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CRACKING CODES BETWEEN THE HEALTH CARE AND THE AGROFOOD SYSTEM: THE DEVELOPMENT OF A FOOD SUPPLEMENT FOR PROSTATE CANCER IN THE NETHERLANDS

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Keyword: food, health, patient movement, prostate cancer, food supplement, short supply chains

Abstract: Both the agrofood system and the health care system are known for their sector specific rules and routines. These routines in general do not favour innovations that transgress the borders of the sector. In earlier documents, Remmers (2014a, b) highlighted the role of patients as emerging and potentially powerful change makers, who cross borders without hesitation, linking the health care and agrofood sector in new organizational arrangements. Patients seem to be to the health and agrofood systems what citizens are in spatial planning: a category whose engagement makes new design (of chains, of products, of areas) more locally adapted, innovative, useful and used.
Core of this paper is a case study of the development of a food supplement for prostate cancer, in which patients play a crucial role. The case study is contextualised by a brief review 1) of the core challenges actors in the health and agro-food system are facing to make food really count for health, and 2) of the emergence of patient movement on food in The Netherlands, to which the author contributes in various roles as a patient advocate, researcher, facilitator and project initiator.
The food supplement for prostate cancer has become available on the market in September 2015, after years of stagnation, through the collaboration between patients, researchers and producers. The paper reviews the process that has led to this sudden acceleration. As a follow-up, the food supplement is now being translated into new, fresh-food based food routines for men at risk of prostate cancer, including the growth and home-delivery of specific crops for prostate cancer. The food supplement is hence paving the way for a new type of producer-consumer relations and short supply chains. The case study suggests that multistakeholder collaboration, geared around a clearly defined and demanding consumer group, is very supportive to make food really count for health, and impact the health and agro-food system.

1. introduction

Both the agro-food system and the health care system are known for their sector specific rules and routines. These routines in general do not favour innovations that transgress the borders of the sector. In earlier documents, Remmers (2014a, b) highlighted the role of patients as emerging and potentially powerful change makers, who cross borders without hesitation, linking the health care and agro-food sector in new organizational arrangements. Patients seem to be to the health and agrofood systems what citizens are in spatial planning: a category whose engagement makes new design (of chains, of products, of areas) more locally adapted, innovative, useful and used.

The paper will first introduce the core challenges that need to be bypassed in order to speed up the incorporation of good food for good health, and align both the healthcare, agro-food sector and the patients movement in their efforts. It then reviews briefly the emergence of the patients movement on food in The Netherlands, singling out the birth of the Dutch Platform Patient and Food. The paper follows with a more detailed case study on the development of a food supplement on prostate

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cancer. It describes the health promise of the food supplement and the development of the coalition that has made its introduction on the market possible, in September 2015, after years of stagnation, through the collaboration between patients, researchers and producers.
In the closing chapter, the potential of the established coalition around the food supplement will be assessed as to impact also the uptake of fresh food for health.

The methodology that supports this paper is participant observation and action research, throughout the development process of the supplement for prostate cancer. The author was chair of the working group on the food supplement, and co-founder of the Platform Patient and Food. All meetings of the working group and of the Platform Patient and Food were carefully documented and accorded in each new step in the process, and a logbook was kept.

2. The challenge: how to make food really count for health?

In recent years, there is abundant attention for the role food plays in maintaining health. On the one hand, a wealth of projects are developed to increase awareness on the need to raise intake of especially vegetables and fruits. Most of these projects are aimed at segments of the population that are most likely to become overweight, in The Netherlands mainly people in lower economic income classes and / or of Moroccan or Turkish descent. These projects are based on conventional notions of ‘good food for good health’, meaning that they depart on the consensuated scientific knowledge on healthy food pattern, condensed in e.g. the ‘Food Guide Pyramid’ in the UK, or the ‘Schijf van Vijf’ in The Netherlands. This consensuated notion is at the same time under attack from a number of “food-guru’s”, who, in a true tsunami of books make a plea for a food pattern that put a different emphasis, either on a much stronger increase in vegetables, or a different perspective on fats etcetera. Whatever may be the exact argument, most approaches coincide in their promise for public health.

Given the load of public attention for food and health, it is remarkable that there is still very little attention, within formal healthcare institution such as hospitals, for a more precisely defined role for food in the process of maintaining or recovering health. Food, so far, is not part of their ‘primary care process’, and hence more subject to budgetary constraints than to medical considerations. This is remarkable, as a recent Dutch survey concluded that dietary intervention for elderly persons in hospitals could save between 15 and 78 million Euros a year (Scholte et al, 2015). A positive exception is the recent initiative of Hospital Gelderse Vallei (Netherlands), who on purpose provides specific food recommendations for patients during hospital stay, to avoid that people receive treatment while being undernourished. These recommendations are based on consensuated notions on the right balance of proteins, carbohydrates, fats etc. Very slowly it becomes evident that this consensuated balance should even be further individualised, as the same food may trigger a very different response in people. A recent Israelian study (Zeevi et, 2015) pointed this out very clearly in relation to the maintenance of sound blood glucose levels. Consensuated knowledge holds that especially food containing fast sugars should be avoided, yet in some people blood glucose peaked more after eating sushi than after ice cream, and in one person the consumption of tomatoes yielded extreme glucose levels.

Given the lack of attention for food in formal health care institutions, the focus on generic recommendations on food for health as part of public health, and the multitude of alternative takes on food present in public media, it is not strange that confusion among consumers is growing. The

question that emerges ever more urgently is: *what food does really work for ME?* In 2014, an appraisal on the business potential of personalised food was conducted, and established more clearly some of the current possibilities, dilemma's and challenges to make food really count for the health of an individual (Remmers, 2014b). One of the promising developments is that, parallel to the incipient initiatives within the health care sector as above described, patients are massively experimenting with food to sustain their health. A study from 2004 estimated food experimentation by cancer patients on 50% (Meijer et al, 2004), while a survey in 2014 measured that up to 75% of patients (of all kinds) experiment with food and food supplements (Meijer et al, 2014). Patients do so in the absence of any formal support from their doctors, who, at best, do not obstruct the patients when experimenting with food. Their food experiments draw on a large variety of health paradigms (Ayurvedic, Chinese Traditional Medicine, homeopathic, paleo, orthomolecular, hand-picked scientific evidence etc), food sources (organic, local, conventional farming) and a mixture of whole foods and food supplements.

The results of these home experiments are not documented, neither by the formal health sector, nor by any independent research. Judging from the claims of the patients themselves, successes and failures are both present.

At the same time, there is a massive amount of nutrition research being performed, trying to pinpoint evidence based causality relations between the consumption of a certain food item with a certain chemical substance, and a health effect. For some areas, the evidence is mounting, as for example with regard to the role of turmeric (from *Curcuma lunga*, mainly grown in India and Pakistan), which is reported to have a positive effect in the control of certain types of cancer[2]. Bitter Gourd (*Momordica Charantia)* is reported to lower the symptoms of Diabetes Melitus type 2[3]. For other areas, the solidity of the evidence is under debate, as is pointed out by Prof. Kampman and collegues (Wageningen University), who have developed a website where lay people can find out what evidence is available regarding food and cancer (www.voedingenkanker.nl).

The problem that emerges time and again is that the knowledge on what food works and what not, is heavily contested even by academic scholars themselves. Hence, it is very difficult for patients to get their doctors back-up their own home experiments. At the same time, food producers cannot claim that their fresh products have a certain health effect, procedures of the European Food Safety Authority (EFSA) regulating food claims being very lengthy, strict and costly. Hence, producers are reluctant to invest in development of crops with enhanced concentration of compounds with specific health effects.

Taken all this together, we witness a paralysis in the uptake of food as a recognised medical intervention and prevention strategy, and even more so as a strategy that can be individualised. Both the biomedical sector, the food producing sector and the patients have legitimate questions to each other as regards the role of food for health (see fig 1.). In fact, uncertainty prevails: either scientific uncertainty if a certain relation between a plant compound and health is solid enough; uncertainty

[2] http://www.tegenkanker.nl/onderzoek/kurkuma/onderzoeksnieuws-kurkuma/ The Amsterdam Medical Centre is currently performing in-depth research as to combine turmeric in combination with a so-called photo-dynamic cancer therapy https://www.amc.nl/web/Het-AMC/Nieuws/Nieuwsoverzicht/Nieuws/Geelwortel-tegen-tumoren.htm

[3] See e.g. Fernandes et al, 2007, and www.bitter-gourd.org

on the side of food producers if the investment in new crop development will be paid off by the expected sales; and patient uncertainty as to what food really matches their health condition.

The core challenge, hence, is to develop a collaborative structure in which these uncertainties can gradually be tackled. The prostate cancer coalition on a food supplement is one such collaborative structure that is being developed, and will be dealt with in detail in paragraph 4.

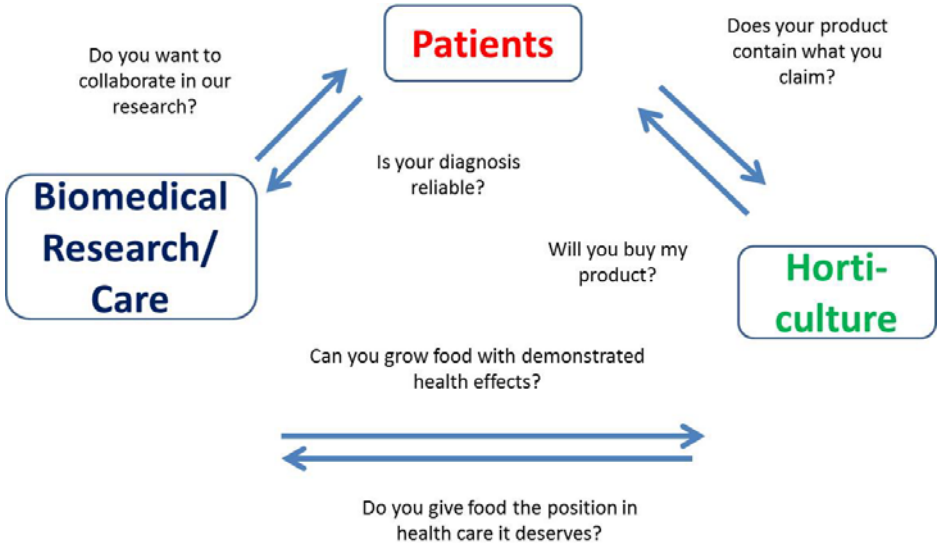

Figure 1. The core actors in health and food, and some of the questions that need to be solved.

3. The emergence of the patients movement on food in The Netherlands

At present, the Netherlands are home to over 400 organisations for people with a specific disease. These diseases concern both physical, mental and psychological/psychiatric diseases. The core areas of work of these organisations are as follows: providing information about the disease, organizing contact between patients that deal with the same disease, and defending the interests of patients with the disease (Smit and De Knecht-van Eekelen, 2015). The organisations are very different in their way of working. Smit and De Knecht (op cit: 15) distinguish patient organisation 1.0 as the traditional organization, working on the core areas with traditional tools; patient organisation 2.0 as the one that involves much more heavily social media; and patient organisations 3.0 as those who deliberately and pro-actively establish collaborations between researchers, patients and business and societal third parties. From the 1.0 to the 3.0 organisation, militancy and focus on patient empowerment increase.

The patient's interest and dedication to food, as highlighted in the previous chapter, contrast quite strongly with the fact that there seems to be hardly any coordinated effort to generate a common patient's perspective on food. Most patient's organisations deal with food only in relation with to their own disease, and when they do it, food is just one of the many items they pay attention to. In 2013, a first attempt to generate a common agenda was formulated in the context of a project born out of the collaboration between two EU patient groups, namely the European Patient's Forum (EPF) and the European Genetic Alliance Network (EGAN). These groups joined forces with the European Nutrition for Health Alliance (ENHA), a multistakeholder group involving dieticians, doctors, food and

pharma industry, working especially on a screening process for malnutrition (Gill’ard, Green and Smit, 2013). Their agenda gathered views of 8 different patient organisations throughout Europe, and is called ‘patients perspectives on nutrition’. The agenda includes several recommendations. The focus is on nutrition, not so much on (fresh) food, and pays predominantly attention to (functional) food for assisting recovery, and little to food as a tool to prevent people from getting sick at all. Using this agenda as a point of reference, a brainstorm was conducted in the course of the Personalised Food project in June 2014. The brainstorm led to the formulation of a series of key issues and recommendations on food and health, summarized here as follows (Remmers et al, 2014):

1. Actors in the health and food sector should collaborate as to empower food to become an acknowledged individualised medical prevention and intervention strategy, tuned to the stage in the treatment process and the phase of life one is in (see figure 2).
2. Improve early diagnostic methods, as to be able to design an adequate food strategy as quickly as possible, and to this purpose use DNA analyses, if possible at birth.
3. Monitor and systematize the experience based knowledge born out of the food experiments of patients and citizens
4. Take serious and validate alternative visions on food and health from other health traditions, e.g. Ayurveda
5. Food is not a single but a multiple drug. Food research should focus on the synergistic health effects of food
6. Healthy food is generated by a healthy food system. Actors should focus on creating a healing environment in all dimensions: natural cropping methods, healthy food offerings where groups are vulnerable and easily seduced (schools, sport canteens etc.), a green and inspiring built environment etc.
7. Make healthy food attractive and tasty. Food is not only medicine, it also enjoyment and social contact. Don’t medicalise food.

The momentum gathered in the appraisal on Personalised Food led to the establishment, in October 2014, of the Platform Patients and Food, an NGO whose mission is ‘to empower food as an acknowledged medical intervention and prevention strategy’. The organization is still very young, but at the same time is attracting quite some clout, with patients and patient organisations of different diseases supporting it: cancer, heart failure, ME/cvs, muscle dystrophy, kidney malfunctioning, lung, immunesystem, to name but a few (www.patientenvoeding.nl). The main topics that the Platform has been working on so far is first, establishing a structure that enables patients wisdom and experience with food to be taken serious and validated, and second, to establish coalitions between health care, food sector and patients as to accelerate the development of good food for good health.

Of note is that while food is the focus of this Platform, the agenda is much broader; food provides merely a prism, that enables to review the integral nature of human health.

4. The development of a food supplement for Prostate Cancer

Food supplements are not equivalent to fresh food as a source of health, but an approximation to it. They form a ‘bridge’ between medicinal drugs on the one hand, and whole foods on the other. Due to the availability of underpinning biomedical research and an accidental match between the researchers and patients, the development of the food supplement for prostate cancer has become an interesting showcase of the challenges that need to be addressed in order to incorporate food as

part of the primary process of health care on the one hand, and product innovation in the fresh food producing sector on the other.

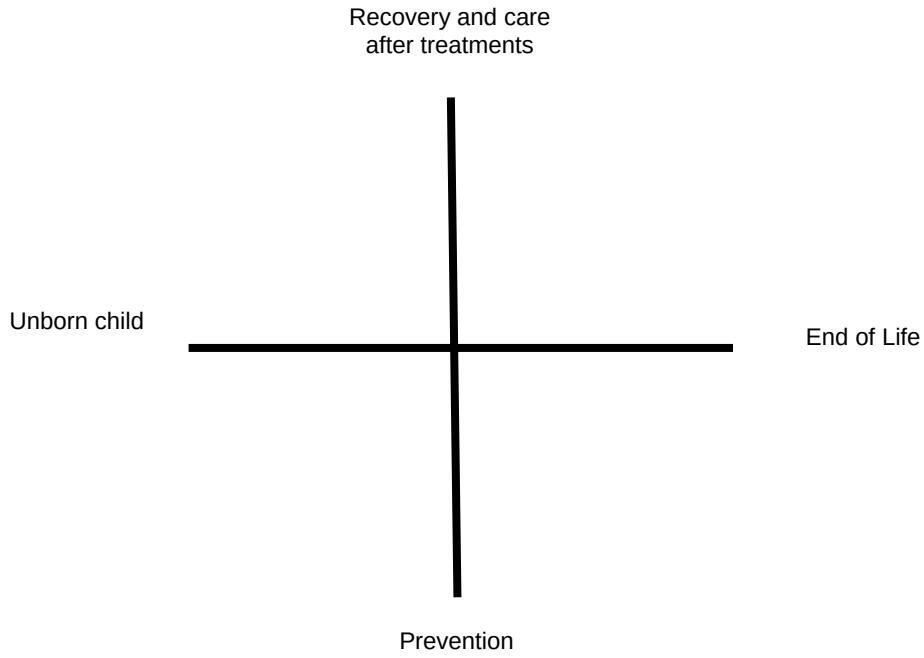

Figure 2. Food should fit both the stage of treatment and the life phase one is in

As part of the appraisal on Personalised Food, in 2014 a coalition was established between researchers and clinicians at the Rotterdam Medical Centre of Erasmus University in Rotterdam, a Dutch producer and wholesaler of food supplements, and the cancer patient movement Inspire2Live.

Source of the collaboration was the research by Erasmus MC on the recipe for a food supplement for prostate cancer. This research had been conducted since 1998, partly autonomously by Erasmus MC, and partly in collaboration by Nutricia and Danone. The elements of the food supplement were based on epidemiological research on the prevalence of prostate cancer in East Asia in relation to diet. In East Asia, the prevalence of prostate cancer is much lower than in Europe or the United States. Lycopene (found in tomatoes), flavonoids found in soya and vitamin E, were the most important components of the supplement, together with a number of accompanying substances. Two types of research had been conducted. First, the supplement was supplied to men which had undergone radical prostatectomy (chirurgical intervention taking away completely the prostate) or radiation. The supplement showed to slow down the doubling time of the PSA-levels (Prostate Specific Antigen, a biomarker that is a measure for the activity of the tumor) with a factor 2.6, as compared to men who had not taken the supplement (Schröder et al, 2005; Kranse et al, 2006). Second, a combination of lycopene and vitamin E was supplied to mice with prostate cancer. Their tumors grew also statistically significant slower (factor 2.6) than in mice who had not been supplied with lycopene and vitamin E (Limpens et al, 2005). These two studies allowed for the assumption that the intake of the food supplement slows down the development of the tumor in humans too. For a 72 year old man, the development of the tumor could be delayed with about 3 years.

These scientific results were available in 2005. The recipe for the supplement was even patented by Nutricia. Yet, it never led to the actual production of the supplement, the main reason being a

business reorientation by the Nutricia. This was much to the frustration of the leader of the research at Erasmus MC, Prof. dr. Schröder, who argued that his patients could not get hold of a soundly researched instrument to manage their health. The situation is quite similar to that of promising, but not yet completely research drugs for patients. Patients who have no other options left, may sometimes use those drugs, known as 'early access to drugs'. This 'early access' almost invariably must be conquered, as the mechanisms as to not allow such use work strongly against it: financial, academic and burocratic[4]. In the case of the prostate cancer food supplement, the supplement was promising not only for the researched group of men who had undergone radical prostatectomy or radiation, but also for men who show to have an elevated level of PSA, but without further signals that would warrant immediate medical action. Those men follow a so-called 'active surveillance' protocol, including regular check-ups of the level of PSA (pers com Prof Schröder). In similar vein, the supplement was possibly of use in a preventive fashion for men over 55 years of age with a history of prostate cancer in their family.

Prof. Schröder's frustration was picked up by Inspire2Live, a cancer patient organisation group based in The Netherlands, advocating strongly for breakthroughs in cancer research, clinical practice and health policy (www.inspire2live.org), and urging for intense collaboration between researchers, clinicians and patients. Their insistence on 'nothing for the patients, without the patient' resembles the advocacy for farmer based research in the 80-ies, when 'Farmer First' became proverbial (Chambers et al, 1989; Scoones and Thompson, 2009). Inspire2Live is composed of so-called 'patient advocates', usually well-educated patients who are primarily interested in advancing the state of the art concerning their disease (patient organisation 3.0). To this end, Inspire2Live differs from many other patient organisation, whose primary concern is to put patients of a certain disease in contact with each other (see chapter 3). Three patient advocates of Inspire2Live, including the author of this paper, established a working group with Prof Schroder and colleagues, that was further complemented by a producer of food supplements (Ars Pro Pharma) and a whole sale company of phytotherapeutic products (Holisan). The Business Development Agency of the province of Flevoland (OMFL) was instrumental in connecting with Ars Pro Pharma, who subsequently connected with Holisan. These partners (Erasmus MC, Inspire2Live and Ars Pro Pharma / Holisan) form the core of a working group, that, since its first meeting in april 2014, has met until, September 2015, approximately every 6 weeks.

In retrospect, the development of the working group has gone through a series of phases, unravelling in a parallel mode several issues. Table 1 gives a concise overview of the different issue that needed to be addressed.

[4] Recently, the case of the drug 'olaparib' made the news in The Netherlands. Olaparib is a drug developed for women with ovary cancer with a specific genetic mutation (BRCA). It happens to provide also excellent results for women with breast cancer with the same genetic mutiation, as praxis has showed. Yet, it will not be covered by health insurance, as the research that underpins its effectiveness, has only been tested in the context of ovary cancer. Result: a potentially curing drug is not available for women, that without it will die. Patient Advocay groups such as Inspire2Live are active in cutting through the obstacles. (http://www.volkskrant.nl/wetenschap/-dit-medicijn-moet-er-komen~a3944132/

Table 1. Phases and issues related to the development of the food supplement for prostate cancer

Phase	Issue	Activity	Milestone
Getting connected	Getting connected	Phone calls, email	Connecting (March-April 2014)
Build up of trust	Getting to know each other	Meetings, exchanging views	Build up of trust, identification of the core collaborators (Aug 2014)
	Establishing trust in the potential market	Calculating the potential number of beneficiaries of the supplement	Holisan says ýes’ and places an order with Ars Pro Pharma (Sep 2014)
	Resolving issues re patent	Getting information on the status of the patent	Decision of the group not to establish new patent, and rely on the built partnership for marketing purposes (Aug 2014)
Getting the supplement on the market	Defining a marketing strategy	Discussing how the supplement could overcome currently blocking mechanism	Decisions regarding the characteristics of the stakeholder collaboration, the composition of the supplement, etiquette and research (Aug 2014 – June 2015)
	Developing additional research	Establishing type of research, finding funding	First proposal submitted for funding (Jan 2015), denied, larger proposal submitted (July 215)
	Fund raising	Search for grants for research and for production of the supplements	Funding for production of the supplement for research purposes secured (Aug 2015)
	Establishing the final recipe	Discussions on what would be wise scientifically and what business wise	Decision to go for the original recipe, without newly promising ‘add-on’s’ (June 2015)
	Defining the text on the etiquette	Consultations with KAG-KOAG about name and further text on etiquette	PROSTAPREV choosen as name for the food supplement (June 2015); supplement available on the market (Sep 2015)
	Establishing a user community	Finding exposure through patients organisations such as Prostate Cancer Foundation, Inspire2Live etc	ongoing
Elaborating a fresh food variant of the supplement	Sensing the interest among new stakeholders (food producers) in a fresh food variant	Talks with a new consortium of pioneering horticulturalists	Project proposal ready (Oct 2015)

4.1 Getting connected

The main stakeholders got connected through the Appraisal on the Business Potential of Personalised Food (Remmers, 2014). This appraisal was commissioned by the Amsterdam Economic Board and Chamber of Commerce, the Province of Flevoland and CAH Vilentum Almere, a University of Applied Sciences, who was able to secure funding through the so-called Centre of Expertise

Greenports, a collaborative network between different Dutch Universities of Applied Sciences. The work was supervised by a Steering Committee, that was staffed, in addition to representatives of the funding organisations, by the Dutch Knowledge Centre of Plant Compounds, Fytagoras (a private research centre on biomedical and plant issues), the Dutch Central Veterinary Service, the project lead of the Green Health Consortium (a collaborative network of a series of Dutch universities of applied science and Small and Medium Enterprises geared towards validating the medical potential of promising plants and cropping techniques), the University of Amsterdam/VU (Prof. H. Westerhoff) and two members of Inspire2Live, a Cancer Patient Organisation. The appraisal was led by Gaston Remmers, in a double role as a professor at CAH Vilentum Almere, and as a patient advocate for Inspire2Live, assisted by the Flevoland Development Agency for Business Development (OMFL).
The first connection was established in January 2014, between Inspire2Live and Prof. Schröder, who had long been a supporter for patient empowerment in cancer care, and an advocate for reducing cancer incidence. The idea of the food supplement was then pitched at a business venue organised by the Dutch Centre of Plant Compounds early March 2014. Later that month, OMFL established a connection with supplement producer Ars Pro Pharma form the city of Lelystad. Several phone calls and emails yielded finally a group of stakeholders, that first met early May 2014.

4.2 Build up of trust

4.2.1 Getting to know each other

A number of meetings was held between May and August 2014. Purpose of these meetings was to figure out the issues to be tackled, the order of actions to be taken, the partners to work with and to gain trust in each other's commitment and capacities. The first session was organised by Prof Schroder in a Rotterdam restaurant. The coming-into-being of the business coalition was first publicly announced a little later on a seminar on Personalised Food (May 2014), organised by the author of this paper, who offered to coordinated the follow-up of the development of the supplement. Meetings were thoroughly documented. About 10 different stakeholders showed interest; by August 2014, the core collaboraters were identified: Erasmus MC, Inspire2Live, Ars Pro Pharma and Holisan, with OMFL on the background.

4.2.2 Establishing trust in the potential market

In order to establish trust in the potential market, it was necessary to become very clear about the potential beneficiaries. On the one hand, this implied a clear identification, by the biomedical researchers, of the target group. Based on the research conducted earlier, the supplement showed results in men having undergone radical prostectomy, a chirurgic intervention taking out the prostate. These men were in principle 'clean', meaning that they had no detectable tumor growing, and were under an 'active surveillance' protocol, following regular check-ups by their doctors. However, the scientists argued that by force of logic, it was very reasonable to conclude that also men who showed to have an elevated level of PSA but without a prostate cancer diagnosis, and men with a so-called 'benign tumor', and who were under active surveillance too, were also likely to benefit from the supplement. These categories sum up for about 3000 men yearly, in The Netherlands alone. Additionally, in general men over 50 years of age were indicated a potential beneficiaries. Prostate cancer will almost invariably develop in men, and most men die with the presence of prostate cancer, without it being the cause of their death. Hence, all men over 50 years of age could potentially benefit from it by means of prevention, although there is no research that

underscores this assertion. The eventual number of potential beneficiaries was hence calculated by the group to be approximately 1.8 million men in The Netherlands, with a core focus group of 3.000.

Another aspect of trust in the market, was the possibility to link the supplement with health claims and the interest in the product by patients. As a vendor of phytotherapeutic products, Holisan had ample experience with products that are not formally regulated as medicine, and knew about the troublesome nature of acquiering health claims. So Holisan was not backed off by the absence of a formal health claim. For Holisan, the solidity of the research and the reputation of Erasmus MC were more important. Also the establishment of the working group, and the promise of active patient involvement, were favourable to its decision to produce the supplement.

This decision was crucial. Between April and September 2014, the working group had met on several occasions, and had at length discussed the potential market and the accompanying activities to further strengthen the biomedical underpinning by additional research. The moment came near that Holisan needed to give a clear signal it was serious with going to market with the product – otherwise the whole exercise was useless. Finally, Holisan said ýes’ in the autumn of 2014 and placed an order with Ars Pro Pharma to acquire the composing substances for the supplement by October 2014.

4.2.3 Resolving issues on patent

The recipe for the supplement was under patent by Nutricia. In the spring of 2014, Nutricia was considering releasing the patent, which it eventually did in September 2014. The coordinating group considered for a few months whether it would be fruitful to buy the patent from Nutricia, the argument being the potential marketing benefits. However, after considerable deliberation, it was decided not to buy the patent, first because of the cost involved, and second because of the limited protection it would provide. If a large company would assemble the supplement without permission, the working group would never have sufficient means to win a legal case against such a company. Hence, the working group would produce a supplement with a recipe that would be available to all.

4.3 Getting the supplement on the market

4.3.1 Defining a marketing strategy

The decision not to work under the ‘protection’ of a patent was crucial, as it highlighted the necessity to find other ways to profile the supplement against other prostate supplements in the market. After all, benchmarking showed that there were a number of supplements available on the shelves of drugstores, that had a some resemblance with the supplement of the working group, that was provisionally named *Prostaprev*.
The benchmarking also raised the question if it was necessary to produce a new supplement at all. The working group considered this to be the case. Main reasons were: a) the already available supplements showed some overlap with Prostaprev, but with considerable variation regarding the concentration of the substances, that were furthermore not very clearly defined; b) the exact effect of these supplements could not be warranted by scientific back-up.
The group then established that the core selling strategy should follow four lines: a) Prostaprev is the first supplement on prostate cancer backed up with a clear line of research behind it; b) the introduction on the market would be accompanied by additional and complementary research as to

even more firmly establish its effectiveness, including also the uptake of promising new ingredients in a follow-up of the supplement; c) the composition of the recipe would not be altered as to enable a reference to ‘prostate’ on the label; d) the build-up of a community of end-users and urologists and oncologists that would be informal promotors of the supplement. In the upcoming paragraphs these issues will be elaborated.

For the three patient advocates involved in the coordinating group, the crucial factor to support the supplement actively was the solidity of the already established research on the supplement, and the promise of the development of additional research accompanying market introduction. The communities of urologists and oncologists were expected, by the Erasmus MC team, to be bit harder to convince, as they were thought to be harnessed more thoroughly in their habitual treatment protocols. In essence, the working group established that its own partnership was the main guarantee to realize a successful market introduction and to develop research.

4.3.2 Developing additional research

Two types of additional research were deemed important. First, research repeating the already established research among men, but with a larger scope. In fact, it concerned a so-called ‘phase 4’ research, the label given to research on drugs that are already available on the market. The second type of research aimed to identify the potential contribution of newly found substances in e.g. pomegranate that might strengthen the effectivity of the supplement. A research proposal for the first research goal was elaborated in January 2015, but was not granted. In July 2015, a larger research proposal combining both research goals was submitted (decision to be expected December 2015). The leadership of these research proposals lies with Erasmus MC, under the supervision of Prof. dr. Bangma, dr. M. Roobol and dr. W van Weerden.

4.3.3 Fund raising

Funds for the research above stated could relatively easily be identified – which doesn’t mean that the procedures to receive a grant were easy. The development of phase 4 research on the supplement introduced another issue. Habitually, it is the manufacturer of the drug who provides the drug without costs for the purposes of the research. Usually, these manufacturers are large pharmaceutical companies. However, in this case the manufacturer was a small player, and by no means capable of providing the supplements for free. Hence, additional funding was needed, and finally found in the form of a grant of the province of Flevoland (August 2015). In this, the OMFL, the Flevoland Development Agency for Business Development, played a crucial role.

4.3.4 Establishing the final recipe

The original recipe that was patented consisted of over 10 different compounds. There were two issues that made a closer look at the recipe necessary. First, it was clear from the outset that the supplement could not have any reference to prostate cancer based on the patented recipe alone. To acquire such a health claim meant submitting it to the European Food Safety Authority (EFSA), implying a lengthy and costly procedure, demanding most probably a lot of additional research. And that was precisely what was meant to be avoided. Yet, there were other substances, already approved of by EFSA in previous decades, that would allow for a reference to a general functioning of the prostate – not to prostate cancer. The exact wording of these health references on medicines

and health products is supervised in The Netherlands by the KOAG-KAG Council[5]. 'Saw Palm' (*Serenoa repens*) and 'Nettle (*Urticae radix*) would qualify for 'for the maintenance of a normal prostate' and 'good for the prostate function'; Saw palm in addition may assert that it is 'good for the urinary tract of men above 45 years'. What both plants exactly do is not mentioned; they do neither affect the development of a prostate tumor. Zinc is another element that is often incorporated in supplements, allowing the statement 'contributing to the maintenance of healthy cells and tissues'. The working group argued back and forth if inclusion of one of these substances would a) affect the working of the recipe that had been researched, and b) if the communicative advantage of a generic referencing to the prostate would outweigh the fact that research had not included such substances. The group finally concluded that although it was not very likely that additional ingredients would interfere negatively with the original ingredients, it could not be excluded either. Second, in terms of public and academic credibility and transparency, it would probably be wiser to stick to the original recipe. These arguments also applied to substances that, in research conducted between 2005 and 2014, to be potentially effective in controlling prostate cancer, such as pomegranate and others (Lin et al, 2015). So, finally, in June 2015, it was decided to stick with original recipe, take it as a reference to on the one hand build additional research, and on the other for product development in the future.

4.3.5 Defining the text on the etiquette

Having decided upon the list of substances, the road to mention on the etiquette an explicit reference to prostate cancer was blocked. Two options were finally left: the name of the food supplement, and a reference to SWOP, the Foundation for Scientific Research on Prostate Cancer, that was a long standing initiative of the Department of Urology of Erasmus MC, aimed at providing funds for scientific research on prostate cancer in particular, and cancers of the urinary tract in general (www.prostaatwijzer.nl). Hence, Holisan designed an etiquette, and submitted it for approval to the before mentioned Dutch KOAG-KAG supervisory council. The name PROSTAPREV was accepted, and also the inclusion of a statement on the etiquette that a part of the sales revenues would be transferred to SWOP. This last option is very interesting, as it also establishes a circular relation between research and product, and guarantees that research is ongoing. Having resolved the issues regarding recipe and etiquette, the supplement could now be introduced in the market, and was launched early September 2015.

4.3.6 Establishing a user community

Establishing a user community forms a corner stone to the successful introduction of the supplement. They are, in fact, the only actors that are legally allowed to link a product to a health claim without the need for a formal approval by EFSA or KOAG-KAG. The vendor of a product has to refrain from any unwarranted claim, and medical scientists and clinicians are to avoid even the least

[5] KOAG stands for "Keuringsraad Openlijke Aanprijzing Geneesmiddelen" (Council for Public Commendation on Medicines) and KAG for "Keuringsraad Aanprijzing Gezondheidsproducten" (Council for Commendation of Health products). Both are foundations, established in 1926, and founded by branche organisations in health care and pharmaceutical industry. In practice, both foundations work closely together in one Council, and are meant to separate false from true public claims (or acceptable from unacceptable claims) by way of self regulation. Source: http://www.koagkag.nl/ See Kasteren et al (2010) for an insightful discussion on European and Dutch regulatory mechanisms around health claims for food, and their dilemma's and paradoxes.

suggestion of a health claim that is not considered to be fully 'evidence based'. So end users are a crucial group that can in fact make or break a product.
The idea was hence to gradually build exposure for the supplement by organising meetings with patients, linking with other patient organisations for prostate cancer, such as the Dutch Prostate Cancer Foundation (PKS), use of social media etcetera. A more comprehensive programme is now being formulated. As a first step, Prostaprev was formally presented at the November 2015 'ProstateDay', a multi-topic conference for prostate cancer patients, clinicians and researchers, organised by a network of specialised prostate cancer treatment centres in the South-West of The Netherlands.

All in all, the development of Prostaprev as a food supplement, has turned out to be as expected: a twisted road with uncertainties on the side of both producers, patients and researchers. The success will depend on the one hand on funding for additional biomedical research, and on the other on the effectiveness with which the user community of prostate cancer patients can be reached.

4.4 Elaborating a fresh food variant of the supplement

As stated earlier, a food supplement is kind of in-between a medicinal drug and healthy food. As such, it is a convenient way for people to sustain their health without changing drastically their food pattern or lifestyle. However, a food supplement, nor a formal medicinal drug, won't help much if the lifestyle is not corresponding. It is obvious that a food supplement that forms part of a diet of fast food and no exercise comes very close to ridiculous. By adopting a healthy diet alone many health problems can already be avoided, no supplement nor drug is needed for that. The case on Diabetes Melitus 2 provides a good example for that. In the context of the food supplement for prostate cancer the question thus emerged: what if it would be possible to translate the supplement 'back' to a healthy food pattern?

Hence, parallel to the development of Prostaprev and with its market launch at hand, an inventory was started to see if the horticultural sector could be interested in producing and delivering specific products for prostate cancer patients. Could a specific 'prostate cancer food basket' be developed? Such a basket would not only include a variety of fresh food commonly available on the market, but also products with higher contents of specific plant compounds, such as lycopene-rich tomatoes. The basket would moreover include a series of cooking recipes and cooking techniques, as the 'food matrix' impacts the uptake and effectiveness of micro- and macronutrients. And it would probably also include some recommendations regarding physical exercise and stress management. When offered in a comprehensive coaching programme, it is expected to yield considerable benefits, as recent research shows (Bourke et al, 2015). Developing such a prostate cancer specific food basket would be a novel development in The Netherlands, and would possibly inspire the horticultural sector to invest more in the development of higher quality products. When combined with home delivery of the food basket including personal preferences, it would take the development of personalised food and personalised logistics a step further. A whole new short supply chain would be born, based on an intense collaboration between patients, biomedical scientists and horticultural producers. The inventory showed that leading Dutch horticultural firms in the Westland production area close to Rotterdam are indeed interested, and at this moment (November 2015), a project proposal is being elaborated.

5. Cracking codes in the health care and food sector: stepping stones

This paper started off with the assumption that patients are possibly to the health care sector what citizens are to formal spatial planning or farmers to dominant agricultural research. Both citizens and farmers have been long neglected as important sources for innovation. Over the past 2 to 3 decades, their involvement has enabled both spatial planning and agricultural technology to become more meaningful and adapted to local ecological, socio-economic and cultural-historical conditions. Patients may do the same for the health care sector, and, as far as food is concerned, also for the agro-food system.

The case study on prostate cancer discussed here departed from the notion that a collaborative approach would be most promising in order to invigorate food as an accepted intervention strategy towards health, while at the same time enabling innovations in horticultural production and providing patients with products they want. In this collaborative approach, uncertainties of all stakeholders could gradually be resolved and institutional barriers could be circumvented. The prostate cancer case has shown that it is indeed possible to find ways to bypass issues on health claims, ánd at the same time to undertake biomedical research to further increase the credibility of the claim. It has also shown that when patients back up an issue, product development and market launch may be accelerated considerably. Note that the recipe for the supplement had been gaining dust for 10 years, before it was ‘awakened’ by the working group. Finally, the case showed that the collaborative network on the food supplement has paved the way to now venture into fresh food as a source for health. With this, suddenly a whole new set of urban-rural linkages emerge, driving farmers to produce vegetables with specific qualities, and demanding them to develop logistic solutions in order to deliver individualized food baskets.

It will take some time before the codes of the health and agrofood sector are cracked to the extent that food can be produced and prescribed for health purposes specifically. We are witnessing a niche innovation, that provides hints as to in what direction future development of short supply chains may go, and where innovation in health and agro-food is to be expected. It is by no means common standard. It seems that the most important thing to do now is to persevere in delivering hands-on successes, gradually engaging dedicated actors from within and outside the dominant health and food regimes.

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