ICT4Depression

User-friendly ICT Tools to Enhance Self-Management and Effective Treatment of Depression in the EU

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Deliverable 5.5:

Proposal for the evaluation of the efficacy and cost-effectiveness of the ICT4Depression system in terms of a randomized controlled trial.

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PU	Public	X
PP	Restricted to other programme participants (including the Commission Services).	
RE	Restricted to a group specified by the consortium (including the Commission Services).	
CO	Confidential, only for members of the consortium (including the Commission Services).	

Contents

1. Introduction

1.1 Background

Major depression is highly prevalent, associated with low quality of life of patients and with increased (co) morbidity and mortality rates (ESEMED, 2004, Saarni et al. 2007). The costs for depression are substantial, estimated yearly at 177 million euro per 1 million inhabitants for major depression (Smit et al. 2006). These costs will increase significantly in the next years as depression will rise from the fourth to the first place of disorders with the highest burden of disease by 2030 (Mathers & Loncar 2006). Efforts to reduce this disease burden may thus be found in increasing the availability and uptake of cost-effective interventions for depression.

The reach and uptake of depression treatment have substantially increased since the availability of Internet-based interventions over the last decade (Riper et al. 2007). Meta-analyses have now shown that these Internet interventions are effective for the treatment of depression (Andersson & Cuijpers 2009, Andrews et al. 2010). The advantages of these low intensity Internet-based interventions relate to their potential to reach broad groups of people and to their qualities of timeliness, (partly) anonymity, 24/7-accessibility, and avoidance of stigma (Andersson & Cuijpers 2008).

Despite these promising results studies have also indicated low therapy adherence rates by users of Internet interventions, low uptake of these interventions by people with a low social economic or migrant background and participants have lacked motivational and personalized support, especially in unguided self-help treatments (Nijland et al. 2010). Currently, a number of innovative strategies are being explored to overcome these problems. One such exploration entails the use of mobile phones for the delivery of interventions (Prociow & Crowe 2010). In terms of potential access these devices appear very suitable as mobile phones are reaching complete coverage in the Netherlands, while smart phone coverage is growing very fast. Smartphones are especially suitable to assess the state and progress of users by using real-time measurements and personalized feedback. Given the importance of mood and activity monitoring in self-help interventions this is an important extension in adjunct to Internet delivered self-help interventions (as participants of Internet interventions are not continuously online).

1.2 ICT4Depression

An example of an innovative intervention for depression treatment that makes use of mobile and Internet technologies is Moodbuster. Moodbuster is developed in a

European project, called ICT4Depression. Moodbuster delivers self-help depression treatment via (1) smartphones for (2) adult patients in primary care within a (3) stepped care framework and by making use of (4) ecological momentary assessment and intervention techniques (EMA and EMI) including the assessment of physiological symptoms in an integrated manner (5) which enables timely interactive feedback and treatment adaptation if needed for patients and professionals alike (Warmerdam et al. 2012). The feasibility and acceptability of Moodbuster are evaluated in a pilot study in the Netherlands as well as in Sweden as part of the ICT4Depression project. The pilot in Sweden included students with an increased level of depressive symptoms. Results of this pilot will be available at the end of the year 2012. The pilot in the Netherlands included adults with a diagnoses of a minor or major depression. Results from this pilot appear at the end of April 2013. Results of these pilots will give an impression of the improvement in depression and deliver input for further optimalisation of Moodbuster. Evaluating the clinical and cost-effectiveness of Moodbuster is a sine qua non for the future implementation of this system in routine practice and will therefore form the next step. In the proposed project we want to evaluate the effectiveness and cost-effectiveness of Moodbuster compared to care as usual for treatment of depression in primary care.

1.3 Research questions

1. Is Moodbuster clinical effective compared to care as usual for adults with depression?
2. Is Moodbuster cost-effective compared to care as usual for adults with depression?

2. Methods

2.1 Design and sample size

This study concerns a randomized controlled trial with two arms; one experimental group which receives Moodbuster and a control group which receives care as usual. Measurements will be taken at baseline, at posttreatment (after 6 weeks) and after 3 and 12 months follow-up.

Based on a power of 0.80, an alpha level of 5% and an expected between group effectsize of 0.35 at the outcome measure, we need 100 participants in each group. Total sample size will be 200.

2.2 Procedure

Recruitment of participants takes place via specialized nurses working in general practices. In the Netherlands, people with common mental health problems are referred to these nurses by the general practitioner. The nurses will inform potential participants of this study by giving them a brochure during a regular consult. Interested participants can sign in for this study via a website. After signing in they receive a screening questionnaire for depressive symptoms by email (Kessler Psychological Distress Scale: K10; Kessler & Mroczek, 1992), and an information brochure and informed consent form by post. Participants who score above the cut-off score of 20 on the K10 are contacted for a telephonic diagnostic interview. Inclusion criteria involve a major or minor depression according the DSM-IV criteria, aged 18 years and older, willingness to wear sensor devices and having a pc with Internet connection. Participants with a high risk on suicide are excluded. Included participants will be randomized according to a computer generated randomization schedule, which is done by an independent researcher. After randomization participants receive the baseline questionnaire by email. In a face-to-face consult participants receive the sensor devices and instructions about the use of Moodbuster. During the study participants can use a smartphone from the University. Participants receive a gratification of 50 Euro at the end of the study.

2.3 Intervention

Moodbuster is an automated self-help treatment that incorporates the following 3 integrated functionalities: 1. Self-help treatment modules, 2. A monitoring system and 3. A reasoning system.

1. *Self-help treatment modules.*

Seven self-management modules are available through the Internet as well as through the mobile phone. The majority of the modules are based on psychological treatments that have been shown to be effective in face-to-face and internet-based treatments.

a) Psycho education. As many people with depression have little knowledge about depression they all start with the psycho education module. This module aims to provide information about depression, its causes and what can be done about it. It also contains a strong motivational component in order to avoid drop out of participants.

b) Exercise therapy. This type of therapy seems be effective in the treatment of depression (Mead et al. 2008). Exercise is a low-threshold, non-stigmatizing

treatment of depression. This module contains information about (different types of) exercise and assignments to get more active.

c) Behavioral activation. Behavioural activation therapy is an effective treatment for depressive disorders as shown in a considerable number of studies and a meta-analysis (Cuijpers et al. 2007). In this module one learns to find a balance between the amount of pleasant activities and necessary activities.

d) Problem-solving. Problem-solving therapies have been found to be effective in the treatment of depression, both in face-to-face therapies (Cuijpers et al. 2007), as well as in internet-based therapies (Van Straten et al. 2008, Warmerdam et al. 2008; 2010). In this module people learn strategies to cope with different kind of problems.

e) Cognitive restructuring. This module also builds on existing evidence-based internet-based interventions for depression (Andersson et al. 2005). In this module the participant learns to recognize negative automatic thougths and to replace them by more positive realistic thoughts.

f) Relapse prevention. Relapse rates after successful treatment of depression are high (Bockting et al., 2005). However, research shows that relapse prevention is possible through the use of longer-term psychological treatments, and treatments specifically aimed at relapse prevention (Vittengl et al., 2007). The relapse prevention module focuses on recognizing signs of a relapse, making plans to cope with these signs and anticipating on future events that could trigger a relapse.

g) Medication adherence module. This module informs the participant about the importance of medication adherence. Exercises are included that try to uncover possible barriers for taking medication. Participants can also see their own medication adherence in a graph.

2. Monitoring system.

Monitoring behavior and emotions is an important component within the treatment of depression. This information is also used to give the participants adequate and personal feedback from the reasoning system. In Moodbuster information is gathered via ecological momentary assessments (EMA; Ebner-Priemer & Trull, 2009). EMA is a valid method to gather real-time data about context, behavior and emotions (Wenze & Miller, 2010). In Moodbuster the mobile phone will be used to prompt the patient for a self-assessment of his mood and feelings, using an intuitive (graphical) interface. Participants will receive daily at random a request to rate their mood on their mobile phone. The minimum amount of required mood ratings is five. In addition, participants are asked to rate their sleep quality and anxiety once a day.

A second aspect of behavior that is monitored concerns biomedical information. Wearable biosensors are developed that measure several reactions of the body to emotional changes, such as electro-dermal activity, respiration, electrocardiography changes.

Medicine intake is the third aspect that is being monitored. Participants who take medication for their depression use an electronic medicine monitoring system. This device is able to detect medicine intake for different types of medication packaging relevant for depression (e.g. blisters, dose organizers, etc.).

3. Reasoning system.

The data obtained from the monitoring system will be interpreted by reasoning modules that can translate sensor information and information provided by patient into therapy information, that can reason about the progress of therapy and that can deduce/advice what therapy is most likely to be successful given the current state of the patient.

The reasoning system is able to provide feedback to both the depressed patient (providing information on progress of the therapy, appropriate therapy models given the state of the patient, motivations and warnings, e.g. concerning compliance with drug descriptions) and to the GP (providing decision support for treatment planning). Patients will receive this personalized automated feedback weekly on the basis of their answers to the prompt questions, home work made and bio-sensors. This is partly done via the cell phone, and partly via a personal website. Simple reminders and motivational messages are best suited for communication via the mobile phone, while a website is more appropriate for detailed progress feedback. In addition, the caregiver will get information about the progress of the patient on a weekly basis.

2.4 Instruments

An overview of the instruments is presented in Table 1. Instruments are divided into 1. screening and diagnosis, 2. primary outcomes and 3. secondary outcomes. Measurements will take place at baseline, at post-treatment and after 3 and 12 months follow-up.

1. Screening and diagnosis

Screening. The 10-item Kessler psychological distress scale (K10; Kessler and Mroczek, 1992) is a measure of non-specific psychological distress in the anxiety-depression spectrum. This screening questionnaire will be used to screen people for depression. Item responses are on a five-point Likert scale (5= “all of the time” to 1=

"none of the time"), total score ranges from 10 (no distress) to 50 (severe distress). Participants with a score of 20 or higher on the K10 are eligible for this study. With this cut-off the K10 shows good sensitivity to capture people with different kind of depressive disorders (Donker et al. 2009).

Diagnostic interview. Study participants will be asked to participate in a telephone diagnostic interview before the start of Moodbuster. To establish a diagnosis we use the Composite International Diagnostic Interview (CIDI). The CIDI (version 2.1), a structured interview developed by the World Health Organisation (WHO, 1990), enables trained interviewers to assess psychiatric diagnosis defined in the Diagnostic and Statistical Manual of the American Psychiatric Association, 4th edition (2001). The assessment typically lasts 30-75 minutes, depending on the mental state of the respondents. In this study, current mental statuses within the last two months will be considered.

Table 1. Instruments and measurements

	Screening	**Baseline (T0)**	**Post-treatment (T1)**	**3 months follow-up (T2)**	**12 months follow-up (T3)**
Screening					
K10	x				
CIDI	x				
Primary outcomes					
CES-D		x	x	x	x
Secondary outcomes					
HADS		x	x	x	x
EQ5D		x	x	x	x
Mastery		x	x	x	x
TIC-P		x	x		

2. *Primary outcome*

The primary outcome is depressive symptoms as measured by the Dutch Center for Epidemiological Studies Depression Scale (CES-D; Bouma et al., 1995). It consists of

20 items and has a total score ranging from 0 to 60. Minimum scores of 16 indicate clinically significant levels of depressive symptoms. The validity of the CES-D has been tested in different populations, for example in self referred elders (Haringsma et al., 2004). Radloff (1977) reports high internal consistencies among different populations (.79 to .92).

3. *Secondary outcomes*

Anxiety symptoms. The 7-item anxiety subscale (Dutch version) of the Hospital Anxiety and Depression Scale (HADS) is used for identifying anxiety symptoms (Zigmond & Snaith 1983). Cronbach`s alpha ranged between 0.81 to 0.84, in different normal and clinical Dutch samples (Spinhoven et al. 1997). Item-responses are on a 0 to 3 scale, total score range is 0-21 with higher scores indicating more anxiety.

Mastery. The 7-items of the Mastery Scale ranges from 1 to 5, total scale score 7-35. A high score (internal mastery) indicates that someone has the feeling to be in control of situations. A low score (external mastery) indicates that someone has the feeling that things are out of their control. The questionnaire has good psychometric properties (Pearlin & Schooler ,1978).

Quality of life. The 5-item self-report Euroqol (EQ5D) measures health-related quality of life and consists of five dimensions (mobility, self-care, main activity, pain and mood), each of which is rated as causing 'no problems', 'some problems', or 'extreme problems'. The EuroQol valuations appear to have good test-retest reliability (Brooks, 1996).

Health care use and costs. Costs will be defined from the societal perspective and encompass (1) intervention costs, (2) costs related to health care uptake, (3) out of pocket expenses for the family and the patient, and (4) costs stemming from production losses due to work loss days and work cutback days. Costs will be calculated in Euros (€). Information on the participants' use of health services and production losses will be obtained with the Trimbos and Institute of Medical Technology Assessment Cost Questionnaire for Psychiatry (TIC-P; Hakkaart – van Roijen, 2002). Data on service use and costs will be collected for 2 periods: the 4 weeks prior to randomization and the 6 weeks following randomization.

The 3 cost categories distinguished are: direct medical costs, direct nonmedical costs, and indirect nonmedical costs. Direct medical costs consisted of intervention costs and uptake of health care services, including costs of medication. Health care services will be costed by multiplying the number of health service units by their standard cost price. Direct nonmedical costs consisted of costs for traveling and parking. Indirect nonmedical costs arise when production losses occur due to

illness. Production losses can occur under 3 conditions. First, people can be absent from paid work due to sick leave (work loss days). Second, production losses may occur when people are ill but continue to work with reduced efficiency (work cutback days). Third, people may also be too ill to perform domestic tasks.

2.5 Analyses

All analyses will be performed on the intention-to-treat sample as well as on the completers only sample. The Linear Mixed Modeling (LMM) procedure will be used for all analyses; LMM includes incomplete cases in the analysis and employs restricted maximum likelihood estimation to calculate parameter estimates. LMM assumes that missing data are missing at random. LMM will be used to investigate treatment differences on the primary and secondary outcome measures. Between-group effect sizes will be calculated according to Cohen's d (Cohen, 1988). Effect sizes of 0.8 can be assumed to be large, while effect sizes of 0.5 are moderate, and effect sizes of 0.2 are small. Clinical significant change will be determined with norms for the outcome measure and with the Reliable Change Index (Jacobson & Truax 1991).

Costs will be determined at 6-weeks follow-up. The economic evaluation consisted of a cost-utility analysis and a cost-effectiveness analysis. For both analyses, the incremental cost-effectiveness ratio (ICER) will be calculated as (C1-C0)/(E1-E0), where C are costs and E is the effect and the experimental and comparator conditions are indexed with the1 and 0 subscripts. The incremental cost-utility ratio will focus on the net costs per QALY gained. The cost-effectiveness ratio focuses on the net costs per reliable and clinically significantly improved case of depression. Nonparametric bootstrap resampling techniques (with 5000 replications) will be used to take into account the stochastic uncertainty of the ICER estimates. Scatter plots of 5000 bootstrapped ICERs on the cost-effectiveness plane will be generated. This helps to produce estimates of the probability that (1) better health is generated for more costs, (2) that the intervention is inferior relative to the control condition because less health is produced at additional costs, (3) that less health is generated for lower costs, and (4) that the intervention dominates because better outcomes are obtained for lower costs.

3. Project group

Prof. dr. Pim Cuijpers, PhD Expertise: head of the Department of Clinical Psychology of VU, Vice Director and one of the program leaders of the Mental Health Programme of VU-EMGO+. His research focuses on prevention and treatment of common mental health disorders including internet-based guided self-help. He has published over 300 peer reviewed papers, chapters, reports and professional publications, including over 100 peer-reviewed international publications, of which 25 (since 2007) on the subject of guided self-help and Internet-based treatments.

Dr. Heleen Riper, Senior researcher, Program Leader eHealth VU University Amsterdam and GGZinGeest Amsterdam. She has been awarded over 25 national research grants and 4 European grants as project leader and collaborated on 6 European projects within the domain of eMental health. She has published in over 50 national and international peer reviewed journals on the development, validation and implementation of Internet and mobile devices to overcome common mental health disorders, including depression.

Dr. E.H. Warmerdam works as a post-doctoral researcher at the Department of Clinical Psychology. She conducted a randomized controlled in which Internet-based interventions for depression were evaluated. She has experience with adapting self-help interventions to make them suitable for use on the Internet and adjusting them for use on the mobile phone.

Dr. M.C.A. Klein, PhD, works as an Assistant Professor in the Agent Systems Research Group at the VUA-FEW since 2007. He has large experience in the field of Artificial Intelligence, especially in the areas of knowledge representation and modelling, knowledge-based systems and dynamic modelling. In addition, he has been intensively involved in the cooperation on depression therapy support between the Clinical Psychology department and the Agent Systems Research group at VUA.

Dr. P. van de Ven, PhD, senior researcher at the University of Limerick, Ireland. He is a specialist in the area of mobility monitoring using wireless sensors and the gathering and analysis of such data on mobile phone platforms and on embedded devices.

Eric Tousset, Senior Mathematician/Statistician, has a master in Mathematics and a master in Biostatistics. He works at Pharmionic Systems as Senior Mathematician/Statistician and has an experience in modelling and simulation using adherence data. He has also participated in the integration of adherence data in a web-based intervention portal.

Dr. A. Rocha, PhD. has been working as a researcher at INESC Porto since 1998. From October 1996 to December 1997 he was an associate member of CERN - European Laboratory for High Energy Physics, IT Division/Web Office. He has participated in several European projects, namely GISEDI, MEDSI and CAALYX, having performed the role of technical coordinator on the latest. His contribution to this project concerns software architecture, system modelling and design, interoperability and service oriented architectures.

Hugo Silva is Chief Innovation Officer at PLUX. He holds a MSc in Electrical and Computers Engineering from Instituto Superior Técnico (IST) and is a researcher at the Communications Theory and Pattern Recognition Group (TCRP) of the Lisbon's pole of Instituto de Telecomunicações (IT). Currently he pursuits his PhD under the supervision of Professor Ana Fred; his main interest areas include biosignal research and system engineering.

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