MOBILE APPLICATION SUPPORTED LIFESTYLE INTERVENTION TO LOWER PROSTATE CANCER RISK

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Abstract: There is an existing Health (e)Coach Solution for supporting intensive lifestyle changes, which may help reduce cancer progression risks in men with low grade prostate cancer. An important challenge is to support and motivate healthy behaviors for the long term (4 years). Smart phones are increasingly used also in this age group. And mobile apps offer significant opportunities for personalized health behavior monitoring and support. Our overall proposition is that an mApps suite, as an extension to an existing online dashboard with automated emails and interpersonal coach sessions, appears promising for improving long term health behavior support. That is, if three conditions are met: 1) Using best of breed mApps from the market (benefits like ease-of-use, continuity, customer support); 2) creating easy and meaningful score conversions (from mApps to personal dashboard); 3) using automated emails as glue between three key aspects personal progress/dashboarding, user attention and motivation, mApp usage.As methodological approach, this paper focuses on two phases from a design research cycle: requirements analysis and a preliminary design solution exploration. In the analysis phase, two questions are addressed: What are effective lifestyle intervention components according to literature? What are solution properties that may enhance motivation and improve health behaviors? In the solution exploration phase our design question is how a proposed mApp extension may likely add value to the existing Health (e)Coach solution.

1 INTRODUCTION

This paper bridges the two worlds of health and ICT (Information & Communication Technology). After the methodology introduction, the first part of the paper explores the extent of potential benefits from extensive lifestyle interventions for prostate cancer patients. The second part analyzes requirements for a proposed extension with smart phone apps in relation to an existing health (e)Coach solution. This is partly based on literature and partly on interviews with the respective health solution provider. Finally, we describe a preliminary solution.

1.1 Propositions

In summary, our **overall proposition** is that a smart phone applications (mApps) suite, as an extension to an existing online dashboard with automated emails (i.e. push notification) and interpersonal coach sessions, appears promising for improving long term health behavior support for low grade prostate cancer patients.

This builds on four sub-**propositions**: 1) A gain may be achieved in quantity and quality of life for low grade prostate cancer by enhancing existing treatments with an intensive healthy lifestyle intervention. 2) An existing health (e)coach program, which uses personal e-dashboarding, intensive health education, interpersonal coaching and automated personal progress emails, offers promising results in terms of health beliefs, health behaviors and health results (Simons and Hampe 2011). Still, more value could be added by bringing the health experiences and feedback even closer to the users. 3) Adding a portfolio of best of breed existing smart phone apps may help improve health awareness, quality of health beliefs, help improve health behaviors, increase transparency, fun and motivation, as well as long term healthy lifestyle adherence. 4) This rests, however, on a number of conditions: a) Using best of breed existing smart phone applications from the market. This brings

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benefits like attractiveness, ease-of-use, low cost implementation, flexible adaptation, continuity, and high quality customer support per application. b) Creating easy and meaningful conversions from the mApps sub-scores to the health progress scores in the personal dashboard. For example: How many calories have been burned with intensive exercise this week? Or: How may fibers or fats have been consumed this week? The mobile applications in the portfolio must be selected to provide these types of sub-scores which can then be translated into the overall health behavior progress scores in the personal dashboard. c) Using automated emails as glue between three key aspects of the solution: facilitating personal progress feedback (based on the e-dashboarding), increasing user health attention and motivation, and automated feedback or compliments on mApp usage. In other words: using the mApps must not be a stand-alone activity. It should visibly increase the value of the personal dashboard and increase health behavior motivation. Whether patients already are active mApp users or not, the weekly email notifications they receive should integrate and explain their personal e-dashboard scores (and when active: mApp scores). Furthermore, this channel mixing increases awareness and it may motivate non-users to start using mApps by showing the benefits this generates.

1.2 Design Research Cycle

Our research approach is based on Information Systems Engineering. It uses the design research cycle of Vaishnavi and Kuechler (2004) with the enhancements towards a pluralistic view as discussed in Frank (2006). Thus we describe the first two stages of the design cycle (Vaishnavi and Kuechler, 2004) in this paper. That is: problem analysis and a motivated suggestion for a design solution for the problem. For the service concept design and service implementation only initial evaluation results are available, a large scale evaluation is missing. Thus we present research in progress. Nonetheless, we propose the general positions and the examplification along the prostate cancer service platform for discussion and improvement to the research community.

2 LIFESTYLE IMPACTS

2.1 Large Differences Worldwide

There are large incidence differences worldwide for several of our common cancers: lung cancer, colorectal cancer, children's cancers, as well as breast cancer and prostate cancer. For prostate cancer, there is a 100-fold difference in age-corrected incidence rates. These vary from 0,5/100.000 persons per year in Qidong County in China in 1997 to around 125/100.000 persons per year in the USA.

These differences are strongly correlated with an affluent (Western) lifestyle and diet. Degree of physical activity, stress and environmental factors likely play a role, but the hypothesis that diet has an independent effect is supported by migration studies which show that Asians who maintain an Asian food pattern through adolescence while living in the West have better cancer protection than those who have adopted Western foods (Wu, 2002).

2.2 Lifestyle Factors

The World Health Organization defines health as consisting of physical, mental and social health. And each of these components has an effect on prostate cancer incidence and mortality. Below we review studies on four aspects: social support, stress, physical activity and food.

2.2.1 Social Support

Furthest away from the field of well-grounded biological pathways is the empirical data regarding **social support** and cancers. (Various immune-, hormonal-, neural- and also behavioral mechanisms have been proposed, but this field is still young.) On the one hand there have been several long term prospective studies over the past decades which have shown correlations between degree of social support early in life and cancer incidence and mortality years later. For example the Alameda study measured degree of social support among Alameda County residents and found significantly raised cancer risks and mortality of all sites during the 17-year follow up period (Berkman, 1995); (Reynolds and Kaplan, 1990). They found it to be an independent and more powerful predictor than age, gender, socioeconomic status and health behaviors. Also marital status has an impact on five year survival for almost every category of age, gender and stage of various cancers (Goodwin, 1987). This was also found specifically for prostate cancer (Krongrad, 1996). These effects have been confirmed in recent meta-analyses: Across 87 controlled studies, having high levels of perceived social support, larger social network, and being married were associated with decreases in

relative risk for mortality of 25%, 20%, and 12%, respectively. There were stronger associations for leukemia/lymphomas and breast cancer, but not enough studies for other cancers to differentiate effect sizes (Pinquart and Duberstein, 2010). And as a generic health effect: across 148 studies, the effect size was OR = 1.50 (95% CI 1.42 to 1.59), 50% more likelihood of survival with stronger social relationships, a finding consistent across age, sex, initial health status, cause of death, and follow-up period (Holt-Lunstad, 2010).

On the other hand, there is the question how effective psycho-social interventions are. There was initial enthusiasm based on successful interventions (Spiegel, 1989); (Fawzy, 1993), but larger RCTs have not been able to replicate these results (Kissane, 2007). Still, it is interesting that in one study, both control and treatment groups had half the mortality risk of those who declined to participate in the study (Boesen, 2007). And another study showed that those who reduced their degree of depression in the first year had improved survival, irrespective of being in the control or treatment group (Giese-Davis, 2011). An important complexity in this field is that seeking support has become very normal, and cancer patients may do so independent of a formal support group. For example, even the simple yes/no answer to the question 'Do you have someone to talk to in the 3 months after your diagnosis?' correlated with a 30% increase (for 'yes') in survival after 7 years (Maunsell, 1995). And a review of the psycho-oncological literature concluded (Garssen, 2004) that one of the most consistent findings is that: the more hopelessness and helplessness are experienced, the more unfavorable the cancer progression is (Watson 1999); (Goldberg, 1996); (Schulz 1996).

2.2.2 Stress

A next potential factor is the effect of **chronic stress**. Potential pathways run via increased cell aging and and telomere shortening (Epel, 2004); (Puterman, 2010), increased DNA damage and hampered DNA repair (Flint, 2007), reduced immune function (Segerstrom, 2004), increased levels of inflammatory cytokines (Bower, 2007), and stress-induced activation of the sympathetic nervous system (SNS) and hypothalamic–pituitary–adrenal (HPA) axis which results in the production of catecholamines and cortisol, which have direct effects on epithelial cell growth and tumor vascularization (McGregor, 2009). Besides, there are higher order mechanisms like stress-induced depression (for example, depression raised mortality in men for melanoma, colon and prostate cancer with 67%: Almeida 2010), reduced self-efficacy and self-care (Miller, 2001) or the 90% increased cancer risk due to low perceived quality of life (Flensborg-Madsen, 2011). For an overview of biological mechanisms, see McGregor (2009). Next, one study found that men who experienced high levels of stress were more than three times as likely to have elevated PSA levels (Prostate Specific Antigen) than were men who experienced low levels of stress (Stone, 1999). And using the breast/prostate cancer analogy, another large study showed that African American women who experienced more emotional stress due to discrimination (on the job, on the street and by the police) had a 48% increased risk of developing cancer after six years (Taylor, 2007).

In terms of interventions, cognitive-behavioral therapy (Philips, 2008) and well as yoga (Raghavendra, 2009) and meditation programs (Biegler, 2009) have resulted in lower cortisol levels, as well as improved mental health and quality of life (Nidich, 2009); (Beard, 2011); (Chambers, 2011). Survival impacts are not always clear or made explicit. When they do appear they seem dependent on improvements in relation to depression (Giese-Davis, 2011) hopelessness (Garssen, 2004) or quality of life (Flensborg-Madsen, 2011); (Spiegel 2011).

2.2.3 Physical Activity

Two different effects exist between physical activity and cancer. The first effect is that sedentary behavior increases cancer risk, independent of BMI (Body Mass Index) or other activity. Sedentary behavior is associated with adverse cardio-metabolic and cancer mortality; in a review of 18 cancer studies has been associated with increased colorectal, endometrial, ovarian, and prostate cancer risk (Lynch, 2010). The second effect is that vigorous exercise helps reduce cancer risk. Already in the College Study, running for over 40 years and following 50.000+ participants, a more than 30% reduction in cancer mortality risk due to physical exercise across all cancers was found, including prostate cancer when exercise is heavy (Paffenbarger, 1986). As one hypothesized pathway, heavy exercise decreases testosterone, which in turn is linked to lower prostate cancer risk.

The EPIC study found an inverse association between advanced prostate cancer risk and occupational physical activity - which is inversely correlated with inactivity throughout the day - but not with leisure activity (Johnsen, 2009). A study

specifically designed for investigating the impact on survival of higher physical activity after prostate cancer diagnosis, found 46% lower overall mortality with increased activity and a 61% lower prostate cancer mortality for those men who had 3 or more hours weekly of vigorous exercise compared with less than 1 hour weekly (Kenfield, 2011). Men exercising vigorously before and after diagnosis had the lowest risk. And a study focusing on degree of progression found that men who walked briskly for 3 h/wk or more had a 57% lower rate of progression than men who walked at an easy pace for less than 3 h/wk (Richman, 2011). Other advantages from physical activity for prostate cancer survivors are improved muscular fitness, physical functioning, fatigue, and quality of life (Thorsen, 2008).

2.2.4 Dietary Factors

One of the best known factors between lifestyle, diet and cancer is **obesity**. This link has been reviewed extensively in the WCRF Research report (WCRF, 2007). Hypothesized pathways include: pro-inflammatory and angiogenic effects of adipose tissue, increased oxidative stress on cells in obese people, and increased blood serum levels in obese people of insulin, glucose and lipids, which all tend to promote cancer cell growth. For various cancers, increased serum levels of insulin, glucose and lipids as caused by dietary fat, have been shown to increase tumor growth and aggressiveness, independent of BMI. For prostate cancer the evidence is still sparse. Glycemic load appears to have limited impact (Nimptsch, 2011), but some protective effects from low fat diets have been found (Aronson, 2010); (Kobayashi, 2008).

The obesity evidence is ‘convincing’ (WCRF 2007) for cancers of the oesophagus, pancreas, colorectum, breast (postmenopause), endometrium and kidney. The link between obesity and prostate cancer is not free of controversy however. Several recent studies suggest that obesity increases the risks of prostate cancer aggressiveness and decreases the risks in relation to low grade cancers (Gong, 2006); (Freedland, 2008). Freedland et al go on to suggest that obesity is biologically associated with increased risk, although this is obscured owing to hemodilution of prostate-specific antigen (PSA) and larger prostate size (which causes cancer-underestimations during diagnosis). This biological link was confirmed in another large study showing that men who lost weight reduced their prostate cancer risk and those with high BMI were at increased risk for aggressive prostate cancer (Rodriguez, 2007).

Chronic inflammation is also relevant: the (modified) Glasgow Prognosic Score, built on CRP (C-Reactive Protein) and albumin measurements, but also other inflammation-based prognostic scores, predict cancer survival, independent of age, sex, tumor stage and for all tumor sites. This includes common cancers like colorectal, breast, lung and prostate cancer (Proctor 2011-1, Proctor 2011-2). This may be a protective link from which fruits/vegetables (Cohen, 2000); (Hodge 2004) and flaxseed/omega 3 PUFA here, besides reducing testosterone and androgens (Demark-Wahnefried, 2001; 2008). Recently it has been found that also aggressive prostate cancer may be attenuated with leafy (-34%) and high carotenoid vegetables (-29%) and promoted (+64%) with high glycemic load foods (Hardin, 2011). Inflammation and CRP levels can be reduced via diet (Middleton 1998), as well as via physical activity (Ford, 2002); (Wegge, 2004) and stress reduction (Fang, 2010); (Oh, 2010). Furthermore, healthy diet can also help reduce depression (Akbaraly, 2009); (Jacka, 2010); (Beezhold, 2010).

Most people are not aware that increased blood **cholesterol** levels also indicate an increased cancer risk, besides increased heart disease risk. This has been shown for several cancers. For prostate cancer there are indications that lower cholesterol levels reduces incidence of the more advanced stages of prostate cancer (Platz, 2009). Unfortunately, pathways are still unclear. Still, diet can create large improvements in cholesterol levels, as can physical activity and stress management.

Western diets (rich in animal foods and low in fiber) also tend to raise **testosterone levels** (Ross, 1994); (Habito, 2001) just like they raise estrogen levels in women (Campbell, 2006). And increased serum testosterone is a known prostate cancer risk factor.

A fifth dietary factor is **IGF-1, in concert with a wider growth factor family** which promote cancer growth. For a review of 194 publications, see Pollak 2008. High circulating levels of IGF’s and low levels of its binding protein IGFPB-3 are associated with increased risk of several cancers, including those of the breast, colorectum (Ma, 2001), lung (Yu, 1999) and prostate (Chan, 2002); (Chan, 1998). IGF-1 levels are relatively high in the West, and our meats and dairy products have seen their IGF-1 levels double over the past decades, whereas IGF-1 has been shown to reach the receptor sites in the gut in its biologically active form (EU Scientific

Committee, 1999). Blood levels of IGF-1 are influenced via diet in multiple ways: most notably via milk, as shown in cohort studies in men (WCRF, 2007); Ma, 2009) and women (Norat, 2007) as well as experimentally: for example a Danish study found a 30% increase in circulating IGF-1 levels when increasing daily milk consumption from 200 ml to 600 ml daily. Besides IGF-1 increases from dairy and more mildly from other animal proteins, IGF-1 reductions were found to correlate with increased vegetable intake (Gunnell, 2003); Norat, 2007).

As a further connection between diet and cancer, there are the **anti-angiogenic properties** of foods. The research groups of Folkman and Li have categorized many food items according to anti-angiogenic strength. It turns out that many foods high in micronutrients (like berries, vegetables, fruits, spices) also potently block the growth of blood vessels towards microtumors. See food items http://www.standup2cancer.org/node/3950?page=1 and effect sizes being compared to anti-cancer drugs www.ted.com/talks/william_li.html. Hence, the microtumors will not become full blown tumors. The anti-angiogenic effect sizes appear similar to several of the recent FDA approved anti-angiogenic drugs, based on the zebrafish vessel formation tests (He, 2009).

On the level of specific dietary product groups and their effects on prostate cancer, the WCRF (2007, p 306-308) reports the following:

- On the basis of 20 studies on pulses (legumes) and 10 studies on soy and soy products: 'Most studies showed decreased risk with increased intake. Meta-analysis of case-control data produced evidence of an association with legume intake, with a clear dose-response relationship.'
- Ten studies investigated processed meat: 'All cohort studies reported increased risk with higher intake; and most case-control studies also showed this effect.'
- 25 Studies investigated milk and dairy and 38 studies investigated milk: 'Most of the studies showed increased risk with increased intake. Meta-analysis of cohort data produced evidence of a clear dose-response relationship between advanced/ aggressive cancer risk with milk intake and between all prostate cancer risk and milk and dairy intake.' The WCRF report mentions 2 pathways between milk and prostate cancer: via the IGF axis, and via downregulation of bioactive vitamin D, thereby increasing cell proliferation in precancerous cells.
- 23 Studies investigated dietary calcium (marker for dairy intake): 'Most [of the 9] cohort studies showed in creased risk with increased calcium intake; case control studies were inconsistent. Meta-analysis of cohort data showed an increased risk of 27% per g/day; [and] an increased risk of 32% per g/day [for advanced or aggressive prostate cancer]'
- On the basis of 10 studies measuring dietary selenium and 23 studies measuring in vivo selenium levels: 'Most studies, including those reporting separately on advanced/aggressive prostate cancer, showed decreased risk with increased intake.'
- On the basis of 42 studies on foods containing lycopene: 'Most of the studies showed decreased risk with increased intake. Meta-analysis [..] showed a 4% decreased risk per 10 microgram lycopene/liter serum.'
- Foods containing vitamin E, in 38 studies: 'Most studies showed decreased risk with increased intake.'

2.2.5 Summary

In summary, social support, stress, physical activity and foods each may have positive influences on mental and physical health. A clinical study with low grade prostate cancer patients is in preparation where these factors will be targets for a lifestyle intervention.

3 REQUIREMENTS & SOLUTION CONCEPT

Elsewhere (Simons and Hampe, 2011) an existing health (e)coach solution is described which supports intensive lifestyle change addressing each of the four lifestyle components: social support, stress, physical activity and food. This solution strongly builds on empowering patients to improve their health: "Health is what happens between doctor's visits." The clinicians and the solution provider are interested in adding an mApp portfolio to improve closeness and feedback to the patients.

The purpose of this section is to formulate a preliminary requirements and solution properties list. Requirements are extracted from literature as well as from two interviews with the solution provider (health coach and innovation manager). The latter interviews also led to the formulation of the preliminary mApp based solution concept.

3.1 Requirements

According to the meta-study of Jimison et al., (2008)

a number of requirements must be fulfilled to create ICT solutions that enhance the value for patients: 1) Ease of use, 2) Perceived usefulness, 3) Relevant information loop: perceived as having health relevance by the patients, 4) Embedding in a treatment cycle: interaction with health providers to decide on the course of action following the information which has been generated, 5) Delivered on technology that patients use every day.

Based on the health providers' interviews, a central goal in this intensive lifestyle intervention is health empowerment and involvement. Related requirements are: 6) Improving transparency and awareness of health effects from lifestyle behaviors, 7) Improving quality of health beliefs, 8) Increasing fun and attractiveness of tracking health behaviors, 9) Increasing motivation for health behaviors.

From the supply side of the health (e)coach provider, the following requirements were mentioned: 10) Operational quality and reliability (customer service of mApps, reliability, continuity, ease of use), 11) Low cost implementation and flexibility (simple to test, adopt and discard mApps, thus gradually improving the portfolio), 12) Creating meaningful conversion scores from mApps into existing e-dashboard, 13) Information flows integration (from mApp to e-dashboard to coach and vice versa).

3.2 Preliminary Solution Concept

In relation to user needs, key elements of the prospected solution are 'closeness', attractiveness and relevance: everyday interfaces are to be used, like email and smart phones. Also fun and attractiveness are important, hence the provider choice for selecting mApps from the most popular, existing mApps. In Aug 2011, smart phone penetration in the Netherlands was 42% http://online.wsj.com/article/BT-CO-20110804-717179.html. In the age group of 60-70 years (core of this patient group) penetration was 20+% and rapidly rising. Also for this age group, smart phones may become a dominant personal ICT platform (in close competition with email, internet and telephone), because of their attractiveness, 24x7 closeness, and intuitive user interfaces.

In terms of functionality, for each health factor (food, physical activity, stress, social support) one or several mApps are selected. Table 1 gives an overview of the functionality and design rationale.

The selected mApps are offered and supported as a portfolio, with a list of recommended mApps, a 'runner up of the month' that is recommended to try out, with a Dutch user manual, and with meta-data generated weekly for the patients (delivered in an automated email) to stimulate mApps usage and show mApps benefits which have been experienced by several of the users, to the rest of the patient group. When patients open their e-dashboard, they see references to the mApps portfolio. And when they enter their weekly health behaviors in the e-dashboard, they see the options to enter mApp generated values.

Table 1: Preliminary Functionality and Rationale.

Functionality	Design rationale
Everyday smartphone & mailbox use.	Increase ease of use and 'closeness'
Portfolio of mApp support options: stress, exercise, food, group support.	Something useful for everyone
Selected mApps are managed as portfolio, including user manual.	Manage and monitor mApps use. And explain value adding in relation to e-dashboarding and coaching activities.
Explicit links into dashboard → if XYZ calories burned: input that value; input from week food report: fibers etc.	Visualize cross-referencing and mutual roles of e-dashboard versus mApps portfolio.
Explicit references in dashboard to mApps: pictures, explanations and dropdowns: 'input value from App'.	Visualize options for mApps use, and trigger non-users to consider using mApps.
Using weekly low intrusion mails (including reports from mHealth data captured.)	Give progress feedback, add relevance, increase awareness.

4 CONCLUSIONS

Based on the preceding argument, our conclusion is as follows: An mApps suite, as an extension to an existing online dashboard with automated emails and interpersonal coach sessions, appears promising for improving long term health behavior support. This rests on the sub-propositions summarized on page 1. Furthermore, we expect that in the coming ten years mApps will revolutionize health self-management, as well as transform the roles and activities of health providers. They will increasingly become coaches of (information- and mApp-) empowered patients that "make health happen in between doctor's visits".

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