Do we have to Include HCI Issues in Clinical Trials of Medical Devices? – A Discussion

Lene Nielsen
IT University, Copenhagen
Denmark
lene@itu.dk

Lars Rune Christensen
IT University, Copenhagen
Denmark
lrc@itu.dk

Anne Sabers
Rigshospitalet
Copenhagen, Denmark
Anne.Sabers@regionh.dk

ABSTRACT

Digital devices play an important role in medical treatment and will in the future play a larger role in connection to cures of health-related issues.

Traditionally medicine has been tested by clinical double blind, randomized trials to document the efficacy and safety profile. When it comes to the use of digital devices in treatments the protocols from the field of medicine is adopted. The question is whether or not this evidence based approach is useful when dealing with digital devices and whether the understanding of the efficiency of a treatment can be obtained without also looking at usability and lifestyle issues.

Based on a case study of epilepsy, a literature study of protocols for investigating treatments using digital medical devices, the set-up of studies, the design of a current protocol for clinical trials, and finally preliminary results, we discuss if clinical trials have to include usability studies to determine if a treatment is effective.*

CCS CONCEPTS

• **Human-centered computing~User studies**

KEYWORDS

Medical devise, Evidence-based medicine, Clinical Trial, Usability, Lifestyle issues

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1 INTRODUCTION

In recent years the number of websites and apps for self-monitoring of health issues from sports performance to tobacco addiction has exploded, apps have been developed for e.g. self-monitoring of illnesses like diabetes, asthma, and bipolar disorder. Following this development, there is an increased interest in researching whether or not the digital systems support health. Examples include behavior change that helps people quit smoking or lose weight, mental health applications that e.g. address depression or anxieties, management of chronic diseases using the Internet and app-based management systems e.g. self-management of diabetes [11] and bipolar disorder [1]. Other examples include patient-accessible personal health records and tailored educational programs for patients [6]. Other technologies support compliance through behavioral changes with different intervention strategies [12].

The number of electronic devices within the area of health are increasing such as an electronic device for the treatment of headaches for migraine patients [20]. A variation of these are devices that uses electric stimulation on a specific nerve or organ. Most are implants with little or no user interaction, but an increasing number stimulates a nerve on the outer body with a demand for user interactions such as the digital device for lowering the number of epileptic attacks for patients with drug-resistant epilepsy, presented later in this paper. Eysenbach et. al. [6] has developed a standard for reporting of randomized controlled trials within eHealth and mHealth trials to provide a broad guidance. The standard includes descriptions of who is involved, the technology, the usage, and the usability test methods. The standard is heavily cited (1014 on Journal of Medical Internet Research (JMIR), 521 on Google Scholar (August. 3, 2017) and has influenced many studies. The standard does include reports on usability tests in the design phase but

does not contain usability issues during the clinical research study.

HCI studies on medical devices typically concern design issues, [1], [3], health management, and coordination issues, [5], [15], [4] Also, long-term studies of behavioral change in order to determine the effectiveness of these technologies are reported. Klasjna, et.al. [12] argues for a narrower notion of efficacy, one that tailors outcome measures to the particular intervention strategies a technology employs. They suggest the construction of a value chain that evaluates the initial, intermediate and distal effects of the technology. This enables HCI researchers to test whether their systems work as intended right from the early stages of development.

Within HCI there are good arguments for doing prototyping and studying early and later use and a large number of literature reports on the design process. But this is not well aligned with the mind-set that medical studies require where the effect of the medical treatment has to be studied in double-blind studies adapting methods from test of drugs in various form. To prove that a technology can reduce attacks or cure an illness other standard has to be applied, such as the drug review process developed by the American Food and Drug Administration (FDA), recognized worldwide as "the gold standard". Thus, when it comes to proving whether or not an app or a device can reduce attacks, heighten compliance, or cure an illness evidence based research from the medical field is introduced. This paper deviates from much of the HCI literature in the medical field as it reports from a study that takes point of departure in evidence-based medicine and the development of a protocol for clinical trials is the focus of this paper.

2 EVIDENCE BASED MEDICINE

The fundamental idea of evidence-based medicine is that not all evidence is created equal – some forms of evidence is deemed stronger than others. When one wants evidence for the efficacy of a (new) treatment the advised method is to conduct a double blind randomized controlled trial, this is referred to as the 'gold standard'. Briefly told, the "gold standard" involves randomly dividing the patients taking part in the trial into two groups. One group of patients is given the active substance under examination, e.g. a drug, and the other group, designated the control group, is given a placebo (sham) treatment designed to have no effect [10].

In medical research, the concept of sham refers to introducing placebo medication for a randomized anonymous test-group. To replicate this protocol for clinical trials in the field of digital devices, some researchers have developed sham devices or used sham data [14] for randomized anonymous test-groups. One example of a sham device is a study of acupuncture versus diazepam in the treatment of pain. In this study, the sham acupuncture introduced real needles at sham acupuncture points [21]. Another sham intervention studied the antiepileptic effect of vagus nerve stimulation using a sham stimulation at the non-vagus nerve innervated earlobe [13]. These sham set-ups have proven problematic; using sham needles and sham acupunctures pressure points might have an impact on the body [10], using a sham earlobe stimulation might affect the patients that can easily find information that the stimulation point is wrong.
Some studies use sham data in connection with testing of eHealth within self-monitoring e.g. [14] these studies focus on usability rather than on actual proof of medication. Other studies create a baseline and compare compliance before, and after introducing a digital stimulation e.g. [20] use a digital device stimulation of the vagus nerve to reduce head ache of chronic migraine patients. Despite the use of a digital device, there is no inclusion of usability issues affecting the utilization.

3 THE CASE

Drug resistant epilepsy is a serious condition that often leads to a major impact on quality of life and poses significant life challenges due to the risk of depression, underemployment, injuries, and death. Despite the critical need, current treatments for this condition are far from satisfactory.

Therapeutic electric brain stimulation techniques provide an option for treating drug resistant epilepsy. The devices act by a variety of mechanisms to decrease neuronal excitability probably by indirect modulation of cortical activity [7], [9]. One method is to stimulate the auricular branch of the vagus nerve in the human ear, so called transcutaneous vagus nerve stimulation (t-VNS) [16]. Studies support the evidence of the efficacy of stimulating the vagus nerve in the ear; including a small clinical and experimental study [19], a subsequent multicenter randomized controlled double blind study based on 70 patients [2]. A Chinese study also found positive results [17]. Side effects were reported including dizziness, headache, local pain, dysaesthesia, and itch at the stimulation site. The side effects seem to be rapidly reversible and disappear soon after the stimulation is terminated. All studies, however, are relatively small and too underpowered to obtain statistically significant results. Based on the above there is a need for a clinical study that can determine if the electric stimulation of the vagus nerve in the outer ear can reduce the number of seizures.

In the reported case, the first attempt to create a protocol involved a sham device and two randomly selected control groups. The rationale for the sham was adopted from the studies on in-operated stimulators [17] [10] [13] [8]. The first ideas to create a sham device involved having it emit a sound or vibration rather than an electrical current, and in that manner, create the illusion of the real device. This had to be abandoned because we found that the patients might readily notice the difference between electrical current and other forms of stimulation such as e.g. vibration or sound if we attempted this approach to making a sham device. The second idea was to not make a sham device as such but to have the device emit a different voltage as sham. We also had to abandon this idea because any voltage might be effective in ways not fully understood and hence not a true placebo. The third and final idea was to give the correct current, but at the wrong place on the ear i.e. place the electrode incorrectly. This also had to be abandoned due to the availability of instruction manuals online

– i.e. a patient seeking information could easily unmask the sham. For these reasons, we had to abandon the whole idea of basing our clinical trial on sham in any form. This echoes the sham trouble describe in the case of acupuncture [21].

Due to the difficulties in establishing a valid sham procedure, as we have seen, we have formulated an alternative within the framework of evidence-based medicine.

Figure 1: The T-VNS device Nemos with the electrode to be placed at the outer ear. The device is the size of a cell phone. The patient interacts with the device to adjust amount of electricity and to follow compliance.

4 DEVELOPING A PROTOCOL FOR A CLINICAL TRIAL INCLUDING DATA ON LIFESTYLE AND USABILITY ISSUES

The idea is to pragmatically provide the best available evidence for the efficacy of t-VNS by indirectly evaluating whether patients continue to use the device after 6 months (end of study) and subsequently after 12 months follow up. Or if they quit use. We hypothesize that if the patient continues t-VNS they most likely experience significant clinical benefits. On the other hand, if the patient discontinues t-VNS it may be due to lack of effect, adverse effects, difficulty in functional handling of the device, or a lack of fit with the lifestyle of the patient.

It is in determining why the patients discontinue the treatment that the need for data on usability and lifestyle issues becomes apparent. It is (partly) through this data generated through questionnaires and interviews that we will be able to determine the root of the reasons for the patients abandoning the t-VNS treatment. Is it because of a lack of effect of the electrical stimulation treatment? Is it because the device is not user-friendly? Is it because the treatment has a bad fit with the lifestyle of the patient (e.g. the patient cannot find the time to use the device for 4 hours every day)? Or is it a combination of these issues? Due to the design of the clinical trial where Informatics and HCI components are included, we are in fact able to answer these questions (both statistically and qualitatively).

To be clear, in this context of a clinical trial, the data on the usability and lifestyle issues are *not* there for design use. They are only there to be able to be taken into consideration when the evidence of the efficacy of the treatment is to be established. That there is a large potential for this data to be used in a device re-design process is of course beneficial, but of secondary importance in this context of evidence-based medicine. Having said that, we are of course interested in redesigning the device in collaboration with its manufacturer in order to ensure a better delivery of the active component, namely, the electrical stimulation. But to spell it out, the contribution of Informatics and HCI to evidence-based medicine, to clinical trials, can be described as being a provider of data, to be used in calculating trial outcome, rather than a design contribution. The design contribution is an afterthought - an important one - but seen from the perspective of evidence-based medicine nonetheless an afterthought.

The following quotes from two patients illustrate the problems of usability and lifestyle issues:

Participant 1: *"It was in the afternoon/evenings I used it. I didn't get it as evenly distributed, as I should. I didn't use it four times for one hour. Most often it was, as you say, afternoon and evenings. Rather one time of two hours and then maybe one hour during the working day. Sometimes longer periods of one and a half hour at afternoons and evenings, because it is easy to wear when you watch television and sit quietly at home."* (Translated from Danish by authors.)

Participant 2: *I use it when I come home from work because I find it highly annoying that you have to clean it all the time. I have sometimes wanted to through the device out of the window (laughs). Because you have to clean your ear all the time*
Interviewer: Ah yes, there is this contact fluid? Do you have to rinse the ear to create contact?

Participant 2: If it is away from the ear then you have to rinse again - both the ear and this thingy." (Translated from Danish by authors.)

Participant 1: "*The problem is if you have a job where you sit down it is no problem. You just have to explain to people around you what it is. If you have a ..., I'm a xx, and walks around, or if you have to do something where you have to move, then it is a bit difficult.*" (Translated from Danish by authors.)

As can be seen from the quotes the difficulties arise from the device - the electrodes easily fall off and the circumstance that you have to clean the ear every time the electrodes fall off. The difficulties also originate from a social context where the patient has to answer questions about the device and electrodes from the surroundings.

We may say, then, that there is reason to think that lifestyle and usability issues will impact the outcome of the trial and data needs to be collected on these issues in a systematic manner, in order to have a valid clinical trial of the medical t-vns device. As indicated, it may not only be because of the electrical stimulation being ineffective that some patients may quit treatment.

5 DISCUSSION

From our case, we argue that when it comes to digital devices "the gold standard" is not enough. HCI needs to be considered when medical devices are clinically tested. Researching the use situations, we can get inspiration from studies that look at proximal effects; intermediate effects, and distal effects that are evaluated through multiyear longitudinal research [18]. We can create transparency in the design and test phases as suggested by [3]. But how can we significantly know to what degree the patient population may be said to quit because of experiencing a lack of efficacy? A lack of fit with their lifestyles? Or an inability to functionally use the device?

Generating data on all of these fronts will, first, provide an empirical basis for evaluating the effect of the device, and second, it will provide a basis for a redesign of the device if the data shows a need for it.

If one fails to generate data on usability and lifestyle issues, for example, the trial design may be biased towards explaining a lack of success with the patient population purely in terms of the efficacy of the active components of the treatment. This may be incorrect, and a may lead investigators to miss an opportunity, for example for a simple redesign of the device, which may in some cases potentially lead to an increased uptake in compliance with what is otherwise treatment with good efficacy.

Similarly, to [12] we propose that HCI researchers should use qualitative studies that focus on people's experiences with the technology in order to understand why and how the system is working and participate in randomized control trials. The question becomes: How can HCI researchers approach the medical field and be accepted into the clinical trials?

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