Healthcare Innovations in an Ageing Society

The Case of Early Diagnostics for Alzheimer's Disease

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Abstract

To meet the grand challenge of ageing, early detection of Alzheimer's disease (AD) is a widely shared goal. Studying emerging early AD diagnostics developments through user-producer interaction (UPI) might increase its societal acceptance. Broadening appears to be quite advanced in early AD diagnostics research in the Netherlands. Producers engage stakeholders in informal discussions about early AD diagnostics impacts by linking up with Dutch Alzheimer Cafes. Upstream involvement takes place by encouraging patients to participate in clinical trials, in which their feedback is obtained on the technological performance of early AD diagnostics. Involving patients in research-agenda building is taking place, and new linkages between researchers and patients are built to improve information transfer via intermediary patient organizations, such as the Alzheimer Society.

Introduction

Longer life expectancy and a shift from acute to chronic diseases are exerting pressure on the capability of healthcare systems to meet the needs of the ageing population. Age-related diseases like Alzheimer's disease (AD) will occur more frequently, nursing care needs to be intensified and a broader, mission-oriented innovation policy is increasingly regarded as being critical for effectively meeting these grand societal challenges. Nowadays, AD is the most common cause of dementia, accounting for approximately 60 % of all cases (Sadowsky & Galvin, 2012). As the damage caused by the pathophysiological mechanisms associated with AD is presumed to be irreversible, earlier detection of AD could offer better future prospects for individuals concerned as patients could benefit from drug therapies, better understanding and more time to prepare for a future with AD (Vestergaard et al., 2006). Furthermore, existing medication, and any future disease-modifying agents, are likely to be more effective when administered earlier in the course of the disease (Van Rossum et al., 2010; Sadowsky & Galvin, 2012). Early detection of AD, therefore, is

a widely shared goal in current biomedical research, and a search is going on for viable AD biomarkers (Boenink et al., 2011). A number of novel technologies are being developed, called 'early AD diagnostics', to enable an earlier and more reliable diagnosis of AD during life based on biomarkers made visible by instruments such as PET, MRI scans and/or CFS-analysis (Handels et al., 2012). The Dutch research consortium, Leiden Alzheimer Research Netherlands (LeARN), amongst others, aims to develop these emerging technologies (CTMM, 2013a).

These new innovations also raise new uncertainties. For example, it remains unclear how desirable future diagnostics are considered by AD patients when treatment is still lacking. Boenink et al. (2011) argue that new biomedical technologies may have a broad set of impacts on medical practice, society and culture, but that society hardly takes these impacts into account when assessing the desirability of a novel technology. Many innovations never make it to daily use in healthcare because they do not fit the needs and values of their targeted users. Therefore, early anticipation of the societal impact of emerging technologies may contribute to more robust and useful technologies. Interaction between users and producers of emerging diagnostic technologies takes place both in laboratory and clinical environments and in the wider society, where the application of healthcare technologies not only meets a medical need but is also accompanied by increased health awareness and growing needs and expectations of citizens due to diagnostic possibilities. While stakeholder involvement in such emerging innovation processes might be beneficial, it remains unclear how to organize it in an effective and efficient way. Uncertainty and flexibility – inherent to emerging technologies - open possibilities for far-reaching stakeholder involvement but at the same time ask for thorough organization of these interactions in the face of ever-changing technology specifications, demands, and configurations of the social network (Rip et al., 1995).

Interaction between the users and producers of biomedical technologies is essential in increasing the success of these innovations in social and economic terms (Moors et al., 2008). Taking into account the preferences of users might facilitate the adoption and implementation of new innovations. Also, the creative potential and experiential knowledge of users might help forming new technologies and putting demands on the agenda of companies and governments (Boon et al., 2011). Moreover, users have a moral right to influence decision-making on innovation processes because it strongly influences their lives (Smits & Boon, 2008). This is especially true for patients considering various treatment options. User-producer interactions (UPI) are indispensable when new technological opportunities are just emerging, which is the case with early AD diagnostics, and are defined by Nahuis et al. (2012, p. 1122) as "interactive learning processes between users and/or producers leading to or aiming at the reduction of uncertainty about the relation between product and demand characteristics".

Previous studies have reflected on the conditions for effective user-producer interaction in biomedical innovation processes. Smits and Boon (2008), for example, have formulated policy measures to involve users in innovation processes in the pharmaceutical industry

in order to improve the quality of innovation processes and increase the acceptance of innovations. In studies of AD, the patient perspective has long been ignored. People with dementia, however, do have the ability to participate in research (Wilkinson, 2002). Empowering patients to take an active role in their own healthcare has been identified as a key factor in the drive to improve health services for patients (Davis et al., 2007). Accordingly, this chapter aims to systematically explore the interactions between users and producers of early AD diagnostics developments in the Netherlands.

The next section briefly describes the methodological approach, followed by the research findings and a conclusion part.

Methodology

Interaction between users and producers (UPI) can increase chances for successful innovations, both in social and in economic terms. It is difficult, however, to fully understand user needs and preferences. After all, users are not always able to articulate their needs, preferences or interests because they might be not fully aware of all latent or future possibilities of a new technology or do not want to share their creative ideas and opinions (Griffin, 1996). Studying user-producer interaction processes helps to identify user needs and preferences and strengthen the role of users in the innovation process (Oudshoorn et al., 2003; Moors et al., 2008). Nahuis et al. (2012) have distinguished various types of UPI in innovation processes, as shown in Table 1. They argue that different contexts demand different types of UPI. These various types of UPI serve as heuristics to methodically explore which interactions take place between users and producers during the development of early AD diagnostics in the Netherlands.

The research is based on qualitative data regarding different interactions between users and producers during the development of early AD diagnostics. Additionally, results are taken into account about improving the ways of involving users. The Dutch LeARN project aims at developing tools for early diagnosis of AD and provides an important source of information. LeARN is funded by the Dutch Centre for Translational Molecular Medicine (CTMM), which is dedicated to enabling earlier and more precise diagnosis of various diseases (e.g. cancer and diabetes) and to the design of personalized therapies (CTMM, 2011). Developments within the CTMM concerning other diseases might also provide insights on user-producer interactions in the context of early AD diagnostics (Handels et al., 2012). Users and producers have different backgrounds and their interactions can be facilitated by intermediary organizations (Boon et al., 2011). Patient organizations for AD represent and promote AD patients' interests and joint research. Therefore, data is also collected about how such intermediary organizations are involved in UPI during the development of early AD diagnostics.

The data is obtained from both scientific literature and from written public sources. The scientific databases Scopus, Google Scholar and PubMed are used for data gathering.

Search terms that are used in these databases are: LeARN, CTMM, biomarkers, PET, MRI, CSF, in vivo, early detect*, early diagn*, Alzheimer's disease, AD, user, patient, involv*, engag*, UPI, user-producer interaction, technology assessment, feedback, clinical trials, decision-making, needs, preferences and combinations of these. Public sources that are consulted include the website of the CTMM, annual reports of the CTMM, the website of the Dutch Research Council NWO and websites of Alzheimer organizations such as Alzheimer's Society and Alzheimer Nederland.

The seven types of UPI described by Nahuis et al. (2012) serve as sensitizing concepts to explore which types of UPI take place in the context of early AD diagnostics. This analytic framework helps to distinguish the different interactions found in this research. Table 11 shows the operationalization of the various UPI concepts.

Type of UPI	Description of UPI types
Broadening	Considering broad societal aspects at early stages of technological development
Constructing linkages	Constructing linkages between users and producers to make the transmission of information more effective
Characterizing users	Giving a representation of who the supposed users are and what they want
Upstream involvement	Users becoming participants in research, design and development, and agenda building
First user enrolment	The selection and enrolment of the first users of new technologies
Feedback	-Focusing on technological performance -Encouraging users and teaching them how to use the technology
Downstream innovation	Users coming up with creative ideas for product development or making improvements themselves

Table 11: Operationalization of the various types of UPI (based on Nahuis et al., 2012)

Research Findings

The process of broadening has been recognized as important for user involvement and put into practice during the development of early AD diagnostics in the Netherlands. Early Medical Technology Assessment (MTA) is a mandatory part of every CTMM research project (CTMM, 2010). The purpose of an MTA is to estimate the effects of medical technologies on the current and future state of health in the patients involved. Besides the analysis of costs and benefits, MTA takes social, ethical and legal considerations into account, indicating that broadening takes place (CTMM, 2013b). The Dutch Research Council, NWO, supports the LeARN project and involves stakeholders in the deliberation and decision-making on the social acceptability and moral desirability of developments in new AD diagnostic technologies (NWO, 2013). This indicates that NWO adds to the process

of broadening in the context of early AD diagnostics. The study of Boenink et al. (2011), supported by NWO, uses the LeARN project for a case study and describes 'possible' sociotechnical futures that reflect on the broad range of potential impacts of technological development in the field of early AD diagnostics. They also predicted the public desirability of these impacts. These scenarios allow for a discussion of what the problems and needs surrounding AD are, and how the attempt to early detect AD influences those problems and needs. Such discussions can be organized with stakeholders in various engagement activities. Boenink et al. (2011) describe two methods to elicit stakeholders' responses. One method is to convene "focus groups" – homogeneous groups of a particular type of stakeholders - to list the conditions that future developments of early AD diagnostics should satisfy for a specific group of stakeholders to accept these developments. Another method is bringing different stakeholders together in a larger, interactive, multistakeholder setting. In such a setting, ultimate conclusions may not just seek to further the interests of one specific group but are based on widely shared values. Cuijpers et al. (2011) presented the current landscape of AD in the Netherlands to get an overview of the various stakeholders and their interests and issues. Besides, they argue that Technology Assessment (TA) does not only take place within formal TA studies but, although not systematic or complete, assessment and anticipation are constantly going on as a part of societal processes. Alzheimer Cafes (ACs) – monthly informal meetings for persons with dementia, their partners, family or caregivers – are then regarded as discursive spaces for informal TA (Rip, 1986) to voice, exchange and assess multiple futures of AD and its diagnostics instruments on an informal basis. Currently, there are over 200 ACs across the Netherlands and the concept is also copied in other countries (Alzheimer Nederland, 2013a). The informal assessment of multiple futures of early AD diagnostics in ACs is an indication that broadening is taking place in the context of early AD diagnostics.

Upstream involvement of users seems to take place in research on early AD diagnostics. First, CTMM tried to facilitate a much greater patient involvement by encouraging them to sign up for future clinical trials (CTMM, 2011). Different Alzheimer patient organizations also encourage patients to participate in clinical trials (Alzheimer Nederland, 2013b; Alzheimer's Association, 2013). For example, Alzheimer Nederland encourages AD patients to participate in research by providing blood samples, brain scans or cerebrospinal fluid for joint research activities at the eight university medical centres in the Netherlands (Alzheimer Nederland, 2013b).

Caron-Flinterman et al. (2007) argue that patients and patient organizations, although highly involved in the biomedical research field as end-user groups, are less influential in terms of decision-making on biomedical research in the Netherlands. Formal decision-making on biomedical research agendas is mainly done by experts. Recent studies, however, show that patients actually are involved in decision-making on research agendas; first, CTMM is trying to enable larger patient involvement by actively consulting patients' opinions on the future direction of translational research (CTMM, 2011). Second, the Research Network of the Alzheimer's Society in the Netherlands involves users in agenda building by working

with people with dementia and carers to select the best dementia research projects for funding (Alzheimer's Society, 2013b). 225 volunteers are involved, working with leading scientists to set the research agenda of the Alzheimer's Society. The Alzheimer's Society is involved in developing new brain scanning techniques for more accurate ways to diagnose dementia (Alzheimer's Society, 2013c). As patients' preferences for research directions are consulted through the Research Network, patients might have an important voice in the involvement in this research. The Dutch Health Council (RGO) has consulted the Dutch government on how to consider the needs of patients and caregivers in the development of research agendas, which indicates that its importance is recognized. This might lead to even stronger user involvement in decision-making on biomedical research (RGO, 2007).

In the first stages of the development of early AD diagnostics, feedback needs to be obtained from AD patients. All diagnostic agents must undergo extensive preclinical and clinical testing before regulatory approval is granted (Frangioni, 2006). In clinical trials, patients provide feedback on the technological performance of diagnostics. They only provide information about the diagnostic value of the technology (RGO, 2011; CTMM, 2013a). Gibson et al. (2004) argue that higher-quality feedback could be obtained through investigating the opinions, experiences and practices of patients during trials by using qualitative methods, such as observational studies, in-depth interviews and textual analyses of written records. The adoption of qualitative methods within clinical trials, when combined effectively with quantitative measures, would allow both researchers and practitioners to gain a better understanding of the improvements that treatments or services provide, and how these improvements are experienced by patients with dementia themselves. By using this feedback, the relevance of outcomes to patients could be improved. Rather than robustly confirming existing hypotheses, qualitative methods can often generate new ideas for further research and provide insights into the experiences of users and carers not immediately accessible through quantitative methods.

CTMM recognized that when patients get involved in translational research, a common language needs to be found that both the researchers and the patients understand (CTMM, 2011). Therefore, they explored the idea of connecting patients and researchers, both associated with the same disease, in one-on-one informal discussions. They argue that this is an adequate way for researchers to find ways of explaining their research in terms that lay people can understand (CTMM, 2011). This illustrates that CTMM constructs linkages between patients and researchers, through which information can more effectively pass. Also, the engagement activities described by Boenink et al. (2011) demand adequate linkages between users and producers. The Alzheimer Cafes also include novel linkages between the researchers, medical experts and patients, and potential/future patients and caregivers to exchange thoughts. Additionally, intermediary user organizations, such as the patient organization Alzheimer Nederland are important linkages between users and producers involved in organizing feedback through encouraging participation in clinical trials. Such intermediary organizations are important when users are involved in agenda building for biomedical research, for example in the Research Network of the Alzheimer's

Society. Boon et al. (2011) argue that intermediary user organizations can facilitate the interactions between users and other actors in several ways. They can function as 'network assemblages' that help to link up networks of patients, clinicians and potential researchers. Or they facilitate boundary conditions and resources of research, such as access to patients for the recruitment of clinical trials.

In summary, the results show that considering broad societal aspects in early technology development is already fairly advanced in research on early AD diagnostics in the Netherlands. Furthermore, researchers could engage various stakeholders (e.g. patients, caregivers) in the informal deliberation of impacts of early AD diagnostics, e.g. by linking up with Alzheimer Cafes. During clinical trials, feedback is obtained from patients on technological performance criteria of early diagnostics. Upstream involvement takes place through encouraging patients to participate in clinical trials. Furthermore, new linkages between researchers and patients and their caregivers are constructed to make the communication of information more effective.

Conclusions and discussion

Adequate linkages between users and producers seem to be important for emerging healthcare innovations, such as early Alzheimer's disease diagnostics. Patient organizations, such as the Alzheimer's Society, play an important intermediary role between users/patients and researchers. Alzheimer Cafes are important places for concerted stakeholder interaction where controversies about early AD diagnostics are articulated, and informal Technology Assessment takes place.

Such concerted stakeholder interactions consist of adaptations of current behaviours of the various stakeholders involved in early AD diagnostics to stimulate healthcare innovation and are the outcome of an alignment process, in which shared research agenda building, feedback and broadening processes play an important role.

Nowadays, there is a lot of attention on the expected but largely uncertain contribution of early diagnostics to healthcare innovations. It would be helpful to manage our expectations based on scenario building and policy coordination (Propp et al., 2009). This research provided insights on how the needs and preferences of patients are taken into account during the innovation process of early AD diagnostics. It investigated how desirable effects of early AD diagnostics can be enhanced and undesirable societal effects prevented, thus leading to ways of responsible diagnostics innovations (Cuijpers et al., 2013). This in turn will reduce the risk of future social and moral controversy and/or low uptake of early AD diagnostics.

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