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Advances in Health Technology Use and Implementation in the Era of Healthy Living: Implications for Precision Medicine

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ABSTRACT

Much of the focus of precision medicine has been directed toward genomics, despite the fact that "lifestyle and behavioral factors" are included in the description of precision medicine. Numerous structured diet and PA interventions have demonstrated success in preventing and/or reducing chronic-disease risk. The use of personal health technologies has expanded exponentially in the health care arena; there are a number of consumer-based technologies yielding health information to individual users. The explosion in technology use provides an opportunity for broader dissemination of health care services and products. In addition, tracking cardiovascular disease risk and lifestyle and behavioral aspects of healthy living (HL) profiles in those products may be an important leveraging interface for precision medicine. This review will discuss and present an overview of current health technologies, their use in promotion of HL metrics and how this data may be integrated into venues that support HL and precision medicine.

Contents

Abbreviations and acronyms: AFib, atrial fibrillation; AI, artificial intelligence; BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; DBP, Diastolic blood pressure; ET, exercise training; HLIs, healthy living interventions; HL, health living; HLM, health living medicine; HTN, hypertension or hypertensive; NCD, non-communicable disease; PHI, protected health information; PA, physical activity; SBP, systolic blood pressure; QOL, quality of life; WT, wearable technology.

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Overview of healthy living and lifestyle in precision medicine

Healthy living (HL) medicine (HLM) is an emerging health concept to promote the prevention of non-communicable disease (NCD). NCD is a global health concern with continually increasing prevalence rates. For example, cardiovascular disease (CVD) is a leading health concern with over one in every three Americans having one or more types of CVD; nearly the same percentage has hypertension (HTN).[1] In fact, nearly 70% of United States (US) adults now meet the revised definition of elevated systolic and diastolic blood pressure (SBP and DBP) according to the most recent guidelines (SBP ≥ 120–<140 mm Hg; DBP ≥ 80– < 90 mm Hg).[1,2] Many of those with elevated BP are not aware of their condition,[1] and very few who receive treatment have their BP under effective control.[1] The links between CVD and HTN show that a cluster of risk factors, including obesity and physical inactivity, occur and significantly contribute to risk. Taking a broader view, NCDs seems to share a cluster of risk factors for their development which include physical inactivity, smoking, high blood sugar, obesity, dyslipidemia, and poor nutrition. The four primary pillars of HLM are ideally suited to combat these risk factors and include: 1) More physical activity (PA) and less sitting; 2) Healthy diet consumption and appropriate caloric load; 3) Healthy body weight maintenance; and 4) Not smoking.[3,4]

The importance of lifestyle as a cornerstone to a prevention intervention can be viewed in light of its ability to reduce the impact of a multitude of CVD risk factors as well as other NCDs. The advocacy for and promotion of HL programs that may prevent or reverse the development of NCD risk factors and their clustering is a critical approach to address these issues in our aging population.[5] In particular the use of emerging and mainstream health technologies by the public and health care systems may provide an important window for HLM integration and implementation across the health care spectrum.[6] However many of the data that support standard recommendations and guidelines to promote HL guidelines, such as 150 min daily of PA and eating diets rich in fruits and vegetables, have not been tested using modern era HL technologies such as mobile health communications, mobile health monitoring, activity tracking and electronic media.[4] Lifestyle interventions that use mobile health technologies to promote HL behaviors will certainly inform the consumer and health professionals about which interventions are most effective. Robust technology-based data and informatics analysis will inform effective prevention, diagnosis, and treatment strategies and PA guidelines focused on precision medicine (see model in Fig 1). Research questions that address how these technologies may be used to implement health living interventions (HLIs) in health care settings and in the community will be important for maximizing technology utilization in the era of precision medicine.

Overview of technology in precision medicine

Precision medicine, innovative in its position on patient care and long-term outcomes, fundamentally relies on the ability to customize and personalize treatment plans specific to a patient's genetic makeup behaviors, and lifestyle. This kind of decision-making in patient care has only become more frequent and more accessible with the rise of massive data collection. With over 160,000 mobile health apps in commercial app stores[7] and an estimated $485 million in annual shipments of wearable technologies by 2018,[8] current smartphone users are commonly collecting their own healthcare data in massive amounts. Patients are using technologies developed from commercial consumer-based perspectives as well as health-organization and academic institutions, often collecting huge stores of personal health data by either inputting tracked information or using wearable technology to submit vitals to a database in real time. Given these developments, informatics researchers, with increases in data mining workshops and education on research methodologies for informatics technology, have been able to conduct broad and pivotal investigations on large population data in addition to making wide contributions in genomics research, attempting to "provide insight into the health of families, communities, and larger populations"[9] and provide "an understanding of how population interactions with our local, regional, and global environments may affect health outcomes."[9] Where these advances in data technology have increased, the prevalence of data mining for informatics research and genomics, decision-making in precision medicine is continuing to rise. However, this boom in accessible patient data collection brings additional challenges for the acceptance and use of this data. As patients track their own statistics technology, data reliability is questioned; furthermore, with collection of patient vitals using wearable technologies, discussed later in detail, protected health information (PHI) privacy and security is questioned as well. Though technology is already being used by both patients and precision medicine practitioners, there are abundant technological resources and little clinical control over the quality of each innovation. That being said, in order to maintain clinical efficiency and truly utilize the power of precision medicine for HLM, current technologies will be necessary for powerful and accurate decision-making in a fast-paced clinical environment in order to individualize care quickly (Fig 2).

State of current technology use in healthy living

A vast range of technologies already exist for personal health management, with focus ranging from daily data entry to new techniques in intrinsic user motivation. Online health and lifestyle management programs, or *e-health* programs, and mobile applications (apps) designed for healthcare, or *m-health* apps, primarily strive to provide

Fig 1. Working model of consumer health-based technologies in the community and during activities of daily living.

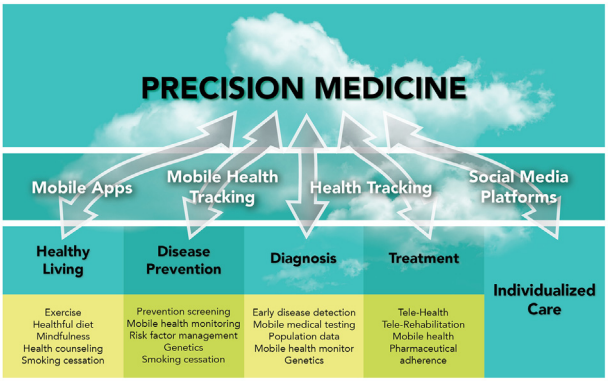

Fig 2. Proposed model of health technology implementation in the health span from prevention to individualized care. Cloud based data analytics through health technologies may provide the tool to implement individualized health and precision medicine.

users with resources for behavioral change, including lifestyle tracking, patient data monitoring, educational content, and accessible support networks.

Currently, with the plethora of available products on the Google Play Store and iOS App Store for healthy lifestyle management, users have limitless options to guide their health, nutrition, and PA using technology. Though many of these eHealth or mHealth initiatives were developed as clinical study stimuli for various health/research organizations, the wide majority are commercially available consumer-based apps, which tend to focus on a larger, more broad audience. One of the most popular consumer-based mHealth apps, *MyFitnessPal*, has reported nearly 100 million installations from both the Google Play Store and iOS App Store[10] in part due to its wide accessibility for users of all demographics and health conditions to begin self-tracking nutrition and PA data. These apps provide users with accountability and improvement metrics, access to curated nutritional and exercise information, and strategies for support in behavioral modification.[10] However, issues with these commercially available apps include a lack of scientific review; though the iOS App Store conducts stringent reviews on the usability and accessibility of each application, mHealth apps have no requirements for their own accuracy, safety, or efficacy.[7] Regarding apps/technologies deployed by health organizations, though information is carefully developed and revised by the scientists involved, many of the products suffer from missing the user experience design of most commercially available apps and a lack of social motivational aspects. There is no question that successful apps have been deployed for both consumers and for research purposes for HLM. However, the most successful initiatives from either development perspective are user-centered and developed iteratively, delaying or inhibiting any analysis of long-term outcomes.

With the massive limitless growth in smartphone,[11] mHealth initiatives in particular have seen immense expansion. Patients that turn to technology for their lifestyle management may already be facing the challenges of poor health lifestyle and difficult physician-patient communication; for both consumer-based and health organization-based mHealth apps, additional challenges for patients include poor user interface design and a disparity between knowledge provided and personal health literacy levels. Many mHealth products provide what is considered a "key component of lifestyle intervention for obesity",[12] self-monitoring, or self-tracking capabilities for diet, weight, and movement. Obesity interventions require self-tracking and management as a major component of lifestyle change, and this kind of mHealth functionality directly contributes to that daily management goal. However, success of those self-monitoring tasks in an app are balanced against the app's ease of use and consistency in data entry; though already identified as highly successful for helping users manage body weight individually, the time-consuming burden of data logging can easily deter users from returning to the app.[13] Other mHealth products pertain to specific disease populations, like mAsthma apps and Diabetes apps that allow for self-monitoring for user-specific vitals to provide management techniques for less broad audiences.[14] In the AsthmaMD app, for example, chronic disease management still required self-surveillance, but the data collected was able to be compared to that population's specific goals and metrics. In one systematic review, Kenner found that overall, mHealth apps truly can "transform the way that health is understood, promoted and managed," however the app's content must be thoroughly evaluated and regulated to give any value to the consumer.[15]

While apps like *MyFitnessPal* request user input to track their own statistics, sometimes facing user drop-off due to time consumption from data-logging, the *wearable technology (*WT) sector of mHealth apps require users to simply wear a product, which will collect corresponding data continuously without necessary user involvement. WTs also include those in the sector of telerehabilitation, using a combination of at-home rehabilitation intervention and mHealth/eHealth products. "With an estimated growth of $485 million in annual shipments by 2018" WT is growing rapidly in the consumer market allowing users to possibly improve or change lifestyles by monitoring PA or vitals with zero data entry for unlimited time.[16,17] Much like general mHealth apps, the large majority of WTs were developed for general audiences, gauging vitals like steps/distance covered walking, heart rate, and sleep patterns.[17] Other types of WTs pertain to specific disease populations, including diabetes, chronic obstructive pulmonary disease, asthma, and CVD.[18] In Pevnick et al.'s framework for cardiology-specific WT, WTs include wearable monitoring devices for: ECG, heart rate, daily activity, and hemodynamic technologies.[9]

In addition to mHealth and WTs, telephone-based and eHealth interventions hold their own value, offering accessibility in rural areas or for poorer populations.[12] What's more, these programs often offer personal feedback that many mHealth and WT initiatives lack, potentially providing a more human connection, understanding, and personal accountability. In one review, it was determined that the most effective eHealth interventions explicitly included regular feedback from interventionists. In another study highlighting diabetes app use, researchers concluded the central drawback of the app was a lack of personal motivational support, often causing the app to be ineffective in aiding self-management. Elements like personal support and real-time feedback from eHealth initiatives hold strong value, but have fallen short in the wake of mHealth research due to massive amounts of promising data from smartphone use.

Current technologies already have a broad influence in healthy lifestyle management in all audiences; however, these technologies fall prey to the same issues that negatively affect more standard interventions, including a lack of consideration toward personal attitudes, environment, and behavior regarding the intervention, leading users to eventually discontinue use from the app or the intervention altogether.

Clinical studies and the state of the evidence

Obesity and diabetes

With the increase in use of smartphones all over the world, their application to healthcare is crucial especially in the realm of lifestyle management. Since smartphones are an item that people carry with them all the time, using them to manage everyday choices such as nutrition, exercise and weight loss is a very effective use of this technology. In fact, they have been shown to be effective at improving people's lifestyle choices. In a 2013 study conducted by Turner-McGrievy, participants were given mobile apps that helped them either with diet management or exercise management, or were placed in the control group which had no mobile app.[19] The groups that did use the mobile apps ate fewer calories and had more PA than their respective counterparts.[19]

Patients with obesity have also benefitted from mobile health from a variety of applications in their weight loss process.[20] There are some studies which have focused on SMS (instant messaging) technology similar to that which is available on most cellular phones.[20] One randomized controlled trial study was designed with two intervention groups whereby obesity-specific text messages were sent to subjects daily, while the control group just had general health and standard-of-care text messages sent to them daily. Importantly, the results showed that the groups with obesity-specific text messages had more weight loss than the control standard of care text messaging group.[21] These findings highlight the importance of personalized content and messaging relative to the disease and designed for optimal weight loss outcomes.[21]

In another study subjects were assigned to either daily text messages and a Facebook group with daily posts, Facebook social media posts alone, or a control group. Results from this study found that the addition of text messages to social media intervention was more effective than Facebook alone at successful weight loss.[22] Other studies in obese adults have noted the importance of combining standard physician interaction care and mobile care that involves self-monitoring of

diet and PA, for achieving significant (>5%) weight loss.[23] In a recent review of clinical trials, Bhardwaj et al.[24] compared the efficacy of various obesity-related mobile health aps on anthropometric indices of weight loss (e.g., body weight, waist circumference and body mass index [BMI]), as well as on lifestyle behavior (dietary and PA), and patient adherence and satisfaction.[24] Of the fourteen studies that tested for a change in body weight, nine studies reported significantly greater weight loss in the mobile app intervention groups. However, the effectiveness of the interventions on body weight reductions were not universal.[25] Of course, there may be various psychological features of the applications which may influence usability and effectiveness in various populations. These features require specific testing in populations in which they are designed to foster weight loss.[25]

Studies that have solely focused on enhancing diet behaviors, using mobile apps such as the SmartAPPetite have demonstrated associations between increased interaction with the app and consumption of healthier food options.[26] Studies that aim to optimize PA have similarly reported increased PA behaviors with mobile app utilization, and intervention participants randomized to the app, particularly demonstrated higher adherence to the app versus controls, suggesting that mobile health apps may help to facilitate long-term behavior change.

Wearable technologies and CVD events

The advent of health tracking wearables and smartphones not only allows for new methods of treatment and therapy, but also serves to help aid in the diagnosis of a medical issue as well. Certain CVD events, such as atrial fibrillation (AFib) and other arrhythmias are potentially life-threatening conditions that affect over 33.5 million people worldwide.[27] According to experts, identification of arrhythmias is crucial to preventing millions of future strokes, heart attacks, and ultimately, hospitalizations.[28]

As with any other physiological disease, identification and diagnosis of the disorder is of the utmost importance. It is a crucial first step that must be taken in order to begin improving a patient's quality of life (QOL). However, arrhythmias are often difficult to diagnose since the symptoms may only appear sporadically and cease before the patient is able to meet with a cardiologist. In such an event, the cardiologist would prescribe the usage of an obtrusive and long-term cardiac monitoring system in an attempt to catch the adverse CVD event. Recently however, another option has become increasingly viable from a cost and quality standpoint. Consumer friendly ECGs such as AliveCor's Kardia Mobile has presented patients and health providers with a lifestyle friendly alternative to the traditional Holter monitor. Offering "30 second EKG" snapshots into the user's cardiac health, the device creates more opportunities to capture and diagnose cardiac events even if the doctor is working remotely. In such a situation, one might be led to believe that a doctor working remotely can be damaging to healthcare, as it is by nature indirect and impersonal. Contrary to these concerns, evidence from remote monitoring studies have shown to reduce the time, effort, and cost required to visit the clinician, with additional improvements demonstrated with patient satisfaction, as well as accuracy of the diagnosis.[29] Another study conducted in a university hospital in Wales, usage of the device even lead to a "4x increase in AFib detection" over a control population in a study of 1000 seniors.[30] Cardiac wearables are also increasingly able to offer healthcare advice on their own with cardiac analysis AI. If a doctor is not immediately available, the device itself is capable of providing diagnosis of certain CVD events with high sensitivity and specificity comparable to professionally read 12-lead EKGs.[30] (https://www.alivecor.com/press/press_release/new-research-confirms-significance-of-alivecors-30-second-ekg/). Even with the availability of a health care provider, for the patient, the ability to conduct a self-recording when symptoms are felt lends agency, security, and most of all efficacy in their own healthcare. In one study, 100% of patients who recorded their ECG after feeling symptoms and self-reported this to a doctor were later diagnosed with a cardiac issue with a median time to diagnosis of as little as nine days.[30] In another study, 93% of patients who used the device said it "lessened AFib-diagnosis anxiety", thus serving to improve not only their physical health, but their mental health as well.[31]

Technology and cancer related complications in precision healthy living

There are almost 13 million cancer survivors in the US.[32] In the last few years, mobile technologies have contributed to prevention, diagnosis, treatment, and follow-up in the field of cancer. In particular, evidence of improved adherence to prevention and screening visits have been effective with mHealth interventions. For example in skin cancer, a study that used text messages as a reminder strategy to improve adherence to wearing sunscreen showed that participants who received text-messages were nearly twice as adherent to a regimen of daily sunscreen application compared with control participants not receiving reminders.[33] Several mHealth intervention strategies have been implemented to address breast cancer. For example a recent investigation of the effect of mHealth with pedometer use on physical function and QOL among breast cancer survivors found that both indices were improved following the mobile health intervention.[34] Quintiliani et al. demonstrated the feasibility of an mHealth-supported behavioral counselling intervention among breast cancer survivors and found some positive physiological (e.g. reduced body weight) and behavioral changes (e.g. increased PA).[35] A patient-centered, Web- and mobile-based educational and behavioral mHealth intervention strategy was used to assess patients' lymphedema symptoms with high reliability and validity, and was able to improve strategies for lymphedema symptom management.[36] Tele medicine may also assist in the precision medicine of cancer care by informing consumers on cancer related complications. For example, a large, prospective, randomized, single-center study of over 700 patients undergoing chemotherapy for metastatic tumors was conducted to follow patient-reported outcomes via a web- based interface for symptom monitoring during treatment.[37] In addition to showing improved health-related QOL in the intervention group, there was also decrease in healthcare utilization in terms of emergency room (ER) visits and hospitalizations in the intervention group.

The benefits of PA in cancer patients is well known to include improved QOL, improved physical function and possible reductions in recurrence rates in some patients.[38] More than 83% of adults aged 50–64 and 56% of adults aged 65 and over have access to high-speed internet making mobile technologies an important opportunity in cancer survivors to engage in a health provider delivered electronic health delivered PA.[39] Courneya et al. particularly found that breast cancer patients undergoing supervised exercise training (either aerobic or resistance exercise) during chemotherapy showed a strong trend ($p = 0.09$) toward improving event free survival and reducing recurrence rates over a median 8 years follow-up.[40]

While the optimal mobile health communication medium is not well established for improving PA in cancer populations, several studies have suggested mobile technology focused interventions are feasible as an outlet to deliver behavior modification recommendations.[41] A study by McConnell et al. found that delivery of an app based weight loss intervention with embedded exercise and nutrition counselling was feasible at reducing body weight.[42] They found that 4 weeks of the intervention was effective in reducing body weight and improving PA (calories expended) in obese cancer survivors with a cancer diagnosis in the previous 3 years.[42] In a comparative analysis another study found that a telemedicine platform (weekly telephone counselling) was more effective at weight loss than a text messaging (3–4 text messages per day) based weight loss intervention in a cohort of women with a diagnosis of endometrial cancer.[43] Interestingly, the same group reported that when both interventions were compared to enhanced usual care, the usual care group demonstrated significantly greater PA than the text and telemedicine arms suggesting that interventions in

this population will require precise optimization based on the targeted outcome (e.g. weight loss vs. PA).[44]

There have been a few randomized controlled trials focused on technology effectiveness on PA in cancer populations. One such example is a recent RCT which showed that a web based health education intervention for 6 weeks showed a greater reduction in insomnia and increased PA measured in daily steps taken than the control group.[45] This program of chronic disease self-management program was implemented with 2 program facilitators who were experienced in chronic disease management and allows for customizable and personalized disease management goals.[45] Further research into the customizability of healthy living interventions using technology in patients with cancer appear warranted.

Role of mHealth in smoking cessation

Tobacco use is a leading preventable cause of death in the US[46] and >480,000 tobacco related deaths per year.[47] While today's smoking rate is lower than years past, progress may have reached a plateau. Furthermore, the increased use of non-cigarette tobacco products and the introduction of new smoking products (e.g. e-cigarettes) maintain tobacco use as a strong lifestyle risk factor that increases the risk of elevated blood pressure and other CVD.[48] Attempts to make the general public aware of the well documented correlation cigarette consumption has with cancer and CVD are still ongoing.[49] Strategies for precision medicine approaches to smoking cessation interventions require matching the unique characteristics of the individual and include: attitudes and self-efficacy for quitting, individualized barriers such as perceived and real weight gain, cultural barriers and factors, and biological nicotine metabolism.[50] Individual tailored interventions for smoking cessation using technology platforms appear to have made some traction. A recent met-analysis found that comprehensive telephone interventions that included exercise education and smoking cession, and dietary advice demonstrated reduced risk for hospitalization following myocardial infarction (MI) and demonstrated more effective rates of smoking cessation.[51] In another recent clinical trial incorporating text messaging with health advice into a primary care implemented smoking cessation program there was a benefit (24%) on effective 6 month cessation rates over those who received health information alone (11%).[52] Another recent trial found that exercise interventions combined with smoking cessation counselling was more effective than health information and counselling alone following the intervention after a year of follow up.[53] A recent systematic review of studies evaluating mobile phone apps aimed at reducing tobacco offered mixed evidence for improvements in quitting rates. Interestingly, user engagement and adherence to app features may be an important feature of whether or not individuals may quite smoking.[54] In one comparative study of smart phone app versus text messaging, those that were assigned the phone application did not demonstrate fast quitting rates than a text messaging intervention in a young adult cohort.[50] Certainly, the implementation of individualized preferences and incentives toward smoking cessation is an important area of future effectiveness research in consumer health technologies for precision medicine.

Emerging technologies

AI developments may be brought into eHealth and mHealth initiatives to supplement apps with personal affect that some users may find lacking in many current products.[55] Giving a customizable, singular, and humanized voice to the product may allow eHealth and mHealth products to "provide specific and congruent feedback to consumers, ask the need for clarification and elaboration, and answer any questions users may have to make sure they understand the information provided and what their different health decision options may be".[55] By humanizing these seemingly time-intensive experiences, AI can strategically promote engagement so that consumers continue daily use and prevent the user drop-off rates seen by so many mHealth products.[55]

Machine Learning initiatives, sharing AI's computational algorithms based on user input, shows great immediate potential for use in precision medicine technologies as well. Much like precision medicine, ML algorithms "have emerged as useful analytical methodologies, undoubtedly due to the rise of big data. Typically, the machine/computer learns from a training set of data where outcomes are mapped to specific data characteristics." One investigation used machine learning to coach users on PA and personalized health training, based[56] on the dataset of the individual participant and creating a tree-algorithm to create specific individual algorithm parameters to predict how to improve patient performance.[53] This creation of personalized goals, using ML, AI, or both, can provide the opportunity for technology to customize itself to an individual's preferences and goals.[57] According to an investigation by Tang et al., non-tailored or non-customized mHealth apps proved difficult to users to integrate into their own lifestyles.[58] Users indicate that they enjoy using and want to use mHealth and eHealth technologies. Similar to precision medicine, developing these technologies to incorporate user data analytics into behaviors and design has great potential to increase user engagement and prevent these patients from discontinuing use of the app.

Direct to consumer genetic testing

There is a number of direct to consumer genetic testing kits that can be purchased online or available over the counter. Examples include 23andMe, Helix, Color. These services are centered on applications that include ancestry analysis and reporting, CVD risk assessment, cancer risk assessment, pharmacogenetics, genetically guided nutritional recommendations etc.

The clinical utility and accuracy of such services have been reviewed by several researchers as reviewed by Covolo et al.[59] While this review is beyond the focus of the current paper, this consumer data is an important aspect of the integration of data on genetics and risk assessment that may be important in future precision medicine clinical trials using technology.

Conclusions and the future of wearables and consumer health technologies in precision medicine

There are opportunities for consumers and health care professionals to leverage health technologies especially mobile health technologies in their daily lives and practices (see model Fig 1). These new technologies will become more broadly used and sought after as the cost for technologies continues to fall. The development and future use of real time, mobile, continuous measures of health metrics such as blood glucose, blood pressure and heart rhythm may be critically important in preventing CVD while also providing consumer driven input on health status in real time. According to the Food and Drug Administration these mobile health apps will require oversight and regulation before approval given the safety implications of such measures.[55] However, once implementable, these data points will also provide robust research opportunities for predictive measures, AI and algorithm development for healthy lifestyle and behavioral interventions in precision medicine and in healthy living (see model presented in Fig 2).

Statement of conflict of interest

None of the authors have any conflicts of interests with regard to this publication.

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