Wilkinson JD, Woolf AD, Wulf S, Yeh PH, Yip P, Zabetian A, Zheng ZJ, Lopez AD, Murray CJ, AlMazroa MA and Memish ZA. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2095-128.



5. Sagner M, McNeil A, Puska P, Auffray C, Price ND, Hood L, Lavie CJ, Han ZG, Chen Z, Brahmachari SK, McEwen BS, Soares MB, Balling R, Epel E and Arena R. The P4 Health Spectrum - A Predictive, Preventive, Personalized and Participatory Continuum for Promoting Healthspan. *Prog Cardiovasc Dis*. 2016.
6. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Després J-P, Fullerton HJ, Howard VJ, Huffman MD, Isasi CR, Jiménez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohler ER, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW and Turner MB. Heart Disease and Stroke Statistics—2016 Update: A Report From the American Heart Association. *Circulation*. 2015.
7. Mechanick JI, Hurley DL and Garvey WT. ADIPOSITY-BASED CHRONIC DISEASE AS A NEW DIAGNOSTIC TERM: AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND THE AMERICAN COLLEGE OF ENDOCRINOLOGY POSITION STATEMENT. *Endocrine Practice*. 0:null.
8. Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, Greenlund K, Daniels S, Nichol G, Tomaselli GF, Arnett DK, Fonarow GC, Ho PM, Lauer MS, Masoudi FA, Robertson RM, Roger V, Schwamm LH, Sorlie P, Yancy CW, Rosamond WD, American Heart Association Strategic Planning Task F and Statistics C. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation*. 2010;121:586-613.
9. Akesson A, Larsson SC, Discacciati A and Wolk A. Low-risk diet and lifestyle habits in the primary prevention of myocardial infarction in men: a population-based prospective cohort study. *J Am Coll Cardiol*. 2014;64:1299-306.
10. Probst-Hensch N, Tanner M, Kessler C, Burri C and Kunzli N. Prevention--a cost-effective way to fight the non-communicable disease epidemic: an academic perspective of the United Nations High-level NCD Meeting. *Swiss Med Wkly*. 2011;141:w13266.
11. Thomas B and Gostin LO. Tackling the global NCD crisis: innovations in law and governance. *J Law Med Ethics*. 2013;41:16-27.
12. Larsson SC, Akesson A and Wolk A. Primary prevention of stroke by a healthy lifestyle in a high-risk group. *Neurology*. 2015;84:2224-8.
13. Khera AV, Emdin CA, Drake I, Natarajan P, Bick AG, Cook NR, Chasman DI, Baber U, Mehran R, Rader DJ, Fuster V, Boerwinkle E, Melander O, Orho-Melander M, Ridker PM and

Kathiresan S. Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease. *N Engl J Med.* 2016;375:2349-2358.

14. Harrington RA, Arena R, Despres JP, Ciarochi A, Croll E and Bloch KD. More than 10 million steps in the right direction: results from the first American Heart Association scientific sessions walking challenge. *Prog Cardiovasc Dis.* 2015;57:296-8.
15. Pratt M, Sarmiento OL, Montes F, Ogilvie D, Marcus BH, Perez LG, Brownson RC and Lancet Physical Activity Series Working G. The implications of megatrends in information and communication technology and transportation for changes in global physical activity. *Lancet.* 2012;380:282-93.
16. Marczak L, O'Rourke K, Shepard D, for the Institute for Health M and Evaluation. When and why people die in the united states, 1990-2013. *Jama.* 2016;315:241-241.
17. Song M and Giovannucci E. Preventable Incidence and Mortality of Carcinoma Associated With Lifestyle Factors Among White Adults in the United States. *JAMA oncology.* 2016.
18. Sallis R. Exercise is medicine: a call to action for physicians to assess and prescribe exercise. *Phys Sportsmed.* 2015;43:22-6.
19. Sallis RE. Exercise is medicine and physicians need to prescribe it! *British journal of sports medicine.* 2009;43:3-4.
20. Arena R, Harrington RA and Despres JP. A message from modern-day healthcare to physical activity and fitness: welcome home! *Prog Cardiovasc Dis.* 2015;57:293-5.
21. Increasing Healthspan: Prosper and Live Long. *EBioMedicine.* 2015;2:1559.
22. Wakim R, Ritchey M, Hockenberry J and Casper M. Geographic Variations in Incremental Costs of Heart Disease Among Medicare Beneficiaries, by Type of Service, 2012. *Prev Chronic Dis.* 2016;13:E180.
23. Heidenreich PA, Trogon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, Finkelstein EA, Hong Y, Johnston SC, Khera A, Lloyd-Jones DM, Nelson SA, Nichol G, Orenstein D, Wilson PW and Woo YJ. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation.* 2011;123:933-44.

24. Folsom AR, Yatsuya H, Nettleton JA, Lutsey PL, Cushman M, Rosamond WD and Investigators AS. Community prevalence of ideal cardiovascular health, by the American Heart Association definition, and relationship with cardiovascular disease incidence. *J Am Coll Cardiol*. 2011;57:1690-6.
25. Younus A, Aneni EC, Spatz ES, Osondu CU, Roberson L, Ogunmoroti O, Malik R, Ali SS, Aziz M, Feldman T, Virani SS, Maziak W, Agatston AS, Veledar E and Nasir K. A Systematic Review of the Prevalence and Outcomes of Ideal Cardiovascular Health in US and Non-US Populations. *Mayo Clin Proc*. 2016;91:649-70.
26. Arena R, Lavie CJ and Guazzi M. Prescribing a Healthy Lifestyle Polypill With High Therapeutic Efficacy in Many Shapes and Sizes. *American Journal of Lifestyle Medicine*. 2015.
27. Medicine USNLo. What is precision medicine? <https://ghr.nlm.nih.gov/primer/precisionmedicine/definition>. Date Accessed: 5/1/2016
28. Kraus WE, Bittner V, Appel L, Blair SN, Church T, Despres JP, Franklin BA, Miller TD, Pate RR, Taylor-Piliae RE, Vafiadis DK and Whitsel L. The National Physical Activity Plan: a call to action from the American Heart Association: a science advisory from the American Heart Association. *Circulation*. 2015;131:1932-40.
29. Arena R, Lavie CJ, Cahalin LP, Briggs PD, Guizilini S, Daugherty J, Chan WM and Borghi-Silva A. Transforming cardiac rehabilitation into broad-based healthy lifestyle programs to combat noncommunicable disease. *Expert review of cardiovascular therapy*. 2016;14:23-36.
30. Arena R, Whitsel LP, Berra K, Lavie CJ, Kaminsky L, Williams M, Hivert MF, Franklin NC, Myers J, Dongel D, Lloyd-Jones DM, Guazzi M, Pinto FJ, Consentino F, Halle M, Gielen S, Dendale P, Niebauer J, Pelliccia A, Giannuzzi P, Corra U, Piepoli M, Lianov L, Guthrie G and Shurney D. Healthy Lifestyle Interventions to Combat Non-Communicable Disease: A Novel Non-Hierarchical Connectivity Model for Key Stakeholders: A Policy Statement from the AHA, ESC, EACPR and ACPM. *Mayo Clin Proc*. 2015;90:1082-1103.