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HEALTH LITERATURE HYBRID AI FOR HEALTH IMPROVEMENT; A DESIGN ANALYSIS FOR DIABETES & HYPERTENSION

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Abstract Increasingly, front runner patients and practitioners want to use state-of-the-art science for rapid lifestyle based cure of diseases of affluence. However, the number of new health studies per year (>500.000) is overwhelming. How to quickly assess state-of-the-art and use new opportunities for rapid patient DIY (Do-It-Yourself) health improvement? In order to develop a health literature hybrid AI to aid DIY rapid health improvement, we analyze user side functional requirements. A cross case design analysis is conducted for hypertension and T2D (Type 2 Diabetes), two major cardiometabolic conditions in our society. Our analysis shows that current DIY health support is ‘watered down’ advise, prone to medicalizing rather than empowering patients. We propose hybrid AI user requirements and discuss how a 2030 hybrid AI health support system can stimulate new ways of working in health and cure.

Keywords:

health,
self
management,
AI
quantifie
self,
service
design,
QFD,
personal
medicine

1 Introduction

When it comes to lifestyle related diseases like cardiovascular disease, Type 2 Diabetes (T2D), dementia and colorectal-, prostate- and other forms of cancer, it turns out that key to our health is our biological self-repair. In virtually all our cells and tissues, damage is being repaired on a continuous basis (Li, 2019). This fact is still largely underutilized by patients and by healthcare professionals. Nor are we using the options to rapidly improve self-repair effectiveness (with biometric progress feedback on a daily basis) from healthy lifestyle choices on foods, exercise, sleep etc (Greger & Stone, 2016).

Already in 2009 Safeway CEO and the corporate Coalition to Advance Healthcare Reform have calculated that 74% of health costs come from only four conditions (cardiovascular disease, type 2 diabetes, obesity and cancer) which are largely preventable or reversible (Burd, 2009). The Lancet EAT committee reiterated this urgency to use options for prevention and reversal of disease more effectively: we cannot afford our current approach, not in health nor in ecology (Willett, 2019).

As discussed elsewhere, health improvement options are welcomed by many (though not all) patients around the moment of diagnosis (Simons, 2020a). There are groups of front runner patients and practitioners who want to use state-of-the-art science for rapid lifestyle based cure of diseases of affluence. Moreover, research increasingly shows that from a biology perspective, health self-repair is more effective than current 'best available' medical treatments (largely because self-repair is biologically more plausible and more advanced, thanks to millions of years of evolution, Greger & Stone, 2016, Li, 2019). The number of well conducted RCT's (Randomized Controlled Trials) showing rapid health improvements within a matter of hours, days or weeks is rapidly growing, largely in the domains of cardio- and metabolic conditions, plus increasingly so in the onco- and neurology domains: depression and even dementia (Greger & Stone, 2016, Bredesen 2017, 2018, Ornish & Ornish 2019, Simons 2020a, 2021a, 2021b).

However, DIY health priorities are difficult to choose, since the number of yearly new studies on health is so large that the field can be overwhelming. For example, even when limiting the search to only the year 2019, Scholar Google finds >500.000 studies on 'health', of which >60.000 are on 'healthy lifestyle'. Furthermore, 2019

has >150.000 studies on ‘obesity’ and >180.000 studies on ‘cardiovascular health’. In short, every working day of the year there are >2000 new studies on health: good luck keeping up with that! And whether you are a practitioner or a patient, you likely have tasks which preclude reading many hours of literature every day. Given this enormous amount of literature, it is also quite easy to get lost in sub-branches, while losing sight of the bigger picture.

In order to help practitioners and DIY patients to navigate this massive amount of science and help them capture, assess and use the best and most recent available evidence on lifestyle interventions for disease reversal, we aim to develop a health literature AI. Thus, the main **research question** is:

What are user requirements for a health literature AI in order to support successful DIY healthy lifestyle choices for health self-repair?

2 Literature

From a biology and health engineering perspective, some of the most promising recent health discoveries use our innate mechanisms for rapid bodily self-repair (Li, 2019). We want to help people experience and measure improved health, possibly within days, with rapid feedback of progress from health measurements.

For design purposes, we take a ‘2030’ view from the future, using ‘optimism by method’: assuming maximum use of the dynamic nature of our biology for self-repair and temporarily ignoring current healthcare barriers. Our aim is to promote cure via rapid health self-repair feedback cycles. This needs an approach with personal iteration cycles, see Figure 1, using (Cross, 1994, Simons, 2020a) goals analysis (problem space), intervention planning (solution space) and measurement portfolio (evaluation space).

We can translate this health iteration cycle into DIY health questions for the hypertension and T2D cases of this paper. DIY health questions for a patient (or a practitioner guiding him/her) may become:

1. What is the underlying biology of the condition (causes, outlook, risk factors)?
(= Problem Space)
2. What are the most effective lifestyle interventions (& their attractiveness)?
(= Solution Space)
3. What are suitable health tracking options (behaviors, symptoms, biometrics)?
(= Evaluation Space)

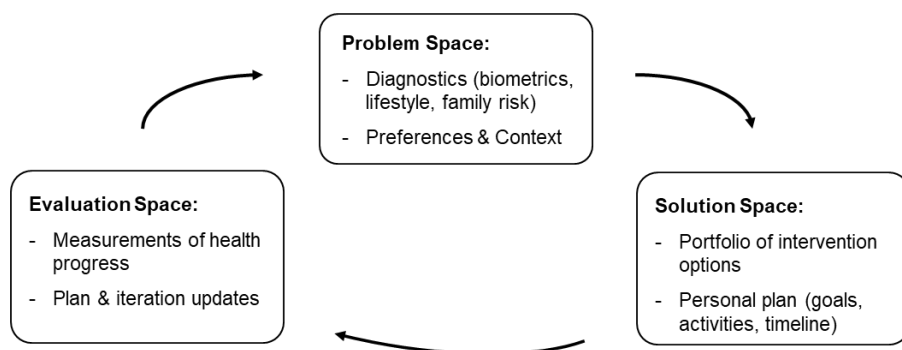


Figure 1: Personal iteration cycles for rapid health self-repair.¹

Various forms of goal setting based on personal preferences and individual coaching, eTool use like microlearning for health, Quantified Self (QS) progress tracking and peer coaching have all been shown to aid success (Simons, 2015, 2016, 2020b). Generally, it is important that patients can set their own priorities and plans, while also using practitioner support (Simons, 2014). This is not only important from a personal perspective (motivation plus a suitable fit with personal preferences and context), but it is also important from the perspective of science and up to date evidence. Lifestyle advice for patients is often outdated, due to slow adoption in health care. On average, new findings take about two decades before they enter standard clinical practice (Balas & Boren, 2000). The practical implication is that for front runner *patients* with ambition in DIY health improvement, science has a lot more effectiveness and evidence to offer than is visible in regular patient lifestyle guidelines. The same challenge exists for *practitioners* wanting to support DIY

¹ Besides biology opportunities of self-repair, overall health iteration success depends on the full picture of choosing personal goals and behaviours that are best suited for one's preferences and context. See Simons (2010, 2013, 2014) for information on intervention planning.

health for their patients. Below, we describe how we use a cross-case analysis to find user requirements that must be fulfilled in order for the health literature AI system to aid DIY health intervention choices.

3 Method

Our research question is a design analysis question. The analysis is an example of design research rather than design science (Vaishnavi & Kuechler, 2004), since design research aims at generating (domain specific) knowledge for solving a given problem. Our analysis will follow design cycle phases 1 and 2 of (Verschuren & Hartog, 2005): '1. first hunch' and '2. assumptions and requirements'. Our first hunch is that we need to explicate the gaps in common sources of information for DIY patients (health care lifestyle guidelines and Google Scholar²). In other words: which needs or gaps should be filled with the health literature AI to aid DIY health intervention choices? Second, can we formulate 'Voice of the Patient' user requirements? We use the first step from QFD (Quality Function Deployment) for software design. This means we explicate 'the voice of the user/patient', using words that users might use themselves (Simons & Verhagen, 2008, Schockert & Herzwurm, 2018), to indicate their needs when using the AI system. (Next, outside the scope of this paper, come steps to validate this with user testing and to form a QFD matrix translating user requirements to technology attributes.)

Since we want a domain-independent structure of the AI health literature support system, we use two different health domains for our DIY case analyses: hypertension and T2D (Type 2 Diabetes). We see them as suitable cases, since they are relevant (with these conditions impacting respectively 50% and 30% of people in affluent countries), different (managed and researched by different specialists) and obviously lifestyle related. We analyze the Dutch situation: What are some of the main health care lifestyle sites and guidelines that patients encounter? What do we observe if we compare that to leading edge lifestyle interventions?

Our approach is similar to action research in the sense that we have a high level of 'access' to the current practices and patients in these domains,³ while at the same

² We take Scholar Google as a reference point for exploring recent studies, since it is so widely used.

³ By providing 6 months of lifestyle coaching (Simons et al., 2010, 2017) for literally thousands of patients and caregivers in these domains, over the course of the past 10 years.

time trying to help them in navigating the information diversity they encounter. Many 'front runner DIY patients' are not average. Although they are higher educated on average, we see their struggles on a daily basis in trying to digest and use the available health science for their DIY health choices. Simultaneously, we see potential for AI to help them. The user analysis in this paper is meant as a first iteration for 'user requirements' that would support their search and decision needs. A fruitful way to start, is to evaluate the current routes/tools they use and analyze the user needs that become apparent from that process.

In the analysis section below, we will take the following steps for our case and user needs analysis (for T2D & hypertension), in two main paragraphs:

1. (a) Case analysis ***Health care advise***: What are some of the main health care lifestyle sites and guidelines that patients encounter for their condition?
1. (b) Evaluation from the design goal perspective: What ***omissions*** do we see if we compare results from step 1(a) to ***leading lifestyle intervention science***?
2. (a) Case analysis ***Science***, via Google Scholar: What is the content, diversity, clarity and applicability of the information found?
2. (b) ***Translation to 'voice of the patient' user requirements***: How could the AI system support my needs and decisions?

4 Analysis, cases T2D & hypertension

4.1 Health care lifestyle guidelines vs. DIY health decisions

As an exemplary search route for a DIY patient with T2D in the Netherlands, we started with a google search (in Dutch) with: "I have diabetes, what can I do?" This led to a top 3 of respectable online sources: www.thuisarts.nl (most visited NL site for family doctor questions), www.diabetesfonds.nl (NL diabetes research & funding) and www.dvn.nl ('Diabetes Vereniging NL' patient association).

Table 1: Case analyses: What is advised vs. omitted on traditional health care sites?

	T2D (Type 2 Diabetes)	Hypertension
Advised (a)	-Lower your blood sugar by eating well (fruits, veggies, nuts, yogurt. No sugary drinks) brisk walk 30 min/day or 60 min/day if overweight. -If that doesn't work: pills. -Manage it well: 3-monthly medical checks.	-Stop smoking, eat well (fruits, veggies, wholegrain, fibers, less saturated fat), less salt, brisk walk 2,5 hrs/week, less stress. -Other factors: weight, alcohol, fatty foods (& some meds) -If cardiac risks: pills. -Discuss checkups with doctor.
Omitted (b)⁴	-T2D is >90% avoidable with healthy lifestyle. -Interventions exist that remove >75% of meds in 4 weeks. -Causes: insulin resistance, lipotoxicity, inflammation: 1-wk reset interventions very effective.	-Hypertension >90% avoidable with healthy lifestyle. -Interventions exist that remove >50% of meds in 4 weeks. -Causes: endothelial function & inflammation: food has more & faster effect than medication.

Apart from the similarities, also summarized in Table 1, it is interesting to see that www.thuisarts.nl is more directed towards medication and 3-monthly checks for complications. Whereas the other two sources explain the causal roles of health behaviors and insulin sensitivity better.



Figure 2: Food page of www.dvn.nl directly contradicts www.dvn.nl advise.

⁴ Sources from longstanding research lines: overall (Roberts & Barnard, 2005), in T2D (Hu, 2001, Fuhrman & Sorensen, 2012, Simons, 2016, 2021a) in hypertension, endothelial health and inflammation (Niskanen, 2004, Franzini, 2012, Rodríguez-Leyva, 2013, Dickinson, 2014, Kapil, 2015, Siervo, 2015, Greger & Stone, 2016).

A similar search for ***hypertension*** gave as top 3 sources: www.thuisarts.nl again, www.hartstichting.nl (cardiac research funding & patient education) and www.zorgkaartnederland.nl (patient association to compare care providers). Of these, www.hartstichting.nl gives most lifestyle support, but not anywhere close to scientific state-of-the-art.

Three aspects are fascinating about these sources: (1) all the relevant and evidence based health ***facts they do not give, see ‘Omitted’ in Table 1*** summary (2) tendencies to medicalize instead of empower patients (3) the ***contradictions and biases*** that persist from Dutch food culture. As two examples of bias, all three T2D sources are clear that saturated fats make things worse. Which they give as one of the reasons that meats should be avoided. Still, Figure 2 shows what the very first picture is on the www.dvn.nl healthy foods page: a meat based dish. And we all know that 1 picture speaks louder than 1000 words... A second example of Dutch food bias is cheese. Despite its high saturated fat content, all three T2D sites say that cheese is perfectly healthy for T2D patients, without providing any justification. The cheese advice is biologically implausible and it contrasts with large empirical studies (Guasch-Ferré, 2017, Drouin-Chartier, 2019) showing clear T2D risk reductions when replacing cheese and butter with less harmful foods⁵.

4.2 Scientific studies vs. DIY health decisions

As illustrated in section 4.1, healthy lifestyle advice on main patient support sites is watered down and prone to cultural and historical biases. In other words: outdated and not suited to patients or practitioners that prefer high impact interventions. Hence, the question is: what if we go directly to the scientific state-of-the-art, how easily will we find clear and actionable answers? Though one could argue that scientific studies are not useful since they are not written for DIY health questions, one could also argue the opposite: when looking for the latest findings and evidence, what better place to look than science? The AI for DIY health we aim for, is meant to bridge both sides of this equation.

⁵ Outside our scope, there are ample discussions (Campbell & Campbell, 2016, Fuhrman & Sorensen, 2012, Greger & Stone, 2016, Greger, 2019) of how our health institutions are living in bubbles of ‘not rocking the boat’, leading to culturally biased and watered down advice. Which is quite different from the high impact interventions that leading edge DIY patients and practitioners are looking for.

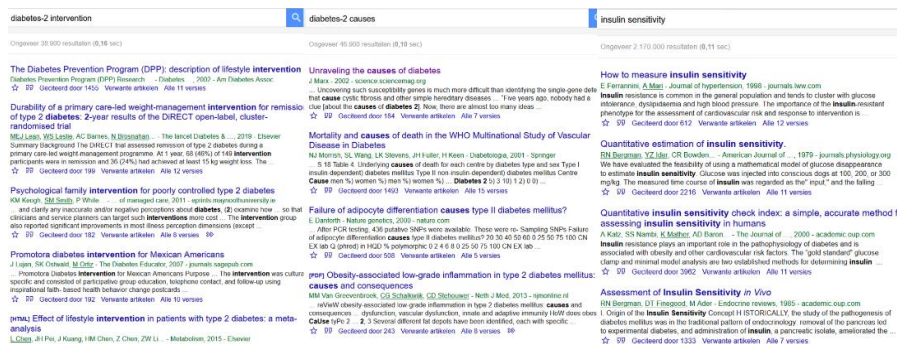


Figure 3: Illustration of study diversity when searching for DIY health answers.

One sees when using Google Scholar, see Figure 3, that the body of scientific studies is not only large, but also highly diverse, with many different subdisciplines in science having their own language and focus. For example, the search results for measuring insulin sensitivity (or -resistance) are way too diverse and technical for helping a patient with his/her daily or weekly progress tracking question. A simple ‘ask your doctor to measure it via an OGTT (Oral Glucose Tolerance Test)’ would be more helpful. In Table 2 we summarize our main Scholar search findings with regard to the section 2 patient questions: causes, interventions and measurements.

Table 2: Use cases science: study overview & contents evaluation

	T2D (Type 2 Diabetes)	Hypertension
Study Search Content	-Causes: diverse papers, many with a genetics, cell or pharma focus, or on complications (cardiac, renal, retina etc). Different results per population. Psycho-socio-cultural factors. -Interventions: widely varying results & difficult to assess why. Reviews= ‘average’ results, not highest impact. -Measuring: either ‘medi-tech’ details or quarterly checks & sugar management or ‘modest’ QS for walking, weight loss etc.	-Causes: many forms (resistant, pulmonary, nondipping, secondary) correlates & co-morbidities of hypertension. -Interventions: apart from many drugs intervention also a long lifestyle interventions tradition. Hard to find and compare dose-response for components: salt, meat, smoke, sports, stress, alcohol, fruits, veggies, fiber etc. -Measuring: Many on 24-h ambulatory monitoring. ‘Manage it’ is checkups (& often drugs).

Another finding is that Google Scholar search results aid in exploring the field, but they are not qualified overviews, see also Figure 3. Overviews exist in the various academic subdisciplines, like literature reviews or meta-analyses, but they often match poorly to the more action-focused ‘voice of the patient’ questions we hear on a daily basis. These are questions on e.g. feasibility of interventions, what is most useful to do and to measure and how to deal with dilemma’s and tradeoffs?

In *answer to our Research Question* and including the concerns above, we get as draft **‘voice of the patient’ user requirements** for the AI system:

1. What are the main causal lifestyle factors that I can potentially influence?
 - 1.1. How large are the effects per causal factor?
 - 1.2. What is the quality of evidence to support this?
2. What are the most effective lifestyle interventions?
 - 2.1 Which are relatively easy and/or attractive for me?
 - 2.2 Which offer rapid, noticeable health results?
3. How can I rapidly measure my health progress?
 - 3.1 Which measurements are low cost & practical for DIY?
 - 3.2 Which are reliable health progress indicators (=have good external validity)?
4. Which attributes above need tradeoff decisions?

If we then look at for example questions 2.1 (intervention ease and attractiveness) or 2.2 (rapid results), we find that most academic overviews are not outlined along these lines. The AI system will need to provide functionality to fill that void and help answer these questions for front runner DIY patients and practitioners.

5 Discussion & Conclusion: AI for next level Quantified Self

An important limitation to our study is that our results still need validation via user testing. Preferably via a Wizard of Oz type of study, with questions like: What would you like to know? Which searches would you use? How would result XYZ help you? What display of results would you like? And in terms of design process, the next QFD step has to be taken: translation of the user requirements to technical attributes which fulfill those requirements for the AI system.

Still, our analyses illustrate that standard lifestyle guidelines are rather meager for health DIY purposes (section 4.1) whereas the scientific information is huge and hard to assess, with many different 'bubbles' within the scientific community whose discussions are highly specialized and disjunct (section 4.2). When designing AI support, there are three reasons for a *hybrid* AI system (which includes expert mediated interpretations) rather than stand-alone AI. First, human interpretation of research design and study validity are needed to counter 'fabricated pseudo-science' lifestyle studies which are often industry-sponsored (Campbell & Campbell, 2016, Greger & Stone, 2016, Simons, 2020a). Second, to avoid 'newness bias'. For example the PCRM (Physicians Committee for Responsible Medicine) show how 'serious scientists' have abandoned studying cholesterol effects of eggs decades ago, since the results were so clear, leaving the field open to biased egg industry studies under labels like 'recent studies show ..' (Barnard, 2019). Third, due to all kinds of confounding factors, lifestyle intervention successes can be difficult to achieve, thus cluttering the scientific field with mediocre results. If 90% of attempts for a certain intervention were less successful, how do we interpret and present the 10% that were very successful? Although this 10% may not form a majority, they often do lead the way forward for new lifestyle successes.

Conclusion

Front runner patients and practitioners aiming for rapid DIY health improvements have a lot to offer for pioneering the frontiers of a more sustainable and effective '2030' healthcare. This will become even more powerful when they have a shared state-of-the-art health literature view thanks to the hybrid AI system we aim to develop. For diseases of affluence, if "health is what happens between doctors' visits", this is a cheaper, more effective way to deliver health care.

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References

- Balas, E. A., & Boren, S. A. (2000). Yearbook of medical informatics: managing clinical knowledge for health care improvement. Stuttgart, Germany.
- Barnard, N. D., Long, M. B., Ferguson, J. M., Flores, R., & Kahleova, H. (2019). Industry Funding and Cholesterol Research: A Systematic Review. *American Journal of Lifestyle Medicine*, 1559827619892198.
- Bredesen, D. (2017). The end of Alzheimer's: The first program to prevent and reverse cognitive decline. Penguin.
- Bredesen, D. E., Sharlin, K., Jenkins, D., Okuno, M. et al (2018). Reversal of cognitive decline: 100 patients. *J Alzheimers Dis Parkinsonism*, 8(450), 2161-0460.
- Burd, Steven A. (2009), "How Safeway Is Cutting Health-Care Costs," *Wall Street Journal*, Eastern Edition, June 12, A15.
- Campbell, T. C., & Campbell II, T. M. (2016). The China Study: Revised and Expanded Edition: The Most Comprehensive Study of Nutrition Ever Conducted and the Startling Implications for Diet, Weight Loss, and Long-Term Health. BenBella Books, Inc.
- Cross, N. (1994). *Engineering Design Methods; Strategies for Product Design* (2nd ed. ed.). Chichester: John Wiley & Sons.
- Dickinson, K. M., Clifton, P. M., Burrell, L. M., Barrett, P. H. R., & Keogh, J. B. (2014). Postprandial effects of a high salt meal on serum sodium, arterial stiffness, markers of nitric oxide production and markers of endothelial function. *Atherosclerosis*, 232(1), 211-216.
- Drouin-Chartier, J. P., Li, Y., Ardisson Korat, A. V., Ding, M., Lamarche, B., Manson, J. E., ... & Hu, F. B. (2019). Changes in dairy product consumption and risk of type 2 diabetes: results from 3 large prospective cohorts of US men and women. *Am J Clin Nutr*, 110(5), 1201-1212.
- Franzini, L., Ardigo, D., Valtuena, S., Pellegrini, N., Del Rio, D., Bianchi, M. A., ... & Zavaroni, I. (2012). Food selection based on high total antioxidant capacity improves endothelial function in a low cardiovascular risk population. *Nutrition, Metabolism and Cardiovascular Diseases*, 22(1), 50-57.
- Fuhrman, J., & Sorensen, C. (2012). *The End of Diabetes*. HarperCollins.
- Greger, M., & Stone, G. (2016). *How not to die: discover the foods scientifically proven to prevent and reverse disease*. Pan Macmillan.
- Greger, M. (2019) *How Not to Diet: The Groundbreaking Science of Healthy, Permanent Weight Loss*. Flatiron Books.
- Guasch-Ferré, M., Becerra-Tomas, N., Ruiz-Canela, M., Corella, D., Schröder, H., Estruch, R., ... & Salas-Salvadó, J. (2017). Total and subtypes of dietary fat intake and risk of type 2 diabetes mellitus in the Prevención con Dieta Mediterránea (PREDIMED) study. *Am J Clin Nutr*, 105(3), 723-735.
- Schockert, S., & Herzwurm, G. (2018). *Agile Software Quality Function Deployment*. Software Engineering und Software Management 2018.
- Hu, F. B., Manson, J. E., Stampfer, M. J., Colditz, G., Liu, S., Solomon, C. G., & Willett, W. C. (2001). Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *New England journal of medicine*, 345(11), 790-797.
- Kapil, V., Khambata, R. S., Robertson, A., Caulfield, M. J., & Ahluwalia, A. (2015). Dietary nitrate provides sustained blood pressure lowering in hypertensive patients: a randomized, phase 2, double-blind, placebo-controlled study. *Hypertension*, 65(2), 320-327.
- Li, W. (2019). *Eat to Beat Disease: The Body's Five Defence Systems and the Foods that Could Save Your Life*. Random House.
- Niskanen, L., Laaksonen, D. E., Nyyssönen, K., Punnonen, K., Valkonen, V. P., Fuentes, R., ... & Salonen, J. T. (2004). Inflammation, abdominal obesity, and smoking as predictors of hypertension. *Hypertension*, 44(6), 859-865.
- Ornish, D., & Ornish, A. (2019). *Undo it!: How simple lifestyle changes can reverse most chronic diseases*. Ballantine Books.

- Roberts, C. K., & Barnard, R. J. (2005). Effects of exercise and diet on chronic disease. *Journal of applied physiology*, 98(1), 3-30.
- Rodriguez-Leyva, D., Weighell, W., Edel, A. L., LaVallee, R., Dibrov, E., Pinneker, R., ... & Pierce, G. N. (2013). Potent antihypertensive action of dietary flaxseed in hypertensive patients. *Hypertension*, 62(6), 1081-1089.
- Siervo, M., Lara, J., Chowdhury, S., Ashor, A., Oggioni, C., & Mathers, J. C. (2015). Effects of the Dietary Approach to Stop Hypertension (DASH) diet on cardiovascular risk factors: a systematic review and meta-analysis. *British Journal of Nutrition*, 113(1), 1-15.
- Simons, LPA & Verhagen, WP. (2008). Applying value-sensitive design and quality function deployment to healthcare ICT: the case of Dutch primary care unit dossiers. *Journal of Design Research* 7 (2): 155-176.
- Simons, L. P. A., & Hampe, J. F. (2010). Service Experience Design for Healthy Living Support; Comparing an In-House with an eHealth Solution. The 23rd Bled eConference, pp. 423-440. Accessed 2010 from www.bledconference.org
- Simons LPA, Hampe JF, Guldemonnd NA. (2013). Designing Healthy Living Support: Mobile applications added to hybrid (e)Coach Solution. *Health and Technology*. 3 (1) pp.85-95. DOI 10.1007/s12553-013-0052-9
- Simons LPA, Hampe JF, Guldemonnd NA. (2014). ICT supported healthy lifestyle interventions: Design Lessons. *Electronic Markets*. 24 pp. 179-192. DOI 10.1007/s12525-014-0157-7.
- Simons LPA, Foerster F., Bruck PA, Motiwalla L & Jonker CM. (2015). Microlearning mApp Raises Health Competence: Hybrid Service Design. *Health and Technology*, 5 pp 35-43. DOI 10.1007/s12553-015-0095-1
- Simons, L. P., Pijl, H., Verhoef, J., Lamb, H. J. et al (2016). Intensive Lifestyle (e) Support to Reverse Diabetes-2. In Bled eConference (p. 24), accessed Dec 20, 2016 www.bledconference.org.
- Simons LPA, Hafkamp MPJ, Bodegom D, Dumaij A, Jonker CM. (2017). Improving Employee Health; Lessons from an RCT. *Int. J. Networking and Virtual Organisations*, Vol. 17, No. 4, pp.341–353. DOI <https://doi.org/10.1504/IJNVO.2017.088485>
- Simons, LPA, (2020a). Health 2050: Bioinformatics for Rapid Self-Repair; A Design Analysis for Future Quantified Self, pp. 247-261, 33rd Bled eConference. June 28-29, Bled, Slovenia, Proceedings retrieval from www.bledconference.org. ISBN-13: 978-961-286-485-9, DOI: <https://doi.org/10.18690/978-961-286-485-9.17>.
- Simons, LPA, Heuvel, AC van den, Jonker CM. (2020b). eHealth WhatsApp for social support: design lessons. *International Journal of Networking and Virtual Organisations*, 23(2), 112-127. DOI <https://doi.org/10.1504/IJNVO.2020.108857>.
- Simons, LPA, Pijl M, Verhoef J, Lamb HJ, van Ommen B, Gerritsen B, Bizino MB, Snel M, Feenstra R, Jonker CM. (2021a). e-Health Diabetes; 50 Weeks Evaluation. *Int. J. Biomedical Engineering and Technology*, Accepted (DOI will follow)
- Simons, LPA, (2021b). Health 2050: Faster Cure via Bioinformatics & Quantified Self; A Design Analysis. *Int. J. Biomedical Engineering and Technology*, Submitted.
- Vaishnavi, V., & Kuechler, W. (2004). Design Research in Information Systems. Accessed Aug 16, 2009 from <http://desrist.org/design-research-in-information-systems>
- Verschuren, P., & Hartog, R. (2005). Evaluation in Design-Oriented Research. *Quality and Quantity*, 39, pp. 733-762.
- Willett, W., Rockström, J., Loken, B., Springmann, et al (2019). Food in the Anthropocene: the EAT–Lancet Commission on healthy diets from sustainable food systems. *The Lancet*, 393(10170), 447-492

