**RC25540 (WAT1507-012) July 8, 2015**
**Computer Science**

# IBM Research Report

## Next Generation Wellness: A Technology Model for Personalizing Healthcare

**Pei-Yun Sabrina Hsueh, Henry Chang, Sreeram Ramakrishnan**
IBM Research Division
Thomas J. Watson Research Center
P.O. Box 218
Yorktown Heights, NY 10598 USA

# Next Generation Wellness: A Technology Model for Personalizing Healthcare

PEI-YUN SABRINA HSUEH, HENRY CHANG, SREERAM RAMAKRISHNAN
IBM T.J. WATSON RESEARCH CENTER

ABSTRACT

Personalization or individualization of care is essential to the behavioral modifications and lifestyle changes that result in patient wellness (for good health or chronic disease management). The implementation of effective personalized care is hampered by the lack of reliable means to collect and process real-time data on individual contexts (preferences, constraints) and on adherence to care protocols and mechanisms to provide timely, customized cognitive coaching that is structured, consistent and informative to users.

The advent of personal embedded biosensors is creating an accumulation of patient-generated data from numerous “touch points” (data interfaces and exchanges between patient and healthcare services before, during and after traditional clinical encounters). A major technical challenge is the establishment of a patient-centered infrastructure that can:

- Provide the customized, timely, evidence/knowledge-driven messaging based on data from multiple touch points for continuous feedback to individual patients
- Support this functionality within an information infrastructure of multiple service providers to provide access to unified views of patients’ data across touch points and time for multiple users (patients, providers, administrators, researchers)

We propose the implementation of a cloud-based platform to support the analytics and other services to implement this infrastructure. From an IT perspective, we explore

- Modeling of patient contexts (preferences, behaviors) within a risk-based framework
- Calibration of individualized, evidence-based recommendations based on patient-generated data
- Deployment of analytics functionalities within the platform model

## 1. INTRODUCTION

### 1.1. PERSONALIZED HEALTH AND CARE

Personalized healthcare [Adams et al. 2010; Goodman 2009; Christensen et al. 2008], highlighted by President Barack Obama’s 2015 initiative on “precision medicine”, can be defined as “[disease] prevention and treatment strategies that take individual variability into account” [Collins and Varmus 2015]. System biologists have extended this concept as “P4 Medicine” (personalized, predictive, preventive, and participatory) [Hood and Friend 2011] to incorporate personalized healthcare that actively engages patients, since it is estimated that more than 60 percent of “health” is based on patient contexts, that is: behavioral patterns, social circumstances and environmental exposures [Schroeder 2007; McGinnis et al. 2002].

As populations age, the prevalence of chronic and pre-morbid conditions (such as obesity) rises, and with them the overall cost of healthcare. In Japan, seniors (those over 65 years) represent 21% of the population and in the United States (US), the ratio of seniors to non-seniors is projected to increase by 80 percent in coming decades [US Census 2012]. According to the Agency for Healthcare Research and Quality [AHRQ 2014], more than 84 percent of US healthcare costs go to chronic care, with its annual cost amounting to $1.65 trillion (or 15% of the gross domestic product (GDP)) [CMS 2012].

Longitudinal studies have shown that tailoring lifestyle interventions can reduce the burden of chronic disease, through primary prevention (e.g., Finnish Diabetes Prevention Study (FIN-D2D) [Saaristo et al. 2001; Tuomeilehto et al. 2007], US Diabetes Prevention Program (DPP) [DPP 2002; DPP 2008], China Da Qing IGT and Diabetes study [Pan et al. 1997]) and secondary prevention via targeted screening (e.g., the US Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (DCCT/EDIC) [DCCT/EDIT 2005] and the UK Prospective Diabetes Study (UK PDS) [Turner et al. 1998]). Quantification of the benefits of such tailored interventions has demonstrated a 42% risk reduction (RR) for all cardiovascular disease events, 57% RR for nonfatal heart attacks, strokes or death from other cardiovascular causes [Stampfer et al. 2010] and 58% RR for Type 2 Diabetes Mellitus for patients with impaired glucose tolerance [Tuomilehto et al. 2001].

Despite this, personalized healthcare has not gained traction as might be expected for wellness, prevention and chronic disease management. Patient-Centered Medical Home (PCMH) models [Peikes et al. 2012] have faced challenges in transforming current encounter-based practice into truly patient-centered care. Improving case management guidelines [CMSA 2004] for coordination of care alone does not appear to solve the problem. There is need to engage and empower patients in their own care, using strategies that incorporate individual variability and that gives patients incentives and access to evidence and data to assert themselves in crucial healthcare discussions and decisions.

## 1.2. CHALLENGES IN ACHIEVING PERSONALIZED HEALTH AND CARE

Existing care delivery is structured on applying evidence-based guidelines to the care of individuals at risk. Guidelines are population-based, that is, they are designed to serve average patients, with the assumption that one guideline “fits all”. An example of this is the standard JNC7 high blood pressure guideline [Chobanian et al. 2003] which uses a single rule, i.e., whether a patient’s systolic blood pressure (SBP) is higher than 135 mm Hg, to determine the prescription of anti-hypertensive therapy, which may not be optimal for diabetic patients (for whom a lower SBP threshold may be more appropriate). Studies have shown that overall, at least 45% of patients do not receive recommended care and that there is large variation in guideline implementation [Grol 2001; McGlynn et al. 2003].

Measuring patient variability is difficult as there are few standard proxy measures to assess different contexts. This difficulty extends into assessing baseline and adaptive contexts (abilities and preferences) in individual responses to specific interventions (that include habit formation, non-adherence, aversion, etc). Thus, patients frequently make “free-style” decisions, without adequate guidance, resulting in low adherence rates (estimated to be less than 50 percent, with one example being a report of 20-30% of prescriptions left unfilled [DiMatteo 2004]).

The financial potential is compelling. The estimated worldwide cost of non-adherence is $30 to $594 billion dollars annually [Luga and McGuire 2014]. In the European Union alone, non-adherence accounts for 194,500 deaths and adds 125 billion euros to the costs per year [PGEU 2008]. In the United States, non-adherence has been estimated to account for 69% of hospital admissions, adding $100 billion and $290 billion annually in terms of excessive hospitalization and avoidable medical spending respectively [IMS 2013]. Stakeholders in healthcare spending, such as self-insured employers, have taken interest and action [RAND 2014].

## 1.3. PERSONALIZED HEALTHCARE, PATIENT EMPOWERMENT AND TECHNOLOGY

To overcome challenges inherent in realizing personalized healthcare:

a) **Physicians and healthcare systems must recognize patients as full partners in the dialogue of evidence-based care**. In this dialogue, the patient is a source of continual, reliable, time-specific data (ongoing reports of point-of-care measurement: serial blood glucose, blood pressure, etc) and physicians and systems provide tools to facilitate active and ongoing two-way communication.

b) **Patients must be actively engaged as full partners in their individualized care.** Patients and families must use education and support to their best ability to make empowered decisions (with support from their providers) about their health and care. Patients must also generate information that prime analytics tools to identify "teachable" moments, to personalize messages according to patient contexts/challenges [Hsueh et al. 2015] and to mediate/mitigate non-adherence risk by tracking and optimizing the effectiveness of incentives [Sherman and Chris 2014].

To support this vision of an active ongoing health dialogue between patient and care team with a bi-directional real-time flow of information to and from the patient, wearable biosensor and cloud technologies are providing new opportunities and possible solutions for exploration.

***Mobile phones:*** The ubiquity of mobile phones provides an open terrain for communication and engagement, with the worldwide mobile health market expected to grow to $49 billion by 2020, with a projected annual growth rate of 49.7% in monitoring services.
One report revealed that 27% of mobile phone users "would like a personalized plan to help guide them through their journey to better health" [CEA 2014].

***Wearable biosensors and cloud platforms:*** Wearable patient monitoring devices are being developed to monitor asthma [Misra et al. 2012] and chronic obstructive pulmonary disease (COPD) [Patel et al. 2009] by tracking physical parameters (movement, heart/respiratory rates) via accelerometers and physiologic sensors. Sensors are also being developed to detect biochemical changes in sweat [Huang et al 2014] and to quantify changes in body movement in patients with Parkinson Disease [Maetzlera et al. 2013]. Non-invasive sensors have been deployed into smoking cessation programs to monitor a patient's smoking habits by monitoring breathing and hand-to-mouth gestures [Lopez-Meyer et al. 2013].

The market of "connected health and wellness devices" is expected to reach $8 billion by 2018. As the Internet of Things (IoT) and Machine to Machine (M2M) technologies and infrastructures mature, 20-50 billion connected devices are predicted to emerge around the world by 2020 [IMS 2012; ABI 2013]. The progressive integration of mobile sensors and cloud technologies is making possible "smart" personal health networks that are raising awareness of healthcare and health. As of 2014, the accumulation of patient-generated health data at finer levels of granularity has stimulated understanding of patient contexts (i.e., disease states, self-management capabilities, and preferences.

## 1.4. PERSONALIZED HEALTHCARE RECOMMENDATIONS AS A PLATFORM-BASED SERVICE

The vision of transforming episodic office-based practice into continuous data-driven patient-centered care requires a paradigm shift to unify care and information transactions (patient-generated data, information and recommendations about care) across "touchpoints" (i.e., all contacts between a patient and healthcare services across time, providers and settings (within and beyond face-to-face encounters)). One possibility, which we are exploring, is the use of a platform, that is, a data-brokering mechanism that connects consumers/patients to services/providers in real-time. In this service model, information can be exchanged wirelessly to provide real-time feedback loops of patient data, assessment and guidance that encourage participatory decision-making.

Cloud-based services are an intrinsic part of the platform approach, but they do not solve the problem entirely. Analytics tools must be available to process incoming health data from multiple sensors into meaningful outputs for interpretation and decision support by users (patients and providers). A major challenge with analytics has been the specification of functionalities to map clinical guideline-based recommendations to personalized care in a safe, effective and sustainable way. As such, healthcare has been slow to implement analytics [Davenport 2007] and thus, progress has been limited.

Other barriers to platform implementation have been:

- ***Uncertainties in the regulation of medical devices and health information assurance:*** As mobile and personal health information technologies mature, the definition of "medical device" becomes less clear. In previous years, the US Food and Drug Administration (FDA) cleared more than one hundred medical mobile applications (MMA) as its 510(k) medical devices, but it has also prioritized safety. The FDA further released the two guidelines on MMA [FDA 2015b] and its associated medical data storage systems (MDDS) [FDA 2015c]. In addition, non-alignment of business interests and the ever-changing regulatory environment for information assurance and security complicate data sharing among federated entities.

- ***Data capacity and costs:*** The sheer size of data has posed challenges to service providers, incurring the need to hire subject matter experts and IT support personnel to handle the quantity and formats of data. The high staffing expense in turn creates barriers to small- and mid-sized providers who do not have enough data volume to justify the costs of analytics and/or cloud services that may be needed.

## 2. A PERSONALZIATION FRAMEWORK

Our research investigates the feasibility of a sustainable wearable sensor-driven cloud-based analytics platform for providing evidence-based feedback based on patient-generated data. We introduce a technical framework for healthcare information personalization, and we begin by asking three questions:

1) How can patient contexts (abilities, preferences, choices, etc.) be modeled within personalized healthcare?
2) How can personalized recommendations be chosen/generated in response to patient data and contexts?
3) What is a vision for implementing these on a service platform?

### 2.1. INDIVIDUALIZED RISK STRATIFICATION

One model of patient contexts (abilities, preferences, choices, etc) poses such attributes in terms of the outcomes risk they confer upon a patient within diseases and treatments. The stratification of risk has been studied with regard to ICD-9 codes and claims data [Sloan et al. 2003] and in relation to patients' self-reported data on their chronic diseases to produce numerical scores [MacKnight and Rockwood 2001], [Charlson et al. 1987], [Elixhauser et al. 1998]. Using this model, analytics techniques have been used with electronic health record (EHR) data to:

- Detect abnormalities in healthcare delivery quality [Sloan et al. 2003]
- Identify significant associations between medication use and disease outcomes (Ex. heart attack risk and use of a specific drug, subsequently removed from the market) [Solomon et al. 2004].
- Identify risk factors for cardiovascular diseases for prediction [d'Agostino et al. 2008].
- Correlate health outcomes of patients with environmental data to analyze behavioral risk factors at the community level [Schaefer et al. 2011]

Similarly, "big data" analytics techniques have been used with genetic biomarkers from genomic databases to capture signals of risk-conferral:

- Correlations between gene expressions and exogenous data, such as physical activity and nutrition intake, have been proposed but not been studied extensively [Thorisson et al. 2005]. Complex diseases, such as obesity and metabolic syndrome may be associated with variable expression of thousands of genes across functional categories.
- High-throughput screening techniques have been applied to identify "dietary signatures" (i.e., sets of distinctive patterns in nutrients, non-nutritive food components and nutritional regimes that can influence the protein expression and regulate the progression of metabolic syndrome) [Roche 2006].
- Molecular analyses (e.g., differences in genes, gene expression, protein expression, and metabolites) are used to assess the relationship between clinical outcomes and individual variations. Such analyses can support individualized interventions based on individual genetic differences in addition to physical activity and other lifestyle choices on chronic disease management for better outcomes [Mori et al. 2009].

The term "sub-health" has been defined by the World Health Organization as a state between health and disease where standard tests may be normal, but in which a patient is in distress or at risk for ailments. This is the conceptual basis for modeling contexts as contributors to a patient's sub-health or risk status [Lloyd-Jones et al. 2010].

## 2.2. INDIVIDUALIZED GUIDELINES FOR WELLNESS MANAGEMENT

An individualized guideline is an ideal that provides patient-specific feedback and recommendations with respect to the patient's contexts and data for optimal wellness management for chronic disease and prevention. As part of individualization, such guidelines (or programs) must include contingencies for acute illness (i.e., "sick" day management), for changes in patient responses over time, for different life circumstances (i.e., home vs work vs vacation vs school) and for their impact on patient contexts (i.e., stress) and management. An individualized guideline should also predict, prevent and overcome treatment resistance and failure.

As an example, the medical management of "diabetes mellitus" (DM) must be individualized:

- Type and severity of disease (Type I DM vs Type II DM) determine pharmacologic approaches. Type I DM typically requires insulin early in the course of the disease, whereas Type II may require it later
- Diabetic patients may be at higher cardiovascular risk (for heart attack and stroke), more so as they age
- Some therapies can increase insulin resistance in some individuals

- Exogenous insulin may increase cardiovascular risk, but better glucose control over time has decreases risk (U.S. Diabetes Control and Complications Trial [DCCT/EDIC 2005] and UK Prospective Diabetes Study (UKPDS) [Turner et al. 1998])
- Some patients with Type I DM may lose their ability to respond to hypoglycemia (low blood glucose) over time.

In this case, individualization of guidelines helps optimize medical care (drug choices depend on specifics of the illness), risk reduction (cardiovascular disease prevention depends on a number of factors, including diabetic management), wellness (day-to-day management depends on diet, exercise, weight management, medication adherence and other factors) and contingencies ("sick" days) to balance physiologic and individual needs as the condition evolves [Abrahamson et al. 2006]. In addition, measures of patients' self-efficacy and literacy may be useful in selecting and developing appropriate educational approaches and partnerships (such as with diabetic educators) [Burke et al. 2014].

Failure to accommodate individual needs may result in mixed effects on different individuals. In many cases, patient-generated health data (including self-reports and monitoring data) can provide important feedback on tailoring and customizing clinical recommendations to individuals. The importance of patient-generated health data in diabetes has been demonstrated in a study at the Juvenile Diabetes Research Foundation (JDRF), which shows that continuous glucose monitoring and individualized insulin adjustment significantly decrease hypoglycemic episodes [JDRF 2008].

## 2.3. COUPLING INFORMATION TO WELLNESS BEST PRACTICES

### 2.3.1.DATA

Mobile and wearable health devices can provide "real-time" patient data (vital signs, exercise, intake and exposure, surveys/assessments, etc.). PricewaterhouseCoopers' Health Research Initiative (HRI) [PwHC 2014] report on "wearables" has demonstrated that 21 percent of Americans are already using personalized technology (wristband/watches to record physical activity, sleep patterns, etc.) to measure and record biometric data. For example, the Apple HealthKit (Apple 2015) supports many observations: date of birth, height, weight, body mass, BMI, body fat percentage, blood pressure, heart rate, RR interval, respiratory rate, body temperature, oxygen saturation, spirometry, peripheral perfusion index, blood glucose, blood alcohol content, dietary intake – carbohydrates, fat, sugar, vitamins, number of times fallen, regular steps, distance, flights climbed, workout information, etc. that may impact on an individual's health. In addition to providing opportunities for health improvement and health IT development, these technologies provide a potential foundation for health and health informatics research, with great opportunities for investigators to develop and explore questions and hypotheses on wellness, interventions, diagnosis, and interventions, with new sensor features providing the potential for a wide array of data on populations (using "big data" techniques).

### 2.3.2.KNOWLEDGE

Knowledge on wellness and prevention that meets the needs and preferences of individuals can been divided into three dimensions:

a) Lifestyle programs that include regimens for managing nutrition, exercise, weight loss, relaxation, pain and stress (Example: customized daily cardiovascular fitness regimens)

b) Messaging tools that deliver timely, contextual messages to users to inform and encourage them at the right time and place (Example: a smartphone reminder about portion control prior to a scheduled social event)

c) Health state analysis and prediction tools that answer patient health questions from the literature and predict outcomes of recommended actions from published guidelines (Example: a patient-friendly summary of the relevant information from the Framingham heart study based on his/her cholesterol level).


In one commercial venture, IBM Watson (artificial intelligence/question answering system) and its capability to process natural language materials is being leveraged to help answer personal health questions from consumers [Welltok 2015]. Through a mobile interface connected to evidence-based knowledge sources, pre-processed by Watson, patients/users can participate more actively in the clinician-prescribed management plans. One challenge to widespread diffusion of this tool and approach is the need to meet the literacy/health literacy needs of patients/users, and its current principal market is employer-based health plans; patients must qualify for self-care (inferring a baseline literacy level for users). One possible vision is that such a tool can provide a focal point for social networking in health condition-related communities (e.g., patientslikeme) to extend patient engagement and empowerment in lifestyle interventions as a part of consumer-driven healthcare.

Fig. 1 “Ask Watson” mobile application

## 3 PLATFORM SUPPORT

We now explore system design requirements for a cloud-based platform that incorporates the personalization framework and support the necessary analytics. The personalization framework consists of four components that fit into clinical information workflow:

- Guideline-based personalized treatment plan: A clinical diagnosis triggers initiation of a condition-specific wellness management plan according to high-level guidelines with constraints. For example, for a diagnosis of “dyslipidemia” the recommended diet constraints are: “carbohydrates 50-60%; protein 10-20%; fat<=30%; total cholesterol <=300 mg; and fiber 25-35 mg” (e.g., National NCEP/ATP III guideline for blood lipid control [Grundy et al. 2002])
- Analytics-driven individualized guideline refinement: Analytics stratify an individual patient’s risk factors according to the patient’s longitudinal record in comparison to a cohort (patients of a similar age, gender and weight, etc.) for disease and risk mitigation strategies according to guidelines, patient/provider preferences and the patient’s needs (according to existing data). For example, a patient with a diagnosis of dyslipidemia with an extremely high fasting cholesterol level may be referred for genetic testing and intensive dietary and medical management.
- In-context outcome-driven personalized recommendation: A user profile specifies guideline recommendations for specific contexts (user preferences and abilities, day-to-day activities, vacation modifications) and filters and ranks them based on the patient’s current context (time of day, event). For example, reminders on diet and portion control may be scheduled prior to dinner at a restaurant (as noted in a patient’s personal calendar).

- Personalized feedback generation and service plan adaptation: Given an incoming data stream by a user, real-time messages provide feedback on adherence/compliance levels in response to defined abnormalities. For example, an unusually high blood pressure measurement may deliver a prompt to a patient for symptoms, inquire about medication adherence and suggest the blood pressure to be re-checked, with an accumulation of high blood pressure events over time.

We define service flow as a sequence of information operations in which some action (knowledge delivery, analytical calculation, mapping to a specific guideline) is invoked by data or other output. Within the personalization framework, the operations of the service flow require inputs from the patient (electronic record data, contexts, sensor data, etc.) and from systematic risk/benefit calculations of specific healthcare interventions (general guidelines) for the patient. These inputs are then mapped to individualized recommendations/guidelines (service plans) that are delivered as specific interventions (services) to the patient for wellness and disease management.

Our cloud platform consists of three layers that use HL7 CDA [Dolin et al. 2006] messaging to interoperate with other health information technology systems for care coordination:

a) The **information service layer** provides analytics utilities connected to other platform components via messaging protocols
b) The **living service layer** orchestrates information services to offer personalization functionalities with application programming interfaces (APIs) that enable programmers to generate personalized information services that can be consumed and delivered
c) The **care solution layer** allows clinical case managers to "jumpstart" personalized care service offerings with simple configuration tools to specify user interactions and interfaces.

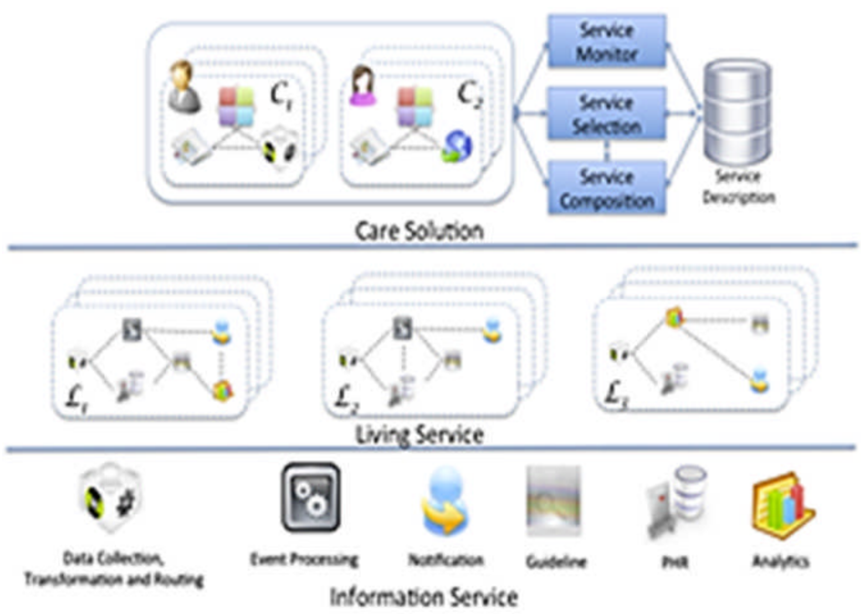


Fig. 2 Platform Support for Personalized Care Application Development

We now focus on analytics (information service layer functions) for three components/tasks of the personalization framework individualized guideline refinement, in-context outcome-driven recommendation and personalized feedback generation (The selection of a guideline-based personalized treatment plan, being triggered principally by diagnosis, requires no analytics within this framework).

### 3.1. SUPPORT FOR ANALYTICS-DRIVEN INDIVIDUALIZED GUIDELINE REFINEMENT

To initiate an active personalization cycle (design and implement an individualized guideline), the platform must absorb patient-centric information from multiple sources and identify predisposing risk factors. The platform must interact with a care provider to allow:

1) Profiling of the patient's personal wellness and health risks
2) Design of effective and interactive presentations of interventions with regard to the profile and contexts
3) Individualizing patient interaction with service options with regard to risk mitigation

To start, clinical and patient-generated data repositories are stored in a patient wellness record (PWR) on the platform [Hsueh et al. 2010]. For each disease or condition, individual risk stratification is performed based on the importance of patient contexts and data in relation to what is known about similar patients and/or what is specified by the care provider. Once the conferral of risks with regard to patient contexts (risk profile) has been performed, specific service plans (recommendations/interventions) are chosen and linked to visual objects/widgets to be presented to the patient for discussion and testing for acceptance and usability.

Therefore, one property that a platform must support is interactive guideline refinement for participatory decision-making, by which clinicians and patients can jointly make health management decisions that fit the patients' contexts (preferences, abilities, constraints, etc.). Once patients have navigated through service plan options with regard to specified constraints and preferences, guidelines can be refined according to perceived importance to generate personalized service plans ready for patient use.

### 3.2. SUPPORT FOR IN-CONTEXT OUTCOME-DRIVEN PERSONALIZED RECOMMENDATION

To complete an active personalization cycle (implement an individualized guideline), the platform must match services/recommendations according to a patient's contextualized needs. It must provide support for services/ recommendations that are reactive to what the patient does, situated in context and proactive to future steps in care.

To accomplish this, our platform provides:

i. Pre-screening (contextual factor analysis) uses analytics utilities that use low-frequency variations across specific risk factors [Pritchard, 2001] to identify risk or susceptibility in complex conditions. For personalized wellness management (in health and chronic disease), these include variations in: nutrition intake, physical activity, social network lifestyle, compliance behavior, and many other external environment factors such as air pollution. This yields a set of contextual risk factors.
ii. Modeling (context-driven personalized query) uses identified contextual risk factors to create context-aware queries as the input to the framework to search for suitable personalized service plans/recommendations.
iii. Post-screening (context-driven user model solicitation) uses filtering utilities to tailor model-generated recommendations with respect to patients' current contexts.

The product of these two components/tasks is a user-centered, context-aware disease management program, which is coupled with adherence monitoring, instant feedback and location-based recommendations.

### 3.3. SUPPORT FOR PERSONALIZED FEEDBACK GENERATION

To sustain the personalized healthcare design framework, the platform must assess incoming data streams for changes, generate interactive feedback and trigger individualized risk mitigation services/recommendation in a reliable and timely fashion. Therefore, two properties that the platform must support are: the detection and reliable identification of significant dynamic changes in incoming data and the ability to monitor for projected changes in incoming signals based on a user's health and wellness status.

## 4. DISCUSSION AND CONCLUSION

### 4.1. THE PLACE OF ANALYTICS IN PERSONALIZED HEALTHCARE

Although existing patient education and participatory decision support approaches that require in-person sessions have been shown as effective in initiating behavioral changes [Brown et al. 2007; Webb et al. 2010], they yielded mixed effects in sustaining behavioral changes. This is largely due to the lack of enforcement and reinforcement based on patient-generated data. The analytics and platform framework to provide this that we have described can help to sustain behavioral change.

The recent acceleration of mobile and sensor development has increased demand for context-aware recommendations systems [van Setten et al. 2004; Adomavicius and Tuzhilin 2008; Abbar et al. 2009] with experimentation to better capture contextual factors that matter for personalized recommendation [Zimmermann et al. 2006]. The rising trend of context awareness and intelligence opens up many new possibilities in the wellness domain (user-centered, context-aware disease management by instant compliance checking and location-based recommendations).

### 4.2. DATA QUALITY

An important issue in deployment of the system we describe is assurance of data quality and integrity. This is especially important for service platform when the data originates from multiple stakeholders (including the patient), more so because of the impact of the service provided (health recommendations to patients at risk).

One approach we have taken is to create a data quality monitor to determine whether an identified risk group is sufficiently representative to be used for predicting risk [Hsueh et al. 2010]. Specifically, the monitor follows possible sources of prediction errors in three major categories: risk group noise, case ambiguity, and noise-adjusted case ambiguity.

- Risk group noise quantifies deviations of the predicted and assigned risk from each risk group identified
- Case ambiguity quantifies average deviation of all predictions yielded on one single case, based on all relevant risk groups
- Noise-adjusted case ambiguity modifies case ambiguity scores reweighted with respect to the noise level of each risk group involved in case ambiguity determination

With the aid of the data quality monitor, developers can implement proactive learning programs to determine which data source to ask for future cases to analyze. When analysis results do not appear to be reliable, the monitor can also help filter cases that are ambiguous.

### 4.3. HEALTH RISK APPRAISALS

Health risk appraisals (HRA) are used by health plans and employer wellness promotion programs. These have also been used to drive treatment for targeted populations. For example, KP Care Management Institute's clinical trial in Hawaii (Eddy et al., 2010) showed that the treatments driven by individualized guidelines could prevent 6,000 myocardial infarctions (MIs) and strokes annually if applied throughout KP. The results can be translated into 43% of improvement over the JNC7 guideline for the same cost.

Despite the successful trials and pilots of HRAs in screening, diagnosis and prognosis, their use in computer-supportive personalized wellness management remains conceptual. Previously, government-sponsored trial programs such as Finnish diabetes prevention study group (Finland D2D) and U.S. Diabetes Prevention Program (DPP) have attempted to provide individualized wellness management by having health professionals manually analyze individual risk and send out personal reminders. However, such a labor-intensive operation is difficult to scale.

The movement to use innovative approaches to make care more patient-centered and accountable and coordinated would benefit from a personalization framework and system design on a service platform that are easily accessible, scalable and elastic.

### 4.4. INNOVATIVE MODELS FOR "OPEN WELLNESS"

Wellness management involves multiple business partners handling different healthcare and wellness issues, including physical examination and screening, physical activity coaching and nutrition regimens, etc. for chronic disease management. Many of these services can be transformed with better understanding of the target users. A service platform business ecosystem can allow health service providers in partnership to provide personalized services based on the shared knowledge of patients' current status and the level of their individual needs. This will help providers tailor patients' personal intervention plans accordingly in the context of their service provisioning.

Emerging opportunities for value-added services such as healthcare data brokering of patient-generated health data for exploratory and comparative effectiveness research, benchmarking for identifying useful attributes for quantifying patient populations of risk and provisioning and repurposing of analytics tools and methods are compelling. The resulting networks of providers could serve to further increase the business ecosystem efficiency and performance of personalization prediction and maintain a competitive edge of the participating service providers.

A major challenge of the ecosystem-based business model is sharing the burden of data protection (Grandison et al, 2012 and Hsueh et al, 2012). In addition to assuring the privacy and security of data within the system, there must consideration of governance regarding proper use and reuse of data and analytics products.

An industry vertical solution is thus expected to fill in the space and provide sustainable system support to the service providers who would like to add a layer of personalization analytics in their own service delivery systems. The development of cloud services that encompass a common personalization analytics component can provide use cases beyond utility computing.

Many new business opportunities, as a result, will emerge from an industry vertical solution that focuses on the ease of employing data-driven analytics approaches that are seemingly too sophisticated in the past and deploying data processing capabilities to handle a large amount of data on an incoming basis.

## 4.5. FUTURE WORK

In addition to the questions outlined in this chapter, our further explorations will involve cognitive modeling to provide insights into the causes of non-compliance and how to devise counter-strategies [Gonzalez et al. 1990; Prochaska et al. 1992; Elder et al. 1999; de Vries et al. 2008]. It is important to tie personalization technology to behavioral medicine regimens that focus on sustaining change.

## ACKNOWLEDGMENTS

Many thanks to our colleagues at the IBM T.J. Watson Center and Taiwan Collaboratory who developed the earlier prototypes of the system described here.

## REFERENCES

ABBAR, S., BOUZEGHOUB, M., AND LOPEZ, S. 2009. Context-aware recommender systems: A service-oriented approach. In *Proceedings of the 3rd VLDB International Workshop on Personalized Access, Profile Management, and Context Awareness in Databases (VLDB PersDB Workshop)*

ABI Research. 2013. More Than 30 Billion Devices Will Wirelessly Connect to the Internet of Everything. Available at: https://www.abiresearch.com/press/more-than-30-billion-devices-will-wirelessly-conne.

ABRAHAMSON, M. et al. 2006. Insulin-Treated Type 2 Diabetes: Balancing Physiologic and Individual Needs. Medscape Education.

ADAMS, J., MOUNIB, E., AND SHABO, A. 2010. IT-Enabled Personalized Healthcare. *IBM Institute for Business Value Report*.

ADOMAVICIUS, G., AND TUZHILIN, A. 2008. Context-Aware Recommender Systems. In Proceedings *of the ACM conference on Recommender systems (RecSys '08)*, 2008.

AHRQ. 2014. Medical Expenditure Panel Survey. Rockville (MD): Agency for Healthcare Research and Quality.

American College of Physicians (ACP). (2011.) Detailed Summary – Medicare Shared Savings/Accountable Care Organization (ACO) Program. Available at: http://www.acponline.org/running_practice/delivery_and_payment_models/aco/aco_detailed_sum.pdf.

American Diabetes Association. Standards of Medical Care in Diabetes—2014. *Diabetes Care* January 2014 vol. 37 no. Supplement 1 S14-S80.

Apple Inc. HealthKit (2015). URL: https://developer.apple.com/healthkit/ [Last accessed 22 April 2015].

Bardel A, Wallander MA, Svärdsudd K. Factors associated with adherence to drug therapy: a population-based study. *Eur J Clin Pharmacol*. 2007;63:307–314.

BROWN, L.L., LUSTRALIA, M.L.A., AND RANKINS, J. 2007. A review of web-Assisted interventions for diabetes management: Maximizing the potential for improving health outcomes. *Journal of Diabetes Science and Technology* 1(6), 164-174.

Butler M, Kane RL, McAlpine D, Kathol, RG, Fu SS, Hagedorn H, Wilt TJ. (2008). Integration of Mental Health/Substance Abuse and Primary Care No. 173 AHRQ Publication No. 09-E003, Agency for Healthcare Research and Quality. October 2008.

CARRELL, S.E., HOEKSTRA, M., AND WEST, J.E. 2010. Is Poor Fitness Contagious? Evidence from Randomly Assigned Friends. *National Bureau of Economic Research Working Paper* No. 16518.

Census Bureau. 2012 national population projections. Washington (DC): Census Bureau. Available from: http://www.census.gov/population/projections/data/national/2012/.
summarytables.html

Consumer Electronics Association (CEA) report. The Connected Health and Wellness Market. Online available at: http://www.ce.org/News/News-Releases/Press-Releases/2013-Press-Releases/CEA-Releases-Report-on-Dramatic-Rise-of-Connected.aspx.

Chang H, Chou PB, and Ramakrishnan S. An Ecosystem Approach for Healthcare Services Cloud. IEEE International Conference on e-Business Engineering, 2009 (ICEBE '09).

CHARLSON, M.E., POMPEI, P., ALES, K.L., AND MACKENZIE, C.R. 1987. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of Chronic Diseases* 40(5), 373-383.

CHOBANIAN, A.V. et al. 2003. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Journal *of the American Medical Association* 289(19), 2560-2571.

CHRISTENSEN, C., GROSSMAN, J., AND HWANG, J. 2008. *The Innovator's Prescription: A Disruptive Solution for Health Care*. McGraw-Hill, New York, NY.

CMS, Office of the Actuary, National Health Statistics Group. 2012. National health expenditures by type of sponsor: calendar years 1987–2012. Baltimore (MD): Centers for Medicare and Medicaid Services. Available at http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/NationalHealthExpendData/Downloads/tables.pdf

CMSA (Case Management Society of America). 2004. The Case Management Adherence Guidelines (CMAG-1). Retrieved October 16, 2004, from http://www.cmsa.org/cmag/[Context Link]

COLLINS, F. S. AND Varmus, H. 2015. A New Initiative on Precision Medicine. *New England Journal of Medicine* Feb 2015.

D'AGOSTINO, R.B. SR,, VASAN, R.S., PENCINA, M.J., WOLF, P.A., COBAIN, M., MASSARO, J.M., AND KANNEL, W.B. 2008. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation* 117(6), 743-753.

DAVENPORT, T. H. AND HARRIS, J. G. 2007. *Competing on Analytics: The New Science of Winning.* Harvard Business School Press, MA.

DCCT/EDIC (THE DIABETES CONTROL AND COMPLICATIONS TRIAL/EPIDEMIOLOGY OF DIABETES INTERVENTIONS AND COMPLICATIONS STUDY RESEARCH GROUP). 2005. Intensive Diabetes Treatment and Cardiovascular Disease in Patients with Type 1 Diabetes. *New England Journal Medicine* 353, 2643-2653.

DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative review of 50 years of research. *Med Care* 2004: 42(3):200-209.

DE VRIES, H., KREMERS, S., SMEETS, T., BRUG, J., AND EIJMAEL, K. 2008. The effectiveness of tailored feedback and action plans in an intervention addressing multiple health behaviors. *American Journal of Health Promotion* 22(6): 417–425.

DOLIN, R.H., ALSCHULER, L., BOYER, B., BEEBE, C., BEHLEN, F.M., BIRON, P.V., AND SHABO, A. 2006. HL7 Clinical Document Architecture, Release 2. *Journal of the American Medical Informatics Association* 13(1), 30-39.

The Diabetes Prevention Program (DPP) Research Group. 2002. The Diabetes Prevention Program (DPP): Description of lifestyle intervention. *Diabetes Care*. 2002 Dec; 25(12): 2165–2171.

DPP (DIABETES PREVENTION PROGRAM). 2008. NIH Publication No. 09-5099, 2008, US Department of Health and Human Services.

EDDY, D., et al. 2011. Individualized Guidelines: the Potential for Increasing Quality and Reducing Costs. *Annals of Internal Medicine*, vol. 154: pp. 627-634.

ELDER, P., AYALA, G., AND HARRIS, S. 1999. Theories and intervention approaches to health-behavior change in primary care. *American Journal of Preventive Medicine*, 17( 4).

ELIXHAUSER, A., STEINER, C., HARRIS, R. AND COFFEY, R. 1998. Comorbidity measures for use with administrative data. *Medical Care* 36(1), 8-27.

FDASIA Health IT Report. 2015. Proposed Strategy and Recommendations for a Risk-Based Framework.
Online available at: http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/UCM391521.pdf

FDA report. 2015. Mobile medication applications: Guidance for Industry and Food and Drug Administration Staff.
http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM263366.pdf

FDA report. 2015. Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices: Guidance for Industry and Food and Drug Administration Staff.
http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm401996.pdf.

Franz MJ, Powers MA, Leontos C, Holzmeister LA, Kulkarni K, Monk A, Wedel N, Gradwell E. The evidence for medical nutrition therapy for type 1 and type 2 diabetes in adults. *J Am Diet Assoc*. 2010 Dec;110(12):1852-89.

FTC Staff. Internet of things: privacy and security in a connected world. FTC staff report. Available at http://www.ftc.gov/system/files/documents/reports/federal-trade-commission-staff-report-november-2013-workshop-entitled-internet-things-privacy/150127iotrpt.pdf.

GOETZ, A.A., DUFF, J.F., AND JBERNSTEIN. .E 1980. Health risk appraisal: the estimation of risk. *Public Health Reports* 95(2), 119–126.

GONZALEZ, V., GOEPPINGER, J. AND LORIG. K. 1990. Four psychosocial theories and their application to patient education and clinical practice. *Arthritis Care Research* 3, 132-143.

GOODMAN, C. 2009. Comparative Effectiveness Research and Personalized Medicine: From Contradiction to Synergy. In *Lewin Group Report prepared for the Conference of Comparative Effectiveness Research and Personalized Medicine: Policy, Science, and Business, National Pharmaceutical Council and Personalized Medicine Coalition*.

GROL, R., AND GRIMSHAW. J. 2003. From best evidence to best practice: effective implementation of change in patients' care. *Lancet* 362, 1225-1230.

GROL, R. 2001. Successes and failures in the implementation of evidence-based guidelines for clinical practice. *Medical Care* 39, 46-54.

GROL, R. 2001. Improving the Quality of Medical Care, *JAMA* 2001; 286(20): 2578-2585.

GRUNDY, S.M. et al. 2002. Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). In the *Third Report of the National Cholesterol Education Program (NCEP) Expert Panel*, NIH Publication No. 02-5215, September 2002.

HARVEY, J. N., AND LAWSON, V. L. 2009. The importance of health belief models in determining self-care behaviour in diabetes. *Diabetic Medicine* 26 (1): 5–13.

Hirst, W. 2014. Connected health and the rise of the patient-consumer. Health Affairs 33:2: 191-193.

Hsueh, P., Lin, R., Hsiao, J., Zeng, L., Ramakrishnan, S. and Chang, H. (2010). Cloud-based Platform for Personalization in a Wellness Management Ecosystem: Why, What, and How. IEEE International Conference of Collaborative Computing.

Hsueh, P,. C Lan, V Deng, and X Zhu. (2012a). From Clinical Requirement to Personalized Wellness Decision Support: A Data-driven Framework for Computer-Supported Guideline Refinement. Proceedings of the 24th European Medical Informatics Conference (MIE 2012).

Hsueh, P., T. Grandison, X. Zhu, H. Pai, and H. Chang. (2012n). Challenges and Requirements on Privacy in Enabling Evidence Use Service on Wellness Cloud, Frontiers in Service Conference, 2012.

Hsueh, P.S., M. Ball, M. Marschollek, F. J. Martin Sanchez, C. Patrovian, V. Patel. Addressing Patient Adherence Issues by Engaging Enabling Technologies. Medical Informatics in Europe (MIE) 2015 Workshop

Ho PM, Bryson LC, Rumsfeld SJ. (2009). Medication Adherence: Its Importance in Cardiovascular Outcomes. *Circulation* 2009;119:3028-3035.

Huang X, Liu Y, Chen K, Shin WJ, Lu CJ, Kong GW, Patnaik D, Lee SH, Cortes JF, Rogers JA. Stretchable, wireless sensors and functional substrates for epidermal characterization of sweat. *Small*. 2014 Aug;10 (15): 3083-90.

Grandison, T., Hsueh, P., Zeng, L., Chang,H., (2011). Privacy Protection Issues for Healthcare Wellness Clouds. Book Chapter in Privacy Protection Measures and Technologies in Business Organizations.

HOOD, L. AND FRIEND, S.H. 2011. Predictive, personalized, preventive, participatory (P4) cancer medicine. Nature Reviews Clinical Oncology 8: 184-187.

Irigaray P, et al. 2007. Lifestyle-related factors and environmental agents causing cancer: An overview. *Biomed Pharmacother* 61(10):640-658.

IMS Institute for health care Informatics. 2012. Press Releases. Available at: http://www.imsresearch.com/news-events/presstemplate.php?pr_id=2743

IMS Institute for health care Informatics. Avoidable Costs in U.S. Health Care: The $200 Billion Opportunity from Using Medicines More Responsibly. June 2013. Available at: http://www.imshealth.com/deployedfiles/imshealth/Global/Content/Corporate/IMS%20Institute/RUOM-2013/IHII_Responsible_Use_Medicines_2013.pdf. Accessed October 10, 2014.

JDRF (THE JUVENILE DIABETES RESEARCH FOUNDATION CONTINUOUS GLUCOSE MONITORING STUDY GROUP). 2008. Continuous Glucose Monitoring and Intensive Treatment of Type 1 Diabetes. *The New England Journal of Medicine* 359: 1--13.

Kansagara D, Englander H, Salanitro A, Kagen D, Theobald C, Freeman M and Kripalani S. Risk Prediction Models for Hospital Readmission: A Systematic Review. VA-ESP Project #05-225; 2011.

KUPER, H., AND MARMOT, M. 2003. Job strain, job demands, decision latitude, and risk of coronary heart disease within the Whitehall II study. *Journal of Epidemiology and Community Health* 57(2), 147–153.

LLOYD-JONES, D.M. et al. 2010. Cardiovascular Risk Prediction: Basic Concepts, Current Status, and Future Directions. *Circulation* 121, 1768-1777.

Lopez-Meyer P, Tiffancy S., Patil, Y., and Sazonov, E. Monitoring of Cigarette Smoking Using Wearable Sensors and Support Vector Machines. *IEEE Transactions on Biomedical Engineering* 2013: 60 (7): 1867-1872.

Luga AO, and McGuire MJ. Adherence and health care costs. *Risk Manag Healthc Policy* 2014: 7: 35–44.

MACKNIGHT, C., AND ROCKWOOD, K. 2001. Use of the chronic disease score to measure comorbidity in the Canadian Study of Health and Aging. *International Psychogeriatrics* 2001,13 Supp 1, 137-142.

Maetzlera W, Domingosc J, Srulijesa K, Ferreirac JJ and Bloemd BR. Quantitative wearable sensors for objective assessment of PD. *Movement Disorders* 28(12): 1628–1637, 2013.

MARMOT, M.G. , ROSE, G. AND SHIPLEY, M., AND HAMILTON, P.J. 1978. Employment grade and coronary heart disease in British civil servants. *Journal of Epidemiology and Community Health* 32 (4), 244–249.

Mayo Clinics Shared Decision Making resource center. Available at http://shareddecisions.mayoclinic.org/resources/general-resources/.

MCGLYNN, E.A., ASCH, S.M. AND KERR. E.A. 2003. Quality of health care delivered to adults in the United States – Reply. *New England Journal of Medicine* 349, 1867-1868.

Mistra V, Bhansali S, Muth J, Jackson T., and Lach J. NSF Nanosystems Engineering Research Center for Advanced Self-Powered Systems of Integrated Sensors and Technologies (ASSIST). Available at: http://www.nsf.gov/awardsearch/showAward?AWD_ID=1160483&HistoricalAwards=false

JH Moore, FW Asselbergs, SM Williams. Bioinformatics challenges for genome-wide association studies. *Bioinformatics* (2010) 26 (4): 445-455.
MORI, M. et al. 2009. Genetic basis of inter-individual variability in the effects of exercise on the alleviation of lifestyle-related diseases. *Journal of Physiology* 587(23), 5577–5584.
MCGINNIS, J.M., Williams-Russo, P., AND Knickman, J.R. 2002. The case for more active policy attention to health promotion. *Health Affairs* 2002, 21(2), 78-93.
Müller M, Kersten S. (2003). Nutrigenomics: Goals and Perspectives. *Nature Reviews Genetics* 4. 315 -322.
PAN X.R. et al. (1997). Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 1997, vol. 20(4), pp. 537-544.
Patel S, Mancinelli C, Bonato P, Healey J, Moy M. Using wearable sensors to monitor physical activities of patients with COPD: a comparison of classifier performance. IEEE Workshop on Wearable and Implantable Body Sensor Networks 2009: 234-239.
Peikes D, Zutshi A, Genevro J, Smith K, Parchman M, Meyers D. Early Evidence on the Patient-Centered Medical Home. Final Report (Prepared by Mathematica Policy Research, under Contract Nos. HHSA290200900019I/HHSA29032002T and HHSA290200900019I/HHSA29032005T). AHRQ Publication No. 12-0020-EF. Rockville, MD: Agency for Healthcare Research and Quality. February 2012.
Pierre, Yong (2010). The Healthcare Imperative: Lowering Costs and Improving Outcomes: Workshop Series Summary. Washington DC: The National Academies Press. p. 141–174.
PRICEWATERCOOPERHOUSE report. Consumer intelligence series: the wearable future. Online available at: http://www.pwc.com/us/en/industry/entertainment-media/publications/consumer-intelligence-series/
Pharmaceutical Group of the EU Staff. Targeting Adherence: Improving Patient Outcomes in Europe through Community Pharmacists' Intervention Adherence. *PGEU policy statement on adherence to medicines*, 2008.
PRITCHARD, J. K. (2001). Are Rare Variants Responsible for Susceptibility to Complex Diseases? *American Journal of Human Genetics* 69(1), 124–137.
PROCHASKA, J.O., DICLEMENTE, C.C., AND NORCROSS, J. C. 1992. In Search of how people change. *American Psychologist* 47(9),.1102-1114.
ROCHE, H. M. 2006. Nutrigenomics—new approaches for human nutrition research. *Journal of the Science of Food and Agriculture* 86(8), 1156–1163.
SAARISTO, T., PELTONEN, M., KEINANEN-KIUKAANNIEMI, S., VANHALA, M., SALTEVO, J., NISKANEN, L., OKSA, H., KORPI-HYOVALTI, E., AND TUOMILEHTO, J. 2007. National type 2 diabetes prevention programme in Finland: FIN-D2D. *International Journal of Circumpolar Health*, 101-112.
SD Burke, D Sherr, and RD Lipman. Partnering with diabetes educators to improve patient outcomes. *Diabetes Metab Syndr Obes*. 2014; 7: 45–53.
SHOJANIA, K.G. et al. 2004. Closing the Quality Gap: A Critical Analysis of Quality Improvement Strategies and Technical Review. *Agency for Healthcare Research and Quality*.
SLOAN, K.L. et al. 2003. Construction and characteristics of the RxRisk-V: a VA-adapted pharmacy-based case-mix instrument. *Medical Care* 41(6), 761-774.
SOLOMON, D.H., SCHNEEWEISS, S., GLYNN, R.J., KIYOTA, Y., LEVIN, R., MOGUN, H., AND AVORN, J. 2004. Relationship Between Selective Cyclooxygenase-2 Inhibitors and Acute Myocardial Infarction in Older Adults. *Circulation* 109(17), 2068-2073.
SCHAEFER, C. et al. 2011. The Kaiser Permanente Research Program on Genes, Environment and Health: A Resource for Genetic Epidemiology in Adult Health and Aging. In *the Proceedings of 17th Annual HMO Research Netowrk Conference*, 2011.
SCHROEDER, S.A. 2007. We Can Do Better — Improving the Health of the American People. *The New England Journal of Medicine* 357(12): 1221-1228.
Scott CT, T Caulfield, E Borgelt and J Illes. (2012). Personal medicine—the new banking crisis. *Nature Biotechnology* 30, 141–147 (2012).
Sherman BW and B Chris. Beyond Incentives: The Impact of Health Care Reform on Employer Population Health Management Strategies. *Population Health Management* April 2014, 17(2): 67-70.
R. A. Sperling, D. M. Rentz, K. A. Johnson, J. Karlawish, M. Donohue, D. P. Salmon, P. Aisen. **The A4 Study: Stopping AD Before Symptoms Begin?** *Science Translational Medicine*, 2014; 6 (228).
THORISSON, G. A., SMITH, A. V., KRISHNAN, L., AND STEIN, L. D. 2005. The International HapMap Project Web site. *Genome Research* 15(11), 1592–1593.
TUOMEILEHTO, J. et al. 2001. Prevention of Type II diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine* 344(18), 1343--1350.
TURNER, R.C. et al. 1998. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom prospective diabetes study. *British Medical Journal* 316(823).
UKPDS Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998; 352: 837–53.
VAN SETTEN, M., POKRAEV, S., AND KOOLWAAIJ, J. 2004. Context-Aware Recommendations in the Mobile Tourist Application COMPASS. In Nejdl, W. & De Bra, P. (Eds.). *Lecture Notes of Computer Science* 3137, 235-244, Springer-Verlag.
Volk RJ, Llewellyn-Thomas H, Stacey D and G Elwyn. (2013). Ten years of the International Patient Decision Aid Standards Collaboration: evolution of the core dimensions for assessing the quality of patient decision aids. *BMC Medical Informatics and Decision Making* 2013, 13 (Suppl 2): S1.
WEBB, T.L., JOSEPH2, J., YARDLEY, L., AND MICHIE, S. (2010). Using the Internet to Promote Health Behavior Change: A Systematic Review and Meta-analysis of the Impact of Theoretical Basis, Use of Behavior Change Techniques, and Mode of Delivery on Efficacy. *Journal of Medical Internet Research* 12(1).
Welltok caféwell concierge introduction. (2015). Available at: http://welltok.com/solutions/cafewell-concierge.html.
ZIMMERMANN, A., SPECHT M., AND LORENZ, A. 2006. Personalization and Context Management. *User modeling and user-adapted interaction* 15(3-4), 275-302.
Gisela Wilcox. Insulin and Insulin Resistance. *Clin Biochem Rev.* 2005 May; 26(2): 19–39.