Delft University of Technology

Document Version
Final published version

Licence
Dutch Copyright Act (Article 25fa)

Citation (APA)
Simons, L. P. A., Murukannaiah, P. K., & Neerincx, M. A. (2026). Dementia Empowerment with Heart Health Intervention and LLM-based Health AI Research Assistant. In *Digital Convergence: Better Solutions for People with Dementia* (pp. 323-345). CRC Press. https://doi.org/10.1201/9781003485681-16

Important note
To cite this publication, please use the final published version (if applicable).
Please check the document version above.

Copyright
In case the licence states “Dutch Copyright Act (Article 25fa)”, this publication was made available Green Open Access via the TU Delft Institutional Repository pursuant to Dutch Copyright Act (Article 25fa, the Taverne amendment). This provision does not affect copyright ownership.
Unless copyright is transferred by contract or statute, it remains with the copyright holder.

Sharing and reuse
Other than for strictly personal use, it is not permitted to download, forward or distribute the text or part of it, without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license such as Creative Commons.

Takedown policy
Please contact us and provide details if you believe this document breaches copyrights.
We will remove access to the work immediately and investigate your claim.

This work is downloaded from Delft University of Technology.

16

Dementia Empowerment with Heart Health Intervention and LLM-based Health AI Research Assistant

Luuk P.A. Simons, Pradeep K. Murukannaiah, and Mark A. Neerincx

This research was (partly) funded by the https://www.hybrid-intelligence-centre.nl/ a 10-year programme funded the Dutch Ministry of Education, Culture and Science through the Netherlands Organisation for Scientific Research, grant number 024.004.022 and by EU H2020 ICT48 project "Humane AI Net" under contract $\# $952026.

16.1 Introduction

Dementia is one of the largest health problems in the world. It is the most expensive disease in most of the industrialized world (Sherzai & Sherzai, 2019), and it places a very large emotional load on caregivers. It is estimated that 15 billion hours of unpaid care are provided yearly to Alzheimer's patients in the USA alone (Alzheimer's Association, 2022). Moreover, it is one of the fasted growing diseases in the world (Sherzai & Sherzai, 2019).

There is a common misconception that dementia cannot be avoided (Hudson, Pollux, Mistry & Hobson, 2012; Cahill, Pierce, Werner, Darley et al., 2015). However, it is largely preventable. For example, the risk scoring system of (Kivipelto, Ngandu, Laatikainen, Winblad et al., 2006) indicates that males of 50 years old can have a factor of 50 times (!!) increase in Alzheimer's risk, depending on lifestyle-related risk factors. In any case, dementia is much better avoidable than treatable (De la Torre, 2010). The summary of that literature is that promoting heart health also promotes brain health (Singh-Manoux, Kivimaki, Glymour, Elbaz et al., 2012). More details follow in Section 16.2, Theory.

Another misconception, or at least a dominant bias from Big Hospital and Big Pharma (Cummings, Lee, Nahed, Kambar, et al., 2022), appears to be the

DOI: 10.1201/9781003485681-16

idea that the best one can hope for in dementia care is alleviation of some of its symptoms, using drugs (Ayton & Bush, 2021). However, biologically, we know that dementia is not a drug deficiency disease, but a cardiovascular-health-related condition (Barnes & Yaffe, 2011; Sabbagh, Perez, Holland, Boustani et al., 2022), building up in our bodies for many decades (Braak & Braak, 1997). There are more than 100,000 recent papers on Alzheimer's (Greger, 2023) and a huge number of them revolve around (pharmaceutical) interventions targeting amyloid plaques. This strategy has been strikingly unsuccessful, with an abysmal 99.6% drug failure rate, the worst of any therapeutic area (Torres-Acosta, O'Keefe, O'Keefe, Isaacson et al., 2020), and some authors labelled this approach as "a congregation of the church of the holy plaque" (Joseph, Shukitt-Hale, Denisova, Martin et al., 2001). This label follows from scientific discussions that it may well be that amyloid plaques and tau tangles are a byproduct of dementia and part of the brain's defence mechanisms, instead of a causal factor (Ayton & Bush, 2021). For a more extensive review, we refer the reader to Greger (2023), chapter "Preserving your mind."

At the same time, interventions that foster brain health, which can improve mental functioning (Barnard, Bush, Ceccarelli, Cooper et al., 2014), dementia biomarkers (Bredesen, 2017; Bredesen et al., 2018), and symptoms of cognitive decline (Williamson, 2019) remain largely unknown and under-utilized. See also our previous work on this underused potential (Simons, 2020, 2023). (There may be a third misconception at work here, namely the assumption that (senior) people will hardly improve their health behaviours (Verweij, Coffeng, van Mechelen & Proper, 2011). An assumption we will refute in Section 16.2, Theory, and Section 16.5, Discussion.)

Given the importance of healthy lifestyle and dementia prevention, an important question becomes ***how to empower patients, caregivers, and their day-to-day health professionals*** (physiotherapists, nurses, dieticians, physician assistants) ***to effectively reduce dementia risk and progression***. As discussed elsewhere (Simons, 2023), the "pill-paradigm" tends to disempower patients, whereas a "self-healing paradigm" is more empowering and biologically better suited for lifestyle-related conditions like dementia. In this chapter, we combine an innovation or design perspective (in which we argue for using "heart health" intervention experiences and a Heart Health AI self-management support (SMS) tool for treating early-stage dementia and cognitive decline) with an empirical element: conducting a user evaluation of the added value of such a Health AI tool with participants who had recent experience with intensive self-management health improvements.

So as a first contribution of this chapter, from an ***innovation and design perspective***, we propose ***two empowerment opportunities***. To start with, based on literature, in Section 16.2, we will propose why and how a daily blood pressure intervention is a cheap, effective, and attractive SMS option for early-stage treatment of dementia and cognitive decline. Secondly, we argue (more details in Section 16.2) that it is becoming increasingly difficult to keep up with the

scientific literature on effective health behaviours for dementia prevention (since there are simply too many new research papers published each year), and that a Health AI Research Assistant may be helpful for health SMS.

Within our design perspective, the empowerment mantra of "Heart health = Brain health" will lead the way, not only because it is biologically relevant and easy to measure daily blood pressure improvements as a proxy for effective dementia prevention, but also since there is so much more intervention experience in the heart health than in the dementia domain, on which we can build. Similarly,

As a second contribution of this chapter, the empirical element is a user evaluation of the added value of a Health AI Research Assistant concept (hereafter also called "Health AI") with n = 8 participants who had just completed a successful heart health intervention, using various information sources. Hence, the focus of the ***user evaluation*** in this chapter is: *For users with hypertension health self-management experience, what are perceived usefulness and intention to use for a Health AI, compared to their other health information sources?*

The Research Questions for the user evaluation are:

1. *In users' solution space, what are their information needs and priorities? What would they most want to ask the Health AI tool?*
2. *How do they use and value other information sources (besides the Health AI)?*
3. *What is their "Technology Acceptance" evaluation and intention to use the Health AI?*

16.2 Theory

In this section we address three topics. Firstly, how heart-healthy behaviours and hypertension management can reduce dementia and cognitive decline risks. Secondly, the power of health SMS and daily social microlearning to achieve large blood pressure improvements through healthier behaviours (thus also reducing dementia risk). Thirdly, we address the design of a Health AI to add value for patients, caregivers, and their health professionals. And we discuss related work on large language models (LLMs) and claims analysis approaches for developing a Health AI.

16.2.1 Improving Blood Pressure and Cardiovascular Health for Dementia

The most common forms of dementia are Alzheimer's disease and cardiovascular dementia. Dementia incidence varies widely worldwide, with patterns very similar to those of heart disease, and with risk levels depending largely on the same health behaviours (Barnes & Yaffe, 2011).

Like in heart disease, consumption of saturated fats (Okereke, Rosner, Kim, Kang et al., 2012; Cao, Li, Han, Tayie et al., 2019), cholesterol (Barnard, 2018), and other foods that worsen atherosclerosis (Roher, Tyas, Maarouf, Daugs et al., 2011) are known risk factors for dementia and cognitive decline, just like blood cholesterol levels are a dementia risk factor (Corsinovi, Biasi, Poli, Leonarduzzi et al., 2011). There is extensive research explaining how pro-atherosclerotic behaviours and pathogenesis promote dementia, which is out of scope of this chapter (Roher, Tyas, Maarouf, Daugs et al., 2011). As is a broader review of the dementia preventive effects of anti-inflammatory, anti-oxidant, and anti-aging foods and lifestyle. Extensive reviews can be found in (Greger & Stone, 2016) and (Greger, 2023).

In this section we focus on the biological benefits of blood pressure reduction for dementia treatment, while at the same time acknowledging that most food and lifestyle choices that lower blood pressure will also lower serum cholesterol levels, systemic inflammation, oxidative stress and other know cardiac- and brain aging risk factors (Bredesen, 2017, Bredesen et al., 2018, Li, 2019, Greger, 2023).

Illustrating heart health relevance for early-stage dementia treatment, Professor Dean Ornish and coworkers have recently shown that their heart health intervention (Ornish, Scherwitz, Billings, Gould, et al., 1998, Ornish, Magbanua, Weidner, Weinberg et al., 2008, Lippman, Stump, Veazey, Guimarães et al., 2024) is surprisingly effective for improving cognitive function in those early-stage Alzheimer's participants that implemented the largest health behaviour improvements (Ornish, Madison, Kivipelto, Kemp et al., 2024).

Blood pressure and vascular function (= elasticity as well as protective and regulative properties of our arteries) are important for brain health, since elastic artery walls function as shock absorbers. As our arteries stiffen, the pressure pulses caused by the pumping of our heart can damage the small vessels in our brain (Pase, Herbert, Grima, Pipingas et al., 2012). This causes three times as many "brain microbleeds" in people with high blood pressure (Henskens, Van Oostenbrugge, Kroon, De Leeuw et al., 2008) and more lacunar infarcts (Kovacic & Fuster, 2012). These lacunar infarcts are small, silent brain infarcts associated with cognitive decline and a double dementia risk (Vermeer, Longstreth & Koudstaal, 2007).

Besides, high blood pressure is linked to brain shrinking, specifically in the memory centre (Beauchet, Celle, Roche, Bartha, et al., 2013). In general, hypertension in midlife is more strongly associated with risks of cognitive decline and dementia at later age than having the APOE Alzheimer's gene (Peila, White, Petrovich, Masaki et al., 2001). In summary of research reviews on the topic: "Fourteen of fifteen cross-sectional studies correlated increased arterial stiffness with impaired cognitive performance, and six of the seven longitudinal studies found that arterial stiffness appeared predictive of cognitive decline" (Singer, Trollor, Baune, Sachdev et al., 2014). Eleven randomized controlled trials (RCTs) show

that reducing sodium intake is one effective way to reduce blood pressure (Filippini, Malavolti, Whelton, Naska et al., 2021), as well as artery stiffness (D'Elia, Galletti, La Fata, Sabino, et al., 2018). And salt is now recognized as a dementia risk factor, independent of its blood pressure effects, caused by the fact that salt impairs artery function (Santisteban & Iadecola, 2018).

One of the largest interventions to show cognitive improvement with blood pressure treatment was published in 2019 (Williamson, Pajewski, Auchus, Bryan et al., 2019). More than 9,000 participants (avg. 68 years old) were randomized to lower their systolic blood pressure to either under 140 or under 120 in the SPRINT trial (Cushman, Ringer, Rodriguez, Evans, et al., 2022). The trial was meant to last six years, but was stopped halfway, since the more intensive drug regimen saved so many more lives, lowering mortality by 27% (unfortunately at the cost of negative side effects like kidney failure etc (Wright, 2015); achieving these results with healthy lifestyle would have been better and would have created positive side effects, instead of negative ones). In terms of neurological outcomes, the 17% reduction in dementia was not statistically significant, but the 19% lower risk of developing mild cognitive impairment was (Williamson, Pajewski, Auchus, Bryan et al., 2019).

16.2.2 Empowerment through Intensive Health Self-Management Support with Daily Blood Pressure Measurements and Social Microlearning

There are many challenges in creating successful health interventions (Simons & Hampe, 2010, Simons, Hampe & Guldemond, 2013, 2014, Simons, Heuvel & Jonker, 2019), and some of the key lessons are (besides the fact that it is indeed not sufficient to just tell people to "eat healthier" Simons, Gerritsen, Wielaard & Neerincx, 2023), also confirmed in the field of health SMS (Jonkman, Schuurmans, Jaarsma, Shortridge-Baggett et al., 2016, Dineen-Griffin, Garcia-Cardenas, Williams, & Benrimoj, 2019). This is because participants have diverse questions and individual support needs. For example, questions about health beliefs and what is healthy, about goal setting and -achievement, about all the automatic daily health choices (what to do for eating/drinking/being physically active, or what not to do, with over 200 "mindless" decision moments per day (Wansink, 2011)); about dealing with potentially unhealthy situations such as social events, including mental preparation- and coping strategies (Simons, Heuvel & Jonker, 2018, 2019, 2020)

Because of these health intervention challenges (see details in Jonkman, Schuurmans, Jaarsma, Shortridge-Baggett et al., 2016, Dineen-Griffin, Garcia-Cardenas, Williams, & Benrimoj, 2019, Simons, Gerritsen, Wielaard & Neerincx, 2024):

a. SMS must be customized, very regular, and very specific.

b. Success experiences and progress confirmation must occur as soon as possible, preferably multiple times per day.
c. It is crucial to coach participants for ownership and experimentation.
d. Patients and caregivers must be guided from "short-term abstinence or willpower strategies" (which are a true pitfall for long-term success (ref Baumeister) to behaviour that fits their (long term) preferences and fosters intrinsic motivations.

In other words: SMS interventions must be attractive for the individual, but also showing biological effectiveness on a relatively short notice. Thus paradoxically, ambitious and high-intensity interventions which use daily experiment-and-measurement feedback cycles to create both biological and psychological successes can be relatively effective and attractive, due to the large benefits that participants experience in a matter of days or weeks (Simons, Pijl, Verhoef, Lamb et al., 2016, 2017, 2022, Simons, Gerritsen, Wielaard & Neerincx, 2024). Blood pressure challenges, with daily self-measurement and achieving −20 to −30 points lower systolic pressure in two weeks on average, are examples of such an approach (Simons, Gerritsen, Wielaard & Neerincx, 2023, 2024).

Given our interventional desire for rapid progress feedback, for dementia and its biologically slow processes, a quicker proxy measurement is needed. Thus, we propose blood pressure challenges as a potentially suitable approach for preventing dementia or treating early-stage cognitive decline.[1] This would have the following benefits for participants: (a) getting a daily biological proxy for biological progress, (b) supporting their ownership and engagement via experiment-and-feedback cycles: which new health behaviours are sufficiently attractive additions to my life as well as biologically effective?

More details on blood pressure challenges are given elsewhere (Simons, Gerritsen, Wielaard & Neerincx, 2023, 2024), but in summary, it is a hybrid eHealth intervention with ***twice-daily blood pressure biofeedback*** consisting of:

- Telephone intake and instructions for BP home measurements
- Start—and final group sessions (two weeks apart, face-to-face)
- Daily MS Teams eCoaching in week 1
- Twice-daily BP measurements and logging email
- Feedback on group progress after first week
- Healthy recipe suggestions
- Content (portal and/or email) on health, BP, and behaviour strategies
- Light weight follow-up support, group sessions in week 5 or 6 and 9 or 10

16.2.3 Health AI Research Assistant for Personalized "Health Hacks" Mining

As stated in our introduction, there are simply too many new health research papers published every year for a human brain to digest. Even if we limit ourselves to "cardiovascular health," more than 6,000,000 studies can be found in Google Scholar. In the years 2023 and 2022, the number of scientific publications on this topic referenced by Google Scholar is 249,000 and 307,000, respectively, per year. Hence, we are looking at artificial intelligence (AI) tools for assistance.

In line with the biology of Sections 16.2.1 and 16.2.2, and to limit our scope in the first phase of our health AI design, we initially focus the AI on cardiovascular health. The AI Research Assistant tool is meant to add value by enabling patients, caregivers, and their everyday healthcare professionals (like physiotherapists, dieticians, nurse practitioners, family doctors, or physician assistants) to self-source the most effective lifestyle choices and the best available medical evidence. For most of these individual optimization questions, the generic and "watered down" suggestions of our main health institutions are not specific enough (Simons, Neerincx & Jonker, 2021, 2022, Simons, Gerritsen, Wielaard & Neerincx, 2023, 2024). As described elsewhere (Simons, Bodegom, Dumaij & Jonker, 2015, Simons, Foerster, Bruck, Motiwalla et al., 2015, Simons, Heuvel & Jonker, 2018, 2019) people face a wide variety of health choices and gain most health benefits and competences when it is not a coach telling them what to do (Simons, 2020), but when they develop their own health patterns which best suite their personal preferences, home situation, social context, etc.

The recent advances in generative AI, LLMs conversing in natural language, and automation in analyzing health claims, open interesting new opportunities for health AI Research Assistant tools. So, as a final step in this section, we summarize related work on (1) LLMs for health, (2) claims analysis in AI (Guo, Schlichtkrull & Vlachos, 2022), and (3) the role of competing tools or information sources when designing and evaluating the added value of new information tools.

In recent years, multiple papers have been published on using *LLMs for healthcare*. Some using a review on opportunities and risks from mostly editorials (Sallam, 2023) or testing several use cases with health professionals (Cascella, Montomoli, Bellini & Bignami, 2023) or interviewing health professionals versus surveying the general public on their ChatGPT use in health (Raina, Mishra & Kumar, 2024). Some of the benefits that are relevant to our research question and generally mentioned in these papers are: utility in health research and benefits for healthcare practice (improving health literacy and efficiency in reviewing the literature). Risks that are often mentioned are: lack of transparency, risk of bias, incorrect citations, and risk of hallucinations. Other papers focusing more on the technology address privacy, security, and data architecture issues (Montagna, Ferretti, Klopfenstein,

Florio et al., 2023) or training and evaluating specialized LLMs to increase natural language qualities like perceived helpfulness, logic, and empathic phrasing (Lai, Shi, Du, Wu et al., 2023). Overall, given that LLMs can be described as "probable-word generators" (Shah, 2023), it is not so surprising that healthcare professionals describe their capabilities as lacking depth and argumentation in health expertise and lacking understanding of complex relationships between personal-, health- and behaviour-aspects (Raina, Mishra & Kumar, 2024).

However, we hold the view that from a design perspective it is not enough to explicate risks of misinformation or lack of transparency of health claims. We must also think about the next steps forward: How to design and enhance generative AI tools such that these risks can be better managed? For instance, when dealing with conflicting claims, mere transparency is insufficient. Metadata and additional tools are necessary to help users weigh different sources and claims. Human domain experts can provide valuable interpretations, creating a "hybrid intelligence" that combines the strengths of artificial and human intelligence (Simons, Neerincx & Jonker, 2021, 2022, Simons, Murukannaiah & Neerincx, 2024). The field of food and health is particularly challenging due to conflicting claims and interests. So, an important question is how to use metadata, information characteristics, and assessment criteria to help evaluate claims.

The task of analyzing claims is studied under the umbrella of *automated fact checking* (Guo, Schlichtkrull & Vlachos, 2022) in the AI (specifically, Natural Language Processing) literature. Automated fact checking typically involves four subtasks: (1) Claim detection involves identifying claims for verification. An important aspect here is identifying claims that are check-worthy (i.e., claims whose truthfulness the public is interested in); (2) Evidence retrieval involves retrieving information which can be used to evaluate the veracity of the claim; (3) Verdict prediction involves determining the veracity of the claim by synthesizing the pieces of evidence retrieved; and (4) Justification production involves generating a justification for why a certain claim was ruled true or not true (or somewhere in between). This is an important and challenging task, considering the black-box nature of the AI tools. The main challenge for us is to formulate these tasks for the domain of our interest in a systematic manner.

Finally, we must borrow some *value evaluation* principles from the field of new product design. This chapter reports on a user evaluation of a Health AI concept (see its description in Section 16.3, Methods and Materials). Besides the general frameworks of Technology Acceptance Model (TAM, Venkatesh & Davis, 2000) and Unified Theory of Acceptance and Use of Technology (UTAUT, Venkatesh, Morris, Davis & Davis, 2003), looking at concepts like perceived usefulness and ease of use, product design aims to specify and design these qualities in detail (Rondini, Pezzotta, Pirola, Rossi et al., 2016). Moreover, the added value of those new qualities should also be considered in comparison to competing alternatives (Herzwurm & Schockert, 2003, Rondini, Pezzotta, Pirola, Rossi et al., 2016). Hence, in our user evaluation, besides

asking feedback on perceived usefulness of various Health AI functions, we will also ask which other information sources are used and/or preferred.

16.3 Methods and Materials

16.3.1 Research Design

Employing a design research approach (Vaishnavi & Kuechler, 2004, Verschuren & Hartog, 2005), we developed a high-level Health AI concept (described below) and gathered feedback from n = 8 participants with recent experience in a hypertension-reduction intervention (see Section 16.4, Results). We utilized a mixed-methods approach, combining quantified surveys, open-ended questions, and action research (during the intervention and user evaluation) to gain in-depth user insights and design suggestions while actively assisting participants[2] in navigating the complexities of health information. The user evaluations revealed a strong need for support in interpreting often ambiguous claims. In Section 16.5, Discussion, we propose several AI tool options to address these user requirements.

16.3.2 Participants

In early February 2024, we collected feedback from n = 8 Dutch participants who had begun an intensive hypertension-reduction intervention on January 15. All participants provided informed consent, and details of the intervention are available elsewhere (Simons, Gerritsen, Wielaard & Neerincx, 2022, 2023, 2024). Consistent with previous findings, average blood pressures were successfully reduced from 140/87 to 122/77 within 12 days through dietary and lifestyle modifications. The participants, all university employees, included two scientists and six support staff. Half were male, half female, with an average age of 45 (ranging from 29 to 58). All participants had experience with LLMs, with two having limited experience, three having average, and three having extensive experience. During the hypertension challenge, they utilized multiple information sources.

16.3.3 The Health AI Concept

- **Initial Scope:** Focussed on food and blood pressure.
- **Training Data:** Includes over 100,000 recent scientific publications in the domain.
- Specific Details are yet to be determined, but the foundation is:
- **User Interface:** Like ChatGPT, Copilot, and Gemini, with added capabilities for interpreting recent health studies.

TABLE 16.1

User Evaluation Topics

Topics Information Use and Health AI Added Value
1. Information usefulness, in general
2. "Voice of the user" Health AI preferences
3. Use of other information sources (during self-management)
4. "Technology acceptance" aspects for the Health AI

- **Language:** Operates in Dutch, allowing users to ask questions and receive answers in plain language.
- **Interactivity:** Supports follow-up questions and provides references to source publications used for answers.

16.3.4 User Evaluation & Data Analysis

When navigating health improvement iterations, participants often cycle through three design spaces: "problem," "solution," and "evaluation" (Simons, 2023). This chapter's user evaluation focuses on information usage within the "solution space" (identifying the most effective and appealing health behaviour options) and the potential benefits of the Health AI. Table 16.1 outlines the evaluation topics.

As discussed in Section 16.2, Theory, we sought insights into participants' general information preferences (topic 1), their desired functionalities and support from the Health AI (topic 2), their use of information sources during lifestyle changes (topic 3), and their technology acceptance feedback (topic 4). For the latter, we employed TAM (Venkatesh & Davis, 2000) and UTAUT (Venkatesh, Morris, Davis & Davis, 2003) to assess user evaluation concepts (perceived usefulness, ease-of-use, ability, trust, feeling, support, intention to use), focusing on individual usage preferences rather than UTAUT's organizational technology adoption processes (Carlsson, Carlsson, Hyvonen, Puhakainen et al., 2006).

Regarding data collection and analysis, we used questionnaire items for quantified evaluation of each topic. Additionally, we encouraged users to provide further input on their values and preferences, aligning with our design evaluation focus.

16.4 Results from the User Evaluation on the Health AI Tool Concept

We begin our results section by presenting the Research Questions (RQs) along with the Tables that summarize the user evaluations:

1. *In users' solution space, what are their information needs and priorities? What would they most want to ask the Health AI tool?* (Table 16.2, *scores and* Table 16.3, *open answers*)
2. *How do they use and value other information sources (besides the Health AI)?* (Table 16.4)
3. *What is their "Technology Acceptance" evaluation and intention to use the Health AI?* (Table 16.5)

In Table 16.2, we address the first Research Question by listing user responses on the usefulness of information, rated on a 7-point Likert scale. The table is divided into two parts: the first part covers general information and opinions, while the second part focuses on the usefulness of the Health AI tool. To highlight user preferences, we marked the top three highest scores in green for each question set.

For general information usefulness, the top three responses indicate that participants prioritize learning which health behaviours are most beneficial for health and hypertension, and how to make those changes easily. Notably, Question 1 received the maximum scores from all participants.

The second part of Table 16.2 reveals the most useful applications of the Health AI tool, according to participants. The top three scores are for understanding the effects of blood pressure and broader health impacts of food, along with practical tips on avoiding unhealthy foods. Just below the top

TABLE 16.2

Information Use and Health AI Preferences (7-Point (Dis)agree, n = 8, Avg = Average)

I Find the Following (General) Information Useful:	**Avg Score**
1. Connections between blood pressure, health, and behaviour	7.0
2. Most effective behaviour changes for hypertension	6.4
3. Knowing blood pressure effect sizes of behaviour changes	6.0
4. Tips for making behaviour changes *easy*	6.6
5. Tips for making behaviour changes *successful*	6.1
The Health AI Tool Would Be Useful for:	
1. Comparing blood pressure effects of foods	5.9
2. Getting health feedback on a specific (supermarket) product	5.8
3. Learning the optimum dosage of a food product	5.0
4. Learning the broader health effects of a food	6.0
5. Comparing effect sizes of foods with other health behaviours	4.9
6. Practical tips on how to increase daily intake of health foods	5.8
7. Tips on how to replace or avoid unhealthy foods	6.1
8. Tips on how to deal with pitfalls/difficult moments	5.8

TABLE 16.3

Information Use and Health AI Preferences (Open Answers)

Other Useful Information Sources Mentioned:
The conversations with the coach were most useful. I would hope the AI could have a similar conversation with us.
The context given during the Challenge in relation to healthy choices was very useful, like for example, "how sugar- and saturated-fat-spikes heighten artery systemic inflammation."
During the Challenge workshops, we heard many things that you would never think of yourself, like, for example, the blood pressure lowering effect of seeds like flaxseeds.
I was happy to hear about the updated hypertension guidelines from the AHA (American Heart Association), this is new for the Dutch context, and I will include this in my conversations with my family physician.
It's nice to see food intervention studies and effect sizes on hypertension.
Other Health AI Usefulness Mentioned:
It would be nice if the Health AI could filter information based on aspects like gender, age, weight, sports background, vegetarianism, etc., to increase relevance for my own situation.
I would like to input my existing breakfast, etc. (which I like) and ask for health improvement suggestions.
If certain foods are useful for my blood pressure, please show me the links to the original studies, so I can read them for myself (See also Table 16.5).
If the blood pressure food advice is distinct from the advice from my dietitian or weight watchers, can the Health AI explain why this may be so?
I want to ask questions on other topics like aspirin or sauna: do they also influence my blood pressure?

three, three items scored 5.8, all with a practical focus: daily eating patterns to increase healthy foods, strategies for dealing with pitfalls and difficult moments, and tips for making healthy choices when shopping.

Interestingly, opinions varied on practical advice items. Some participants preferred receiving practical tips from other participants, including context on usage and adoption. As one participant noted: "*By interacting with others about what works and why, our conversations become part of our usage intention. The goal is to apply these insights ourselves, making the* ***conversation a part of our behaviour change*** *rather than just information gathering.*"

However, others preferred the AI tool for practical advice, while favouring the coach for understanding the broader health picture and its relevant connections. In Table 16.3, we list the main open answer inputs given in the user evaluation, regarding (1) the information sources that were found useful, and (2) other Health AI usefulness ideas and preferences.

In response to Research Question 2, Table 16.4 details the extent to which participants used various information sources during the two-week Challenge period. These sources can be seen as alternatives potentially competing with the Health AI we plan to introduce. All participants reported regular use of coach inputs, and all but one found inputs from other participants useful. The third most utilized source was official health institutes. Regarding the fourth source, personal networks, most participants indicated

TABLE 16.4

Use of Other Information Sources (Number of Times, n = 8, Avg Nr = Average Number of Times)

Number of Times during Challenge (of 2 Weeks)	Avg Nr
1. My personal network (family, friends, etc.)[3]	1.7
2. My physician or other health professionals	0.4
3. Sites/info from official health institutes	2.3
4. Other Internet sources	0.5
5. Google Scholar, PubMed, or similar	0.3
6. Individual scientific papers	0.9
7. Inputs/remarks from other Challenge participants	5.8
8. Inputs from Challenge coach	7.6

that these were more about sharing information rather than receiving it, although they did receive practical advice on implementing healthy lifestyle behaviours. Other Internet sources were often described as containing too much confusing or low-quality information.

When asked which information was most useful (open question), all participants cited the ***Challenge workshops as the most beneficial***. This included materials, PowerPoints, references, an online portal with health information, and the explanations provided. *Reasons given included: providing a good summary, the value of practical tips, reflecting on their own behaviours, specific links and literature for focused follow-up, saving time, and not feeling the need to conduct their own research because the provided information was sufficient*.

Regarding Research Question 3, Table 16.5 presents responses to various aspects of Technology Acceptance. Since three of the highest-scoring items

TABLE 16.5

Technology Acceptance Factors (7-Point (Dis)Agree, n = 8, Avg = Average)

The Health AI Tool..:	Avg Score
1. is interesting	6.1
2. is useful for insights on improving my health	5.5
3. is easy to use for asking questions	6.0
4. is easy to interpret when presenting conflicting articles	4.9
5. will gain my trust, following the degree of clarity of its sources	6.1
6. I find it useful to discuss its outputs with other Challenge participants	5.5
7. I find it useful to discuss its outputs with the Challenge coach	6.5
8. I find it useful to practice its use in Challenge workshops	5.8
9. I would certainly use the Health AI	6.1

received the same score (6.1), we highlighted the top four in green. These responses indicate that participants find the Health AI interesting and intend to use it. However, it was also clear (from items 2, 4, and 6, as well as from open responses) that all participants were cautious about the risk of receiving unreliable answers from LLM tools like the Health AI. This concern is reflected in two of the top four items in Table 16.5: 5. ("it will gain my trust, following the degree of clarity of its sources") and 7. ("I find it useful to discuss the Health AI outputs with the coach").

Participants valued the ability to critically assess and interpret Health AI responses, especially when guided by human experts. They viewed this "hybrid intelligence" approach as a beneficial way to utilize the technology. However, they found interpretations from less knowledgeable participants to be less helpful.

Regarding ***future Health AI use***, preferences varied ((in line with the variation in Table 16.2 answers). Some desired introductory training on how to use (or not use) the technology effectively, while others preferred a more hands-on approach. Similarly, some wanted to ask a wide range of health, food, and blood pressure questions, while others focused on scientific research or practical daily health tips. Additionally, some expressed interest in discussing potential Health AI suggestions with other participants during workshop sessions.

16.5 Discussion

16.5.1 Empowerment of Patients, Caregivers, and Health Professionals

In this chapter, we proposed two empowerment strategies for patients, caregivers, and healthcare professionals. Firstly, we showed how the successes in cardiac health, which have motivated senior citizens to make significant lifestyle changes, can be applied to the treatment of early-stage dementia and cognitive decline. This approach leverages the biological link between blood pressure, cardiovascular health, and dementia outcomes. Practically, it provides daily feedback on progress, empowering patients in their health improvement efforts. Secondly, we introduced and tested an AI Health Research Assistant designed to extract the most relevant lifestyle findings from the vast amount of new health literature published each year, ensuring that patients and professionals stay informed with the latest research.

Regarding the first point of lifestyle changes and despite the behaviour change challenges we discussed in Section 16.2, over the years we have seen many examples of large enthusiasm and satisfaction (even one or more years later, Simons, Bodegom, Dumaij & Jonker, 2015, Simons, Foerster, Bruck, Motiwalla et al., 2015, Simons, Pijl, Verhoef, Lamb et al., 2017, Simons, Pijl,

Verhoef, Lamb et al., 2022), based on the fact that participants were challenged to make large health behaviour improvements. This fostered empowerment, engagement, and satisfaction because of the short- and long-term health benefits that participants achieved. Results are very motivating. Especially when the health behaviours that one chooses fit well with one's preferences, personal life, and health ambitions (Simons, Hampe & Guldemond, 2014, Simons, Heuvel & Jonker 2019, Simons, 2023).

Whereas the large results in the blood pressure challenge we previously published were mostly realized in (busy) working populations (Simons, Gerritsen, Wielaard & Neerincx, 2023, 2024), these results were recently replicated in older, community-participant groups, see Figure 16.1. These results have yet to be more extensively analyzed and published, but this gives a preliminary idea of the large average systolic pressure drop in the most recent elderly community group (n = 7, avg age of 75 years old) over the course of 9 weeks (2 weeks intensive + 7 weeks light weight follow up), with average recommendation and satisfaction scores of 8.6 and 8.8 (out of 10).

In relation to the Health AI, participant evaluations were surprisingly positive, but also nuanced. This response fits well with previous other health content and tool evaluations in the context of intensive lifestyle interventions. Even though not every tool is equally valued by each participant, most participants appreciate and use at least several of the tools and content sources, since they feel that it helps them forward (Simons, Pijl, Verhoef, Lamb et al., 2016, 2017, Simons, Heuvel & Jonker, 2019, 2020, Simons, Pijl, Verhoef, Lamb et al., 2022).

When discussing the limitations of the empirical user evaluation of this chapter, a first limitation is its explorative nature, with only n = 8 participants. Still, for reaching input saturation at this design stage this appears sufficient; sometimes even five, six, or seven users are enough (Faulkner, 2003). Second,

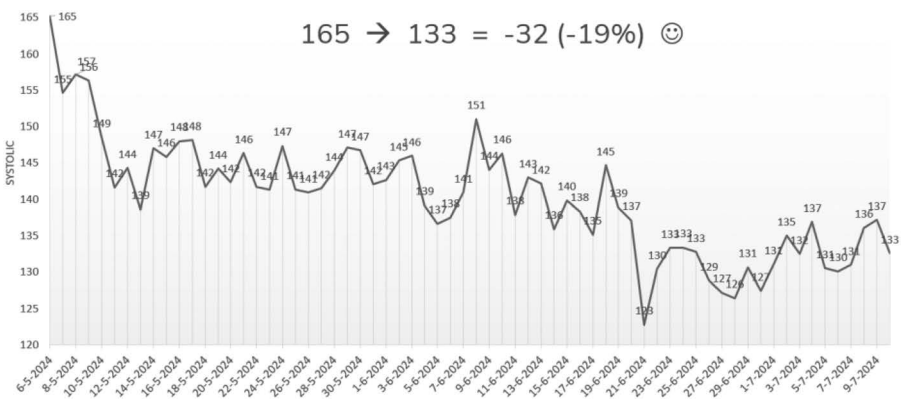


FIGURE 16.1
Average systolic pressure improvements (n = 7, avg. 75 yrs).

TABLE 16.6

Claims Evaluation Criteria

Evaluation Criteria and Interpretation Examples from Literature:

1. ***Time Evolution of Claims:*** Tools that track changes in health claims over time can be valuable. Dr. Neal Barnard (2018) highlights how claims about the cardiac health of eggs have evolved, often inaccurately becoming more positive in recent decades. This shift is attributed to the overwhelming negative evidence from earlier research, which led to a decline in serious investigation into the topic. This void was subsequently exploited by the egg industry to promote studies with questionable claims.
2. ***Consistency of Claims:*** A prime example of consistent scientific evidence is the established health benefits of fruits and vegetables. Despite this overwhelming consensus, some individuals, including intervention participants, online sources, and occasionally even dietitians, advise against consuming more than two servings of fruit per day due to concerns about their sugar content. While refined sugars may pose health risks, the consistent positive findings from numerous studies regarding the overall health benefits of fruits are clear and should prevail.
3. ***Body of Evidence:*** As a leading expert in health behaviours and risks highlights (Willett, 2012), it's crucial to evaluate the strength of scientific evidence. For over a century, a vast body of research, including animal studies, large-scale human migration studies, and randomized controlled trials, has consistently demonstrated a causal link between saturated fats, blood cholesterol, and cardiovascular disease.
4. ***Burden of Proof:*** Occasionally, new claims challenge prevailing scientific consensus. This can either represent a groundbreaking discovery or an error. A notorious example of the latter is the tobacco industry's claim that smoking is beneficial because it reduces the risk of Parkinson's disease (Greger & Stone, 2016, p.265). While it's true that tobacco and tomato plants contain substances with potential neuroprotective properties, this alone is insufficient. The burden of proof dictates that when overwhelming evidence points in one direction (smoking is harmful), extraordinary evidence is required to support the opposite claim (smoking is beneficial).
5. ***Explicit Arguments and Proof for Conflicting Claims:*** When introducing a claim that contradicts existing *body of evidence*, the *burden of proof* lies with the proponent to provide compelling arguments and/or evidence supporting the new claim, despite conflicting data. The health effects of soy consumption in humans are a case in point. While early animal studies suggested a potential link between high soy intake and cancer risk, this conflicted with the observed health of Asian populations with a high soy diet. Subsequent research revealed that rodents metabolize soy differently than humans, resolving this apparent contradiction (Setchell, Brown, Zhao, Lindley et al., 2011).
6. ***Weighing Claims for Type of Study:*** The soy example highlights a crucial principle in health research: large-scale, double-blind randomized controlled trials in humans provide significantly stronger evidence than animal studies or observational studies. While this may be evident to some, a Health AI can clarify and effectively utilize this distinction.
7. ***Claimer and Industry Affiliation Analysis:*** The prevalence of industry affiliations and conflicts of interest among scientists in the food sciences is alarming. Even the US Dietary Guidelines Advisory Committee, where objectivity should be paramount, has been found to have 19 out of 20 members with industry ties (Mialon, Serodio, Crosbie, Teicholz et al., 2022). To assess claim validity, a metadata analysis examining the identity of claimers and their industry affiliations can provide valuable insights.

the Health AI is only evaluated in concept. The next step in our research is to test a real prototype. Still, also on a concept level, their user inputs are useful, especially given their recent experience in dealing with ambiguous or conflicting claims from food and hypertension literature.

16.5.2 Health AI: Evaluation and Metadata Criteria for Ambiguous Claims

For a Health AI, besides analyzing and summarizing claims in scientific literature, there are other metadata that can be used to help evaluate the reliability of claims. In our health AI user evaluation, we heard several concerns regarding reliability and transparency of the answers. As a possible interpretation aid for users, Table 16.6 lists several criteria against which (possibly contradicting) claims can be evaluated. This is still early-stage design thinking, but we think these types of criteria are important for future AI transparency and usefulness.

16.5.3 Hybrid Intelligence for Ambiguity "Rationale capturing"

To summarize and conclude the user evaluation, it confirmed the importance of information quality and of scientific evidence for healthy lifestyle choices. Participants expressed particular concern regarding ambiguous or conflicting claims and emphasized the value of human expert support for interpreting such information. Based on their feedback, we believe this finding likely extends to other health domains, including cognition and dementia research.

Regarding the "hybrid intelligence" approach, providing expert explanations for confusing claims was deemed valuable. This addresses users' key questions of "How to interpret claims?" and "Is there an underlying reason for the ambiguity?" A hybrid solution, combining AI tools with expert human guidance, appears to be effective. In this model, the AI assists experts, while the final advice is grounded in human expertise, addressing users' primary concerns about claim confusion in the food and health domain.

16.6 Conclusion

Dementia is one of the most feared diagnoses in medicine (Greger, 2023). The aim of this chapter was to help empower patients, caregivers, and health professionals in becoming proactive in reducing future burdens of dementia and cognitive decline. For this purpose, we use biological causality: significantly reducing hypertension and improving cardiovascular health offers important potential to improve future dementia outcomes. We have attempted to

illustrate how a specific form of intensive hypertension SMS, with daily blood pressure measurements, social learning, large health behaviour changes, and multiple microlearning moments per day, helps motivate people and can lead to large improvements in cardiovascular health, even within several weeks. Moreover, it is a type of intervention which has been shown to raise health self-management competencies and which leads to high satisfaction and recommendation scores, even in the long run.

In an empowerment approach like this, participants regularly take on a lot of ownership and they want to self-source information about their options regarding health choices. For this purpose, a Health AI Research Assistant can be valuable to help mine the vast amount of new health findings published every year. User evaluations have shown that experienced lifestyle participants have positive but nuanced expectations of such a Health AI, including risks of AI hallucinations, information in-transparency, or conflicting messages. To help with transparency and information evaluation, we have proposed several metadata criteria to be used by future versions of Health AI Research Assistant tools.

Notes

1 Moreover, since there are about 30% of misdiagnoses of Alzheimer's (Viña & Sanz-Ros, 2018), caused by other underlying issues like sleep problems, depression, or side effects of (ironically) cardiovascular or sleep medications causing cognitive impairment. In our experience, blood pressure challenges also help people tackle issues like sleep problems, depressive symptoms, or overmedication. Thus we can help solve cognitive impairment via the "positive side effects" of healthy lifestyle.

2 By supporting individuals during hypertension lifestyle interventions, as well as providing six months of healthy lifestyle coaching (Simons & Hampe, 2010, 2017) for literally thousands of participants and caregivers in these domains, over the course of the past ten years.

3 One of the participants was an outlier with score 15, hence excluded from this item average. Moreover, all participants said it was more about sharing information than receiving information, except for practical tips/discussions on how to implement health behaviours.

References

Alzheimer's Association. (2022). Alzheimer's disease facts and figures. Special Report More than normal aging. https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf. Alzheimer's Association. Accessed January 8, 2003.

Ayton, S., & Bush, A. I. (2021). β-amyloid: the known unknowns. *Ageing Research Reviews*, *65*, 101212.

Barnard, R. J. (2018). How the Egg Industry Skews Science. YouTube, accessed 26-2-2024: https://www.youtube.com/watch?v=FyG8wr0gWIA.

Barnard, N. D., Bush, A. I., Ceccarelli, A., Cooper, J., de Jager, C. A., Erickson, K. I., … & Squitti, R. (2014). Dietary and lifestyle guidelines for the prevention of Alzheimer's disease. *Neurobiology of Aging*, *35*, S74–S78.

Barnes, D. E., & Yaffe, K. (2011). The projected effect of risk factor reduction on Alzheimer's disease prevalence. *The Lancet Neurology*, *10*(9), 819–828.

Beauchet, O., Celle, S., Roche, F., Bartha, R., Montero-Odasso, M., Allali, G., & Annweiler, C. (2013). Blood pressure levels and brain volume reduction: a systematic review and meta-analysis. *Journal of Hypertension*, *31*(8), 1502–1516.

Braak, H., & Braak, E. (1997). Frequency of stages of Alzheimer-related lesions in different age categories. *Neurobiology of Aging*, *18*(4), 351–357.

Cahill, S., Pierce, M., Werner, P., Darley, A., & Bobersky, A. (2015). A systematic review of the public's knowledge and understanding of Alzheimer's disease and dementia. *Alzheimer Disease & Associated Disorders*, *29*(3), 255–275.

Cao, G. Y., Li, M., Han, L., Tayie, F., Yao, S. S., Huang, Z., … & Xu, B. (2019). Dietary fat intake and cognitive function among older populations: a systematic review and meta-analysis. *The Journal of Prevention of Alzheimer's Disease*, *6*, 204–211.

Carlsson, C., Carlsson, J., Hyvonen, K., Puhakainen, J., & Walden, P. (2006). Adoption of mobile devices/services—searching for answers with the UTAUT. In *System Sciences, 2006. HICSS'06. Proceedings of the 39th Annual Hawaii International Conference on* (Vol. 6, pp. 132a–133a). IEEE.

Cascella, M., Montomoli, J., Bellini, V., & Bignami, E. (2023). Evaluating the feasibility of ChatGPT in healthcare: an analysis of multiple clinical and research scenarios. *Journal of Medical Systems*, *47*(1), 33.

Corsinovi, L., Biasi, F., Poli, G., Leonarduzzi, G., & Isaia, G. (2011). Dietary lipids and their oxidized products in Alzheimer's disease. *Molecular Nutrition & Food Research*, *55*(S2), S161–SS172.

Cummings, J., Lee, G., Nahed, P., Kambar, M. E. Z. N., Zhong, K., Fonseca, J., & Taghva, K. (2022). Alzheimer's disease drug development pipeline: 2022. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *8*(1), e12295.

Cushman, W. C., Ringer, R. J., Rodriguez, C. J., Evans, G. W., Bates, J. T., & Cutler, J. A., … & SPRINT Research Group. (2022). Blood pressure intervention and control in SPRINT. *Hypertension*, *79*(9), 2071–2080.

D'Elia, L., Galletti, F., La Fata, E., Sabino, P., & Strazzullo, P. (2018). Effect of dietary sodium restriction on arterial stiffness: systematic review and meta-analysis of the randomized controlled trials. *Journal of Hypertension*, *36*(4), 734–743.

De la Torre, J. C. (2010). Alzheimer's disease is incurable but preventable. *Journal of Alzheimer's Disease*, *20*(3), 861–870.

Dineen-Griffin, S., Garcia-Cardenas, V., Williams, K., & Benrimoj, S. I. (2019). Helping patients help themselves: a systematic review of self-management support strategies in primary health care practice. *PLoS One*, *14*(8), e0220116.

Faulkner, L. (2003). Beyond the five-user assumption: benefits of increased sample sizes in usability testing. *Behavior Research Methods, Instruments, & Computers*, *35*, 379–383.

Filippini, T., Malavolti, M., Whelton, P. K., Naska, A., Orsini, N., & Vinceti, M. (2021). Blood pressure effects of sodium reduction: dose–response meta-analysis of experimental studies. *Circulation*, *143*(16), 1542–1567.

Greger, M. (2023). *How not to age: the scientific approach to getting healthier as you get older.* Flatiron Books, New York.

Greger, M., & Stone, G. (2016). *How not to die: discover the foods scientifically proven to prevent and reverse disease*. Pan Macmillan, New York City.

Guo, Z., Schlichtkrull, M., & Vlachos, A. (2022). A survey on automated fact-checking. *Transactions of the Association for Computational Linguistics*, *10*, 178–206.

Henskens, L. H., Van Oostenbrugge, R. J., Kroon, A. A., De Leeuw, P. W., & Lodder, J. (2008). Brain microbleeds are associated with ambulatory blood pressure levels in a hypertensive population. *Hypertension*, *51*(1), 62–68.

Herzwurm, G., & Schockert, S. (2003). The leading edge in QFD for software and electronic business. *International Journal of Quality & Reliability Management*, *20*(1), 36–55.

Hudson, J. M., Pollux, P. M., Mistry, B., & Hobson, S. (2012). Beliefs about Alzheimer's disease in Britain. *Aging & Mental Health*, *16*(7), 828–835.

Jonkman, N. H., Schuurmans, M. J., Jaarsma, T., Shortridge-Baggett, L. M., Hoes, A. W., & Trappenburg, J. C. (2016). Self-management interventions: proposal and validation of a new operational definition. *Journal of Clinical Epidemiology*, *80*(12), 34–42.

Joseph, J., Shukitt-Hale, B., Denisova, N. A., Martin, A., Perry, G., & Smith, M. A. (2001). Copernicus revisited: amyloid beta in Alzheimer's disease. *Neurobiology of Aging*, *22*(1), 131–146.

Kivipelto, M., Ngandu, T., Laatikainen, T., Winblad, B., Soininen, H., & Tuomilehto, J. (2006). Risk score for the prediction of dementia risk in 20 years among middle aged people: a longitudinal, population-based study. *The Lancet Neurology*, *5*(9), 735–741.

Kovacic, J. C., & Fuster, V. (2012). Atherosclerotic risk factors, vascular cognitive impairment, and Alzheimer disease. *Mount Sinai Journal of Medicine: A Journal of Translational and Personalized Medicine*, *79*(6), 664–673.

Lai, T., Shi, Y., Du, Z., Wu, J., Fu, K., Dou, Y., & Wang, Z. (2023). Psy-LLM: Scaling up global mental health psychological services with AI-based large language models. *arXiv preprint arXiv:2307.11991*.

Li, W. W. (2019). *Eat to beat disease: the new science of how your body can heal itself.* Hachette UK.

Lippman, D., Stump, M., Veazey, E., Guimarães, S. T., Rosenfeld, R., Kelly, J. H., … & Katz, D. L. (2024). Foundations of lifestyle medicine and its evolution. *Mayo Clinic Proceedings: Innovations, Quality & Outcomes*, *8*(1), 97–111.

Mialon, M., Serodio, P., Crosbie, E., Teicholz, N., Naik, A., & Carriedo, A. (2022). Conflicts of interest for members of the US 2020 Dietary Guidelines Advisory Committee. *Public Health Nutrition*, 27(1), 1–28.

Montagna, S., Ferretti, S., Klopfenstein, L. C., Florio, A., & Pengo, M. F. (2023). Data decentralisation of LLM-based chatbot systems in chronic disease self-management. In *Proceedings of the 2023 ACM Conference on Information Technology for Social Good, Lisbon, Portugal, Sept 6 2023 to Sept 8 2023,* (pp. 205–212).

Okereke, O. I., Rosner, B. A., Kim, D. H., Kang, J. H., Cook, N. R., Manson, J. E., … & Grodstein, F. (2012). Dietary fat types and 4-year cognitive change in community-dwelling older women. *Annals of Neurology*, *72*(1), 124–134.

Ornish, D., Madison, C., Kivipelto, M., Kemp, C., McCulloch, C. E., Galasko, D., … & Arnold, S. E. (2024). Effects of intensive lifestyle changes on the progression

of mild cognitive impairment or early dementia due to Alzheimer's disease: a randomized, controlled clinical trial. *Alzheimer's Research & Therapy*, *16*(1), 122.

Ornish, D., Magbanua, M. J. M., Weidner, G., Weinberg, V., Kemp, C., Green, C., … & Carroll, P. R. (2008). Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention. *Proceedings of the National Academy of Sciences*, *105*(24), 8369–8374.

Ornish, D., Scherwitz, L. W., Billings, J. H., Gould, K. L., Merritt, T. A., Sparler, S., … & Brand, R. J. (1998). Intensive lifestyle changes for reversal of coronary heart disease. *JAMA*, *280*(23), 2001–2007.

Pase, M. P., Herbert, A., Grima, N. A., Pipingas, A., & O'Rourke, M. F. (2012). Arterial stiffness as a cause of cognitive decline and dementia: a systematic review and meta-analysis. *Internal Medicine Journal*, *42*(7), 808–815.

Peila, R., White, L. R., Petrovich, H., Masaki, K., Ross, G. W., Havlik, R. J., & Launer, L. J. (2001). Joint effect of the APOE gene and midlife systolic blood pressure on late-life cognitive impairment: the Honolulu-Asia aging study. *Stroke*, *32*(12), 2882–2889.

Raina, A., Mishra, P., & Kumar, D. (2024). AI as a Medical Ally: Evaluating ChatGPT's Usage and Impact in Indian Healthcare. *arXiv preprint arXiv:2401.15605*.

Roher, A. E., Tyas, S. L., Maarouf, C. L., Daugs, I. D., Kokjohn, T. A., Emmerling, M. R., … & Beach, T. G. (2011). Intracranial atherosclerosis as a contributing factor to Alzheimer's disease dementia. *Alzheimer's & Dementia*, *7*(4), 436–444.

Rondini, A., Pezzotta, G., Pirola, F., Rossi, M., & Pina, P. (2016). How to design and evaluate early PSS concepts: the product service concept tree. *Procedia CIRP*, *50*, 366–371.

Sabbagh, M. N., Perez, A., Holland, T. M., Boustani, M., Peabody, S. R., Yaffe, K., … & Tanzi, R. E. (2022). Primary prevention recommendations to reduce the risk of cognitive decline. *Alzheimer's & Dementia*, *18*(8), 1569–1579.

Sallam, M. (2023). ChatGPT utility in healthcare education, research, and practice: systematic review on the promising perspectives and valid concerns. *Healthcare MDPI*, *11*(6), 887.

Santisteban, M. M., & Iadecola, C. (2018). Hypertension, dietary salt and cognitive impairment. *Journal of Cerebral Blood Flow & Metabolism*, *38*(12), 2112–2128.

Setchell, K. D., Brown, N. M., Zhao, X., Lindley, S. L., Heubi, J. E., King, E. C., & Messina, M. J. (2011). Soy isoflavone phase II metabolism differs between rodents and humans: implications for the effect on breast cancer risk. *The American Journal of Clinical Nutrition*, *94*(5), 1284–1294.

Sherzai, D., & Sherzai, A. (2019). Preventing Alzheimer's: our most urgent health care priority. *American Journal of Lifestyle Medicine*, *13*(5), 451–461.

Simons, L. P. A., (2020). 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: 978-961-286-362-3. https://doi.org/10.18690/978-961-286-362-3.17.

Simons, L. P. A., (2023). Health 2050: faster cure via bioinformatics & quantified self; A design analysis. *International Journal of Networking and Virtual Organisations*, *28*(1), 36–52. https://doi.org/10.1504/IJNVO.2023.130957

Simons, L. P. A., Bodegom, D., Dumaij, A., & Jonker, C. M. (2015a). Design Lessons from an RCT to Test Efficacy of a Hybrid eHealth Solution for Work Site Health. Paper *presented at the 28th Bled eConference*. Bled, Slovenia, from www.bledconference.org.

Simons, L. P. A., Foerster, F., Bruck, P. A., Motiwalla, L., & Jonker, C. M. (2015b). Microlearning mApp raises health competence: hybrid service design. *Health and Technology*, *5*, 35–43. doi:10.1007/s12553-015-0095-1

Simons, L. P. A., Gerritsen, B., Wielaard, B., & Neerincx, M. A. (2023). Hypertension Self-Management Success in 2 weeks; 3 Pilot Studies, pp. 19–34, *36th Bled eConference*. June 25–28, Bled, Slovenia, Proceedings retrieval www.bledconference.org. ISBN-13: 978-961-286-751-5. https://research.tudelft.nl/en/publications/hypertension-self-management-success-in-2-weeks-3-pilot-studies/

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. Retrieved from www.bledconference.org

Simons, L. P. A., Hampe, J. F., & Guldemond, N. A. (2013). Designing healthy living support: mobile applications added to hybrid (e)Coach solution. *Health and Technology*, *3*(1), 85–95. doi:10.1007/s12553-013-0052-9

Simons, L. P. A., Hampe, J. F., & Guldemond, N. A. (2014). ICT supported healthy lifestyle interventions: design lessons. *Electronic Markets*, *24*, 179–192. doi:10.1007/s12525-014-0157-7

Simons, L. P. A., Heuvel, AC van den, & Jonker, C. M. (2018). eHealth WhatsApp Group for Social Support; Preliminary Results, pp. 225–237, *Presented at the 31st Bled eConference*. Bled, Slovenia, Proceedings retrieval from www.bledconference.org. ISBN-13: 978-961-286-170-4. https://doi.org/10.18690/978-961-286-170-4

Simons, L. P. A., Heuvel, AC van den, & Jonker, C. M. (2020). eHealth WhatsApp for social support: design lessons. *International Journal of Networking and Virtual Organisations*, *23*(2), 112–127. https://doi.org/10.1504/IJNVO.2020.108857

Simons, L. P. A., Gerritsen, B., Wielaard, B., & Neerincx, M. A. (2024). Employee hypertension self-management support with microlearning and social learning. *International Journal of Networking and Virtual Organisations*, *30*(4), 350–365.

Simons, L. P. A., Murukannaiah, P. K., & Neerincx, M. A. (2024). Designing and Evaluating an LLM-based Health AI Research Assistant for Hypertension Self-Management; Using Health Claims Metadata Criteria, pp. 283–298, *37th Bled eConference*. June 9–12, Bled, Slovenia, Proceedings. ISBN-13: 978-961-286-871-0. doi:10.18690/um.fov.4.2024

Simons, L. P. A., Neerincx, M. A., & Jonker, C. M. (2021). Health Literature Hybrid AI for Health Improvement; A Design Analysis for Diabetes & Hypertension, pp. 184–197, *34th Bled eConference*. June 27–30, Bled, Slovenia, Proceedings retrieval from www.bledconference.org. ISBN-13: 978-961-286-385-9. https://aisel.aisnet.org/bled2021/5

Simons, L. P. A., Pijl, M., Verhoef, J., Lamb, H. J., van Ommen, B., Gerritsen, B., Bizino, M. B., Snel, M., Feenstra, R., & Jonker, C. M. (2016). Intensive Lifestyle (e)Support to Reverse Diabetes-2. Paper *presented at the 29th Bled eConference*. Bled, Slovenia, from www.bledconference.org. and http://aisel.aisnet.org/cgi/viewcontent.cgi?article=1023&context=bled2016

Simons, L. P. A., Pijl, H., Verhoef, J., Lamb, H. J., van Ommen, B., Gerritsen, B., Bizino, M. B., Snel, M., Feenstra, R., & Jonker, C. M. (2017). Diabetes Lifestyle (e)Coaching 50 Weeks Follow Up; Technology Acceptance & e-Relationships, pp. 545–560, *presented at the 30th Bled eConference*. Bled, Slovenia, Proceedings retrieval from www.bledconference.org. ISBN 978-961-286-043-1. https://doi.org/10.18690/978-961-286-043-1

Simons, L. P. A., Neerincx, M. A., & Jonker, C. M. (2022). Is Google making us smart? Health self-management for high performance employees & organisations.

International Journal of Networking and Virtual Organisations, *27*(3), 200–216. doi:10.1504/IJNVO.2022.10053605

Simons, L. P. A., Gerritsen, B., Wielaard, B., & Neerincx, M. A. (2022). Health Self-Management Support with Microlearning to Improve Hypertension, pp. 511–524, *35th Bled eConference*. June 26–29, Bled, Slovenia, Proceedings retrieval from www.bledconference.org. ISBN-13: 978-961-286-616-7. doi:10.18690/um/fov.4.2022

Simons, L. P. A., Pijl, H., Verhoef, J., Lamb, H. J., van Ommen, B., Gerritsen, B., Bizino, M. B., Snel, M., Feenstra, R., & Jonker, C. M. (2022). E-health diabetes; 50 weeks evaluation. *International Journal of Biomedical Engineering and Technology*, *38*(1), 81–98.

Simons, L. P. A., van den Heuvel, W. A., & Jonker, C. M. (2019). WhatsApp Peer Coaching Lessons for eHealth. In *Handbook of research on optimizing healthcare management techniques* (pp. 16–32). IGI Global, ISBN 9781799813712.

Singer, J., Trollor, J. N., Baune, B. T., Sachdev, P. S., & Smith, E. (2014). Arterial stiffness, the brain and cognition: a systematic review. *Ageing Research Reviews*, *15*, 16–27.

Singh-Manoux, A., Kivimaki, M., Glymour, M. M., Elbaz, A., Berr, C., Ebmeier, K. P., … & Dugravot, A. (2012). Timing of onset of cognitive decline: results from Whitehall II prospective cohort study. *BMJ*, *344*, 1–8.

Torres-Acosta, N., O'Keefe, J. H., O'Keefe, E. L., Isaacson, R., & Small, G. (2020). Therapeutic potential of TNF-α inhibition for Alzheimer's disease prevention. *Journal of Alzheimer's Disease*, *78*(2), 619–626.

Vaishnavi, V., & Kuechler, W. (2004). Design Research in Information Systems. Last updated August 16, 2009, from https://scholar.google.com/citations?user=2AUiwBoAAAAJ&hl=en

Venkatesh, V., & Davis, F. D. (2000). A theoretical extension of the technology acceptance model: four longitudinal field studies. *Management Science*, *46*, 186–204.

Venkatesh, V., Morris, M. G., Davis, G. B., & Davis, F. D. (2003). User acceptance of information technology: toward a unified view. *MIS Quarterly*, *27*(3), 425–478.

Vermeer, S. E., Longstreth, W. T., & Koudstaal, P. J. (2007). Silent brain infarcts: a systematic review. *The Lancet Neurology*, *6*(7), 611–619.

Verschuren, P., & Hartog, R. (2005). Evaluation in design-oriented research. *Quality and Quantity*, *39*, 733–762.

Verweij, L. M., Coffeng, J., van Mechelen, W., & Proper, K. I. (2011). Meta-analyses of workplace physical activity and dietary behaviour interventions on weight outcomes. *Obesity Reviews*, *12*, 406–429.

Viña, J., & Sanz-Ros, J. (2018). Alzheimer's disease: only prevention makes sense. *European Journal of Clinical Investigation*, *48*(10), e13005.

Wansink, B. (2011). *Mindless eating*. Hay House UK Limited, London.

Willett, W. C. (2012). Dietary fats and coronary heart disease. *Journal of Internal Medicine*, *272*(1), 13–24.

Williamson, J. D., Pajewski, N. M., Auchus, A. P., Bryan, R. N., Chelune, G., & Cheung, A. K., … & Sprint Mind Investigators for the SPRINT Research Group. (2019). Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial. *JAMA*, *321*(6), 553–561.