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Reaching for Cardio-Metabolic Fitness and Resilience through Self-Healing and Guided Individualized Cyber-Therapy: An Opportunity to Reenergize Primary Care

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ABSTRACT

Background: There is a need to facilitate efforts to reduce metabolic, cardiovascular, and stress-related risks with a healthy lifestyle and improve cardio metabolic and cardio-vegetative health and longevity with self-management and guided therapy. We recently introduced a Cyber-Physical System (CPS) to facilitate this process. CPS is a mobile technology integrating sensory data from various mobile devices into individualized dynamic mathematical models of physiological processes, allowing for analysis and prediction and maximizing user control and supported by the primary provider.

Methods: Closely mimicking HOMA-IR (a practical laboratory measurement of insulin resistance) is our metric allowing for the noninvasive observation of insulin resistance changes by estimating R or Rw-ratio which are defined as R=ΔL/ΔF and Rw=ΔW/ΔF where ΔL, ΔW and ΔF are lean mass, weight and fat mass change over 24 hrs. We can estimate R or Rw-ratio either with use of our Self-Adaptive Model of the Energy Metabolism (SAM-HEM) demanding precise calorie counting or with our Weight, Fat weight, Energy balance (WFE) model without mandatory calorie counting by serially measuring weight, fat weight, and energy balance. The verification of this concept was performed using data from 12 clinical studies with 39 clinical study arms and with total number of patients n=2010.

Results: The correlation between changes of HOMA-IR and changes of daily WFE calculated Rw-ratio was -0.6745 with a P value of 0.0000024.

Conclusion: Our cyber-physical system along with a sensor system can provide a truly individualized strategy for estimation, measurement, and prediction of physiological variables of the metabolism including changes of insulin resistance which are essential for prevention and treatment diabetes and cardiovascular disease in primary care.

Keywords: Medical cybernetics; Machine learning; Self-adaptive individualized mathematical modeling; Non-invasive monitoring; Observing aging health; Risk prediction; Metabolic health; Insulin resistance; Cardiorespiratory fitness; Cardio-vegetative stress

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INTRODUCTION

I am perhaps a rare breed of practicing internist with previous training in Bio-Medical Cybernetics (MC) before entering medical school and a post-doctoral research fellowship in non-invasive cardiology. This engineering training together with my experiences in primary care in academic and non-academic environments have inspired my vision for unleashing the potential of MC to help reenergize primary care.

Central to the mission of primary care is fighting the burden of non-communicable chronic diseases including the most prominent one, Cardiovascular Disease (CVD) [1]. There is a need to facilitate efforts to reduce CVD risks such as insulin resistance with healthy lifestyle and to improve cardiometabolic fitness for improved health and longevity with both self-management and guided therapy. A viewpoint article in JAMA by Philip A. Pizzo [2] recommends to us a "prescription" for longevity focused on three issues:

- Having purpose
- Seeking social engagement
- Embracing a positive lifestyle

In primary care we must be prepared to guide our patients not just to improve morbidity and mortality but also to "improve the life journey" and promote healthy aging by individualized care. This article will outline how self-healing and guided individualized cyber-therapy by a Healthy Lifestyle Team approach could be realized with methods of MC organized into a cloud-based Cyber-Physical System (CPS).

Medical cybernetics is mostly concerned with exploring regulatory systems in humans-their structures, constraints, and possibilities using mathematical modeling. Cyber-therapy is defined here as the combined use of individualized mathematical-statistical modeling, prediction, planning for change and gaining control by feedback of information on components of the human energy metabolism of an individual for self-management of the modifiable components of cardiometabolic and cardio-vegetative functioning of the body with option for guided therapy. Our machine learning mathematical modeling techniques of the human energy metabolism such as the Self-Adaptive model of the Human Energy Metabolism (SAM-HEM) [3-5] and the serial Weight, Fat weight, and Energy balance (WFE) models [6,7] are tools to observe and predict the difficult to measure State Variables (SV's) of the human energy metabolism, such as slow occurring body composition changes including lean mass, protein mass, fat mass, or practically impossible to measure outside of a laboratory variables like changes of insulin resistance, utilized macronutrient intake and fat oxidation rates.

This paper is to show how MC could be used to prevent and fight the pandemic of obesity and insulin resistance with its associated cardiovascular disease complications caused by increased endothelial inflammation, dysfunction, and oxidative stress. The significance of the MC technology for primary care is that it could augment self-management of lifestyle disorders that are preventable or reversible in an early stage of the chronic disease with lifestyle interventions. Examples include prediabetes, diabetes type 2, atherosclerosis, cancer, and neurodegeneration [8].

The need for prevention or reversal of early stages of chronic disease is heightened by the devastation of the concurrent occurrence of the pandemic of obesity and the epidemic of Coronavirus 19 with ferocious consequences in our communities: obesity and associated insulin resistance worsened the outcome of Coronavirus 19 [9]. The most important link is the state of metabolic inflammation that predisposes patients to an enhanced release of cytokines. Metabolic inflammation will also compromise the immune system, reducing the body's ability to tackle the infection, impairing the healing process, and prolonging the recovery [10]. Though, laboratory methods to evaluate oxidative stress and profiling of the endovascular functioning with methods such as brachial artery Flow-Mediated Dilatation (FMD) are available to identify high risk for endothelial inflammation, but these methods provide only a snapshot or one point in time assessment and are not able to predict the future development. Improvement of sugar control and insulin resistance are key in the battle to reduce the proinflammatory state leading to morbidity and mortality [10]. Recent recommendations by academic authors to treat type 2 Diabetes (DM2) and complications like Cardiovascular Disease (CVD) call for "a patient-centered approach that addresses patients' multimorbidities, needs, preferences, and barriers and includes diabetes education and lifestyle interventions as well as pharmacologic treatment" [11]. However, the most important question of "how?" remains answered only with traditional approaches. Clearly, a paradigm shift in risk assessment with long term observation [12] and personalized prediction [13] with appropriate intervention is needed.

This article gives me the opportunity to outline my vision on the most important question of "how" to achieve goals of continuous personalized risk assessment with monitoring aging health status and providing support for improved lifestyle management using tools of MC. The overall goal of individualized cyber-therapy with use of a CPS is to provide risk assessment, monitoring, and support for better control of the metabolism. Instrumental in creating the necessary tools are the already widely available information technologies like smart phones, cloud computing, and sensor devices of the fitness industry. All these could be put together into a CPS that includes the SAM-HEM and WFE models.

MATERIALS AND METHODS

Our CPS [6,7] compresses the sensory data into individualized dynamic mathematical models of physiological processes allowing for analysis, prediction, and maximizing control by user. We invented self-adjusting mathematical models [3-7], allowing for the noninvasive observation of metabolic State Variables (SV's) including insulin resistance changes by estimating R or Rw-ratio which are defined as $R=\Delta L/\Delta F$ and $Rw=\Delta W/\Delta F$ where ΔL, ΔW and ΔF are lean mass, weight and fat mass change over 24 hrs. We use our mathematical models to estimate these variables [6,7]. We utilize state space modeling where process models and measurement models work in unison and update each other's a priori and a posteriori model calculation with the help of the minimum variance Kalman filter. We can estimate R or Rw-ratio either with SAM-HEM demanding precise calorie counting or with our Weight, Fat weight, Energy balance (WFE) model without mandatory calorie counting by serially measuring weight, fat weight, and energy balance [6,7]. Further, we extended its WFE model calculations (WFE-DNL-AT) for the assessment of *de novo* Lipogenesis (DNL), Adaptive Thermogenesis (AT), and of 24 hr Respiratory Quotient (RQ) [7]. WFE-DNL-AT calculations, however, require daily macronutrient energy intake counting.

The feasibility of the concept that R-ratio and/or Rw-ratio to track changes of insulin resistance was performed using data from 12 clinical studies with 39 clinical study arms and with total number of patients n=2010 [7]. We performed verification also for the WFE-DNL-AT model and its estimation of DNL, AT and RQ. The model calculations were graphically compared to the measured RQ's [7] which were taken by 24 h respiratory chamber in the clinical study entitled "Calorie for calorie, dietary fat restriction results in more body fat loss than carbohydrate restriction in people with obesity" [14].

RESULTS

The results of the met analysis showed a strong correlation between changes of HOMA-IR and changes of daily WFE calculated Rw-ratio, weight change velocity ΔW_k, changes of fat oxidation *vs.* carbohydrate oxidation ΔFox/Cox, and daily changes of fat mass ΔF_k as in **Table 1** [7]. The strongest correlation was found between HOMA-IR and Rw-ratio changes, supporting our modeling proposition to use Rw-ratio as a surrogate measure for HOMA-IR. **Figure 1** shows the data scattering of ΔHOMA-IR *vs.* ΔRw across the 39 study arms and depicts the calculated linear correlation function. WFE-DNL-AT calculations predicted the measured values of DNL, AT, and RQ with quite acceptable accuracy by visual comparison of the graphical representations of the measured RQ's by a 24 h respiratory chamber with the calculated RQ's by the WFE-DNL-AT model.

Table 1: Correlation results from 39 clinical trial arms.

State variable	HOMA-IR	P value
ΔRw-ratio	-0.6745	0.0000024
ΔW_k	0.6413	0.0000108
Fox/Cox	0.6218	0.0000238
ΔF_k	0.4748	0.0022542

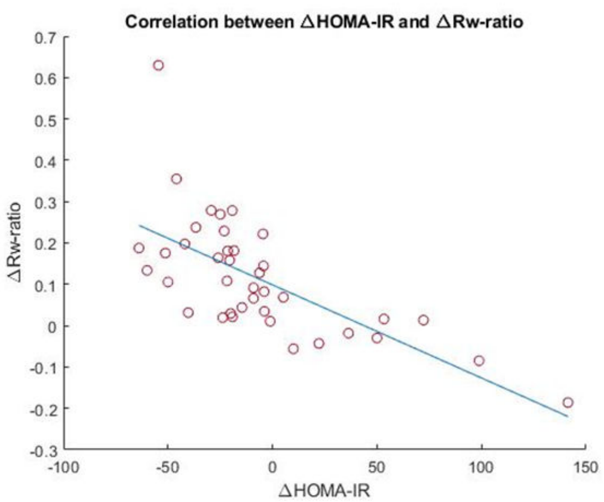

Figure 1: Correlation between changes of HOMA-IR and Rw-ratio.

Propositions for Risk Management

Our extended model calculations from serial fat and weight measurements and energy balance estimates can help unmask changes of insulin resistance in response to user's diet and exercise habits, creating the necessary tools to measure metabolic processes indirectly [6,7] and allow for estimating the otherwise difficult or impossible to measure changes of State Variables (SV's) of the metabolism such as 24 h non-protein respiratory quotient, utilized macronutrient energies, fat oxidation rate, carbohydrate oxidation rates, *de novo* lipogenesis, and adaptive thermogenesis. The core innovation is here that we can estimate the unknown parameters of the metabolic stochastic difference equations using principles established in physics such as the principle of "least action" or "stationary action" along with utilizing principles of indirect calorimetry [6,7].

The ultimate outcome measure of any clinical intervention is mortality, including CVD and all-cause mortality. Applying CPS offers a wholistic view of a lifespan where all the observed and appropriately chosen variables can be assigned to risk calculations in terms morbidity and mortality creating clear targets to maximize control over them. We consider here three intertwined areas of healthy aging with implications for significant mortality risks:

- Metabolic health
- Cardiovascular health
- Cardio-vegetative health

The justification for these areas of focusing are:

Insulin resistance is an independent risk factor for CVD mortality [15]. A CPS is empowered to calculate trends and trajectories of insulin resistance as measured with R or Rw-ratio and fat mass, which can also be translated into predicted changes of visceral fat mass and waist circumference. Because all these variables have been shown to have high correlation to cardiovascular mortality [16] CPS is uniquely suitable for real time monitoring of the metabolic health status. CPS uses the following physiological System Variables (SV's) in its process models: Weight, lean mass, fat mass, Waist Circumference (WCF), insulin resistance associated R-ratio or Rw-ratio, Fat oxidation *vs.* Carbohydrate oxidation (Fox/Cox), and 24 h non-protein Respiratory Quotient (RQ).

Maximal oxygen uptake and exercise test duration represent the strongest predictors of mortality [17-19]. We estimate indirectly the maximum oxygen uptake (VO_2max) from Heart Rate (HR) and measuring maximal Activity Energy Expenditure (aEEmax) during graded exercise. The VO_2max calculation model uses multiple linear regression with data on age, sex, height, percent body fat, aEEmax, and the slope between HR and physical activity energy expenditure [20]. The model is self-adapting (self-learning) from the daily incoming data and assesses changes of VO_2max, exercise capacity, and Heart Rate Reserve (HRR). We adopted the critical power model from [21] which is defined as the maximal sustainable aerobic power not causing "fatigue" to measure exercise capacity. The Heart Rate Reserve (HRR), and Heart Rate Variability (HRV) are directly measured through the wearable sensor system.

Imbalance of the autonomic nervous system functioning in terms of sympathetic-parasympathetic balance is associated with all-cause mortality and sudden cardiac death [22-24]. The variables measuring functioning of the autonomous nervous system and estimating imbalance between sympathetic vs. parasympathetic activity are the heart rate and HRV with time domain as well as frequency domain power spectrum indicators such as the power in Low Frequency band (LF) and High Frequency band (HF) and their ratio LF/HF characterizing autonomic nervous system functioning in terms of sympathetic-parasympathetic balance [23,24].

CPS generates SV's and metrics in each domain of use (1-3) and displays the results quasi real time on the screen of a mobile and web app, the Metabolic Health Monitor (MHM) which has a user and provider functionality. MHM is designed for displaying the SV's quasi real time and providing feedback by personal trainer or primary provider. The web app has functionality for the personal trainer/ primary provider(s) or the user himself/ herself for analysis, prediction, goal setting of the calculated SV's and metrics. MHM enables also planning for lifestyle change and evaluating progress and outcome.

The overarching holistic approach is here the individualized tracking and construction of predicted trajectories over a lifespan from collected data of essential physiological variables (SV's) in all three domains of health with major implications to morbidity/mortality, determine their physiological reserve in a continuum with preventive purposes before reaching significant disease, decompensation, or death. Importantly all these variables can be used to constant risk calculations and assessment keeping goals in clear perspectives. This concept is visualized in **Table 2** entitled the life diagram.

Table 2: The life diagram.

Domains of health and MC models	Physiological range and proposed variables for monitoring	Pathological range and possible interventions	Major morbidity with crisis
Morbidity/Mortality risk			
Physiological reserve			Organ failure and crisis
Metabolic health	Weight, lean mass, fat mass, WCF, insulin resistance R, Rw-ratio, Fox/Cox, 24 h RQ	Behavior modification/lifestyle change/dynamic behavioral modification with CPS	Metabolic catastrophe
Cardiovascular health	MaxO2, HRR, HRV	Cardiopulmonary exercise/ dynamic exercises planning with CPS	Cardiorespiratory failure
Cardio-vegetative health	HR, HRV, LF/HF	Care by cardiologist/dynamic planned interactions supported with metrics from CPS	Nerve exhaustion/pending sudden cardiac death

The increasing risk of major morbidity/mortality is represented by a thickening red stripe as the physiological reserve capacity diminishes. Note that the tapering arrow in blue symbolizes diminishing reserve capacity and represents target of improvement. The diagram shows also major tools how vanishing physiological reserve in each health category could be improved and potentially help restore age adequate health. Our value proposition and main research idea is to use CPS to collect highly impactful data, compress them into MC models, determine the model parameters which become target for optimization of physiological functioning to reduce risk for morbidity/mortality. Along with this the goal is to improve cardio-metabolic fitness, and psychological resilience with result driven predictive feedback control (showing self-efficacy with effort-result analysis with implications for self-control strategy and tactics). MC modelling can provide special insight into processes, giving the expected direction of change of a data point in the future *i.e.* connecting the dots or putting them on a model trajectory and explaining the changes. The benefit is that instead of comparing the user's data against a group average, the individualized modeling and data trajectory creation allows for individualized interventions.

The MC models with trajectories and predictions allow for quantifying progress and for providing metrics for dynamic behavioral interventions supported by smart portable devices as it is suggested [25]. The undeniable advantage of modern portable electronics is that they can provide resources and powerful data for self-healing in a non-judgmental way without stigmatization associated with obesity. The self-explaining context of the state variables has the potential to raise self-awareness and draw attention to risk reduction and individual responsibility in the fight against modifiable non-communicative disease processes. The derived metrics provided by CPS have the potential to give the opportunity for education and learning about risks for health, develop new skills to fight risks, build motivation as well as measure self-efficacy in the fight against modifiable risks. The same CPS metrics can be used by a lead team or therapist for teaching, guiding needed changes of lifestyle or behavior, and suggesting counter measures to tackle poorly managed stress. CPS derived data could open avenues to machine learning to optimize performance.

We are in the process of developing our CPS cloud-based software platform to accept data from wearable sensors of the fitness industry. In this process we are adapting a so-called webhook technology of Metriport Co. that can access the data through 3rd party APIs potentially from the following wearable sensors: Dexcom, Fitbit, Garmin, Oura, Whoop, Withings, Cronometer, Apple health, and Google fit. In addition, we are developing our body-composition hydration analyzer photo-plethysmography equipped stand-up scale [26]. This can provide bioimpedance measurement to detect daily changes of body composition along with the Rw-ratio. The Photoplethysmography (PG) sensors are to monitor systolic (SBP) and Diastolic (DBP) blood pressures. The PG sensor can measure also Pulse Wave Velocity (PWV) to track changes of total arterial compliance.

For the recognition of Major Morbidity with crisis (**Table 2**), we are in the process of developing an extended version of CPS *i.e.*, the Integrated CPS (ICPS) [27]. We reviewed recently how wearable sensors can support recognition of medical urgencies [28] and support diagnostic excellence in emergencies [29]. From a medicolegal standpoint it is important to emphasize the distinction between a CPS, which is a nonmedical software, versus ICPS which still must be approved by FDA to become a medical software. The distinction between CPS and ICPS is also needed regarding appropriate response to the identified problems: CPS is designed for self-management of lifestyle issues and for guided interventions by health coaches. ICPS requires medical supervision. Importantly, ICPS extends the CPS non-invasive monitoring capabilities in physiological functioning into the field of pathological functioning with far reaching implications for telemonitoring, telemedicine, rehabilitation, prehabilitation, prehospital care and supporting also first responders to medical emergencies.

Table 3 entitled the pathways to maximize control gives conceptual summary how CPS derived metrics can help interventions across lifespan promoting healthy aging when state variables are in physiological range or in the pathological range. For the former education is the most important tool about processes of healthy aging. When SV's deviate from a healthy life trajectory than behavior modification is needed or when significant disease or decompensated state ensues than rescue measures are required. In all categories CPS can support a truly individualized strategy for estimation, measurement, and prediction of physiological variables and create metrics for optimized self-control and dynamic interventions based on the targeted metrics, leading to self-healing and cyber-therapy supervised by health care providers. Machine learning could help maximize control.

Table 3: The pathways to maximize control.

Intervention type	Physiological range methods of choice	Pathological range possible interventions	Major morbidity with crisis
Self care	Self-education	Self-healing with behavior modification and using CPS	Optimized learned behaviors to secure survival until rescue
Managed care using information from CPS	Teaching/learning how to improve health with use of CPS	Interventions by health care provider team to guide therapy also using information from CPS	Lifesaving interventions by rescue team using data also from CPS
Cyber-therapy	Machine learning of healthy baseline functioning	Autonomous computer-generated optimal control to maximize results and realize individualized "precision" medicine with strict supervision by health professional	Autonomous machine directed therapies which can be overruled by physician

DISCUSSION

From primary health care point of view the innovation is that CPS captures the metrics in 3 intertwined domains of physiological functioning in the user's natural environment to obtain data from the metabolic, cardiovascular, and cardio-vegetative health domains. An all-encompassing risk assessment by CPS allows quasi-real time monitoring for the user and the primary care giver. Analysis, prediction, and planning for change can be performed either at home or in the primary provider's office through a MHM mobile and web app and display of results on the user's smartphone. Unique to our effort is that our suggested state variables are connected to risks of morbidity and mortality [26] and allow risk assessment continuously over a lifespan, raising self-awareness, enhancing motivation, and underscoring self-responsibility to reduce modifiable risks as much as possible.

Based on our simulation studies of serial fat and weight measurements, CPS is a suitable concept to indirectly measure and predict the otherwise very difficult- or impossible-to-measure slow changes of State Variables (SV's) of the metabolism such as insulin resistance, 24 h non-protein respiratory quotient, utilized macronutrient energies, fat oxidation rate, carbohydrate oxidation rates, de novo lipogenesis, adaptive thermogenesis, and capture them for the first time noninvasively in the user's natural environment. Metabolic health goals, like improved metabolic flexibility, improved insulin resistance along with greater lean mass and optimized fat versus carbohydrate burning can be approached with the help of CPS through feedback of information from a personalized self-adaptive mathematical model of the energy metabolism with optional coaching by a health care provider team. CPS can also help optimize cardiorespiratory fitness level by providing feedback of indirectly estimated VO_2max uptake. CPS can be realized already with a Garmin smart watch and Index scale.

Recognizing the powerful predictive values of VO_2max uptake, exercise capacity, and HRV in terms of all-cause morbidity and mortality, these system variables can be used to track the time course of training adaptation/maladaptation to physical training or physical therapy. These variables can help set the optimal training loads, leading to improved physical resilience. Uniquely, CPS could provide HRV derived metrics to gauge cardio-vegetative stress and the recovery time after stress and give quantitative data regarding vegetative stress. HRV just may be useful to track the 3 stages of vegetative stress defined by Janos Selye:

- Alarm reaction
- Resistance stage
- Exhaustion stage

Together with other clinical data HRV related metrics may offer the opportunity to recognize the 3rd stage. Once crisis is recognized its mitigation becomes paramount to avoid its greatest danger which is sudden cardiac death [23,24].

Undoubtably, major challenges remain ahead to be tackled before CPS can become widely available. The technical hurdle is to create a scalable versatile mobile and cloud computing platform for CPS which can potentially be used with a variety of mobile health products on the market. While intend to make CPS potentially usable with various mobile health products, this effort may be stifled because of a lack of interoperability of various fitness devices and because data are stored in "data silos," preventing users and health professionals from getting an integrated view of health and fitness data [30]. The current practice is for third-party developers to retrieve the data via an open API with permission of the owner of the API and the user. The key risk and challenge are to make users' data accessible for cloud computing systems like CPS.

A short list of other problems to be overcome before widespread usage is as follows: data privacy and security, to create a marketable product which is only a fitness device at this stage of development and does not fall into a medical device category, creating tools for easy calorie intake counting, creating tools for visceral fat mass measurement, and in general creating a culture of health where health as a value is elevated to the highest level. After proper consenting, secondary analysis of metabolic data could help not only clinical research but also insurance companies to calculate costs and potentially reimburse the treatment/self-treatment and improvement of risk factors for CVD. A value-based health delivery system holds potential to incentivize participants to improve their lifestyle, especially if insurance companies would honor participants with a discount on the premiums for those who were successful in lowering their cardiovascular risk.

For reenergizing primary care, we must open the world of digital health to our patients and make the modifiable risk factors observable as they evolve in quasi real time, so that patients can be fully in charge of their destiny with respect to cardiometabolic processes and what is generally understood and wished for as health, fitness, and strength. Most recent recommendations by academic authors for patient-centered care [11] could be approached by using tools of MC and the concept of CPS. CPS can facilitate five strategic goals essential to our patients:

- It can provide metrics of cardiometabolic health to monitor and support healthy aging.
- It can promote education.
- It can connect all participants in local health care services and related entities of the nutrition, fitness and wellness industry.
- It could ignite social entrepreneurships and unite activists, local small businesses and other entities related to health to build health conscientious communities.
- Insurance companies could learn more about risks with implications for value-based reimbursement of services.

My additions to Dr. Pizzo's "prescription" for longevity [2] are the following: Taking individual responsibly for our lifestyle throughout lifetime not just for our sake but also for our family, community, and society at large with self-discipline, strong resolve, motivation, and self-efficacy. Teaching and becoming role model example and helping our communities to develop a culture of health for the next generation to come. Physicians could play an important role in achieving healthy lifestyle interventions [1] and help develop physical and mental resilience. This could occur through connecting the patient through MHM smart phone and web app used by a Healthy Lifestyle Team [1]. Therapists can identify the risk factors for change and a reasonable personal intervention strategy that can be constantly modified in small strategic steps customized to users' needs. CPS may be used to dole out small daily achievable tasks and allow users to accomplish their daily goals. Past successes in achieving the set goals may translate to improving motivation, compliance, and self-efficacy in making needed lifestyle changes. The tool for reaching longevity is incomplete without heeding the words of Iuvenalis: "A healthy mind in a healthy body" to express the theory that healthy nutrition and physical exercise is an important or essential part of mental and physical well-being and developing resilience i.e. adapting and responding positively to stress and misfortune. Resilient people tend to maintain a more positive outlook and cope with stress more effectively.

CONCLUSION

In conclusion, CPS can serve as an appropriate quasi real-time tool to monitor and optimally adjust modifiable risk factors. The trends/trajectories of metabolic values calculated by the mathematical models can serve as tools, allowing for planning and executing dynamic changes of behavior for optimization and control of these values. All-encompassing CVD risk scores calculated by the mathematical models can serve as outcome measures to be tracked by the user and therapist to fight CVD burden and optimize lifestyle real time. CPS is applicable in resource-limited settings with reasonably low investment.

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REFERENCES

1. Arena R, Guazzi M, Lianov L, Whitsel L, Berra K, et al. (2015) Healthy lifestyle interventions to combat noncommunicable disease-a novel nonhierarchical connectivity model for key stakeholders: A policy statement from the American heart association, European society of cardiology, European association for cardiovascular prevention and rehabilitation, and American college of preventive medicine. Euro Heart J. 36(31):2097-2109.
2. Pizzo PA (2020) A prescription for longevity in the 21st century: Renewing purpose, building and sustaining social engagement, and embracing a positive lifestyle. JAMA. 323(5):415-416.
3. Ori ZP (2017) Parametric recursive system identification and self-adaptive modeling of the human energy metabolism for adaptive control of fat weight. Med Biol Eng Comput. 55(5):759-767.
4. Ori Z, Ori I (2016) Fighting weight problems and insulin resistance with the metabolic health monitor app for patients in the setting of limited access to health care in rural America. 2016 IEEE Global Humanitarian Technology Conference (GHTC).
5. Ori Z, Ori I (2016) Canonical representation of the human energy metabolism of lean mass, fat mass, and insulin resistance. 2016 IEEE 7th Annual Ubiquitous Computing, Electronics and Mobile Communication Conference (UEMCON).
6. Ori ZP (2019) Cyber-physical system for management and self-management of cardiometabolic health. Type 2 diabetes-from pathophysiology to modern management. IntechOpen.
7. Ori ZP (2019) Metabolic health analysis and forecasting with mobile computing. Mobile Comput. pp. 123.
8. Phillips MC (2022) Metabolic strategies in healthcare: A new era. Aging Dis. 13(3):655.
9. Sanchis-Gomar F, Lavie CJ, Mehra MR, Henry BM, Lippi G (2020) Obesity and outcomes in COVID-19: When an epidemic and pandemic collide. Mayo Clin Proceed. 95(7):1445-1453.
10. Bornstein SR, Dalan R, Hopkins D, Mingrone G, Boehm BO (2020) Endocrine and metabolic link to coronavirus infection. Nat Rev Endocrinol. 16(6):297-298.
11. Harris SB, Cheng AY, Davies MJ, Gerstein HC, Green JB, et al. Person-centered, outcomes-driven treatment: A new paradigm for type 2 diabetes in primary care.
12. McEvoy JW, Diamond GA, Detrano RC, Kaul S, Blaha MJ, et al. (2014) Risk and the physics of clinical prediction. Am J Cardiol. 113(8):1429-1435.
13. Localio AR, Mulrow CD, Griswold ME (2020) Advancing personalized medicine through prediction. Ann Intern Med. 172(1):63-64.
14. Hall KD, Bemis T, Brychta R, Chen KY, Courville A, et al. (2015) Calorie for calorie, dietary fat restriction results in more body fat loss than carbohydrate restriction in people with obesity. Cell Metabolism. 22(3):427-436.
15. Godsland IF, Lecamwasam K, Johnston DG (2011) A systematic evaluation of the insulin resistance syndrome as an independent risk factor for cardiovascular disease mortality and derivation of a clinical index. Metabolism. 60(10):1442-1448.
16. Dallongeville J, Bhatt DL, Steg PG, Ravaud P, Wilson PW, et al. (2012) Relation between body mass index, waist circumference, and cardiovascular outcomes in 19,579 diabetic patients with established vascular disease: The REACH registry. Euro J Prev Cardiol. 19(2):241-249.
17. Laukkanen JA, Lakka TA, Rauramaa R, Kuhanen R, Salonen R, et al. (2001) Cardiovascular fitness as a predictor of mortality in men. Arch Intern Med. 161(6): 825-831.
18. Myers J, McAuley P, Lavie CJ, Despres JP, Arena R, et al. (2015) Physical activity and cardiorespiratory fitness as major markers of cardiovascular risk: Their independent and interwoven importance to health status. Prog Cardiovasc Dis. 57(4):306-314.
19. Lee DC, Sui X, Artero EG, Lee IM, Church TS, et al. (2011) Long-term effects of changes in cardiorespiratory fitness and body mass index on all-cause and cardiovascular

disease mortality in men: The aerobics center longitudinal study. Circulation. 124(23):2483-2490.

20. Kwon SB, Ahn JW, Lee SM, Lee J, Lee D, et al. (2019) Estimating maximal oxygen uptake from daily activity data measured by a watch-type fitness tracker: Cross-sectional study. JMIR Mhealth Uhealth. 7(6):e13327.
21. Clarke DC, Skiba PF (2013) Rationale and resources for teaching the mathematical modeling of athletic training and performance. Adv Physiol Educ. 37(2):134-152.
22. Thayer JF, Yamamoto SS, Brosschot JF (2010) The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. Int J Cardiol. 141(2):122-131.
23. Ori Z, Monir G, Weiss J, Sayhouni X, Singer DH (1992) Heart rate variability: Frequency domain analysis. Cardiol Clin. 10(3):499-533.
24. Singer DH, Ori Z (1995) Changes in heart rate variability associated with sudden cardiac death. Heart Rate Variability. pp. 429-448.
25. Spruijt-Metz D, Hekler E, Saranummi N, Intille S, Korhonen I, et al. (2015) Building new computational models to support health behavior change and maintenance: new opportunities in behavioral research. Transl Behav Med. 5(3):335-346.
26. Ori ZP (2021) Medical cybernetics for continuous risk assessment and management of insulin resistance and related complications. 2021 International Symposium on Biomedical Engineering and Computational Biology. pp. 1-5.
27. Ori ZP (2019) Integrated cyber-physical system to support early diagnosis and prevention of prediabetes and complications of type 2 diabetes. Type 2 Diabetes-From Pathophysiology to Cyber Systems.
28. Ori Z (2022) Wearable sensors for monitoring personal health and supporting recognition of medical urgencies. Curr Res Emerg Med. 2(4):1032.
29. Ori Z (2022) Striving for diagnostic excellence in emergencies by using principles of personalized prevention and medical cybernetics. Curr Res Emerg Med. 2(7):1047.
30. Gay V, Leijdekkers P (2015) Bringing health and fitness data together for connected health care: mobile apps as enablers of interoperability. J Med Internet Res. 17(11):e260.