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FACULTY OF PSYCHOLOGY AND EDUCATIONAL SCIENCES
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PAXonline. Computer mediated psychotherapy for anxiety disorders

EXTENDED ABSTRACT OF THE PHD THESIS

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Note. The author of this thesis, doctoral candidate Amalia Maria Ciuca, certifies the following:

a. This thesis includes the results of the research conducted by Amalia Maria Ciuca (author) for obtaining Doctor in Psychology degree.

b. Parts of this thesis have been accepted for publication or have been presented in conferences; appropriate quotes of those works were included in the thesis. The works accepted for publication and/ or presented in conferences include other co-authors that substantially contributed to writing, data interpretation, etc.

c. This thesis was written according to scientific standards. The whole text and the extended abstracts were written by Amalia Maria Ciuca, who assumes full responsibility for adhering to academic standards.

Table of Contents

Short abstract

There are major imbalances between demand and supply of quality psychological services, both at national and global level, causing significant suffering for individuals, families and communities. Mental health must become a priority, and the ultimate scope of this research is to improve access to quality psychological services through the use of computer mediated psychotherapy (CMP). In this sense, our aim was to create and validate an online professional platform for the prevention and psychotherapy of anxiety disorders.

Rigorous analyses conducted led to development of PAXonline, a multi-user platform build upon principles from e-learning and cognitive science, offering all the necessary resources for addressing anxiety problems and comorbid depression.

We have conducted a randomized controlled trial in which we successfully tested both the efficacy of the first CMP program for panic disorder in Romania, and the integration of therapeutic guidance sessions offered through secured Skype. Analyses have shown that PAXPD treatment with or without guidance is efficient in treating panic disorder with comorbidity, and also for secondary outcomes, such as functional impairment and associated depression symptoms.

Results of this research program have theoretical and practical implications as to counseling and psychotherapy service delivery and use. Overall, results from the studies presented in this doctoral thesis clearly support the efficacy and acceptability of computer mediated psychotherapy for anxiety disorders.

Keywords: computer mediated psychotherapy (CMP), anxiety disorders, panic disorder, guided internet-based cognitive behavioral therapy (ICBT), paxonline, randomized controlled trial (RCT), treatment predictors

Chapter 1 - Theorethical background

1.1. Project motivation

1.1.1. The gap between mental health needs and services

Hundreds of millions of people are affected by mental health disorders worldwide and failing to adequately address this issue brings significant suffering, disability and economic loss. The lifetime prevalence for mental health disorders in general is above 46%. The highest prevalence is recorded for anxiety disorders (28.8%) and affective disorders (20.8%), with anxiety disorders tending to have an early onset (R. C. Kessler et al., 2005). Every year over 38.2% (164.7 million people) of the total EU population suffer from at least one mental disorder and the resulting economic costs rise at 3-4% of EU Gross Domestic Product (GDP) (Wittchen et al., 2011). One third of medical consultations made by general practitioners are in fact provided for mental health problems (Linzer et al., 1996; Shah, 1992; Strain, 1982). A report released by WHO (World Health Organization) and WONCA (World Organization of Family Doctors) in 2008 stated that „up to 60% of people attending primary care clinics have a diagnosable mental disorder" (WHO&Wonca, 2008, p. VII). The most frequent problems seem to be anxiety and depression, and their evolution is generally chronic (White, Jones, & McGarry, 2000).

Despite the potential to successfully treat mental disorders, only a small minority receive even the most basic kind of treatment. Studies have shown that 60% of those in need receive no treatment at all, and only 32.7% of those who receive treatment get it at minimal quality standards (Wang, Lane, et al., 2005). In Europe, 48.3% of those in need of assistance do not benefit from it (Alonso et al., 2007). The main population that requires and refuses psychological treatment are young people between the age of 15-28 (Rickwood, Deane, & Wilson, 2007). Even if there is some progress in this area, we are still far from adequately meeting current needs (R. C. Kessler et al., 2005). Furthermore, there are numerous barriers to accessing mental health services, thus the treatment is provided only with a significant delay from the onset of the disorder (after 9-23 years for anxiety disorders and 6-8 years for mood disorders) (Wang, Berglund, et al., 2005).

1.1.2. The context of mental health problems in Romania

Statistics regarding mental health problems in Romania are scarce and unclear. According to the Romanian League for Mental Health, at the national level there seems to be approximately 600.000 individuals with mental health problems (of which 300.000 are considered severe

cases). Florescu et al. (Florescu et al., 2009) conducted a study on a representative sample of 2537 participants aged over 18. Results of the study show a cumulative lifetime prevalence of mental health problems of **13.4%**, of which 6.9% - anxiety disorders, 4.3% - mood disorders, 3.4% - substance abuse and dependence and 2.1% - impulse control disorders. In regard to comorbidity, from the 13.4% of the sample that exhibited at least one mental disorder, 4.5% had at least two and 1.4 % had at least three disorders. The research coordinated by Florescu was part of an European initiative, where mental health disorders and related problems were investigated (http://www.eu-wmh.org, 2011). Compared to the other 9 countries, Romania seemed to have the smallest lifetime prevalence for mental health problems.

Can we draw the conclusion that Romanians are healthier or that our mental health services are more efficient? There are some other direct or indirect data about this topic, and they indicate that is mostly a matter of low recognition of problems and high stigma. In an European ranking of the number of patients with mental disorders (http://www.eu-wmh.org, 2011), Romania is ranked third out of 23 countries, with 1100 affected individuals per 100.000. It seems that the number of cases with mental disorders recorded at hospital discharge has increased in the past years (Mănăilă, 2013). According to the Romanian Association for Psychiatry and Psychotherapy (Ștefănescu, 2014), the prevalence of anxiety disorders in Romania reaches international rates, i.e. between 25-28%. The same study conducted by Florescu and collaborators shows that 76.4% of those with mental health problems do not benefit from any kind of treatment whatsoever, and barely 11.5% receive mental health care services, specifically 9.5% psychiatric treatment and 4% psychological treatment. The others attend general care (13.5%) and religious counselling (0.8%). When compared to 29 other countries in Europe, Romania is ranked last in regard to treatment access (EIU, 2014).

1.2. Barriers to treating mental health problems

The World Health Organization (WHO) recommends that mental health should become a global priority, considering disorders in this spectrum as „the core health challenge of the 21st century" (Wittchen et al., 2011, p. 670).

How can we explain this paradox between the high prevalence of mental health disorders and the low percentage of people who benefit from adequate treatment? What are the barriers and obstacles that hinder access to treatment? Our analysis has revealed multiple barriers: at the individual level, general practitioner (GP) level, mental health professionals (psychiatrists, psychotherapist and counselors) level, and also at the system level.

Almost two thirds of the individuals with diagnosable mental health problems do not seek treatment (Goldman, Rye, & Sirovatka, 1999). Information provided by Florescu et al. in 2009 show that in Romania the situation is the same: only 2-3% of those affected by anxiety and substance abuse problems and 10.2% of those presenting mood disorders actually seek treatment in the first year of illness onset.

The main barriers at **individual level** are:

- Reduced perception of the need for treatment. People tend to perceive mental problems as transitory, denying or minimizing their severity (Eisenberg, Golberstein, & Gollust, 2007; Mojtabai, Olfson, & Mechanic, 2002; Prins, Verhaak, van der Meer, Penninx, & Bensing, 2009).
- Desire to solve problems on one's own; 40 to 65% of those who are aware of their problems report they would prefer to manage them on their own (Andrade et al., 2014; Andrews, Henderson, & Hall, 2001; Gulliver, Griffiths, & Christensen, 2010; Lang, 2005; Rickwood et al., 2007).
- Stigma associated to mental health problems (C. Brown et al., 2010; Craske et al., 2005; Gulliver et al., 2010; Sussman, Robins, & Earls, 1987).
- Tendency to first ask for informal help from relatives and friends (J. Brown et al., 2014). If this solution does not work, individuals seek for professional help.
- Lack of information about efficient available treatments and negative stereotypes regarding treatments (Christiana et al., 2000; Sareen, Cox, Afifi, Clara, & Yu, 2005).
- People are not ready for change, according to Prochaska stages of change model (O'Hare, 1996; Prochaska et al., 1994).
- Practical issues: financial costs and lack of time; lack of geographic accessibility.

Approximately 83% of individuals suffering from anxiety and depression first turn to general practitioners and usually stop after this stage (K. A. Collins, Westra, Dozois, & Burns, 2004; Ohayon, Shapiro, & Kennedy, 2000). The main barriers **at general practitioner level** are:

- Lack of screening instruments and other adequate resources for managing mental health problems: only 15% of anxiety disorders and 36% of mood disorders and identified by GPs (D. Kessler, Lloyd, Lewis, & Gray, 1999; Kroenke, Spitzer, Williams, Monahan, & Lowe, 2007).

- Insufficient GP training for managing mental health problems. For example, of those identified as having a mental disorder, only 28% (Weisberg, Beard, Moitra, Dyck, & Keller, 2014) to 41% (Stein et al., 2011) receive adequate treatment (medication and/ or psychotherapy).
- Structure of GP services. The focus is on organic illness and there are considerable time constrains (K. A. Collins et al., 2004).
- Lack of integration between primary care services and secondary and tertiary care provided by mental health professionals (P. Y. Collins, Insel, Chockalingam, Daar, & Maddox, 2013), which leads to major treatment delays mentioned above (between 9 and 23 years from disease onset) (Wang, Berglund, et al., 2005).

The main barriers at **professional level** are:

- Lack of available specialists, resulting from the scarcity of counsellors, psychiatrist and clinicians, but also from inconsistent geographic distribution (WHO, 2011). Other factors are high prices for medication or therapy, lack of fit between client-therapist schedule, etc.
- Insufficient training in evidence-based treatments. Empirical data shows that CBT treatments are the most efficient psychological treatments for anxiety and mood disorders (Butler, Chapman, Forman, & Beck, 2006; Chambless & Ollendick, 2001; Deacon & Abramowitz, 2004; Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012), but few people benefit from them (11%) (Gunter & Whittal, 2010), in part due to insufficient CBT therapist who would provide such quality services (G. Andersson, 2015; Lovell & Richards, 2000).
- Cultural and axiological differences between clients and psychotherapists.
- Stigma associated to psychological treatments, but also low compliance to treatment, which leads to premature drop-out rates (35-47%) (Marks, Cavanagh, & Gega, 2007).
- Limited treatment efficiency and high relapse rate. For example, success rate for CBT treatment of anxiety and depression is a little bit more over 50% (Butler et al., 2006; NICE, 2006)

Therefore, there is a major gap between the number of individuals requiring treatment and individuals who truly benefit from adequate intervention. In order to make real changes within the system, psychological treatments must be focused on the individual, rather that the

institutions or the professionals who deliver them (WHO, 2008). We need to find solutions for reducing internal barriers and improving access to treatments; training the medical staff that provides primary care (GPs, nurses) and provide them with efficient screening instruments; improving access to evidence-base treatments and increasing their efficiency.

1.3. Internet use - the digital generation

Information and communications technology (ICT) have substantially changed many of our daily activities, having a major impact at all levels of our functioning. For example, the majority of the population uses internet as the main source of information in the decision-making process (Horrigan & Rainie, 2006). The number of internet users grows exponentially each year. The table below shows the dynamic rise of global internet use in the past 20 years.

Table 1 Global internet use

1995	1999	2002	2005	2008	2011	2013	2015
0.4%	4.1%	8.6%	15.7%	23.5%	32.7%	39%	**42.4%**

Romania is the country with the lowest percentage of internet use among European countries – 56.3%; this percentage has risen, though, with approximately 4 units each year.

Table 2 Internet use in Romania

2000	2004	2006	2010	2012	2014
3.6%	18.7%	23.4%	35.5%	44.1%	**56.3%**

Therefore, it is very important to consider globalization and the mind of the „digital generation". Digital natives, or digital born, are the generation born after 1995 that has interacted daily with digital media growing up: computer games, mobile phones, e-mail, internet, etc. Their daily life is constantly structured by digital media. Ongoing interaction with technology has created a new form of mind – the digital mind – that is different from the mind of „digital immigrants". The digital mind is used to easy and fast access to rich and multimedia information, personalizing products and services, producing and editing e-content, permanent connection and rapid feedback.

In addition to all of these changes, 62% of individuals seek information on mental health on the internet (Lorence & Greenberg, 2006); in Romania, the percentage is also high – 71.4% (Costache, Ciuca, & Miclea, 2014).

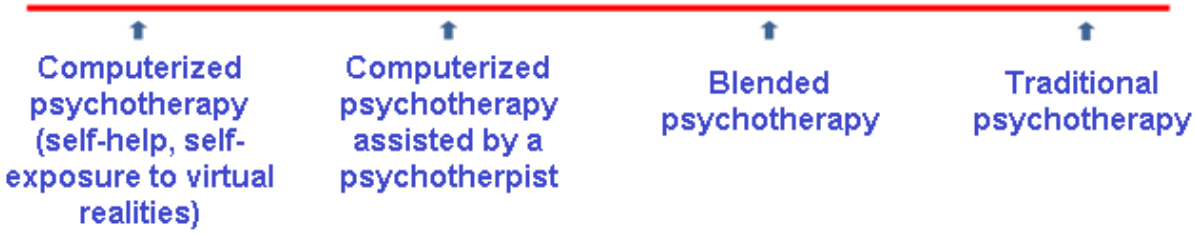
1.4. Proposed solutions - Computer mediated psychotherapy (CMP)

In order to balance the demand and supply of psychological services and to improve their accessibility, psychotherapy must reconsider certain principles and delivery modalities (M. Miclea, Miclea, & Ciuca, 2008). Psychotherapist- and relationship-focused psychotherapy (i.e. psychotherapy is a service offered by the psychotherapist within a therapeutic relationship/ alliance) has unfortunately proven its limits. Without denying the importance and benefits and seeking to build upon them, we propose PROCESS focused psychotherapy (i.e. psychotherapy is the change within the patient that occurs through the use of multiple resources: bibliotherapy, multimedia content, real/ virtual support groups, computer-assisted intervention, GPs etc.).

Given the aspects highlighted thus far, we propose **promoting computer mediated psychotherapy (CMP).** In short, CMP means offering counseling and psychotherapy services through the use of technology (internet, computers, mobile phones, tablets). In this paper we will use interchangeably two of the most common phrases for this concept: computer mediated psychotherapy (CMP) and internet cognitive-behavioral therapy (ICBT). CMP therefore combines the information technology and the human abilities and aims to reduce psychological problems and to create opportunities for personal development, by engaging the client in a variety of evidence-based therapeutic activities (M. Miclea, Miclea, Ciuca, & Budau, 2010). Modern computer mediated psychotherapy programs are meant to provide an user-friendly interface and can be used instead of (self-help) or in combination with face to face therapy, thereby creating an environment rich in resources that subsequently contribute to activating the psychotherapeutic process in the mind of the patient, either with or without therapist guidance (M Miclea & Kallay, 2012).

The use of computers and information technology within the psychotherapeutic process is flexible and goes along a continuum, as figure 1 shows.

Figure 1 Types of CMP



1.4.1. Computer mediated psychotherapy types and programs

In reaction to identified issues regarding the treatment of mental health problems, ICBT solutions have been tested in recent years. Some programs have reached an adequate level of

development and their efficacy and efficiency has been empirically proven. There are many computerized programs worldwide, most of them designed for the treatment of mild and moderate depression and anxiety disorders (phobias and panic attacks). *Beating the Blues*, *Overcoming Depression*, *Restoring the Balance*, *Good Days Ahead: The Multimedia Program for Cognitive Therapy*, *Fearfighter*, *Cope*, *BT Steps*, *MoodGym* or *Cool Teens CD-ROM* are just a few of the most popular programs.

We will employ Barak's (Barak, Klein, & Proudfoot, 2009) classification of computerized psychotherapeutic interventions: web-based internet interventions, online counseling and psychotherapy, internet-operated therapeutic software and other online activities (e.g. blogs, support groups, multimedia resources). Our research concerns only the first three categories, described in details below:

Web-based internet interventions have several main components: psychoeducational content of the program, multimedia resource use (graphs, animations, and audio-video materials), online interactive activities (self-report sheets, exercises) and feedback or psychological assistance. The combination of these components results in various web-based applications that contribute to improving physical or mental health problems.

Online counseling describes all the communication pathways via internet, either synchronous or asynchronous - e-mail, chat, audio-video (e.g. Skype) -, that facilitate access to long-distance psychotherapeutic services.

Internet-operated therapeutic software draw on the principles of artificial intelligence and use the latest technology in order to create therapeutic games or 3D virtual environments (e.g. *Second Life*), therapeutic robots that simulate therapy (e.g. *Eliza* program) and rule-based expert systems (for assessment, treatment selection and progress monitoring). These are used especially in exposure techniques via virtual reality, for problems such as specific phobias, social anxiety, sexual dysfunction, but also to help pain management.

1.4.2. Efficacy of computer mediated psychotherapy

In recent years, the efficacy and effectiveness of CMP/ ICBT has been investigated in hundreds of studies and dozens of meta-analyses, regarding a variety of disorders or psychological-related problems (for example: anxiety disorders, depression, substance addiction, eating disorders, weight control, smoking cessation, pain, tinnitus, irritable bowel syndrome, procrastination etc.). Overall results from these studies have been positive and promising (G. Andersson & Cuijpers, 2009; Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Barak, Hen,

Boniel-Nissim, & Shapira, 2008; Hedman, Ljotsson, & Lindefors, 2012; Kaltenthaler et al., 2006).

Table 3 Illustrative effect size from meta-analyses of treatment outcome studies

No.	Treatment type	Effect size	No. of studies or meta-analyses	Reference
1.	Various therapies and disorders	0.75	18 meta-analyses	Lipsey & Wilson, 1993
2.	CBT and behavior therapy, various disorders	0.62	23 meta-analyses	Lipsey & Wilson, 1993
3.	CMP, various disorders	0.53	92 studies	Barak et al., 2008
4.	CMP, anxiety disorders	.95	27 studies	Mewton et al., 2014
5.	Antidepressant (FDA registered studies 1987-2004)	0.31	74 studies	Turner et al., 2008
6.	CMP vs. face to face CBT	-0.02	24 studies	Cuijpers et al., 2010

Note. FDA – US Food and Drug Administration.

In the light of recent studies, CMP seems to be as efficient as face to face psychotherapy, having a long-lasting effect (G. Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Barak et al., 2008; Cuijpers, Donker, van Straten, Li, & Andersson, 2010), especially when assisted or supported by human intervention (G. Andersson & Titov, 2014), for the age group between 19-39 years old and individuals suffering from anxiety (Spek et al., 2007). In addition, online psychotherapy based on an cognitive-behavioral approach demonstrated best results (Barak et al., 2008), with highest effect sizes for post-traumatic stress disorder (0.88), panic (0.80) and smoking cessation (0.62) (Barak et al., 2008).

1.4.3. Limits and benefits of computer mediated psychotherapy

The main benefits of CMP highlighted by several authors (Amstadter, Broman-Fulks, Zinzow, Ruggiero, & Cercone, 2009; G. Andersson & Titov, 2014; Proudfoot et al., 2004) are:

- ✓ Large scale dissemination of standardized and empirically supported treatments;
- ✓ Online screening and diagnostic instruments;
- ✓ Lower financial and time costs compared to face to face therapy;
- ✓ Increased temporal and spatial accessibility;
- ✓ Chance to avoid the social stigma associated to mental health service use;
- ✓ Improved outcome and progress monitoring and self-monitoring;
- ✓ Opportunity to provide users with systematic feedback;
- ✓ The therapist can manage more patients, due to reduced time per patient;

- ✓ High variety of psychotherapeutic resources and the chance to access them whenever needed;
- ✓ Use of multimedia content that can improve understanding and encoding;
- ✓ Ongoing guidance and practical support.

In addition to advantages brought on by CMP, there are a series of arguments against and issues regarding its use (G. Andersson & Titov, 2014; Barak et al., 2008):

- o Lack of direct visual contact;
- o Completely automatic use of screening and diagnostic instruments is problematic and recommended against;
- o High costs of developing and accrediting CMP programs;
- o One size does not fit all;
- o Lack of motivation or necessary ability to operate in online environments;
- o Inability to detect and solve patient complications (crisis management);
- o Ethical dilemmas in practicing psychotherapy online: patient identity, confidentiality, impersonal relationship with the patient;
- o Lack of clear rules and laws to cover all potential situations resulting from use of CMP;
- o Practical and technical issues (ex. intervention depends on electricity).

While some of these problems still exist, some have been overcome at least partially, due to recent developments. Therefore, numerous psychotherapists and clients now use and benefit from this innovative treatment solution (G. Andersson & Titov, 2014; King et al., 2006).

Chapter 2 - Research objectives

Mental health problems affect the quality of life at the individual, social and also economic level because of direct and indirect costs that they entail. Mental health must become a global priority, and the fundamental scope of this research is to improve access to quality psychological services through the use of computer mediated psychotherapy. Therefore, our general objective is creating and validating a professional online platform for the prevention and psychotherapy of anxiety.

Specific objectives are:

- Developing an optimal multi-user CMP solution (PAXonline Platform);
- Evaluating the efficacy of PAXonline Platform;
- Identifying patient characteristics and other factors that might predict the efficiency of the platform in treating anxiety disorders;
- Analyzing and illustrating the course of treatment within the intervention program for panic disorder (PAXPD).

Chapter 3 - Study 1. The development of PAXonline, a professional platform for the prevention and treatment of anxiety disorders

Because it is a relatively new field, there still aren't guidelines for the development of an efficient CMP-type intervention program; therefore, we have focused our attention towards *e-learning*. We have started from the assumption that psychotherapy (mainly the cognitive-behavioral one) is a learning process; consequently, the CMP solution had to be created so as to sustain and facilitate the learning process and, implicitly, the therapeutic process of change. In the same time, e-learning solutions have been already applied in the field of education, and things are even more advanced due to the already accumulated experience (R. C. Clark & Mayer, 2003; Kozma, 2001; Mayer & Moreno, 2003). Hence, we aimed to apply the useful aspects of instructional design (ID) in the development of our CMP solution. The instructional design is defined as the empirical and iterative process of analysis, planning, development and management of learning that has as primary purpose to improve the efficiency of the learning process (Reiser & Dempsey, 2007) and implies several essential intermingling stages:

1. The analysis stage, which involves the analysis of the target users and of the learning context;
2. The planning and development stage, which involves the clear definition of the learning objectives, in terms of knowledge, attitudes and abilities; establishing the structure of the e-content and its delivery; the selection of learning materials or resources; the creation of learning activities.
3. The implementation stage, the actual use of the platform by the target audience.
4. The evaluation stage – determining the formative and summative evaluation methods, of the users' performances;
5. The management – integrating the solution into the system and the continuous management of the users, the database etc.

The working definition that has lead us in the development of the online platform for the prevention and therapy of anxiety, describes a CMP program as a computer application that meets three essential conditions:

- is explicitly created to serve a psychotherapeutic purpose,
- implements the principles and methods of bona fide psychotherapy (ex. CBT, psychodynamic therapy),

- actively involves the patient into a range of psychotherapeutic activities; *psychotherapy is centered on the process,* the person is the active agent who implements the *change,* using the existing resources to produce psychotherapeutic effects (M. Miclea et al., 2010).

From the very beginning our aim was two-fold:

a. improving the effects of psychotherapy;
b. improving the patients' behavior of asking for help, by overcoming the barriers mentioned in the previous chapter.

Taking into account the recommended instructional design stages, our definition of the CMP solution and the envisaged purposes, the development of the online platform for the prevention and therapy of anxiety involved several stages:

1. The rigorous analysis of the needs and features of the users (patients, therapists, general practitioners), as well as the obstacles faced by the patients in their search for help for their mental health problems;
2. The critical analysis of similar products;
3. The review of the literature on CMP and the existing standards (ex. NICE, ISRII);
4. The analysis of the e-learning domain and the transfer of the relevant principles;
5. The analysis of the treatment guidelines for anxiety disorders (Clark & Beck, 2011; Leahy & Holland, 2000; Andrew, 2003) and the content of psychotherapeutic resources;
6. Determining the general architecture and the specifications of the platform;
7. Testing the functionality and usability of the platform (a reiterative process, carried out during the entire development of the solution).

3.1. The needs and characteristics of the users

Given the process of searching for help for mental health issues and the fact that one is confronted with barriers at all levels, we decided to dedicate the platform to clients/patients, as well as to the general practitioners and therapists (counsellors, psychologists and psychiatrists). The main purpose of a multi-user prevention and intervention platform is to create a therapeutic community.

The patient needs: access to specialists, properly validated psychotherapy programs; personal improvement and development techniques; specific and easy-to-use resources; evaluation instruments and worksheets; motivation, guide and support throughout the

intervention. All these offered by means of personal control and flexibility – i.e., the patient has access to all these "therapeutic resources" where, when and as much as he/she needs.

The therapist needs: to promote the psychotherapeutic resources to a larger number of clients; a "virtual" private practice; access to scientifically validated psychotherapy programs; access to numerous intervention techniques and indications for their personalized and maximized effects; access to evaluation instruments and worksheets; access to a scientific community to communicate ideas, cases and to receive suggestions, additional materials etc.; the possibility to reflect a more efficient management of the patients (the digital psychotherapeutic agenda) – all offered in a flexible manner and under personal control.

The general practitioner needs: access to a scientifically validated information sources and specific training programs; access to fast and efficient screening instruments; access to a scientific community; a place where to send his patients when their problems transcend his competence and where he can collaborate with mental health specialists; a digital medical agenda for a more efficient management of patients - all offered in a flexible manner and under personal control.

3.2. The analysis of similar existing products

In view of identifying some common points, differences and the weaker points of the already existing cognitive-behavioral programs, we analyzed several of them: *Beating the Blues* (anxiety and/or depression), *COPE* (depression), *Overcoming depression: A Five Areas Approach* (depression), *Fear Fighter* (specific phobia, panic), *BTSteps* (obsessive-compulsive disorder), *Panic Centre* (anxiety and panic), *Moodgym* (depression and anxiety in teenagers and young people).

Table 5 shows, in a structured manner, the main characteristics of the best known and most tested online programs. In the same time, in order to facilitate the comparison, we added the characteristics of the online prevention and intervention program developed by us, named PAXonline.

Table 5 PAXonline and other CMP programs

Characteristics	***PAXonline***	***Beating the Blues***	***Fear Fighter***	***Panic Center***	***Moodgym***
Who is it addressed to? Beneficiaries	Patients (adults), Psychoterapists General practitioners	Patients Specialists can use the program in their activity as additional help, but it is not especially designed for them.	Patients (adults)	Patients (adults)	Patients – 15-25 years old
Addressed issues	Prevention and psychotherapy of anxiety; comorbid depression; personal development	Anxiety and depression, with a focus on depression	Panic and specific phobias	Panic and agoraphobia	Prevention of depression and anxiety in teenagers
Duration; number of sessions	3 months for patients 1 year for psychotherapists 3 years for general practitioners Introductory video sessions 10-14 modules per program	Introductory video sessions 15min; 8 sessions of 50 minutes	10 weeks (3 months) 9 modules	16 weeks 9 main modules and other 7 auxiliary modules (secondary problems)	6 weeks 5 modules
User's instructions – locations, accessibility	Online; can be accessed directly, either with referral from the general practitioner or the psychotherapist	Organized context - clinics, private practices; there is also an online version. The referral from the general practitioner is mandatory.	Standalone FF, NetFF FF education Only with referral from the general practitioner	Online	Online
Available human support	Psychotherapeutic assistance available upon request, by mail, messenger and video chat (secured Skype). Support group on the forum	5 minutes before each session and another maximum 15 minutes after each session (at the clinic).	5 minutes before each session and another maximum 15 minutes after each session (at the clinic). Helpline facilitators, by phone or e-mail (netFF) – 1h maximum	Support group on the forum, plus conversation on instant messenger with other patients or the forum's moderators.	Only automatic feedback generated by the program.
Performed evaluations	Initial screening (the independent use is not recommended by the persons with psychotic problems, bipolar disorders, suicidal risk, substance consumption).	An initial evaluation is performed and the persons with psychotic problems, bipolar disorders, suicidal risk, substance consumption are not accepted	An initial evaluation is performed and the persons with psychotic problems, bipolar disorders, suicidal risk, substance consumption are not accepted	Initial and final general evaluation, plus shorter evaluation during every session or whenever requested by the patient.	At the beginning of each module 2 questionnaires are filled in, one for anxiety and one for depression.

	Advanced evaluations Specific pre-post intervention evaluations Short evaluation at the beginning and end of each module	Initial and final general evaluation, plus shorter evaluation during every session.	Initial and final general evaluation, plus shorter evaluation during every session		
Components	Psychoeducation Cognitive-behavioral therapy plus elements of positive psychology and mindfulness Homework	Psychoeducation Cognitive-behavioral therapy Homework	Psychoeducation Cognitive-behavioral therapy Homework	Psychoeducation – questions and elaborated answers Cognitive-behavioral therapy Homework	Psychoeducation Cognitive-behavioral therapy Online exercises Homework
Additional options	Personal portfolio Forum, basic and personal resources and information, Symptomatology personal sheet Rewards within the programs, personal diary, explicative dictionary Patient Register Synchronic and Asynchronic Psychotherapeutic Assistance Video materials that present case studies in order to stimulate the vicariant learning Technical support	Diary or user's notebook Setting goals 5 case studies are used for providing examples – video format. Technical support	Setting goals. Troubleshooting – support in case of technical problems or difficulties. Real life stories – short quotes, evaluations and opinions. Technical support	Dictionary for the medicine and disorders. Support group– forum mediated by the specialists. Instant messenger Mood Tracker – a kind of diary that can be filled in online, daily regarding the personal status, panic attacks. Setting goals. "Testimonials" of other users Technical support	Diary or user's notebook Games and animations Fictional characters that help illustrate the intervention. Technical support
The navigation pattern	Recommended pathway, but the choice belongs to the user. Modules can be revisited any time. Flexibility, independence and personal control are promoted. The psychotherapist can personalize the intervention for each patient.	Compulsory navigation path A session per week	Compulsory navigation path A session per week	The first, longer, session is mandatory; the others can be chosen by the user. Modules can be revisited anytime.	Compulsory navigation path, the modules can be accesses step by step. Modules can be revisited anytime.

3.3. The analysis of the field of *e-learning* and the transfer of the relevant principles

Although there are several clinical guidelines that make recommendations regarding the use of online/ computer-based solutions for mental health (NICE, 2006; Proudfoot et al., 2011; Ritterband, Thorndike, Cox, Kovatchev, & Gonder-Frederick, 2009), the literature does not talk about the way in which proper contents must be created for this kind of solutions. That is why we needed a set of guidelines or rules regarding the creation of contents for the online mental health solutions. In our opinion, these rules are strongly influenced by the answers given to four categories of questions:

1. ***Users:*** What kind of people will use that particular mental health solution? What are their goals and particular features? Which is their daily routine in which the *e-mental health* solution is intended to be integrated? How do we expect them to react online?
2. ***Relationships:*** What type of relationships should be created among the users? How can these relationships be developed online? What is our role, as psychotherapists and also creators of *e-content*?
3. ***Content and format:*** Which are the most relevant and useful contents? Which is the most proper format in order to communicate the desired contents?
4. ***Work environment:*** How can the optimal digital environment be created in order to support the users in reaching their goals? Which are the necessary architecture and design to optimize the learning process?

The main conclusions drawn after the analysis and integration of the classical psychotherapy with the *e-learning* are as follows.

1. Optimized scanning

Recent data show that in the online environment the information is not cited in a linear manner, but it is rather scanned or overflown (Campbell, 2004). Readers scan the text to identify the most important ideas, in order to understand how these are linked to each other and to extract the information they need. In the same time, reading off a screen is different in many aspects from reading off paper (e.g. image resolution, reading speed, fatigue and the need of breaks). Based on these principles we can outline the following recommendations: (a) the use of shorter sentences and paragraphs, with simpler topics; (b) marking the more important sections by short and informative titles and subtitles; (c) organizing and structuring information by using different types of subtitles (Kilian, 2001); (d) the possibility to increase or decrease the used font and the predilect use of a constant, familiar font; (e) brighter colors to attract attention.

2. Information and knowledge organized in learning objects

In order to optimize the learning process, information should be presented in a structured and organized manner. In the digital environment, the most frequent organization involves the use of learning objects, i.e. a group of information surrounding a certain learning goal, which allows a specific evaluation and which is relatively independent, i.e. it contains all the necessary information to fulfill the set objectives (Polsani, 2006). In the same time, a learning object can be used flexibly, in more courses or programs.

3. Facilitated interactions and improved work alliance

The patient is the key factor for change: he/she decides how to utilize the resources and the possible assistance of the therapist offered through the CMP. We can thus talk about an interaction with the online intervention program. In order to make the patient more responsible and offer him/her more control, several rules should be applied: (a) presenting the information on three levels of depth. First level: general framework and essential information; second level: more details - audio, video or graphic, dynamic materials; third level: detailed scientific information. (b) flexible curriculum that allows the browsing through the intervention program depending on the stage in which each user is situated. (c) personalized intervention and (d) Interaction with multimedia materials.

4. Increased involvement and in-depth processing through multimedia contents. The efficient use of the multimedia format

The use of digital technologies provides extended possibilities to use contents in various multimedia formats for the CMP solutions, for example: animations or audio-video materials to explain the processes that take place at the neurophysiological level, a certain case study or a particular therapeutic technique. The research on e-learning (Mayer & Moreno, 2003; Kozma, 2001) has led to the elaboration of several instructions: (a) chunking the video materials /animation in smaller sequences. (b) providing a balance between oral materials and the visual or audio elements. (c) displaying the images, animations or graphics in the immediate proximity of the adjacent verbal content. (d) The audio-video elements should not present concepts that are different from those treated in the adjacent texts (Hannafin & Hooper, 1989). (e) providing information about the used multimedia elements, in order to assist the user to make informed decisions on their use.

3.4. The analysis of the treatment protocols for anxiety disorders

The studies show that the prevalence of anxiety disorders during a lifetime is of approx. 30%, and its prevalence over the course of a year is of 19% (R. C. Kessler et al., 2005). The evolution of the anxiety disorders is chronic, and in the lack of a proper treatment the patients have to endure major costs over a long period of time. Anxiety disorders can present themselves under several forms (e.g., panic disorders, specific phobia, social phobia, obsessive-compulsive disorder, generalized anxiety disorders, post-traumatic stress disorder) and have a complex etiology, being the result of diverse interactions among social, biological and psychological factors.

According to the guidelines published by international authorities in the field of mental health, such as the guidelines of the American Psychiatric Association (APA, 2009) or the guidelines of the National Institute for Health and Care Excellence from Great Britain (NICE, 2011) anxiety disorders can be treated efficiently by means of two types of therapy, applied independently or together: cognitive-behavioral therapy and pharmacotherapy.

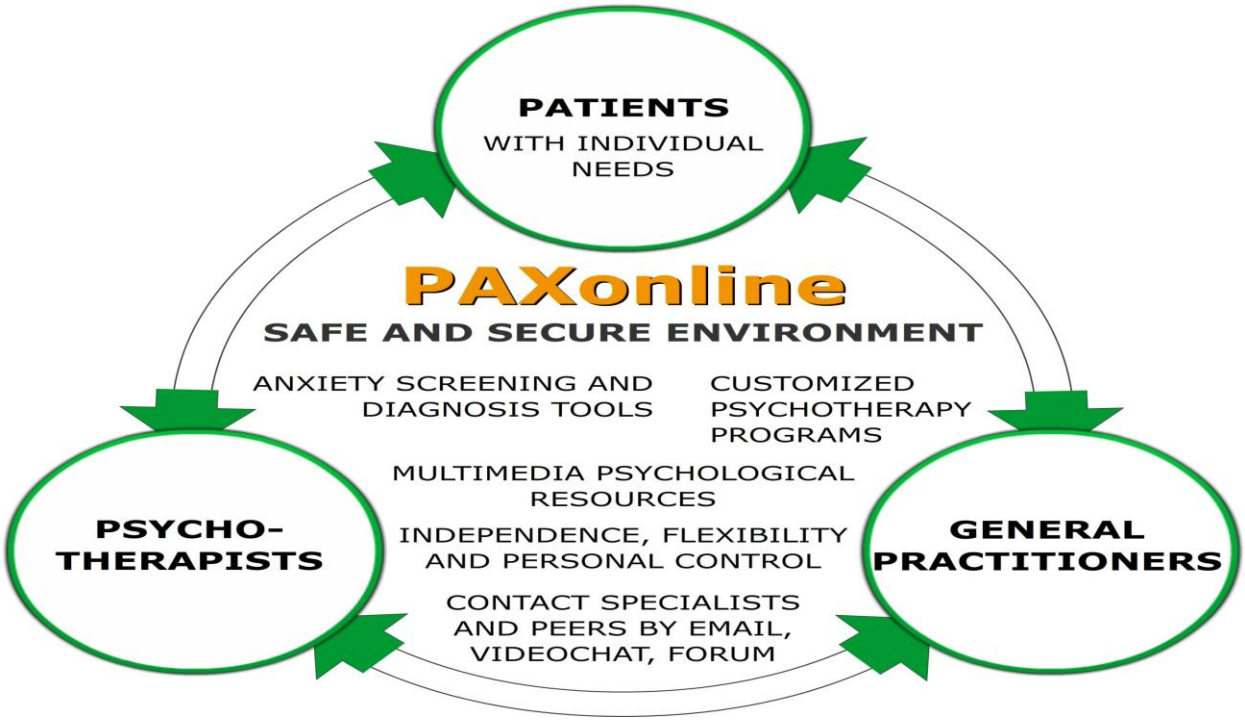
The cognitive-behavioral (CBT) is the most studied form of psychological treatment for anxiety disorders, and the results of over three decades of clinical studies support its efficiency (Butler et al., 2006; Deacon & Abramowitz, 2004). A very important aspect of the cognitive-behavioral interventions is that the obtained positive effects are maintained over a long period of time (DiMauro, Domingues, Fernandez, & Tolin, 2013; Durham et al., 2005). Recently, the beneficial effect of the CBT on the brain has been demonstrated. More precisely, it was proven that through psychotherapy, a correction takes place in the way the cerebral circuits involved in the detection of dangers, the engagement of the anxiety reactions and the control of the anxiety function (Beauregard, 2014; Porto et al., 2009; Straube, Glauer, Dilger, Mentzel, & Miltner, 2006).

After an analysis of the intervention protocols for anxiety problems we selected the main strategies for intervention that we would use in view of creating the programs and implicitly of the intervention modules from PAXonline. These are: psychoeducation, the reduction of the neurophysiological hyper activation, the change of attentional biases, the change of the thinking process, fighting the avoidance and the prevention of subsequent falls. As additional methods we used the problem solving technique, the development of positive emotions and the reduction of the comorbid depression symptoms through methods of behavioral activation.

3.5. The conclusions of the performed analysis – The specifications of the PAXonline platform

The PAXonline concept, resulted from the performed analyses could be summarized through the following graphic illustration:

Figure 2 – Graphical illustration of the PAXonline concept



3.6. Testing the functionality and usability of the PAXonline platform

Testing the computer programs represented an essential stage in the development process, which enabled the detection of errors and the compliance with quality standards. Testing the functionality of the PAXonline platform was accomplished in two steps, two complete circles, at approximatively one month distance from each other. We tested the system both globally and at the level of units, modules and subsystems. On this occasion we also performed the corrective maintenance, that is the troubleshooting or the elimination of bugs, and we made functional improvements.

Procedure

a) The first testing. Aimed to test the functionality of the platform by seven psychologists experienced in the development and testing of software, for four hours a day, over a period of ten days, who submitted their observations in a final report. These were classified by the research

team according to their importance. Most observations were implemented on the spot (70 of 160 observations).

b) The second testing. Involved 17 persons with university degrees in psychology, Masters student and doctoral candidates from the Faculty of Psychology and Educational Sciences, the "Babeș-Bolyai" University of Cluj-Napoca, as well as five persons with certain anxiety problems. For three weeks, each participant fulfilled the role of patient, therapist and general practitioner (a role per week). The persons manifesting anxiety problems performed only the role of patient. The software specialists operated the changes identified at the end of each week. The tests were made both individually, and in pairs (general practitioner – patient or therapist - patient) or in group (testing the synchronic communication, video-chat and discussion forums).

The testing stage aimed to identify the functionality errors and to make the suggestions for the improvement of the online platform.

The following **aspects and functionality principles** were taken into consideration:

a) **Transmitting the information and messages among the users** (therapist - patient, doctor - patient) **and between the user and the system in due time**, under **conditions of maximum security** and with an **extremely flexible architecture**. The data security is of the highest level, due to software that can crypt and decrypt data, sign messages with digital signatures, verifies, identify and certify the keys distributed for entities at a distance. The software automatically crypts the information, being able to manage various types of algorithms;

b) **Integrating other attached systems in the online platform**, such as forum and video chat options;

c) Using **simple procedures, preferable to complex endeavors**, which would uselessly complicate the process;

d) Introducing some **internal link structures, folder structures, URLs** and the necessary amount of time to download;

e) Carefully designing the **site management** component.

3.7. Pilot Study - testing the PAXonline platform within an observational study

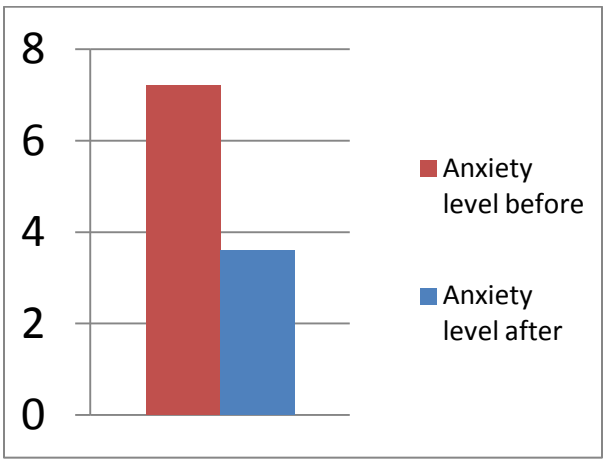
Over a period of three months, from May to July 2012, the platform was tested within an observational study by 1 100 clinical psychologists, 700 patients and 50 general practitioners. At the end of this period, participants were invited to fill in a feedback questionnaire. The questionnaire was designed to help evaluate several aspects related to the functionality of the

PAXonline platform, its usefulness, the perceived quality and importance of the PAX components, its efficiency in reducing the anxiety symptoms, the user's general satisfaction and possible recommendations for improvement.

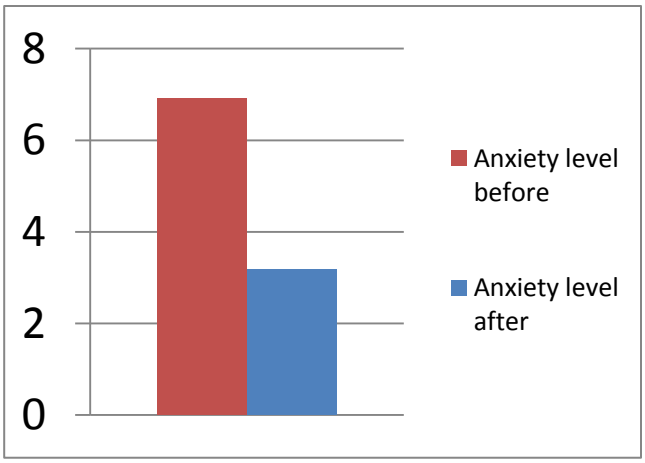
The feedback questionnaire was filled in by 640 specialists (clinical psychologists or therapists) and 49 patients. 95% of the specialists and 75% of the patients answered that they found it "easy" or "very easy" to use the platform. The importance of all the components was evaluated at maximum levels by both the specialists (the graphics, the images and the audio-video materials were considered the most important), and the patients (the text content of the modules). The platform component that was considered to be the least important was the discussion forum, especially among the patients. All elements were evaluated at the highest quality standards by the respondents, both specialists and patients, the most appreciated being: "the text content of the modules" (over 85% of the specialists, 81.63% of patients,) and "graphics, images, audio-video materials" (83% of specialists and patients).

In order to evaluate the efficiency of the platform in reducing the anxiety problems, both the patients and their therapists specified the degree of these problems before and after the intervention. The severity of the anxiety problems was evaluated on a scale from 0 to 10, where 0 means the lack of anxiety and 10 means its highest intensity. The graphic representations of the received answers are shown in Graphic no. 3 for therapists and no.4 for patients.

Graphic no.3 Therapists



Graphic no 4. Patients



The results of these evaluations were extremely similar, representing an additional guarantee of their validity. Both the specialists and the patients evaluated the pre-intervention anxiety problems at an intensity around 7 points, and after the intervention this intensity dropped to approximately 3.4 points. The difference pre-post intervention was statistically significant in both situations (see Table 33).

Table 33 - Reduction of the anxiety symptoms after using the PAXonline platform

Evaluation	N	Pre-treatment M (SD)	Post-treatment M (SD)	
Therapists	149	7.22 (1.75)	3.6 (1.63)	t(148)=25.865, p<.001
Patients	33	6.92 (2.33)	3.18 (1.75)	t (32)=10.046, p<.001

All patients who used the PAXonline platform within the pilot study answered positively to the question "Would you recommend the platform to other people with anxiety problems?", which indicates a high level of satisfaction and trust. When answering open questions, the specialists wrote that they mostly appreciated the innovative concept, the qualitative scientific resources and the fact that it offers them a rigorous structure and well-articulated treatment plans. The patients appreciated the module content and its utility, as well as its presentation (video format); homework; high accessibility and language.

The feedback received in the pilot study was extremely important. Firstly, it was proven that the platform is ready to be used in subsequent studies (high functionality, easy-to-use, high satisfaction of users and the appreciation for the PAX quality and component utility) and encouraging evidence was procured regarding its efficiency in the treatment of anxiety disorders.

3.8. The description of the platform through which the online therapy is carried out

PAXonline is a Professional Platform for the Prevention and Therapy of Anxiety, which works online. It implements a new concept about psychotherapy through a software application, which combines the principles of the cognitive-behavioral therapy with the available features of the information and communication technology.

The platform has **two levels** (visitor and user) and **three categories of users**: patient, therapist and general practitioner. In the same time, PAXonline has **three main functions:**

- screening and psychological evaluation;
- prevention, psychotherapy and personal development;
- psychological and technical assistance.

As a **visitor**, anybody can benefit from the resources and primary assistance for anxiety problems (brief articles about anxiety disorders, existing types of treatment and their efficiency, dictionary, frequent questions) and access to two **screening instruments** that automatically inform the persons if it is **possible** they suffer from an anxiety disorder, and then which disorder is more **likely to be present** in that particular case.

THE PATIENT is the main user of the platform. The central element is the **psychotherapy program**, developed for each anxiety disorders and consisting of a series of module. Each module focuses on a particular component of the therapy process (e.g. the conceptualization of the case, exposure, relaxation, identification and fight against the dysfunctional cognitions etc.). The modules are organized in a certain order, but the program is flexible, some modules being optional. The modules have multimedia contents, and the content is organized in order to maximize the assimilation of resources and the therapeutic change. The patient is constantly activated in order to use the resources for getting better, through the answer that he must provide to the therapeutic questions, through teach-back, links to additional resources, the worksheets etc. Practically, the browsing of a module is not a **reading endeavor**, but it rather involves a **range of therapeutic activities** that the patient must carry out (e.g. answer the questions, teach-back, fill in worksheets, etc.). The results of these activities are saved in the **Personal portfolio**, in order to **permanently monitor** the evolution of a patient. In the Personal portfolio any multimedia files from **Specific Resources** can be saved.

If he/she feels the need for additional assistance, the patient can access a therapist from within the program. The communication with the therapist can be asynchronic (via messenger) or synchronic (via Skype). The therapist has an automatic access to the Personal Portfolio of the patient; therefore, based on the records from the Portfolio, the therapist can support, monitor, offer feed-back and explicitly plan some activities. Besides the resources provided by PAXonline, the therapist can upload, for any of his patients, additional personalized resources.

The patient also benefits from an electronic **Personal Diary** that is saved in the **personal Portfolio**. At the end of the therapy, the patient can download all the resources saved in the Portfolio. In addition, the patient becomes a part of a virtual therapy community, through a **Forum**, moderated by an experienced therapist.

All in all, PAXonline provides the patient with a personal space, where professional resources and specialized assistance are available (support, supervision, feed-back, planning), to maximize the therapeutic process. The patient performs a guided range of activities with these resources, and his progresses are attentively monitored. The platform places him in a therapeutic community which he can benefit from.

THE THERAPIST, the second user of the PAXonline platform, benefits from a range of specific opportunities. He can use the platform either as an instrument between two classic therapy session or within them (computer assisted classic therapy), or to assist (guide, evaluation, supervision, intervention) the patients who registered on PAXonline (computer therapy assisted

by therapist). PAXonline offers the therapist the possibility to perform a computer evaluation of the symptomatology with the help from a range of instruments, an asynchronic communication or via video chat with his own patients, discussions via the Forum with other therapists interested in the therapy of anxiety, registered on PAXonline, an instrument that manages the patients and their clinical evolution, through the **Patient Register** and the possibility to offer personalized resources to the online patients. As a supervision and learning instrument, PAXonline creates a **community of practice and learning**.

THE GENERAL PRACTITIONER gets access to PAXonline by simply registering, but he/she has to participate in an introductory training course. With the help of PAXonline, the general practitioner: a) can provide a better primary care to the patients with anxiety disorders from the private practice; b) can perform the screening of these disorders; c) can refer the patients to the resources and assistance offered by PAXonline, also soothing the weight of the stigma.

In conclusion, PAXonline represents a technical solution meant to improve the anxiety therapy in the digital era. It is based on a new conception on the structure of therapy, in accordance to the human mind of today and the world of digital technology.

3.8.1. The principles implemented within the PAXonline platform. The presentation of the structure of a standard module

The components of a standard module standard of the platform are as follows:

1. **The evaluation of the emotional state and the intensity of the anxiety problems**

At the beginning and end of each module there is a mandatory evaluation of the emotional state over the previous 24 h (scale from -10 to +10) and the intensity of anxiety problems (scale from 0 to 10) manifested by the patient. We monitor the record of the evolution over time and the effect of each module.

2. **The objectives of the module**

There are two or three objectives for each module, and their role is to orient, guide and motivate going over each module.

3. **The content with information and exercises**

We present here *in extenso* all the relevant information, explanatory videos are shown, worksheets and various exercises are solved. For an easier and more flexible browsing, the content was divided in sections. The information is presented in a simple language, and the delivered format alternates, the same information being presented in at least two formats (e.g.

graphic and animated). Most worksheets must be downloaded and filled in on the personal computer.

4. **Case presentation**

Each module contains multimedia case presentations, related to the treated topic or topics. They sum up clearly and concisely the content of the module, facilitate its understanding and shape the application of the recommended exercises (e.g. the adjustment of breathing exercise).

5. **The summed up module**

In each module, the presented information is summarized in text, table or graphic format, in order to be better fixed and memorized.

6. **Exercises**

The patient receives at the end of the module homework associated to the treated topic, that is, actual behaviors to implement or exercises, individual follow-up sheets etc.

7. **Testing the knowledge**

This evaluation takes place at the end of each module in two ways: multiple-choice questions, followed by an immediate feedback and the teach-back method, known as "teach another". It is considered that this method leads to better understanding and higher treatment compliance (Dinh, Clark, Bonner, & Hines, 2013).

8. **Finishing the module and offering a reward**

The last step or the last component of a standard module is to finish and take the prize, the reward (funny videos, games or songs). This section is aimed at increasing the motivation by repaying the effort and introducing a positive emotion.

3.9. Conclusions and recommendations for using the platform

PAXonline represents a therapy design that is focused more on the therapy process and less on the relationship between the therapist and the patient/client. This means that the entire endeavor of designing the platform was centered on the idea that the therapy interventions can be performed in various locations (the therapist's or the general practitioner's practice or the patient's home) and with different resources (multimedia contents, virtual or real support groups, computer assisted intervention programs etc.), in the most diverse formats (text, graphic, audio, audio-video) able to accelerate the therapy process that takes place in the patient's mind. Therefore, the creation and implementation of this professional platform for the prevention and therapy of anxiety was based on the rigorous analysis of the features and needs of the users of mental health services, such as patients, therapists and general practitioners.

We tried to build PAXonline according to the EU international norms, regarding the development of instruments of psychological assistance and, as an *e-mental health* solution, according to the NICE (*National Institute for Clinical Excellence - UK*) recommendations, one of the most advanced in this field. They recommend a sequential approach, on stages, of the mental health issues, which involves a progressive intensity of the clinical intervention, depending on the initial severity and the response to therapy.

The first level of the sequential approach is that of the ***primary assistance***, from the general practitioner. The interventions are minimal: self-administered therapies, bibliotherapy, and computer-based therapy. On the **second level**, for the cases with a ***moderate clinical symptomatology***, interventions of an increased intensity are recommended, such as the psychoeducation, psychological counselling, psychological services for personal optimization, anxiolytic medication. **The third level** of intervention in the field of mental health implies a multi-disciplinary approach, additionally intensified, involving specialized psychiatric services, therapy, and medical assistance pertaining to different specialties, depending on the particular case.

Within this three-layered model, **PAXonline** is situated above the primary intervention level, because it **integrates the digital resources of therapy with the actual assistance offered by a therapist.** The computer mediated therapy, and implicitly PAXonline, do not replace the face-to-face therapy, but rather represent a viable alternative for the people who wouldn't otherwise benefit from any kind of treatment for their mental health problems. In addition, PAXonline, used as a support for the classic therapy, may enhance its efficiency.

Chapter 4 – Study 2. Testing the efficacy of PAXPD program for treating panic disorder

4.1. Background - theoretical review

Hundreds of millions of people are affected by mental health disorders worldwide. Every year over 38.2% (164.7 million people) of the total EU population suffer from at least one mental disorder and the resulting economic costs rise at 3-4% of EU Gross Domestic Product (GDP) (Wittchen et al., 2011). A report released in 2008 showed that „up to 60% of people attending primary care clinics have a diagnosable mental disorder" " (WHO&Wonca, 2008). Still, there is an alarming underdetection of mental health problems – for example, detection rates of anxiety and mood disorders in general practice reach only 15% and 36%, respectively % (Üstün & Sartorius, 1995; White et al., 2000). Despite the potential to successfully treat mental disorders, because of multiple barriers only a small minority receive even the most basic treatment, at minimal standards.

Computer and Internet-based cognitive behavioral treatments (ICBT) represent recent attempts to innovate the psychotherapeutic process, matching both the existent demands of the market, and the new attitudes of those who seek help in the digital era. Research on internet-based treatments has grown rapidly in the past decade, gathering more than 100 controlled studies that successfully tested various intervention programs for anxiety disorders, mood disorders, or other psychiatric conditions (Hedman et al., 2012; Mewton, Smith, Rossouw, & Andrews, 2014; Richards & Richardson, 2012). Because half of all lifetime cases of mental disorders start by age 14 years and the median age of onset for anxiety is 11 years (R. C. Kessler et al., 2005), it should be mentioned that ICBT shows promising results not just for adults, but also for treating anxiety and depression in youth (Ebert et al., 2015; Silfvernagel, Gren-Landell, Emanuelsson, Carlbring, & Andersson, 2015).

So far, the literature suggests a superiority of guided versus unguided self-help treatments in terms of efficacy, adherence to treatment and drop-out rates (G. Andersson & Titov, 2014; Johansson & Andersson, 2012; Palmqvist, Carlbring, & Andersson, 2007; Richards & Richardson, 2012), but the conclusions are based on few studies and mainly limited to depression and social anxiety disorder, thus restricting the generalizability of the findings (Baumeister, Reichler, Munzinger, & Lin, 2014). The role of therapist guidance and its impact on treatment outcome is central to the development of ICBT programs and needs to be addressed directly.

In guided programs, asynchronous communication (emails or text messages) is most commonly used and, on average, patient guidance does not take more than 10 minutes per week (G. Andersson, 2015). So far, research is very limited regarding web-based treatment programs that provide guidance through synchronous (real time) audio-video communication (e.g. video chat programs such as Skype). On the other hand, there is growing evidence that the efficacy of CBT delivered via videoconference is equivalent to face-to-face treatment for mood and anxiety disorders (Bouchard et al., 2004; Germain, Marchand, Bouchard, Drouin, & Guay, 2009; Hilty et al., 2013; Stubbings, Rees, Roberts, & Kane, 2013; Théberge-Lapointe, Marchand, Langlois, Gosselin, & Watts, 2015; Yuen et al., 2013). This type of communication closely matches face-to-face therapy and enables access to important face-to-face cues such as verbal tone, facial expressions, and body language. Furthermore, this type of contact may facilitate higher engagement, feelings of accountability and social support, and reduce the risk of misunderstandings, compared to emails and instant messaging (Abbott, Klein, & Ciechomski, 2008). All of the above could also facilitate the development of a better therapeutic alliance (Simpson & Reid, 2014), a factor that has consistently proven to be a key predictor for therapeutic change in face-to-face therapy (Horvath, Del Re, Fluckiger, & Symonds, 2011; Martin, Garske, & Davis, 2000). So far, there is mixed evidence regarding the importance of the therapeutic alliance in guided ICBT (G. Andersson, 2015). Even if contact with the therapist is only minimal, patients seem to develop a strong alliance, but this makes no difference for the outcome, at least for self-help interventions with rather low-intensity guidance (G. Andersson, 2015). However, the therapeutic alliance in internet-based treatments that include video conferencing is yet to be investigated (Sucala et al., 2012).

4.1.1. Objectives and research questions

The aim of the present trial is to investigate the clinical efficacy of an internet-based self-help treatment program for panic disorder with therapist guidance via secured Skype in Romanian adults. The program (PAXonline for panic disorder) has been developed de novo by the authors, based on empirically validated cognitive behavioral models of anxiety disorders (Andrews, 2003; D. A. Clark & Beck, 2011; Leahy & Holland, 2000), and it is currently the only available psychological treatment of this kind in Romania. A secondary objective was to compare the guided self-help intervention (audio-video synchronous therapist communication) to a similar but unguided intervention program, considering clinical outcomes, adherence to treatment and drop-out.

4.2. Methods

The study design is reported in line with the CONSORT 2010 statement (Consolidated Standards of Reporting Trials)(Schulz, Altman, & Moher, 2010) and the SPIRIT 2013 Statement (Standard Protocol Items: Recommendations for Interventional Trials) (Chan et al., 2013).

4.2.1. Study design

This study is a randomized controlled trial with two active treatment conditions and a waiting list control group. A one-factor experimental design (parallel-group, superiority trial) has been used. The three conditions are:

1. *Web-based self-help program for panic disorder with intensive guidance (PAXPD-guided)*
2. *Web-based self-help program (PAX-unguided)*
3. *Waiting list control group*

4.2.2. Ethical approval

The study has been approved by the Ethical Review Board of The Center for the Management of Scientific Research Babes-Bolyai University (No. 31697/ 12.05.2014), and has been prospectively registered in Australian New Zealand Clinical Trials Registry (ACTRN12614000547640, 22/05/2014).

4.2.3. Participants

Native Romanian speakers with Panic Disorder (n=86) were recruited via media (TV news, internet advertisements, and social media), promotional advertising displayed in emergency rooms, and direct recommendations made by a network of general practitioners and psychotherapists.

Inclusion and exclusion criteria

Participants were included in the study if the following conditions were met: (1) their symptomatology fulfilled the diagnostic criteria for panic disorder according to DSM IV-TR (APA, 2000); (2) their age is within the range of 18-65 years; (3) they have access to a computer with internet connection; (4) they are native Romanian speakers; (5) they provided a written informed consent.

Participants were excluded if any of the following criteria were met: (1) they were at that time enrolled in a different psychotherapeutic program or have received psychotherapy in the previous 3 months; (2) they presented severe comorbidities, other than a different anxiety

disorder or mild depression (e.g. bipolar disorders, psychotic disorders, substance abuse); (3) they suffered from mental retardation; (4) their symptoms were aggravated by a severe medical problem (e.g. ventricular tachycardia, heart attack, stroke, pulmonary fibrosis, hyperthyroidism, epilepsy); (5) they presented suicidal ideation or behaviors.

Medication use was permitted, but only if the dosage had been constant in the previous month and the same dosage must remain constant during the trial. Benzodiazepines were not allowed, according to existing recommendations (Kumar & Malone, 2008; NICE, 2011; Otto, McHugh, & Kantak, 2010).

4.2.4. Procedure

The participants started the screening process on the study website (http://studiu.paxonline.ro), by filling out several online forms, anonymously. Eligible participants were contacted by email to schedule a semi-structured clinical interview via secured Skype or telephone. The interviews were conducted by a trained clinical psychologist, who sought to verify and confirm the diagnosis of panic disorder and compliance with all the inclusion/ exclusion criteria. At this point, participants who remained eligible after the interview received an email with a detailed informed consent and a link to fill out the online pre-treatment questionnaires. Participants were required to give their express consent to be included in the study. Participants who consented to this procedure were then randomly allocated to one of the three study groups.

Participants from group 1 (PAXPD guided), received a document with the recommended pathway for the entire course of treatment, along with instructions on how to communicate with their psychotherapist in the platform. They had a few days to explore the platform and read the first recommended module before scheduling their first Skype session with their psychotherapist. All the Skype sessions were audio recorded by the psychotherapists.

Participants from group 2 (PAXPD unguided) received a document with the recommended pathway for the entire course of treatment and were informed that they may ask for help with technical problems.

The waiting list control group did not receive treatment for 12 weeks. Afterwards, they could choose to follow the PAXonline treatment for panic disorder either independently or with guidance from a therapist.

4.2.5. Interventions

The PAXonline Program for Panic Disorder is a 12-week internet-based treatment, which consists of cognitive-behavioral therapy modules, delivered with or without assistance from a therapist. The Panic Disorder Program contains 16 modules which address important cognitive behavioral psychotherapy elements such as: psychoeducation on the disorder and means of intervention; techniques for decreasing neurophysiological hyperarousal; cognitive restructuring; exposure to feared somatic sensations, alongside with situational (in vivo) exposures to reduce agoraphobic avoidance; positive emotions training; problem-solving training; behavioral activation and cognitive restructuring exercises to reduce symptoms of depression; relapse prevention. Each module can be completed in 15-40 minutes and the participants were provided with a recommended timetable (one or two modules per week, depending on the complexity of the content and the homework assignments).

Guidance. Both treatment groups used the same intervention, but the first group also received guidance from a licensed psychotherapist. The participants in this group had regular 15-30 minutes Skype sessions (the length depends on the complexity of the modules and the needs of each patient) with their psychotherapist. In total, there were 10 Skype sessions programmed. During these sessions, held over secured Skype, the psychotherapist checked if the participant had completed and understood each module, answered questions, and helped the participant carry out the recommended exercises.

Therapists. Three licensed psychotherapists with formal training in cognitive behavioral therapy and a minimum of 3 years of clinical experience worked with the participants allocated in the first treatment group. The guidance was delivered according to a standard treatment protocol, but it has also been personalized according to each participant's need.

4.2.6. Instruments

The selected instruments have already been well validated and are frequently used in CBT clinical trials for panic disorder in particular, as well as for other anxiety and mood disorders. Measures were taken at baseline (pre-treatment), 6 weeks after the intervention started (mid-treatment), directly after the intervention (post-treatment, 12 weeks after baseline), 1, 3, 6 and 12 months after the intervention ended.

4.2.6.1. Primary outcome measures

The primary outcomes are the diagnostic status of the participants at post-assessment and symptoms of panic disorder as assessed with the Panic Disorder Severity Scale – Self Report

(PDSS-SR). PDSS is originally a face-to-face interview and was adapted to a self-report questionnaire by Houck et al. (Houck, Spiegel, Shear, & Rucci, 2002). The questionnaire has good psychometric properties (Cronbach's alpha = 0.92, test-retest reliability is 0.83) and is sensitive to changes following treatment (Houck et al., 2002). A cut-off score of six may discriminate between the presence and absence of current DSM-IV panic disorder and a cut-off score of fourteen may discriminate between mild and severe panic disorder (Furukawa et al., 2009).

Panic Disorder is assessed using the Romanian adapted version of Psychiatric Diagnostic Screening Questionnaire (PDSQ) (Ciuca et al., 2011; Zimmerman & Mattia, 2001), which comprises a self-report screening scale, followed by a semi-structured interview delivered by a clinician.

4.2.6.2. Secondary outcome measures

Secondary treatment outcomes concerned a series of aspects, measured by specific scales:

- *Symptoms of depression* - Patient Health Questionnaire (PHQ-9) (Kroenke, Spitzer, Williams, & Lowe, 2010)
- *Functional impairment* - Work and Social Adjustment Scale (WSAS) (Mundt, Marks, Shear, & Greist, 2002)
- *Attention biases* - Body Vigilance Scale (BVS) (Schmidt, Lerew, & Trakowski, 1997)
- *Fear of body sensations* - Body Sensations Questionnaire (BSQ) (Chambless, Caputo, Bright, & Gallagher, 1984)
- *Catastrophic cognitions relevant to panic attacks and agoraphobia* - Panic Attack Cognition Questionnaire (PACQ) (Clum, Broyles, Borden, & Watkins, 1990) and Agoraphobic Cognitions Questionnaire (ACQ) (Chambless et al., 1984).

4.2.6.3. Additional measures

We also included some additional measures. For some we constructed brief questionnaires.

- *Treatment credibility and patient expectancies* - Credibility/Expectancy Questionnaire (CEQ) (Devilly & Borkovec, 2000)
- *Working alliance* - Working Alliance Inventory – Short Form (WAI-S) (Horvath & Greenberg, 1989; Tracey & Kokotovic, 1989)

- *Personality traits (dependent personality and personal autonomy)* - OMNI-IV (Loranger, 2001) and Personal Autonomy Questionnaire (PAQ) (Albu, 2007)
- *Perceived social support* - SS-5, an abbreviated version of the Medical Outcomes Study Social Support Scale (MOS-SSS) (Sherbourne & Stewart, 1991)
- *Usability* - System Usability Scale (SUS) (Broke, 1986)
- *Sociodemographic questionnaire*
- *Psychoeducation* - Psycho-Education Questionnaire (PEQ)
- *Adherence to treatment and homework compliance*
- *Frequency of use of anxiety reduction strategies*
- *Patient satisfaction* - Patient Feedback Questionnaire (PFQ)
- *Drop-out Reasons*

4.2.7. Randomization

Participants who returned the informed consent and met all the required criteria were randomly allocated to one of the three conditions. The randomization process was done by a software developed to implement a minimization algorithm (Pocock & Simon, 1975) that assured a balanced randomization between groups with respect to certain predefined prognostic (stratification) factors (chronicity and severity).

4.2.8. Blinding

Taking the characteristics of our research into consideration, it was impossible to keep patients or psychotherapists blind to the study procedures and intervention. All participants were provided with detailed information about the aims and the methodology of the study. They were able to request more information about the study and they had the right to terminate participation at any time. The clinical psychologists in charge with the clinical interviews, on the other hand, were blind to the treatment group allocation.

4.2.9. Statistical analysis

All statistical analyses will be performed using the IBM SPSS Statistics version 20. In order to compare between group differences at pre-treatment, we will use ANOVA test and chi-square. Primary analysis will be performed on all randomized participants (regardless of protocol adherence), according to intention-to-treat paradigm. In line with current standards (G. Andersson et al., 2012; Ivarsson et al., 2014), we chose to use the approach called *linear mixed effects models with full information maximum likelihood estimation.* Significance tests for

dichotomous data (such as diagnostic status) will be conducted with chi-square tests. Calculations of within- and between-groups effect sizes (Hedges's g) will be based on the pooled standard deviations. Regression analyses will be used to identify predictors of treatment outcome and of pre-post change.

4.3. Results

According to existing recommendations (Pintea, 2010) the results are reported from several perspectives: statistical significance, practical significance (effect sizes) and clinical significance.

4.3.1. Pre-treatment evaluation

Groups did not differ significantly with regard to age, F (2, 56) = .60, p = .55 or other demographic characteristics, χ^2 (2-10) = .17-11.59, p > .31. Most of the participants were women - 71%, a percentage similar with those reported in other ICBT studies; the education level was quite high, 55% having a university diploma. The mean age was 35 years, the youngest participant having 21 years, and the oldest 64 years. In regard to the occupational status, 77% were active (students, employees or antrepreneurs), and the rest were staying home parents, unemployed or retired. The big majority, 79% were either in a relationship, or married.

There were no significant pretreatment differences between the study groups on the primary and secondary measures, which shows that the minimization method worked well and the groups were quite similar before the treatment commencement, F(2, 69-83)=.03-1.63, p>.20. The severity of panic disorder, measured with PDSS-SR, was high (m=15.97, SD=4.74), above the values reported in similar ICBT studies (Bergstrom et al., 2010; El Alaoui et al., 2013; Hedman, Ljotsson, Ruck, Bergstrom, Andersson, Kaldo, et al., 2013).

4.3.2. Main results

Given current literature guidelines, and also the high drop-out rate in our study (24%), we chose to test the effects of our intervention through linear mixed regression models (Gueorguieva & Krystal, 2004). This approach uses all available data on each subject and does not involve the substitution of missing values but estimates parameters about missing values. Furthermore, mixed models account for the correlation between the repeated measurements. As a method of estimation, we chose restricted maximum likelihood (RELM) model and an unstructured covariance. Therefore, based on our linear mixed models (group by time), we found highly significant time effects on all three outcomes used, PDSS-SR - F (2, 63.96) = 93.05, p=.000; WSAS - F (2, 58.2) =29.32, p=.000; PHQ-9 - F (2, 62.61) =28.1, p=.000. Also, we found statistically significant group by time interaction effects, which means that groups evolved

differently in time. Therefore, symptomatology decreases were recorded in all three groups, but analysis shows significant differences in regard to evolution, F (4, 64.14) =9.22, p=.000; F (4, 58.73) =9.83, p=.000; F (4, 63.29) =7.21, p=.000.

Additionally, we ran post-hoc comparisons to identify significant differences between certain groups and certain points of evaluation. Results show statistically significant differences between group 1 (PAX guided) and control group at mid-term evaluation, Bonferroni t (64) = 2.46, p=.049. At post-treatment, both treatment groups had significant differences when compared to control group, Bonferroni t (70) = 4.94, p =.000, Bonferroni t (71) =3.14, p=.007. Post-hoc comparison between the two treatment groups was not significant on either mid-term, Bonferroni t (64) =0.86, p=1, or post-treatment evaluation, Bonferroni t (71) =1.88, p=.193. These results indicate that both forms of treatment, PAX guided and PAX unguided, are efficient in reducing panic symptoms.

The same statistical analysis has been conducted in regard to variables directly targeted in the PAXPD treatment: catastrophic cognitions (measured by PACQ and ACQ), fear of body sensations (BSQ) and hypervigilance towards physical sensations (BVS).

After conducting comparison analysis between the three experimental groups, we can conclude that both groups that received PAXonline treatment, guided or unguided, had significantly better outcomes that the control group. Significant differences were recorded both in regard to primary (severity of panic disorder) and secondary results (functional impairment and severity of depression symptoms) of treatment, and also in regard to variables that account for the process of change in cognitive-behavioral therapy (catastrophic cognitions and interpretations, hypervigilance towards own body and fear of physical sensations). Although the guided intervention group showed some superiority as to measured outcomes, this difference has not proven statistically significant at post-treatment. Moreover, we have found that the unguided group had lower catastrophic cognitions and interpretations in the first six weeks of treatment. However, differences at mid-treatment evaluation have not been statistically significant.

4.3.3. Practical significance of the results – effect sizes

As already noted, it is extremely important to calculate and report effect sizes. This aspect is deemed as a necessity, as there is no clear direct connection between statistical significance coefficients and the actual difference between two groups (Durlak, 2009). In order to compute the magnitude of effects between pre-test and post-test (within effect sizes), but also between the three groups at post-treatment (between effect sizes), we used Hedges's d coefficient.

For PDSS-SR scale, which measures panic symptoms and represents the primary outcome of treatment, the within effect size was 2.22, 95% CI (1.55, 2.88) for the guided PAX group and 1.59, 95% CI (1.00, 2.18) for the unguided PAX group. Both values indicate large within effect sizes, even a bit larger than the ones reported in previous studies; medium effect size computed in a recent meta-analysis for CMP intervention for panic was 1.32, 95% CI (0.79, 1.97) (Hedman, Ljotsson, Ruck, Bergstrom, Andersson, Kaldo, et al., 2013).

Large within effect sizes were also obtained for secondary outcomes, functional impairment and severity of associated depression symptoms. For WSAS scale, which measures functional impairment associated to panic disorder, the effect size was 1.38, CI (.75, 2.01) for the guided PAX group and 1.04, CI (.44, 1.64) for the unguided group. In regard to PHQ-9 scale, which measures severity of depression symptoms associated to panic disorder, effect size was 1.44, CI (.79, 2.09) for the guided PAX group and .97, CI (.37, 1.57) for the unguided group.

Large within effect sizes have also been demonstrated for catastrophic cognitions measured with PACQ, both for the guided PAX group g=1.54, CI (.93, 2.15), and for the unguided PAX group, g=.99, CI (.42, 1.57). In regard to BVS, which measures vigilance towards own body, effect size is 1.66, CI (1.04, 2.28) for the guided PAX group and 1.06, CI (.48, 1.65) for the unguided group. For BSQ, which measures intensity of fear towards own physical sensations, effect size is 1.42, CI (.78, 2.05) for the guided PAX group and .81, CI (.25, 1.38) for the unguided PAX group. For ACQ, which measures catastrophic cognitions related to loss of control and own body sensations, effect size is 1.24, CI (.62, 1.85) for the guided group and .55, CI (0, 1.1) for the unguided. Therefore, all the effect size measurements of pre-post effect of treatment for the two intervention groups are medium, .55 to large, .99 and very large, 2.22.

For PDSS-SR scale, which measures the severity of panic symptoms and represents the primary outcome of treatment, the effect size between guided PAX group and control group is large, g=1.29, CI (.72, 1.86); and between unguided PAX and control is also large, g=.81, CI (.28, 1.35). Both values show large effect sizes of treatment versus control group, very similar to ones reported in classic face to face CBT; the medium effect size computed in a recent meta-analysis for classic CBT intervention in panic disorder was 1.04, 95% CI (0.85, 1.23) (Sanchez-Meca, Rosa-Alcazar, Marin-Martinez, & Gomez-Conesa, 2010). The between effect size for the treatment groups, guided PAX and unguided PAX, was a medium one, g=.49, CI (.03-1.02).

Table 43 – Between effect sizes at post-treatment

Scale	Between effect-sizes		
	PAX guided vs. PAX unguided	**PAX guided** vs. waitlist	**PAX unguided** vs. waitlist
PDSS-SR	0.49 95% CI [.03- 1.02]	**1.29** CI [.72-1.86]	**0.81** CI [.28-1.35]
WSAS	0.36	**1.19** CI [.60 – 1.78]	**0.85** CI [.29 – 1.42]
PHQ-9	0.28	**1.16** CI [.56 – 1.75]	**0.90** CI [.32 – 1.47]
PACQ	.45 CI [.09-1.00]	**1.42** CI [.83-2.02]	**1.00** CI [.43-1.56]
BVS	.59 CI [.04-1.14]	**1.27** CI [.69-1.85]	**.7** CI [.44-1.58]
BSQ	.29	**1.27** CI [.67-1.87]	**1.01** CI [.44-1.58]
ACQ	.24	**1.07** CI [.49-1.65]	**.83** CI [.27-1.38]

PDSS-SR – Panic Disorder Severity Scale – Self Report; WSAS – Work and Social Adjustment Scale; PHQ-9 – Patient Health Questionnaire; PACQ – Panic Attack Cognitions Questionnaire; BSQ – Body Sensations Questionnaire; ACQ – Agoraphobic Cognitions Questionnaire; BVS – Body Vigilance Scale.

4.3.4. Clinical significance of the results

There are multiple ways to calculate and assess the clinical significance, and we have chosen to use the following two: percentage of participants in each group who score below cut-off point at the end of treatment, and also the percentage of participants who do not meet the diagnostic criteria for panic disorder at diagnostic interview. The table below summarizes the results of this analysis.

Table 44 – RCT results in terms of clinical significance

Group	Methods	Post-Treatment	
		Without panic	**With panic**
Guide PAX	Clinical interview	20 (**71%**)	8 (29%) 6 missing
	Cut-off PDSS-SR	19 (**68%**)	9 (32%) 7 missing
	Cut-off PDSQ	19 (**68%**)	9 (32%) 7 missing
Unguided PAX	Clinical interview	8 (**28%**)	21 (72%) 11 missing
	Cut-off PDSS-SR	11 (**38%**)	18 (62%) 7 missing
	Cut-off PDSQ	11 (**38%**)	18 (62%) 9 missing
Waitlist	Clinical interview	3 (**10%**)	26 (90%) 6 missing
	Cut-off PDSS-SR	5 (**17%**)	24 (83%) 7 missing
	Cut-off PDSQ	5 (**17%**)	24 83%) 8 missing

Using the intention-to-treat procedure (regarding dropouts as treatment failures), 38% (n = 11) of the participants in the unguided self-help group, 68% (n = 19) of the participants in the guided self-help group, and 17% (n = 5) in the waiting-list condition were below the cut-off scores for both PDSS-SR and PDSQ scales. When clinical interview results were used, 71% (n=20) of the participants in the guided PAX group, 28% (n=8) of the participants in the unguided PAX group and 10% (n=3) in the waiting list no longer met criteria for a panic disorder diagnostic. The differences between the three groups were significant, χ^2 (2) = 24.42, p=.000. Moreover, the difference between the two treatment groups was significant according to the post-treatment clinical interview results, χ^2 (1) = 10.97, p=.001.

4.3.5. Treatment adherence and compliance

Analysis of treatment adherence has shown significant differences between the two treatment groups as measured through the number of modules completed within the platform, but not the time spent in PAXPD intervention program. These results are consistent regardless of the paradigm we employed, either intention to treat (t (53) = 2.14, p =.037 and t (54) = 1.83, p =.073) or treatment completers (t (29) = 2.33, p=.027 and t (41) = 1.87, p=.069). There is a clear tendency towards higher adherence in the guided group, but this superiority is statistically significant only in regard to number of modules completed. Effect sizes are medium to large.

Table 45 – Treatment adherence and compliance

	Guided PAX		Unguided PAX			Hedges's g
	M (SD)	Mdn	M (SD)	Mdn		
No. of modules	10.61 (5.02) (0-17) 12.48 (2.58) (7-17)	12 13	7.41 (6.2) (0-17) 9.23 (5.98) (0-17)	5 9	t (53) = 2.14, p =.037 t (29) = 2.33, p=.027	.56 .76
Time spent in PAXPD	22.26 (15.46) (0-62.6h) 26.98 (14.23) (7.3-62.6h)	20.67 29.27	14.59 (15.93) (0-47.85h) 18.09 (16.42) (0-47.85h)	7.2 12.76	t (54) = 1.83, p =.073 t (41) = 1.87, p=.069	.48 .57
No. of sessions	7.75 (3.71)	10				
Time spent in sessions	4.23h (2.22)	5.24h				
Breathing regulation	2.64 (1.66) 3.52 (.68)	3 4	1.79 (1.66) 2.36 (1.5)	2 3	U = 280.5, p=.036 U = 119.5, p=.004	.50 .97
Autogenic training	2.61 (1.66) 3.48 (.75)	3 4	1.31 (1.37) 1.73 (1.32)	1 2	U = 220.5, p=.002 U = 63, p=.000	.84 1.59
Physical exercise	2.04 (1.4) 2.71 (.85)	2.5 3	1.38 (1.55) 1.82 (1.53)	1 2	U = 306.5, p=.101 U = 149, p=.041	.44 .70
Attention	2.25 (1.48)	3	1.17 (1.34)	1	U = 240, p=.006	.76

regulation	3 (.78)	3	1.55 (1.34)	2	U = 86, p=.000	1.29
ICAR 1	2.14 (1.46) 2.86 (.85)	2.5 3	1.21 (1.32) 1.59 (1.3)	1 2	U = 259, p=.015 U = 105, p=.002	.66 1.13
ICAR 2	2.14 (1.46) 2.86 (.85)	2 3	1.31 (1.42) 1.73 (1.39)	1 2	U = 279, p=.035 U = 121.5, p=.006	.57 .96
Interoceptive exposure	1.86 (1.35) 2.48 (.93)	2 2	.48 (.83) .64 (.90)	0 0	U = 176, p=.000 U = 43, p=.000	1.22 1.97
Exteroceptive exposure	2.25 (1.6) 3 (1.05)	3 3	1.34 (1.54) 1.77 (1.54)	0 2	U = 278, p=.032 U = 124, p=.007	.57 .91
Positive emotions development	2.04 (1.5) 2.71 (1.06)	2 3	1.38 (1.66) 1.82 (1.68)	0 2	U = 316, p=.133 U = 162, p=.085	.41 .62
Problem solving	2 (1.44) 2.67 (.97)	2 3	1.34 (1.57) 1.77 (1.57)	0 2	U = 312, p=.116 U = 158, p=.067	.43 .67

Note. Mdn – median; ICAR 1 – cognitive restructuring technique for conscious maladaptive cognitions; tehnica de restructurare cognitivă a cogniților conștiente; ICAR 2 - cognitive restructuring technique for unconscious beliefs; read colour is used for treatment completers.

In order to assess how frequent the anxiety reduction techniques were used (treatment compliance) we have developed a 10 items questionnaire. Eight of these questions are scored on a 5-point Likert scale (0-never and 4-daily or almost daily) and the last two are open ended questions: "Which techniques helped you the most?" and "Which are the techniques that you plan on using after the end of the intervention?". Mann-Whitney test of compliance to treatment indicates that frequency of anxiety reducing techniques was significantly higher in the guided PAX group than in unguided PAX group, except for techniques to improve positive emotions and problem solving (optional module), where there is no difference between the two groups. Results were similar in paradigms used, intention to treat and treatment completers, U=176-280, p<.036, U=43-149, p<.041 respectively. Effect sizes are medium to large. The largest difference between the two groups is in regard to interoceptive exposure practice. It seems that very few of the unguided participants managed to practice this technique frequently.

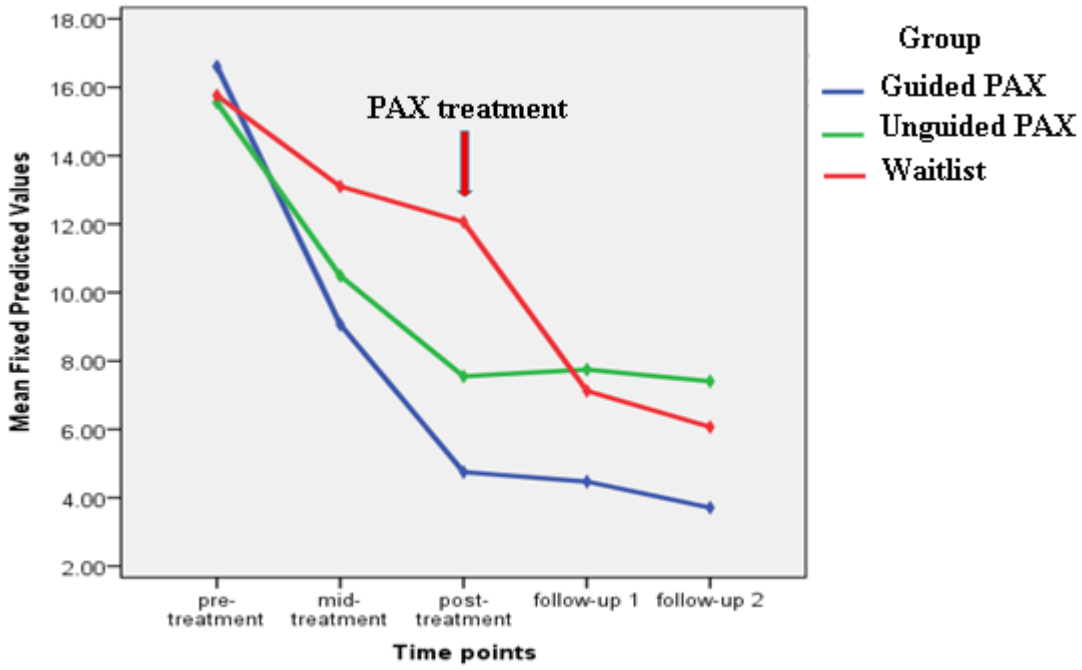
4.3.6. Follow-up results

Participant evolution and status were also monitored after termination of the 12 weeks treatment. They were invited to submit a set of self-report questionnaires at 1 month, 3 months, 6 months and 12 months. Here we are reporting only on the results registered on the first two time points, 1 month and 3 months.

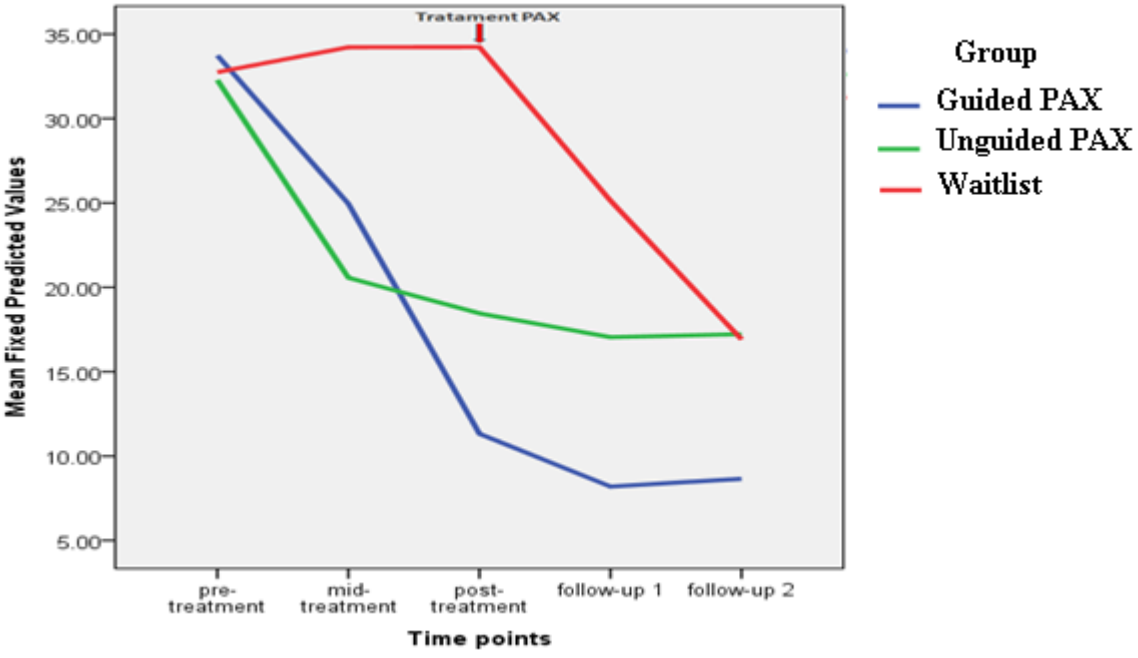
As to primary, secondary and additional measures, the effect of treatment were maintained at follow-up for both intervention groups. Moreover, in group 1 (guided PAX) the symptomatology continued to decrease, and at three month follow-up the difference between the two experimental groups increased and became statistically significant in regard to multiple

outcomes. As expected, group 3 (control group) that received PAX treatment guided or unguided, had significant lower symptomatology levels at post-treatment – pre-post effect sizes were large, between .98 and 1.3. We illustrate below graphs 16 and 19, presenting the evolution of panic attacks symptoms and catastrophic cognitions as measured by the Panic Attacks Cognitions Questionnaire.

Graph no 16. PDSR-SR results from pre-treatment to follow-up



Graph no 19. PACQ results from pre-treatment to follow-up



4.3.7. Patient satisfaction with PAXPD treatment

Besides evaluating the clinical efficacy of PAXPD treatment for panic disorder and comorbid symptoms, it is also important to evaluate the degree of patient acceptance and satisfaction with this treatment.

Of the 49 respondents, 18 reported that they had used other forms of treatment before entering the study (5 medication, 5 counselling or psychotherapy and 7 both medication and counselling/ psychotherapy), and 83.3% considered the PAXPD intervention program as superior to whatever treatment(s) they had previously received.

Several aspects were mentioned as suggestions for improvements: more time available for using PAXPD program; more video materials and better quality; more interactivity and the need for therapeutic support (as mentioned by the participants in the unguided group); access to the platform from the personal phone or other operating systems; simplifying worksheets and assessment questionnaires completion; increasing discussion in the forum. Also, 35% of respondents answered that no improvements are needed.

As to the most appreciated elements in the platform, we mention the following: module content; video materials; psychotherapeutic assistance (half of the guided participants mentioned high regard for their therapist); attractive design and information structure; clear and explicit presentations; practical recommendation; flexible use. To note that 27% of those responding to this questions answered “everything”.

3.1. Discussion

The prevalence of mental health problems is very high and bears considerable suffering and burden worldwide. However, only a small percentage of the affected individuals reach out and receive treatment for their problems. There are many barriers at different levels, yet a viable solution to increase access to quality treatment resides in the possibilities provided by internet-based cognitive behavioral treatments. Although several ICBT programs have been tested with strong positive results and even integrated into regular health care (Hedman, Ljotsson, Ruck, Bergstrom, Andersson, & Kaldo, 2013), there are countries where validated internet based interventions are yet to be developed. The present trial aims both to validate the overall efficacy of the first Romanian ICBT program for panic disorder, and to investigate aspects that are novel to ICBT, such as brief therapist guidance sessions via secured Skype.

A central focus of our trial has been to test the additive effect of therapeutic guidance via secured Skype in self-help ICBT programs. Specifically, the current study design allowed us to

assess the effect of the same self-help intervention modules in two treatment conditions: therapist guided via Skype vs. unguided self-directed intervention.

Analysis has shown that PAXPD treatment is efficient in reducing panic disorder symptoms, but also secondary outcomes, such as functional impairments and associated depression symptoms, regardless of delivery form. Moreover, PAXPD treatment and efficacy has also been proven for change process variables: catastrophic cognitions and interpretations, attentional biases and fear towards own physical sensations.

By directly comparing the two PAX treatment groups, with or without therapist support, we have found no statistical difference at post-treatment assessment, but Skype guided treatment proved superiority through larger effect sizes and a clear higher percentage showing clinical significance. Additionally, treatment effects were maintained and even continued to increase after treatment termination. The difference between PAX guided and unguided became statistically significant at 3 months after treatment completion, which again shows the beneficial role of therapeutic assistance in long term perpetuating and maintaining mental health.

The results in this study confirm the short and long term efficiency of PAXPD program in reducing panic symptoms and associated problems, with high and promising degree of patient acceptance and satisfaction. Clearly, in order to increase the uptake of CMP solutions, we need to continue the ongoing development of such interventions, and also to conduct new rigorous clinical trials in real life context. Hopefully, this will increase the positive impact of psychotherapy and counselling services on the quality of life at individual and national levels.

Chapter 5 – Study no. 3. Identifying potential predictors for the efficacy of PAXPD program

5.1. Study objectives

There is good quality evidence that ICBT treatments, especially guided interventions, are both efficacious and effective, either compared with waiting-list or with face to face interventions, but there is no intervention that is suitable for everyone (Andersson, 2015). A key aspect of this study was identifying the characteristics of patients that would benefit the most from CMP interventions. Therefore, in order to be able to make recommendations for certain individuals, with certain characteristics, we need to know more about potential variables that can predict the effects of PAXPD therapeutic intervention. Unfortunately, the studies conducted so far have shown few stable predictors across studies and diagnostic (El Alaoui et al., 2013). For example, treatment adherence was considered as a potential predictor variable, but there are inconsistencies, with some studies finding an association between adherence and clinical outcomes (Gerhard Andersson et al., 2005; Hilvert-Bruce, Rossouw, Wong, Sunderland, & Andrews, 2012; Meyer et al., 2009) and others not (El Alaoui et al., 2013; Farrer, Griffiths, Christensen, Mackinnon, & Batterham, 2014; Hoifodt et al., 2015). Another example is the severity of the disorder at baseline. In one study, a high baseline severity predicted better outcomes (Warmerdam, Van Straten, Twisk, & Cuijpers, 2013), while another study showed the contrary, low levels of panic symptom severity predicting better outcomes (El Alaoui et al., 2013). Another interesting result concerns the role of comorbidity. A recent study showed that having a comorbid anxiety disorder was associated with a better treatment outcome among patients with panic disorder but not patients with social anxiety disorder (Haug et al., 2015), while others found no significant association (El Alaoui et al., 2013; Vernmark et al., 2010).

Given these facts and based on our small sample size, we chose an exploratory approach, in an effort to comply with persistent recommendations about the need to include and report such analysis in controlled clinical studies (Hoifodt et al., 2015; MacKinnon & Luecken, 2008).

5.2. Research variables and data analysis procedure

We categorized potential predictors based on moment of evaluation: pre-treatment, mid-treatment and post-treatment. Apart from this classification, some variables remain stable (e.g. age and sex), while others are dynamic and change according to therapy progress (e.g. therapeutic relationship evolves based on progress made by the patient). Furthermore, because

the dynamic of some variables is better investigated through mediation and moderation analysis for identifying mechanisms of change, this aspect remains a future research direction.

Statistical analysis was conducted in two successive stages; first, we computed the correlation between variables and afterwards, based on those results, we conducted a set of multiple regression analysis. As criterion (outcome) variables we used post-treatment scores for severity of panic disorder, level of functional impairment and severity of associated depression symptoms, and the degree of change between pre-post treatment scores for each of these variables. We decided to add the second criterion due to the information it provides about the dynamics of our targeted variables (Moldovan & Pintea, 2015). Both methods come with disadvantages; therefore, by using both types of criteria, we hope to raise the validity of our results and conclusions. Literature emphasizes pros and cons regarding the use of pre-post treatment degree of change, some authors preferring another option, i.e. residualized change scores (Steketee & Chambless, 1992). The main critics against using raw scores measuring degree of change include issues such as regression towards the mean and influence of pre-treatment scores on degree of change. Nevertheless, we decided to use the pre-post treatment degree of change called delta change score (difference score), since we had a high reliability for the degree of change in our study. According to recommendations by MacKinnon, reliability of pre-posttest degree of change is estimated based on assessment instrument reliability and correlation between outcomes at the two moments of assessment, pretest and posttest. In our case, the internal consistency of PDSS-SR, WSAS and PHQ-9 scales is high (.89 for PDSS-SR and PHQ and.90 for WSAS) and the correlation between pre and post treatment scores for the three mentioned variables is under or a little over 0.5, for both paradigms: intention to treat and treatment completers (.36 and .17 for PDSS-SR, .54 and .47 for WSAS, .44 and .37. for PHQ-9), which indicates that degree of change variable is reliable enough (MacKinnon, 2008).

In the case of intention to treat procedure, which includes all the randomized participants into analysis (regardless of treatment adherence or assessment instruments completion), we decided to replace missing data from mid- and post-treatment assessment with the last score reported by premature drop-out participants (last observation carried forward – LOCF procedure). In order to reduce bias inherent to this method, we tried to identify results as close as possible to the targeted assessment time. Specifically, this means that beyond the main assessments (pre-, mid- and post-treatment), we also included periodic assessment results conducted in PAXonline platform (e.g. for symptom severity assessment, participants in the

study received a message every two weeks inviting them to complete the PDSS-SR questionnaire).

In order to gain a clearer perspective on the investigated aspects and to raise the accuracy of the conclusions, we decided to supplement the intention to treat method with treatment completers analysis. Specifically, we will conduct the same analysis using only the available data, without any method of imputation, since this can induce various types of bias. In this context, *treatment completers,* does not refer to the way participants used the treatment; it means that in our analysis, we will use only data from the participants that filled the necessary assessment questionnaires.

In order to raise the statistical power of our study and the chance to identify existing predictors, we also included the participants that were first randomized to control group, and then received PAXPD treatment with or without therapist guidance by choice.

5.3. Results

Due to small sample sizes and exploratory approach, our aim was not to identify a general prediction model, but to find the best predictors related to the three investigated categories. For this reason, we will present the conclusions sequentially, first for the pre-treatment variables and then for the other two categories. We will try to integrate the results according to the two paradigms and the two types of criteria.

5.3.1. Pre-treatment variables that predict outcomes

Participants age correlated significantly with treatment outcomes on both groups, regardless of the method (intention to treat or treatment completers) and the type of criterion variable used (degree of change or post-treatment score). Interestingly, the direction of the correlation is contrasting: in the guided group, younger participants had better outcomes; in the PAX unguided group, older participants had better outcomes. The link between age and treatment adherence and compliance might be a potential explanation for these results. Next sub-chapter provides more detail on this matter, and the pre-treatment predictor analysis will we resumed following this section.

5.3.1.1. Predictors of treatment adherence and compliance

In the guided PAX group, adherence to treatment (number of completed modules) correlates with computer skills, platform usability and social support. Age is strongly negatively correlated, but not statistically significant (r = -.24, p=.071). Compliance to treatment correlated

significantly with participant age: r=-.38, p=.009 (hyperactivation reducing techniques), r=-.48, p=.001 (cognitive techniques), r=-.50, p=.001 (exposure techniques). Therefore, younger participants had higher compliance rates, especially in using exposure techniques.

With treatment completers, the situation is a bit different: adherence to treatment correlates best with computer skills (r=.50, p=.003), education level (r=.33, p=.042) and occupational status (r=.42, p=.012). As to compliance to treatment, completing relaxation techniques correlated positively with personal autonomy (r=.55, p=.007) and level of education (r=.43, p=.011). Restructuring and exposure techniques still correlated negatively with age, r=-.44, p=.009 and r=-.48, p=.004.

In the case of unguided PAX group, adherence to treatment strongly correlates with platform usability, r=.63, p=.000 and participant age, p=.42, p=.005. Compliance to treatment correlates significantly with platform usability and participant age, but not as strongly as with exposure techniques. Personal autonomy correlates positively with cognitive restructuring and exposure techniques, r=.57, p=.013 and r=.46, p=.043, respectively. Results do not vary much between the two paradigms, intention to treat and treatment completers.

Returning to conclusions on pre-treatment predictors of outcomes, we have found that age and initial symptom severity predict the degree of pre-post change in panic symptom severity, regardless of applied paradigm. For secondary outcomes, i.e. functional impairment and depression symptoms, the best predictor is also initial symptom severity. There are differences, though, between the two paradigms, when using final scores as criterion variables. For treatment completers, pre-treatment variables that predict final scores are dependent personality traits in regard to panic symptom severity and depression symptoms, but only for the guided PAX group.

5.3.2. Mid-treatment variables that predict outcomes

For the guided PAX group, severity of depression symptoms at mid-treatment and therapeutic alliance measured after the first guidance session are the best predictors of treatment (there are no major differences on account of variables used as outcomes, i.e. degree of pre-post change or post-treatment scores of symptomatology).

In the unguided PAX group, the best predictors of symptomatology are functional impairment and depression symptom severity as measured at mid-treatment, but also platform usability and initial treatment credibility (there are small differences depending on the criteria used).

Analysis conducted on a small set of data from treatment completers show that the main mid-treatment predictors are severity of depression symptoms for guided PAX group and platform usability and initial treatment credibility for unguided PAX group (both when using degree of change as outcome variable). When using final scores as criteria, the main predictors for guided PAX group are platform usability, panic symptom severity and treatment credibility. For unguided PAX group, we identified symptom severity and platform usability as mid-treatment predictors.

5.3.3. Treatment adherence and compliance as predictors of outcome

For the guided PAX group, the number of therapeutic sessions (adherence to treatment) can predict the primary and secondary outcomes of treatment, regardless of the type of variable used as outcome. As to compliance, frequency of participant use of in vivo exposure and breathing regulation techniques predict treatment outcomes. Specifically, physical exercise can predict outcomes related to depression.

For the unguided PAX group, adherence to treatment does not predict outcomes, and the best predictor related to treatment compliance is use of autogenic training.

Results are similar for both groups also in the treatment completers paradigm, except that adherence to treatment also does not correlate with outcomes in the guided PAX group.

Once again we are emphasizing the fact that our small and at some places very small sample does not allow us to draw firm conclusions regarding variables that predict treatment outcomes. This investigation must be repeated in future studies and larger samples, but the analysis conducted in this study can provide us with important clues and help us select potentially relevant predictors for further investigation.

Chapter 6 - Study 4. The experience of using PAXPD treatment, a CMP solution for treating panic disorder

Research about individual paths in therapy, how patients utilize and experience these interventions has been scarce. Our study documents how the individual process of psychological treatment unravels during an internet-based treatment program for panic disorder, with therapist guidance, via Skype. The two client cases in this chapter are presented using Fishman's Individual Case Comparison method and have registered two different outcomes. Internet-based interventions have been proven to be a successful and substantial contributor to increasing access and availability to high quality psychological treatment. Yet, in order to be most efficient, these interventions need to be customized according to each client's specific traits (i.e. severity of symptoms and comorbidity problems, personality traits, life context, stage of change process etc.). Real-time audio-video guidance has proven to be a way of customizing the interventions and has increased their positive impact.

6.1. Case context and Method

Hundreds of millions of lives are affected worldwide by mental health disorders, leading to major socioeconomic losses. However, 60% of the people affected never undergo treatment for their problems. New technology-based solutions have been proposed in the last decade, aiming to increase access to high quality treatment. Though their format and delivery may vary, their main characteristic consists of offering psychotherapy services through computers, mobile devices and internet technology.

This type of solutions can be categorized in three specific groups: internet-based interventions, online therapy and blended therapy. The first category comprises of web-based interventions that are primarily self-guided, serve a specific purpose and implements principles and methods from bona fide psychotherapy (M. Miclea et al., 2010). This type of intervention involves the client in psychotherapeutic activities through an interactive web interface. The second category consists of offering traditional therapy through synchronous (such as Skype) or asynchronous communication (such as e-mail) (G. Andersson, 2015). The third category uses technology in all its forms to assist face-to-face sessions (Krieger et al., 2014).

Analyzed further, internet-based interventions can fit into two categories, based on the offering of additional support: guided or unguided interventions. Albeit some web-based programs have registered strong positive results in the treatment of anxiety disorders, mood

disorders and other psychiatric conditions, there are still countries where this type of intervention has not been developed or tested (G. Andersson & Titov, 2014).

Evidence shows that the web-based guided programs and face-to-face therapy have produced equivalent overall effects (G. Andersson et al., 2014).

Due to the general success of web-based interventions and the scarcity of access to quality psychological treatment in Romania (where 76.4% receive no treatment at all) (Florescu et al., 2009), we have developed PAXonline, an ICBT platform that deals with the prevention and treatment of anxiety disorders. The platform allows patients to follow multimedia intervention modules clustered in therapeutic programs addressing several types of anxiety disorders. The patient has the possibility of using these modules alone or assisted by a therapist via Skype.

We have conducted a randomized controlled trial (RCT) to test the efficacy of the platform, focusing our research on testing the augmentative effect of therapeutic guidance offered via Skype. Preliminary results of the study show that PAXonline is an effective ICBT solution for treating panic disorder (Ciuca, Berger, Crisan, & Miclea, 2015).

Our RCT undertakes a qualitative approach and aims to provide further insight into the patients' individual paths in therapy, how they use this type of intervention and how they experience the process of therapy.

Our approach is grounded in the Individual Case-Comparison paradigm proposed by Fishman (Fishman, 2011) and makes use of the "mixed methods" model in psychotherapy research formulated by Dattilio et al., who views the best therapy practice as an integration of the results of quantitative, group-based treatment research with case-based, contextualized clinical expertise and the idiographic tailoring of therapy (Dattilio, Edwards, & Fishman, 2010). At the same time, individual time course data provides us with the opportunity to shift focus on how change occurs rather than on whether it does. Although the ICC method has not been previously used in illustrating the use of web interventions, we believe it can provide us with a better "bottom-up" understanding. The main purpose of the study is to document how the individual process of psychological treatment unfolds during a therapist-guided web-based treatment program.

6.1.1. Treatment context

In our RCT, participants meeting the diagnostic criteria have been randomly assigned to three conditions: unguided use of the web-based self-help PAXonline, therapist-guided use of PAXonline and the wait-list control group.Both clients described in the paper, whose identities have been disguised, have been a part of the treatment program guided via Skype. In order to

ensure the rigor of our study, our methodological approach required audio-recording the therapy sessions, collecting qualitative data from self-report questionnaires and platform usage details and we have used an independent evaluator to asses the clients before and after therapy.

6.1.2. Measures used

Symptoms of panic disorder and diagnostic status were considered our primary outcomes. Secondarily, we evaluated quality of life and depression. Several other measures were included in the measurements in order to investigate the specific effects of treatment components or other potentially relevant aspects. Measures were taken at baseline, during the treatment, post-treatment and follow-up, at 1, 3, 6 and 12 months after the treatment completed. All self report measures were administered online. Panic disorder diagnostic status was assessed using the Romanian adapted version of Psychiatric Diagnostic Screening Questionnaire (Ciuca et al., 2011; Zimmerman & Mattia, 2001), which consists of a self-report screening scale and a semi-structured interview conducted by a clinician through phone or Skype. Panic disorder symptoms were evaluated every two weeks during the treatment with the Panic Disorder Screening Scale – Self Report (Houck et al., 2002). The Credibility/Expectancy Questionnaire (CEQ) (Devilly & Borkovec, 2000) and Working Alliance Inventory-Short Form (WAI-S) (Horvath & Greenberg, 1989) were administered twice, after the 1st and 4th Skype meeting.

6.2. The Guiding Conception: ICBT for Panic Disorder

Panic disorder is generally conceptualized as an acquired fear of somatic sensations of autonomic arousal (Craske & Barlow, 2007). The CBT model we have used in our treatment program distinguishes between general vulnerability factors like neuroticism, key specific factors and maintenance factors. It also explains how a panic attack may occur and how panic disorder may develop.

Based on the CBT model, the panic attack can occur when a person experiences increased physiological arousal, interprets the changes as being threatening and focuses excessively on them. Hypervigilance increases the arousal, convincing the individual further that they are in danger, triggering a false alarm and causing a full panic attack. Developing hypervigilance towards somatic changes and anticipatory anxiety coupled with avoidance and excessive safety behaviors after the panic attack increase the likelihood of developing a panic disorder (Leahy & Holland, 2000).

A multicomponent CBT intervention includes techniques to lower physiological arousal, reduce cognitive misinterpretation, develop coping skills, reduce fear toward somatic sensations

and reduce counterproductive avoidance behaviors. Evidence has shown that CBT has been very successfully used in the treatment of agoraphobia, with long-term therapeutic effects (Leahy & Holland, 2000). In vivo exposure seems to generate the greatest benefits while the inclusion of homework may improve overall treatment efficacy (Sanchez-Meca et al., 2010).

6.2.1. Treatment description

PAXonline is a 12-week web-based treatment consisting of cognitive-behavioral therapy module, delivered with or without therapist guidance. The platform aims to provide individuals with a safe and secure environment where the patients are empowered and ready to get involved in the process of change. PAXPD comprises of 16 module addressing cognitive behavioral therapy elements. The modules are based on existing principles of e-learning and cognitive sciences so as to enhance user experience and support the development of skills, behavior/goal auditing and goal tracking. Modules are structured on the following sequence: mood checking, goal setting, presentation of content, summary, checking the level of understanding, homework and reward. The information is presented in multimedia format and can be completed in 15-40 minutes. The participants are provided with a recommended timetable.

In our study, we provided patients with guidance through synchronous audio-video communication; a choice that we believe closely matches face-to-face therapy and enables access to face-to-face cues. Real-time communication confers therapists the possibility of customizing the feedback and support for each patient, thus forming a better therapeutic alliance.

Online sessions of 15-30 minutes were used to asses the state of the patient, the level of understanding, compliance with program and therapist recommendations and support in carrying out exercises. Sessions are schedules through a secure messaging system available on the treatment platform. A total of 10 Skype sessions is available for each participant.

6.3. The Clients - Assessment of the Problems, Goals, Strengths, and History

Maria was a young woman, 21 years old, studying away from her family. She had just her mother and a younger sister; her father left before she was even born and never recognized her as his daughter. When she started the intervention, she had a severe panic disorder and agoraphobia and needed to be in the company of someone even when staying at home. She had comorbid depressive and generalized anxiety disorder symptoms. Maria's first panic attack was 8 months prior to treatment. She was very tired and feeling restless and her mother offered her half of a

Xanax pill to help. Her symptoms worsened and her panic attack ended at the emergency room. Afterwards she experienced 2-3 panic attacks per day. She underwent extensive medical examination which revealed no somatic problems. Referred to a psychiatrist, she was prescribed Xanax and Paroxetine, but did not take the medication. The attacks worsened while she was trying to cope with them on her own, she started avoiding going out alone, staying home alone and gave up physical exercise. At the start of treatment, she was convinced she had an underlying, life-threatening physical condition. The main symptoms during her panic attacks were palpitations, heat and pressure in the chest, dizziness, breathing problems, a lump in her throat, the left side of her body getting numb and thoughts that she would die.

Andreea was a 38-year old woman, specialized in literature but working as an assistant manager. She lived with her mother throughout her life and went through the loss of her father 18 months prior to starting treatment. She was unable to leave the house unaccompanied. Some of her panic symptoms were occasionally aggravated by cervical spondylosis. She had gone through a major depressive episode 14 years prior and a mixed subclinical anxiety-depression after losing her father. At the beginning of the treatment for panic disorder, she showed symptoms of depression, OCD and GAD, but did not fulfill the diagnostic criteria. At the start of the treatment she was single and still living with her mother. She had had three long-distance relationships in her life, one of them a virtual relationship spanning several years that she described as "toxic". She was a highly educated and cultured woman, but extremely anxious and overwhelmed by catastrophic scenarios. At the beginning of the treatment, she had completely isolated herself out of fear of having a panic attack in public. She gave up physical exercise, walking, shopping, reading, etc., thus keeping herself in the house, which lead to her feeling trapped and developing depression symptoms.

Both clients presented a high level of catastrophic cognitions, high attentional focus on attentional focus on interoceptive activity, high fear of losing control over their body, intense preoccupation with physical sensations, and intense fear of bodily sensations.

6.4. Case Formulation and Treatment Plan

In web-based interventions, the treatment is very standardized and treatment components are determined beforehand. In PAXPD, the treatment can be tailored by the therapist or through available optional treatment modules.

Both patients were sensitive individuals, were vulnerable towards anxiety and had anxious role models when growing up. Their first panic attacks happened in particularly negative life

situations which activated their general vulnerability. In Maria's case, the panic attack occurred after a very tiring week and after having taken the troubling decision of breaking up with her boyfriend. After the panic attack, she got back together with her boyfriend and avoided all the situations which had caused her trouble, consolidating her fear response.

Andreea had often felt very sad or worried about her ability of taking care of herself after the loss of her father and sister's support. Her underlying physical problem, cervical spondylosis, triggered her first panic attack. She developed a vicious cycle of panic, from sensations to catastrophic cognitions. Consequently, she demanded to be accompanied every morning, eventually switched from public transit to cabs and she limited social activities, even giving up shopping at the nearby market.

Both patients were enrolled in the panic disorder program on PAXonline, during the RCT, and both received guidance via Skype from the same therapist. The treatment of both patients included goals and strategies that were embedded in the program modules.

6.5. Course of treatment

Maria was very motivated, curious and eager at the beginning of the program and read more than recommended in the first sessions. Her first session (38 minutes) consisted of covering her panic attack history and her reactions to it. She was provided with information about her condition and filled out the required questionnaires and monitoring sheets. Her treatment plan was customized based on her personal experience with panic attacks. As homework she was asked to monitor the frequency and describe her panic attacks. The second session (33 minutes) focused on introducing breathing techniques to help reduce hyperarousal symptoms and she was guided through a series of exercises. Her depression symptoms were also discussed briefly and she was recommended to consider returning to physical exercise. Homework consisted of recording her symptoms, practicing the breathing exercises and taking short walks. The third session (43 minutes) focused on relaxation through autogenic training. Maria found autogenic training difficult and was offered the alternative of progressive muscle relaxation technique. She was guided by the therapist through a series of exercises. Homework consisted of breathing exercises and autogenic training twice a day. The fourth session centered on attentional biases and Maria was offered a set of solutions. A second focus of the session was on a new symptom she was experiencing. As a consequence, the therapist decided to prioritize addressing her comorbid depression symptoms and introduce one of the optional modules, dedicated to overcoming learned helplessness and practicing behavioral activation. During the fifth session

Maria reported not having had any panic attacks in a week. They discussed the module on depressive symptoms and decided on an action plan. Due to Maria's experience with autogenic training, the therapist decided to introduce a new relaxation method, the progressive muscle relaxation. The sixth session focused on changing maladaptive conscious cognitions. Maria reported having had a great week and that the progressive muscle relaxation technique was proving to be more efficient than autogenic training. She had used the breathing technique to minimize the impact of a panic attack that had happened at school prior to the treatment session. In the second part of the meeting she was taught a restructuring technique and given restructuring worksheets to deal with catastrophic cognitions. During session seven, Maria estimated her well-being at 10 out of 10. She had successfully used the cognitive restructuring technique and challenged 4 of her most important dysfunctional beliefs. This allowed her to believe that she could beat her anxiety. The session focused on cognitive restructuring of unconscious dysfunctional cognitions. Maria had trouble identifying her dysfunctional beliefs so the therapist provided her with more information and guided her through the process. Her homework was to continue her work with cognitive restructuring of her conscious and unconscious beliefs and use an exercise to identify her core values and principles. Session eight was dedicated to planning and practicing the interoceptive exposure technique. Maria had experienced a limited panic attack, seemingly triggered by alcohol consumption. She reported that her attitude towards panic attacks had changed and they had become more manageable. Maria understood how avoidance maintained her anxiety and the importance of interoceptive exposure exercises. Together with her therapist, she practiced some of the exercises and was instructed to repeat them 4 times a week. Session number nine came 4 weeks after the previous one. Maria chose to read module 10, "Avoidance reduction through exteroceptive exposure" and then put the exposure exercises in practice by herself. During the break between sessions, she went through a new panic attack while visiting her family. She experienced heart palpitation for a longer time and her mother called an ambulance. Although the episode made her question the success of her efforts, she continued with the exposure exercises. During the session, the importance of cultivating positive emotions was discussed and Maria was guided in finding the best strategies and methods for herself. The tenth session was centered on relapse prevention. Maria was feeling insecure, so the therapist helped her develop an action plan for the next months. She acknowledged the progress she made in the last weeks, but she knew a lot of work still had to be done.

Andreea was extremely happy to find a treatment option that did not require for her to leave her home. She felt that face-to-face treatment would have been impossible for her, at that time. The first session (38 minutes) focused on symptomatology normalization, understanding the differences between fear and anxiety, the development of anxiety disorders, setting appropriate expectations and information on the use of the platform. Andreea worked on identifying her personal circumstances and vulnerabilities. She noted having always had difficulties with decision making and how losing her father had felt "unbearable". Her homework consisted of auditing the frequency and descriptions of her panic attacks using a worksheet. The second session took more than 15 minutes longer than planned due to questions unrelated to the treatment plan. Andreea hadn't read the recommended modules so the therapist spent time on presenting the treatment program and then on practicing breathing techniques. As homework she was asked to continue monitoring her symptoms and practice her breathing exercises twice a day. The third session was centered on the explanatory model in module 1 and relaxation exercises. While these topics were covered in the end, the session took longer than expected because Andreea continuously discussed her emotions and her avoidance attitude. She was encouraged to stop avoiding behaviors and start facing her problems. Andreea manifested her concern regarding the danger of some postures in the autogenic training. The fourth session began with a discussion about homework assignments. Andreea was very stressed because she hadn't managed to do all her exercises and proceeded to complain about herself. The therapist offered her a brief time management technique. A few minutes were spent on instructing Andreea on technical aspects regarding the platform. Andreea had skipped some steps in the Autogenic Training and the heart exercises from AT scared her. The importance of following the program thoroughly was explained again. In order to improve her low mood, she was recommended to focus on positive things throughout the day and writing them down. Andreea had not read the module dedicated to the fourth session, "Optimizing attentional functioning" so the last part of the session was spent on consolidating the knowledge gained previously. Session 5 (57 minutes) was focused on attentional biases and the cognitive restructuring of conscious automatic thoughts and catastrophic cognitions. For the first part, the therapist modeled two exercises and recommended practicing them twice a day. For the second part, Andreea complained about feeling overwhelmed by the information she was receiving and the amount of exercises. The therapist had to address Andrea's unrealistic expectations, her strong need for control and perfectionism. Further, she reintroduced Andrea to the technique in Module 8, helped her identify the thoughts that made her anxious and showed her how to challenge them. Andreea

was also shown how to address her tendency to exaggerate certain consequences. In this session, Andreea reported that she was no longer experiencing panic attacks, but she was still terrified of them. The therapist decided to approach an additional module dedicated to dealing with worries, during the sixth session. Andreea complained about her performance in reading the recommended modules and continued saying she would not be tricked into doing exposure modules. The therapist emphasized the importance of doing the exercises she had learned until that point in order to be ready to the exposure exercises. Session 7 centered around changing maladaptive unconscious cognitions. The therapist offered a model for identifying and challenging unconscious beliefs. Although the frequency and intensity of her panic attacks had diminished significantly since the beginning of the treatment, Andreea continued to be extremely afraid of the panic attacks. The therapist encouraged her to continue practicing the anxiety reducing exercises and to start considering making life changes. Session 8 was dedicated to interoceptive exposure. Andreea practiced some exercises together with the therapist and finally admitted things had gone better than expected. Her homework was to continue with the exercises and practice interoceptive exposure every other day. Session 9 focused on discussing and planning exteroceptive exposure exercises. By this time, Andreea had been taking short walks on her own. She developed an exposure plan together with her therapist and promised to practice her exercises more. The tenth session was dedicated to positive emotions, making life changes and finding the strength to cultivate her passions. The importance of continuing the strategies she learned was emphasized, along with ways to prevent and manage a relapse. She acknowledged her progress and the work that still needed to be done and admitted to feeling sad about losing the support of her therapist.

6.5.1. Special aspects about offering treatment for panic disorder through a web-based intervention and Skype

Both patients found that working from home was less threatening than face-to-face therapy and that by the end of the treatment seeing their therapist would not have been a problem. They appreciated the possibility of revisiting each module on the platform, without restrictions. Both Andreea and Maria found the platform well organized, comprehensive and useful. Andreea mentioned experiencing problems with the sound in some videos and when filling in the questionnaires and worksheets and uploading them to the platform. Both the clients and the therapist found that using asynchronous and synchronous communication provided more flexibility, was more time efficient and made rescheduling easier even on short notice.

Technical problems arose with both clients. Andreea's first session took place after two

unsuccessful trials due to poor internet connectivity. Similar technical problems occurred during treatment, too. These situations caused the sessions to last longer and sometimes affected the practice of some exercises. Real time video communication offers both advantages and disadvantages. While it can provide the therapist with good visual cues, this can also create the feeling of being to close to the other person, leading both patients to sometimes avoid eye contact with the therapist. Lighting conditions also influenced the process – Maria's improperly lit room lead the therapist to misperceive some sounds and interpret a cold as crying.

Though the therapist had good results working with PAXonline assisted by Skype, she sometimes would have found it helpful to be in the same room as her clients, in order to fully and properly convey all her positive energy.

6.6. Therapy monitoring. Program use – time spent in the platform and homework compliance

Maria was committed to the program and relied a lot on the sessions she had with her therapist. Her total 10 sessions summed up to 312 minutes, ranging between 21 and 43 minutes per session, with an average of 31.2 minutes. Some sessions were longer due to the comorbidity problems that needed to be addressed. She went through the recommended module once or twice and uploaded most of the required worksheets. In total, she spent 494 minutes on the treatment modules. Asynchronous communication was used a total of 15 minutes during her treatment, mostly about the planning of a next Skype session. Maria spent more time on practicing the recommended exercises and integrating them into her life. She kept a panic attack frequency monitoring sheet and checked her mood at the beginning and end of each module.

Maria's mood was low in the first weeks, while she was still having panic attacks and her depressive symptoms worsened. Adding the module dealing with comorbid depression proved to be the correct therapeutic decision and Maria started to feel better, with the exception of low point 3 weeks before the end of the treatment. During this time, she experienced a new panic attack, but fortunately she did not allow it to stop her progress and continued her exposure activities. Her mood had already improved by the time she completed the relapse prevention module.

Maria's anxiety levels changed during treatment, ranging from high at the beginning and decreasing after each module, except the 4th and the 10th. The time spent at home also spiked her anxiety level to 6 out of 10, but it dropped shortly after to 4 and then 3 as reported in the feedback questionnaire.

Andreea was committed to the program even through she was afraid of doing the

exercises. She needed a lot of support from her therapist and developed a strong therapeutic relationship. The time range for her sessions was between 28 and 57 minutes, totaling 434 minutes and having an average of 43.4 minutes. Andreea went through the modules multiple times and uploaded most of the worksheets. Her behavior on the platform seemed rather confused at the beginning. She frequently used the personal diary feature to write about her experience and spent a total of 1936 minutes on the treatment modules. Asynchronous communication was used a total of 20 times during treatment, mostly regarding setting up Skype sessions and technical aspects of the PAXonline platform. Although Andreea used the platform more than Maria, she managed to transfer less into her everyday life. While she tried to put the exercises into practice, she found it difficult to fit them in her schedule. She practiced the breathing technique and autogenic training just once a day and did not implement the recommendations for physical exercise. She practiced the exposure exercises inconsistently, for about 2 weeks, two or three times per week. In the last weeks of treatment, she showed progress by going to a market alone, passing through a crowded intersection she had avoided and going out with a friend twice and returning home alone once.

As shown by her panic attack frequency monitoring sheets, Andreea's had a low mood for the first weeks of the program and still had intense panic attacks. Her mood improved when the panic attacks disappeared. An unexpected panic attack made her mood drop once again, but she recovered and was able to maintain her mood at a positive level. She was still unhappy about being single, separated from her sister and in a job she hated. She still experienced panic attacks in the last part of the treatment but their intensity was lower and most happened during exposure exercises. Although the level dropped as she adjusted to the treatment, Andreea's anxiety continued to be high even in the last weeks of the treatment.

6.7. Concluding Evaluation of the Therapy's Process and Outcome

Post-treatment, both clients filled in the required questionnaires and were evaluated by a clinical psychologist via Skype.

6.7.1. Results on primary and secondary outcomes

Maria's initial PDSS-SR score was 18, dropped to 8, then 5 during treatment and she scored 3 during post-treatment. The diagnostic report after the clinical interview stated that she no longer had a panic disorder, only residual symptoms and subclinical agoraphobia. She no longer experienced depressive symptoms and her GAF scored went from 50 at the beginning to 80. From an anxiety level of 10/10 at the beginning of the treatment, she went to 3/10 post-

treatment.

Andreea's initial PDSS-SR score was 18. During treatment it dropped to 14, then 12 and at post-treatment she scored 11. The diagnostic report after the clinical interview revealed that she still had a panic disorder with agoraphobia, but the intensity dropped from severe to moderate. She experienced depressive and GAD symptoms, but their intensity had also dropped. Her GAF score improved from 45 at the beginning of the program to 65. Her anxiety level dropped from 10/10 to 6/10 at the end of the treatment.

6.7.2. Additional measures

Social support and therapeutic alliance. Maria benefitted from high levels of social support, but the same was not true for Andreea. In her case, social support scored 19 on SS-5 scale, later dropping to 15.

The therapeutic alliance, measured after the 1st and 4th sessions, was high at both points for Maria. Andreea showed a slightly lower level at the beginning and showed a maximum at the second time point.

Treatment credibility. Expectancy and credibility ratings differed for the clients. At the beginning, Maria thought of the program as highly credible and expected it to be successful, Andreea showed less credibility and lower expectancies for improvement. At the second time point, both patients had improved their expectancies and showed higher credibility.

Personality traits were measured at the beginning of the intervention. Maria scored in the normal range in the OMNI IV Dependent Personality Subscale (Loranger, 2001). Andreea's results were above the cut-off point, confirming her therapists' observations that she was suffering from a dependent personality disorder. She also showed low levels of autonomy on the Personal Autonomy Scale (Albu, 2007), especially in the cognitive and behavioral subscales. Maria's scores on the Personal Autonomy Scale ranked in the normal range, but she did show lower emotional autonomy.

Program usability. The usability of the PAXonline platform was assessed using the System Usability Scale designed by Broke. Maria had very high usability scored from the beginning until the end, whereas Andreea showed significantly lower usability scores. Andreea was able to complete her tasks, but she requested additional technical support.

6.7.3. Client's mental status at follow up

In Maria's case, the good results were maintained at follow-up evaluations. She had not had any relapses, even though she had gone through losing someone dear to her. She continued

practicing the exercises and that helped her avoid a relapse and kept her good mental health status.

Andreea's post-treatment evaluation showed she still suffered from panic disorder with agoraphobia, but had a clear tendency towards improvement. Her measurements improved from one follow-up to the next. We are unfortunately unable to know if she recovered from her panic disorder and agoraphobia since there was no follow-up clinical interview.

6.7.4. Discusion

At the beginning, both patients were suffering from severe panic disorder with agoraphobia. During treatment, both clients showed significant improvements while undergoing therapy through the same online platform, guided by the same therapist. However, at the end of the treatment, only Maria had recovered from panic disorder. Andreea still fulfilled the diagnostic criteria for panic disorder with agoraphobia, with moderate intensity.

Life contexts differed greatly for the two patients. One, who registered better outcomes, was a young student with a strong social support and lots of opportunities and the other, with poorer outcomes, was an older woman with lower levels of social support, an unfulfilling job, no personal projects or plans for the future and very much afraid of physical sensations. At the same time, Andreea showed a dependent personality disorder and lower levels of personal autonomy. She practiced the recommended strategies inconsistently and showed ambivalence towards them.

Patterns of change. After the end of the program, Andreea continued working on the platform by reading the additional modules regarding problem solving and reducing depressive symptoms. Based on her journal entries, she was able to identify her main problems and was determined to address them one at a time. According to Prochaska's stages of change, the two clients were in different stages at the beginning of treatment, and "the amount of progress clients make during treatment tends to be a function of their pretreatment stage of change" (Prochaska, Norcross, & DiClemente, 2013, p. 13). Maria was an action-oriented person, prepared to implement change and benefitted from social support. Andreea was a more reflective person, initially overwhelmed by her situation. She needed more time to develop trust in the course of action and start putting a consistent effort into applying the exercises in real life. Andreea needed more from the therapy, even though the panic attacks and severe agoraphobia were main concerns. Unfortunately, the standardized program was unable to completely meet Andreea's needs and additional problems. While the therapist tried to be supportive and address the symptoms of depression and GAD, the RCT also required for her to be directive and task-

oriented.

In Maria's case, the therapist immediately addressed the depressive symptoms and changed the relaxation technique when necessary. In Andreea's case, the therapist approached the GAD symptoms only in the second part of the treatment. The agenda was constantly delayed by Andreea's avoidant style and the confusion at the beginning. Therefore, less time was spent on exposure exercises, which may explain the slower progress registered at post-treatment and the improvement noticed at the 1-month follow-up.

6.7.5. Conclusions

These case studies lead us to several conclusions. Firstly, for each of our patients, PAXonline plus guidance sessions have been useful. Most of the participants in the study showed significant improvements. However, the impact of the guidance sessions may be influenced by factors such as personal life context. Also, ICBT programs are not sensitive of the serendipities in patients' lives, but this can be compensated for by the therapist through the Skype sessions. Patients' comorbidities and personality traits also need to be factored in, since they may be projected upon the therapeutic models.

Secondly, a conclusion can be drawn regarding the role of therapists. In ICBT plus guidance sessions via Skype, the therapist is more of a facilitator in the assimilation process of the modules. The psychotherapist facilitates the understanding of the modules, the practice of the exercises and serves to motivate the clients.

Based on the existing evidence, we believe that web-based interventions may contribute largely to bridging the gap between mental health care needs and high quality treatment. In order for ICBT programs to generate the most value, we need to discover the best customized solutions, tailored specifically to individual needs. Offering real-time audio-video guidance is one way of tailoring these interventions and increasing their positive impact, but each patient has an own internal process of change and an individual pace, and that is a significant variable that we need to consider for treatment delivery.

Chapter 7 - General conclusions and discussion

7.1. Theoretical and practical implications

The main motivation behind this research endeavor resided in a practical problem with major individual, social and economic consequences. We have recurrently emphasized the statistics that show the extremely high percentage of individuals suffering from mental health problems and the low percentage of those seeking and receiving help. The current situation, i.e. the major gap between need for treatment and the extent that treatment is offered and accessed, calls for major changes. Existing systems have focused too much on reducing symptoms, without taking client needs and help-seeking behavior into consideration. The consequence is that we have reactive systems that can indeed offer viable solutions, but do so only for a small number of individuals. We must admit that the impact of psychiatry and psychology on the quality of life of people has been extremely low. As a global consequence, medical services must reform so that they focus on the individual, not on the institutions or the service providers (WHO, 2008).

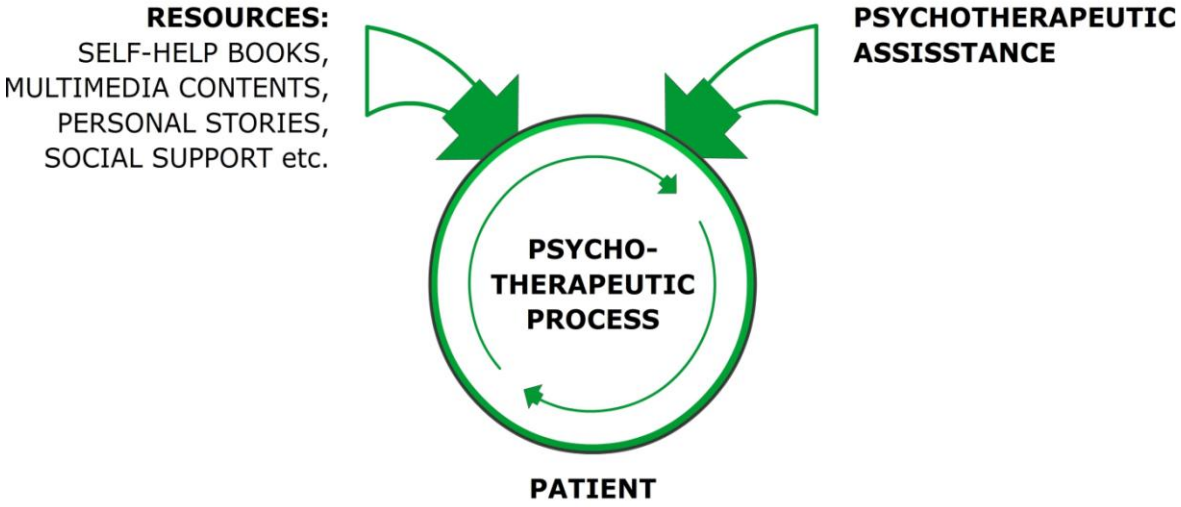
Based on concrete needs and existing obstacles that we identified, we sought to contribute to finding solutions for reducing internal barriers and facilitating access to treatment; training primary care staff (general practitioners and nurses) and providing them with efficient screening instruments; improving access to evidence-based treatments and increasing their efficiency. We consider that computer mediated psychotherapy field (offering long-distance counselling and psychotherapy services through the use of technology – internet, computer, mobile phones, and tablets), may provide an adequate answer and offer viabile solutions complementary to classical methods.

Results of this research program have a series of practical and theoretical implications for the way counseling and psychotherapy services for anxiety disorders are being delivered and used. Overall, the results of the conducted and presented studies in this doctoral thesis clearly support the efficacy and acceptability of computer mediated psychotherapy for anxiety disorders.

In study 1, our goal was to develop a multi-user platform that offers prevention and psychotherapy services for anxiety disorders. The explicit scope of the platform was from the beginning twofold: to facilitate the therapeutic process and to optimize the effects of psychotherapy, but also to improve the help-seeking behavior of patients. Our approach was rigorous and thorough, starting from the detailed analysis of targeted user needs and characteristics and continuing with a review of similar product analysis and a study of existing guidelines. In order to overcome the weaker aspects of current CMP solutions, we started

investigating the e-learning and cognitive science fields. The conclusions of our investigations have been organized in a set of essential principles that we then applied in developing PAXonline platform.

- It must be focused not only on psychotherapy but also on the help-seeking behavior of the person in need.
- The general practitioner has an important role in addressing mental health problems.
- It creates a community of learning and practice and becomes a part of a stepped care system.
- An e-mental health solution is not only a toolbox but a psychotherapeutic environment, where the users have personal control, flexibility and independence.
- It is useful for psychotherapeutic design to assimilate valuable findings from instructional design (e-learning) and cognitive science.
- The main aim of psychotherapeutic designs in e-health is to catalyze the psychotherapeutic process in the mind of the people. Patient (not the treatment) is the active agent of change. Psychotherapy is for the psychotherapeutic process what teaching is for learning.



The functionality, usability and acceptability of the platform were tested in multiple stages, both by specialists and by individuals suffering from anxiety. The results of the pilot study showed that the platform is ready for use and for further investigation (showing high functionality, ease of use, high user satisfaction and appreciation of the quality and utility of PAX components). Also, there were promising data regarding platform efficiency in treating anxiety disorders.

Over 175 studies conducted by independent research teams have proven the efficacy and effectiveness of CMP in treating mood and anxiety disorders and other problems (irritable bowel syndrome, chronic pain, tinnitus, sexual dysfunction, insomnia, eating disorders, stress etc.). However, the evidence is not consistent yet in regard to the level and type of therapeutic assistance needed in ICBT. Previous studies show inconsistent results on the role of therapeutic assistance and its impact on treatment outcomes. This problem plays a central role in the development of ICBT programs and must be tested directly. Consequentially, **in study 2** we aimed to determine the benefits of regular therapeutic guidance offered through real-time audio-video communication (i.e. Skype) compared to independent, unguided use of self-help ICBT program for panic disorder. Both treatments were compared to a wait-list control group.

To the best of our knowledge, this study represented the first effort to investigate the efficacy of self-help internet intervention offering therapeutic assistance through real-time audio-video communication. For the first time, a self-help intervention with therapist guidance was compared to one without therapist guidance in treating panic disorder. Analysis conducted have shown that PAXPD program is efficient in treating panic disorder with comorbidities, and also for secondary outcomes, such as functional impairment and associated depression symptoms, regardless of the delivery modality. Effect sizes are very similar to ones reported in classic CBT therapy (Sanchez-Meca et al., 2010), and even larger than the ones reported in similar previous studies investigating ICBT (Hedman, Ljotsson, Ruck, Bergstrom, Andersson, Kaldo, et al., 2013). The efficacy of PAXPD treatment was also demonstrated for variables accounting for the process of change in cognitive-behavioral therapy: catastrophic cognitions and interpretations, attentional biases and fear towards one's own physical sensations.

By directly comparing the two groups that received the PAX treatment, with and without therapist guidance, our results were similar to the ones reported in other studies (Berger, Caspar, et al., 2011; Berger, Hammerli, Gubser, Andersson, & Caspar, 2011; Botella et al., 2010; Furmark et al., 2009; Olthuis, Watt, Bailey, Hayden, & Stewart, 2015; Titov, Andrews, Choi, Schwencke, & Johnston, 2009). Although at the end of intervention the differences between treatment groups were not statistically significant, the Skype guided treatment proves superiority through larger effect sizes and higher percentage of clinical significance (71% of participants did not fulfill diagnostic criteria for panic disorder). Moreover, the effects of treatment were maintained and even increased after treatment completion. The difference between guided and unguided PAX groups became statistically significant at 3 months follow-up, which again indicates the benefic role of therapeutic assistance in perpetuating and maintaining long term

mental health. As to premature drop-out rates, no statistically significant differences were recorded between the two groups (25% and 24% respectively), but there was a clear superiority of the guided PAX treatment in regard to adherence (i.e. number of modules completed and total time spent in the online intervention program) and treatment compliance (frequently of use for the main anxiety reducing techniques).

Another proof supporting the efficacy of PAXPD intervention is the progress of the control group after the waiting/ monitoring period. As expected, participants in this group (who received the PAX treatment with or without assistance after waiting 12 weeks) significantly reduced their symptomatology at the end of treatment – effect sizes for pre-post intervention were large for all outcomes, between 0.98 and 1.3.

In **study 3** we tried to contribute to one of the key aspects of recent research: identifying the characteristics of patients that would benefit the most from CMP interventions. Multiple types of potential predictive variables were assessed: pre-treatment variables (demographic and clinical characteristics), mid-treatment (therapeutic alliance, treatment credibility and expectancy, online platform usability) and variables related to treatment adherence and compliance. Our approach was exploratory and we tried using two paradigms and two types of criterion variables in order to improve the validity of our efforts. Identified predictors include: age and initial severity of symptoms, dependent personality traits; severity of depression symptoms recorded at mid-treatment, platform usability, treatment credibility and therapeutic alliance; number of therapy sessions (to measure adherence to treatment), frequency of use of breathing regulation, autogenic training and in vivo exposure techniques.

Our study was one of the few that identified the therapeutic relationship as a predictor of outcomes in the CMP/ ICBT field. As we mentioned before, using real-time audio-video communication could facilitate the development of a better therapeutic relationship (Simpson & Reid, 2014). Even if therapeutic relationship is a key predictor in face to face interventions (Horvath et al., 2011; Martin et al., 2000), up until this point the results have been inconsistent in regard to ICBT (G. Andersson, 2015).

Other interesting results concern the rhythm of change, depending on initial panic symptom severity and comorbidity of depression symptoms. Initial panic symptom severity is a good predictor of treatment outcome for the unguided PAXPD group – the higher the initial severity of panic disorder symptoms, the higher the scores at post-treatment. However, for patients receiving therapist guidance, the initial severity of symptoms did not count as much. Regardless of their

starting point, the outcomes recorded at the end of treatment have been very similar. These results once again support the importance of therapeutic guidance in ICBT therapies, and also the fact that guided PAXPD program is efficient even for more severe cases.

In study 4 we blended the quantitative and the qualitative approaches and we used a particular method for mixed research – Individual-Case-Comparison – ICC, proposed by Fishman in 2008, which allowed us to illustrate the individual treatment process within PAXPD program. In this way, we were able to derive a few conclusions about factors that enable or hinder the change process in computer mediated psychotherapy (e.g. life context, personal history, comorbidity, stage of change, patient personality traits). Our view is that in guided ICBT, the role of the psychotherapist is rather to enable the process of assimilation of therapeutic opportunities available in each module. The therapist facilitates understanding of modules and practice of certain exercises (through modeling) and aims to raise patient motivation.

7.2. Limitations and future research directions

Our results have inherent limitations in regard to documenting and analyzing the phenomenon under investigation. Despite our best efforts to assure the high quality and validity of research, there are certain limits that must be mentioned and taken into consideration in order to have an accurate perspective upon these findings.

First of all, although the size of the sample in study 2 was large enough for us to reach our main research objectives, it was much more difficult to conduct detailed subgroup analysis. The small and in some places very small sample does not allow us to draw firm conclusions about potential predictors for the outcomes of treatment. There are also several limitations related to statistical procedures (e.g. use of LOCF method). Although analysis should be repeated in future studies and on larger samples, the findings in this study can provide important clues and can help us select potential relevant predictors for future investigations.

Secondly, for ethical reasons, the control group received treatment in the second part of the study. Therefore, there was no follow-up data for the control group. This represents a limit that we have assumed from the very beginning, but it also allowed us to document the positive effect of the treatment by comparing the progress of the control group participants before and after treatment use.

Another aspect points to the inherent limits of controlled clinical studies – i.e. having high internal validity, but limited generalizability of the results. We did try to reduce the exclusion criteria as much as possible and our study could be regarded as a pragmatic randomized control

study, but in the future, more effectiveness and field studies are needed in order to evaluate PAXonline platform. The recommended DSM or ICD diagnostic criteria are hard to apply, and is pretty difficult to find a „clear-cut" panic disorder in practice. In our study, like in other studies, many potential participants were excluded after clinical interview because they did not meet diagnostic criteria. Obviously, individuals suffering form mild or even subclinical mental disorders also require treatment and we intent to conduct further studies to investigate the clinical efficacy of PAXonline for subclinical anxiety disorders.

Recruitment was conducted among the members of the general community, by mass-media advertising and through the study website, and this might have led to a self-selected participant sample. A series of studies, though, suggest that the sampling bias does not automatically lead to ungeneralizable results in CMP studies (Donkin et al., 2012; Titov, Andrews, Kemp, & Robinson, 2010).

There isn't very much to be done about the treatment drop-out rate, especially since it was similar to the one recorded in face to face therapy studies. Clearly, though, the treatment adherence and compliance can be improved. In this sense we are currently working on optimizing PAXonline platform, both technologically (e.g. responsive interface, adding new mobile applications that can facilitate the process of change even further), and content-wise. We have carefully reviewed the recommendations sent by our study participants; we hope that their (direct or indirect) feedback will help us improve CMP treatment usability and credibility. In order to make the PAXonline platform available internationally for testing by other research teams, it will soon be available in English.

The efficacy and effectiveness of the studies conducted so far bring hope that computer mediated psychotherapy might substantially contribute to reducing the gap between mental health needs and service use by improving access to quality psychological treatments. Our efforts, however, have only just begun. In order to apply these services more efficiently, we need to find the best way to adjust and tailor interventions according to individual patient characteristics (severity of symptoms and comorbid problems, personality traits, life context, stage of change, etc.). Real-time audio-video guidance is a viable method for adjusting these interventions and improving their positive impact, but treatment delivery must always allow for the fact that each patient has their own internal process of change and their own rhythm for making the necessary changes in their lives.

Selective references

Abbott, J.-A. M., Klein, B., & Ciechomski, L. (2008). Best practices in online therapy. *Journal of Technology in Human Services, 26*(2-4), 360-375.

Albu, M. (2007). Un nou instrument pentru evaluarea autonomiei personale la adolescenţi/ A new instrument for personal autonomy evaluation in adolescents. *Anuarul Institutului de Istorie George Bariţ din Cluj-Napoca. Seria Humanistica, V*, 99-114.

Alonso, J., Codony, M., Kovess, V., Angermeyer, M. C., Katz, S. J., Haro, J. M., . . . Brugha, T. S. (2007). Population level of unmet need for mental healthcare in Europe. *The British Journal of Psychiatry, 190*(4), 299-306. doi: 10.1192/bjp.bp.106.022004

Amstadter, A. B., Broman-Fulks, J., Zinzow, H., Ruggiero, K. J., & Cercone, J. (2009). Internet-based interventions for traumatic stress-related mental health problems: a review and suggestion for future research. *Clinical Psychology Review, 29*(5), 410-420. doi: 10.1016/j.cpr.2009.04.001

Andersson, G. (2015). *The Internet and CBT: a clinical guide*: CRC Press, Taylor& Francis.

Andersson, G., BergstrÖM, J. A. N., HollÄNdare, F., Carlbring, P. E. R., Kaldo, V., & Ekselius, L. (2005). Internet-based self-help for depression: randomised controlled trial. *The British Journal of Psychiatry, 187*(5), 456-461.

Andersson, G., & Cuijpers, P. (2009). Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. *Cogn Behav Ther, 38*(4), 196-205. doi: 10.1080/16506070903318960

Andersson, G., Cuijpers, P., Carlbring, P., Riper, H., & Hedman, E. (2014). Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. *World Psychiatry, 13*(3), 288-295. doi: Doi 10.1002/Wps.20151

Andersson, G., Paxling, B., Roch-Norlund, P., Ostman, G., Norgren, A., Almlov, J., . . . Silverberg, F. (2012). Internet-based psychodynamic versus cognitive behavioral guided self-help for generalized anxiety disorder: a randomized controlled trial. *Psychother Psychosom, 81*(6), 344-355. doi: 10.1159/000339371

Andersson, G., & Titov, N. (2014). Advantages and limitations of Internet-based interventions for common mental disorders. *World Psychiatry, 13*(1), 4-11. doi: 10.1002/wps.20083

Andrade, L. H., Alonso, J., Mneimneh, Z., Wells, J. E., Al-Hamzawi, A., Borges, G., . . . Kessler, R. C. (2014). Barriers to Mental Health Treatment: Results from the WHO World Mental Health (WMH) Surveys. *Psychol Med, 44*(6), 1303-1317. doi: 10.1017/S0033291713001943

Andrews, G. (2003). *The treatment of anxiety disorders : clinician's guide and patient manuals* (2nd ed.). Cambridge: Cambridge University Press.

Andrews, G., Cuijpers, P., Craske, M. G., McEvoy, P., & Titov, N. (2010). Computer therapy for the anxiety and depressive disorders is effective, acceptable and practical health care: a meta-analysis. *PLoS One, 5*(10), e13196. doi: 10.1371/journal.pone.0013196

Andrews, G., Henderson, S., & Hall, W. (2001). Prevalence, comorbidity, disability and service utilisation. Overview of the Australian National Mental Health Survey. *Br J Psychiatry, 178*, 145-153.

APA. (2009). Practice Guideline for the Treatment of Patients With Panic Disorder. Retrieved 07.01.2012, from American Psychiatric Association http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/panicdisorder.pdf

Barak, A., Hen, L., Boniel-Nissim, M., & Shapira, N. (2008). A comprehensive review and a meta-analysis of the effectiveness of internet-based psychotherapeutic interventions. *Journal of Technology in Human Services, 26*(2-4), 109-160.

Barak, A., Klein, B., & Proudfoot, J. G. (2009). Defining internet-supported therapeutic interventions. *Ann Behav Med, 38*(1), 4-17. doi: 10.1007/s12160-009-9130-7

Baumeister, H., Reichler, L., Munzinger, M., & Lin, J. (2014). The impact of guidance on Internet-based mental health interventions—A systematic review. *Internet Interventions, 1*(4), 205-215.

Beauregard, M. (2014). Functional neuroimaging studies of the effects of psychotherapy. *Dialogues in Clinical Neuroscience, 16*(1), 75-81.

Berger, T., Caspar, F., Richardson, R., Kneubühler, B., Sutter, D., & Andersson, G. (2011). Internet-based treatment of social phobia: a randomized controlled trial comparing unguided with two types of guided self-help. *Behav Res Ther, 49*(3), 158-169.

Berger, T., Hammerli, K., Gubser, N., Andersson, G., & Caspar, F. (2011). Internet-based treatment of depression: a randomized controlled trial comparing guided with unguided self-help. *Cogn Behav Ther, 40*(4), 251-266. doi: 10.1080/16506073.2011.616531

Bergstrom, J., Andersson, G., Ljotsson, B., Ruck, C., Andreewitch, S., Karlsson, A., . . . Lindefors, N. (2010). Internet-versus group-administered cognitive behaviour therapy for panic disorder in a psychiatric setting: a randomised trial. *Bmc Psychiatry, 10*. doi: 10.1186/1471-244x-10-54

Botella, C., Gallego, M. J., Garcia-Palacios, A., Guillen, V., Banos, R. M., Quero, S., & Alcaniz, M. (2010). An Internet-Based Self-Help Treatment for Fear of Public Speaking: A Controlled Trial. *Cyberpsychology Behavior and Social Networking, 13*(4), 407-421. doi: DOI 10.1089/cyber.2009.0224

Bouchard, S., Paquin, B., Payeur, R., Allard, M., Rivard, V., Fournier, T., . . . Lapierre, J. (2004). Delivering cognitive-behavior therapy for panic disorder with agoraphobia in videoconference. *Telemed J E Health, 10*(1), 13-25. doi: 10.1089/153056204773644535

Brown, C., Conner, K. O., Copeland, V. C., Grote, N., Beach, S., Battista, D., & Reynolds, C. F. (2010). DEPRESSION STIGMA, RACE, AND TREATMENT SEEKING BEHAVIOR AND ATTITUDES. *Journal of community psychology, 38*(3), 350-368. doi: 10.1002/jcop.20368

Brown, J., Evans-Lacko, S., Aschan, L., Henderson, M. J., Hatch, S. L., & Hotopf, M. (2014). Seeking informal and formal help for mental health problems in the community: a secondary analysis from a psychiatric morbidity survey in South London. *Bmc Psychiatry, 14*(1), 275. doi: 10.1186/preaccept-2067133308130116

Butler, A. C., Chapman, J. E., Forman, E. M., & Beck, A. T. (2006). The empirical status of cognitive-behavioral therapy: a review of meta-analyses. *Clinical Psychology Review, 26*(1), 17-31. doi: 10.1016/j.cpr.2005.07.003

Campbell, K. (2004). *E-ffective writing for e-learning environments*. London InformationScience Publishing.

Chambless, D. L., Caputo, G. C., Bright, P., & Gallagher, R. (1984). Assessment of Fear of Fear in Agoraphobics - the Body Sensations Questionnaire and the Agoraphobic Cognitions Questionnaire. *Journal of Consulting and Clinical Psychology, 52*(6), 1090-1097. doi: Doi 10.1037/0022-006x.52.6.1090

Chambless, D. L., & Ollendick, T. H. (2001). Empirically supported psychological interventions: controversies and evidence. *Annu Rev Psychol, 52*, 685-716. doi: 10.1146/annurev.psych.52.1.685

Chan, A. W., Tetzlaff, J. M., Altman, D. G., Laupacis, A., Gotzsche, P. C., Krleza-Jeric, K., . . . Moher, D. (2013). SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med, 158*(3), 200-207. doi: 10.7326/0003-4819-158-3-201302050-00583

Christiana, J. M., Gilman, S. E., Guardino, M., Mickelson, K., Morselli, P. L., Olfson, M., & Kessler, R. C. (2000). Duration between onset and time of obtaining initial treatment among people with anxiety and mood disorders: an international survey of members of mental health patient advocate groups. *Psychol Med, 30*(3), 693-703.

Ciuca, A. M., Albu, M., Perţe, A., Budău, O., Miclea, Ş., & Miclea, M. (2011). The Romanian adaptation of the Psychiatric Diagnostic Screening Questionnaire (PDSQ). *Cognition,Brain,Behavior, XV*, 69-93.

Ciuca, A. M., Berger, T., Crisan, L. G., & Miclea, M. (2015). *Internet-based treatment for Romanian adults with panic disorder: a randomized controlled trial comparing a Skype-guided with an unguided self-help intervention*. Paper presented at the ESRII 3rd Conference, Warsaw, Poland.

Clark, D. A., & Beck, A. T. (2011). *Cognitive therapy of anxiety disorders: Science and practice*: Guilford Press.

Clark, R. C., & Mayer, R. E. (2003). *E-learning and the science of instruction*. San Francisco: Pfeiffer.

Clum, G. A., Broyles, S., Borden, J., & Watkins, P. L. (1990). Validity and Reliability of the Panic Attack Symptoms and Cognitions Questionnaires. *Journal of Psychopathology and Behavioral Assessment, 12*(3), 233-245. doi: Doi 10.1007/Bf00960620

Collins, K. A., Westra, H. A., Dozois, D. J., & Burns, D. D. (2004). Gaps in accessing treatment for anxiety and depression: challenges for the delivery of care. *Clinical Psychology Review, 24*(5), 583-616. doi: 10.1016/j.cpr.2004.06.001

Collins, P. Y., Insel, T. R., Chockalingam, A., Daar, A., & Maddox, Y. T. (2013). Grand challenges in global mental health: integration in research, policy, and practice. *PLoS Med, 10*(4), e1001434. doi: 10.1371/journal.pmed.1001434

Costache, R., Ciuca, A. M., & Miclea, M. (2014). *Psychologists' and potential patients' attitudes towards computer-mediated psychotherapy*. Paper presented at the 35th STAR Conference, Cluj-Napoca, Romania.

Craske, M. G., & Barlow, D. H. (2007). Panic Disorder and Agoraphobia. In D. H. Barlow (Ed.), *Clinical Handbook of Psychological Disorders: A Step-by-Step Treatment Manual* (4th ed.).

Craske, M. G., Edlund, M. J., Sullivan, G., Roy-Byrne, P., Sherbourne, C., Bystritsky, A., & Stein, M. B. (2005). Perceived unmet need for mental health treatment and barriers to care among patients with panic disorder. *Psychiatr Serv, 56*(8), 988-994. doi: 10.1176/appi.ps.56.8.988

Cuijpers, P., Donker, T., van Straten, A., Li, J., & Andersson, G. (2010). Is guided self-help as effective as face-to-face psychotherapy for depression and anxiety disorders? A systematic review and meta-analysis of comparative outcome studies. *Psychol Med, 40*(12), 1943-1957. doi: 10.1017/s0033291710000772

Dattilio, F. M., Edwards, D. J., & Fishman, D. B. (2010). Case studies within a mixed methods paradigm: toward a resolution of the alienation between researcher and practitioner in psychotherapy research. *Psychotherapy (Chic), 47*(4), 427-441. doi: 10.1037/a0021181

Deacon, B. J., & Abramowitz, J. S. (2004). Cognitive and behavioral treatments for anxiety disorders: a review of meta-analytic findings. *Journal of Clinical Psychology, 60*(4), 429-441. doi: 10.1002/jclp.10255

Devilly, G. J., & Borkovec, T. D. (2000). Psychometric properties of the credibility/expectancy questionnaire. *Journal of Behavior Therapy and Experimental Psychiatry, 31*(2), 73-86. doi: Doi 10.1016/S0005-7916(00)00012-4

DiMauro, J., Domingues, J., Fernandez, G., & Tolin, D. F. (2013). Long-term effectiveness of CBT for anxiety disorders in an adult outpatient clinic sample: a follow-up study. *Behav Res Ther, 51*(2), 82-86. doi: 10.1016/j.brat.2012.10.003

Dinh, H. T. T., Clark, R., Bonner, A., & Hines, S. (2013). The effectiveness of health education using the teach-back method on adherence and self-management in chronic disease: a systematic review protocol. *2013, 11*(10 <!-- jbi edits -->), 12 <!-- jbi edits -->. doi: 10.11124/jbisrir-2013-900

Donkin, L., Hickie, I. B., Christensen, H., Naismith, S. L., Neal, B., Cockayne, N. L., & Glozier, N. (2012). Sampling bias in an internet treatment trial for depression. *Translational Psychiatry, 2*(10), e174. doi: 10.1038/tp.2012.100

Durham, R. C., Chambers, J. A., Power, K. G., Sharp, D. M., Macdonald, R. R., Major, K. A., . . . Gumley, A. I. (2005). Long-term outcome of cognitive behaviour therapy clinical trials in central Scotland. *Health Technol Assess, 9*(42), 1-174.

Durlak, J. A. (2009). How to Select, Calculate, and Interpret Effect Sizes. *Journal of Pediatric Psychology, 34*(9), 917-928. doi: 10.1093/jpepsy/jsp004

Ebert, D. D., Zarski, A.-C., Christensen, H., Stikkelbroek, Y., Cuijpers, P., Berking, M., & Riper, H. (2015). Internet and Computer-Based Cognitive Behavioral Therapy for Anxiety and Depression in Youth: A Meta-Analysis of Randomized Controlled Outcome Trials. *PLoS One, 10*(3), e0119895. doi: 10.1371/journal.pone.0119895

Eisenberg, D., Golberstein, E., & Gollust, S. E. (2007). Help-seeking and access to mental health care in a university student population. *Med Care, 45*(7), 594-601. doi: 10.1097/MLR.0b013e31803bb4c1

EIU, T. E. I. U. (2014). Mental health and integration. Provision for supporting people with mental illness: a comparison of 30 european countries. http://mentalhealthintegration.com/media/whitepaper/eiu-janssen_mental_health.pdf: The Economist Intelligence Unit Limited.

El Alaoui, S., Hedman, E., Ljótsson, B., Bergström, J., Andersson, E., Rück, C., . . . Lindefors, N. (2013). Predictors and Moderators of Internet- and Group-Based Cognitive Behaviour Therapy for Panic Disorder. *PLoS One, 8*(11), e79024. doi: 10.1371/journal.pone.0079024

Farrer, L., Griffiths, K., Christensen, H., Mackinnon, A., & Batterham, P. (2014). Predictors of Adherence and Outcome in Internet-Based Cognitive Behavior Therapy Delivered in a Telephone Counseling Setting. *Cognitive Therapy and Research, 38*(3), 358-367. doi: 10.1007/s10608-013-9589-1

Fishman, D. B. (Producer). (2011). The "Individual-Case-Comparison" method for systematically comparing good-outcome and poor-outcome RCT clients: Editor's introduction. *Pragmatic Case Studies in Psychotherapy*.

Florescu, S., Ciutan, M., Popovici, G., Galaon, M., Ladea, M., & Petukhova, M. (2009). The Romanian Mental Health Study: main aspects of lifetime prevalence and service use of DSM-IV disorders [Romanian] *Management in Health, 13*(3), 22–30.

Furmark, T., Carlbring, P., Hedman, E., Sonnenstein, A., Clevberger, P., Bohman, B., . . . Andersson, G. (2009). Guided and unguided self-help for social anxiety disorder: randomised controlled trial. *British Journal of Psychiatry, 195*(5), 440-447. doi: DOI 10.1192/bjp.bp.108.060996

Furukawa, T. A., Shear, M. K., Barlow, D. H., Gorman, J. M., Woods, S. W., Money, R., . . . Leucht, S. (2009). Evidence-Based Guidelines for Interpretation of the Panic Disorder Severity Scale. *Depression and Anxiety, 26*(10), 922-929. doi: Doi 10.1002/Da.20532

Germain, V., Marchand, A., Bouchard, S., Drouin, M. S., & Guay, S. (2009). Effectiveness of Cognitive Behavioural Therapy Administered by Videoconference for Posttraumatic Stress Disorder. *Cogn Behav Ther, 38*(1), 42-53. doi: 10.1080/16506070802473494

Goldman, H. H., Rye, P., & Sirovatka, P. (1999). *Mental Health: A Report of the Surgeon General*. Washington DC: Department of Health and Human Services.

Gueorguieva, R., & Krystal, J. H. (2004). Move over ANOVA: progress in analyzing repeated-measures data and its reflection in papers published in the Archives of General Psychiatry. *Arch Gen Psychiatry, 61*(3), 310-317. doi: 10.1001/archpsyc.61.3.310

Gulliver, A., Griffiths, K. M., & Christensen, H. (2010). Perceived barriers and facilitators to mental health help-seeking in young people: a systematic review. *Bmc Psychiatry, 10*(1), 1-9. doi: 10.1186/1471-244x-10-113

Gunter, R. W., & Whittal, M. L. (2010). Dissemination of cognitive-behavioral treatments for anxiety disorders: Overcoming barriers and improving patient access. *Clinical Psychology Review, 30*(2), 194-202. doi: 10.1016/j.cpr.2009.11.001

Hannafin, M. J., & Hooper, S. (1989). An integrated framework for CBI screen design and layout. *Computers in Human Behavior, 5*(3), 155-165. doi: http://dx.doi.org/10.1016/0747-5632(89)90009-5

Haug, T., Nordgreen, T., Öst, L. G., Kvale, G., Tangen, T., Andersson, G., . . . Havik, O. E. (2015). Stepped care versus face-to–face cognitive behavior therapy for panic disorder and social anxiety disorder: Predictors and moderators of outcome. *Behav Res Ther, 71*, 76-89. doi: http://dx.doi.org/10.1016/j.brat.2015.06.002

Hedman, E., Ljotsson, B., & Lindefors, N. (2012). Cognitive behavior therapy via the Internet: a systematic review of applications, clinical efficacy and cost-effectiveness. *Expert Rev Pharmacoecon Outcomes Res, 12*(6), 745-764. doi: 10.1586/erp.12.67

Hedman, E., Ljotsson, B., Ruck, C., Bergstrom, J., Andersson, G., & Kaldo, V. (2013). Effectiveness of Internet-based cognitive behaviour therapy for panic disorder in routine psychiatric care. *Acta Psychiatr Scand, 128*. doi: 10.1111/acps.12079

Hedman, E., Ljotsson, B., Ruck, C., Bergstrom, J., Andersson, G., Kaldo, V., . . . Lindefors, N. (2013). Effectiveness of Internet-based cognitive behaviour therapy for panic disorder in routine psychiatric care. *Acta Psychiatrica Scandinavica, 128*(6), 457-467. doi: Doi 10.1111/Acps.12079

Hilty, D. M., Ferrer, D. C., Parish, M. B., Johnston, B., Callahan, E. J., & Yellowlees, P. M. (2013). The effectiveness of telemental health: a 2013 review. *Telemed J E Health, 19*(6), 444-454. doi: 10.1089/tmj.2013.0075

Hilvert-Bruce, Z., Rossouw, P. J., Wong, N., Sunderland, M., & Andrews, G. (2012). Adherence as a determinant of effectiveness of internet cognitive behavioural therapy for anxiety and depressive disorders. *Behav Res Ther, 50*(7-8), 463-468. doi: 10.1016/j.brat.2012.04.001

Hofmann, S. G., Asnaani, A., Vonk, I. J. J., Sawyer, A. T., & Fang, A. (2012). The Efficacy of Cognitive Behavioral Therapy: A Review of Meta-analyses. *Cognitive Therapy and Research, 36*(5), 427-440. doi: 10.1007/s10608-012-9476-1

Hoifodt, R. S., Mittner, M., Lillevoll, K., Katla, S. K., Kolstrup, N., Eisemann, M., . . . Waterloo, K. (2015). Predictors of Response to Web-Based Cognitive Behavioral Therapy With High-Intensity Face-to-Face Therapist Guidance for Depression: A Bayesian Analysis. *J Med Internet Res, 17*(9), e197. doi: 10.2196/jmir.4351

Horrigan, J., & Rainie, L. (2006). The internet's growing role in life's major moments. *Pew Internet & American Life Project.* Retrieved from http://www.pewinternet.org/2006/04/19/the-internets-growing-role-in-lifes-major-moments/ website:

Horvath, A. O., Del Re, A. C., Fluckiger, C., & Symonds, D. (2011). Alliance in Individual Psychotherapy. *Psychotherapy, 48*(1), 9-16.

Horvath, A. O., & Greenberg, L. S. (1989). Development and validation of the Working Alliance Inventory. *Journal of counseling psychology, 36*(2), 223.

Houck, P. R., Spiegel, D. A., Shear, M. K., & Rucci, P. (2002). Reliability of the self-report version of the Panic Disorder Severity Scale. *Depression and Anxiety, 15*(4), 183-185. doi: Doi 10.1002/Da.10049

http://www.eu-wmh.org. (2011). The Burden of Mental Disorders in the European Union Retrieved 15 Martie, 2013

Ivarsson, D., Blom, M., Hesser, H., Carlbring, P., Enderby, P., Nordberg, R., & Andersson, G. (2014). Guided internet-delivered cognitive behavior therapy for post-traumatic stress disorder: A randomized controlled trial. *Internet Interventions, 1*(1), 33-40. doi: http://dx.doi.org/10.1016/j.invent.2014.03.002

Johansson, R., & Andersson, G. (2012). Internet-based psychological treatments for depression. *Expert Review of Neurotherapeutics, 12*(7), 861-869.

Kaltenthaler, E., Brazier, J., De Nigris, E., Tumur, I., Ferriter, M., Beverley, C., . . . Sutcliffe, P. (2006). Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation. *Health technology assessment, 10*(33), 1-186.

Kessler, D., Lloyd, K., Lewis, G., & Gray, D. P. (1999). Cross sectional study of symptom attribution and recognition of depression and anxiety in primary care. *Bmj, 318*(7181), 436-439.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry, 62*(6), 593-602. doi: 10.1001/archpsyc.62.6.593

Kilian, C. (2001). Effective web writing. Retrieved August 9, 2012, from http://www.webtechniques.com/archives/2001/02/kilian/

King, R., Bambling, M., Lloyd, C., Gomurra, R., Smith, S., Reid, W., & Wegner, K. (2006). Online counselling: The motives and experiences of young people who choose the Internet instead of face to face or telephone counselling. *Counselling and Psychotherapy Research, 6*(3), 169-174. doi: 10.1080/14733140600848179

Kozma, R. B. (2001). Robert Kozma's Counterpoint theory of "learning with media". In R. E. Clark (Ed.), *Learning from media. Arguments, analysis and evidences.* Greenwich, Connecticut: Information Age Publishers.

Krieger, T., Meyer, B., Sude, K., Urech, A., Maercker, A., & Berger, T. (2014). Evaluating an e-mental health program ("deprexis") as adjunctive treatment tool in psychotherapy for depression: design of a pragmatic randomized controlled trial. *Bmc Psychiatry, 14*(1), 285.

Kroenke, K., Spitzer, R. L., Williams, J. B., Monahan, P. O., & Lowe, B. (2007). Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med, 146*(5), 317-325.

Kroenke, K., Spitzer, R. L., Williams, J. B. W., & Lowe, B. (2010). The Patient Health Questionnaire Somatic, Anxiety, and Depressive Symptom Scales: a systematic review. *General Hospital Psychiatry, 32*(4), 345-359. doi: DOI 10.1016/j.genhosppsych.2010.03.006

Kumar, S., & Malone, D. (2008). Panic disorder. *BMJ Clinical Evidence*, 1010.

Lang, A. J. (2005). Mental health treatment preferences of primary care patients. *J Behav Med, 28*(6), 581-586. doi: 10.1007/s10865-005-9019-2

Leahy, R. L., & Holland, S. J. (2000). *Treatment plans and interventions for depression and anxiety disorders*. New York ; London: Guilford Press.

Linzer, M., Spitzer, R., Kroenke, K., Williams, J. B., Hahn, S., Brody, D., & deGruy, F. (1996). Gender, quality of life, and mental disorders in primary care: results from the PRIME-MD 1000 study. *Am J Med, 101*(5), 526-533.

Lipsey, M. V., & Wilson, D. B. (1993). The efficacy of psychological, educational, and behavioral treatment: Confirmation from meta-analysis. *American Psychologist, 48,* 1181-1209.

Loranger, A. (2001). OMNI Personality inventories. Professional manual. *Lutz, FL: Psychological Assessment Resources*.

Lorence, D. P., & Greenberg, L. (2006). The Zeitgeist of Online Health Search: Implications for a Consumer-Centric Health System. *Journal of General Internal Medicine, 21*(2), 134-139. doi: 10.1111/j.1525-1497.2005.0295.x

Lovell, K., & Richards, D. (2000). MULTIPLE ACCESS POINTS AND LEVELS OF ENTRY (MAPLE): ENSURING CHOICE, ACCESSIBILITY AND EQUITY FOR CBT SERVICES. *Behavioural and Cognitive Psychotherapy, 28*(04), 379-391. doi: doi:null

Mănăilă, A. (2013, 15.03. 2013). Numarul pacientilor romani cu tulburari mentale a crescut cu 25%. Retrieved 15.03., 2013

Marks, I. M., Cavanagh, K., & Gega, L. (2007). Computer-aided psychotherapy: revolution or bubble? *Br J Psychiatry, 191*, 471-473. doi: 10.1192/bjp.bp.107.041152

Martin, D. J., Garske, J. P., & Davis, M. K. (2000). Relation of the therapeutic alliance with outcome and other variables: A meta-analytic review. *Journal of Consulting and Clinical Psychology, 68*(3), 438-450. doi: Doi 10.1037//0022-006x.68.3.438

Mayer, R. E., & Moreno, R. (2003). Nine Ways to Reduce Cognitive Load in Multimedia Learning. *Educational Psychologist, 38*(1), 43-52. doi: 10.1207/S15326985EP3801_6

Mewton, L., Smith, J., Rossouw, P., & Andrews, G. (2014). Current perspectives on Internet-delivered cognitive behavioral therapy for adults with anxiety and related disorders. *Psychol Res Behav Manag, 7*, 37-46. doi: 10.2147/PRBM.S40879

Meyer, B., Berger, T., Caspar, F., Beevers, C. G., Andersson, G., & Weiss, M. (2009). Effectiveness of a novel integrative online treatment for depression (Deprexis): randomized controlled trial. *J Med Internet Res, 11*(2), e15. doi: 10.2196/jmir.1151

Miclea, M., & Kallay, E. (2012). The computer-mediated therapy of anxiety. from http://dspace.bcucluj.ro/handle/123456789/32700

Miclea, M., Miclea, Ş., & Ciuca, A. M. (2008). Computer-supported psychotherapy should pay attention to e-learning. *Cognitie, Creier, Comportament/Cognition, Brain, Behavior, 12*(1), 131.

Miclea, M., Miclea, Ş., Ciuca, A. M., & Budau, O. (2010). Computer-mediated psychotherapy. Present and prospects. A developer perspective. *Cognition, Brain, Behavior: An Interdisciplinary Journal, 14*, 185-208.

Mojtabai, R., Olfson, M., & Mechanic, D. (2002). Perceived need and help-seeking in adults with mood, anxiety, or substance use disorders. *Arch Gen Psychiatry, 59*(1), 77-84.

Moldovan, R., & Pintea, S. (2015). Mechanisms of change in psychotherapy: methodological and statistical considerations. *Cognition, Brain, Behavior. An Interdisciplinary Journal, 14(4)*, 299-311.

Mundt, J. C., Marks, I. M., Shear, M. K., & Greist, J. H. (2002). The Work and Social Adjustment Scale: a simple measure of impairment in functioning. *British Journal of Psychiatry, 180*, 461-464. doi: DOI 10.1192/bjp.180.5.461

NICE. (2006). Guidance on the use of computerized cognitive-behavioral therapy for anxiety and depression. Retrieved 6.01.2012, from National Institute of Health and Clinical Excellence https://www.nice.org.uk/guidance/ta97

NICE. (2011). Generalised Anxiety Disorder and Panic Disorder (With Or Without Agoraphobia) in Adults: Management in Primary, Secondary and Community Care. *NICE clinical guideline 113*.

O'Hare, T. (1996). Court-Ordered versus Voluntary Clients: Problem Differences and Readiness for Change. *Social Work, 41*(4), 417-422. doi: 10.1093/sw/41.4.417

Ohayon, M. M., Shapiro, C. M., & Kennedy, S. H. (2000). Differentiating DSM-IV anxiety and depressive disorders in the general population: comorbidity and treatment consequences. *Can J Psychiatry, 45*(2), 166-172.

Olthuis, J. V., Watt, M. C., Bailey, K., Hayden, J. A., & Stewart, S. H. (2015). Therapist-supported Internet cognitive behavioural therapy for anxiety disorders in adults. *Cochrane Database Syst Rev, 3*, Cd011565. doi: 10.1002/14651858.cd011565

Otto, M. W., McHugh, R. K., & Kantak, K. M. (2010). Combined Pharmacotherapy and Cognitive-Behavioral Therapy for Anxiety Disorders: Medication Effects, Glucocorticoids, and Attenuated Treatment Outcomes. *Clinical Psychology: Science and Practice, 17*(2), 91-103. doi: 10.1111/j.1468-2850.2010.01198.x

Palmqvist, B., Carlbring, P., & Andersson, G. (2007). Internet-delivered treatments with or without therapist input: does the therapist factor have implications for efficacy and cost?

Pintea, S. (2010).The relevance of results in clinical research: statistical, practical, and clinical significance. *Journal of Cognitive and Behavioral Psychotherapies, 10(1),* 101-114.

Polsani, P. R. (2006). Use and Abuse of Reusable Learning Objects. *2006, 3*(4).

Porto, P. R., Oliveira, L., Mari, J., Volchan, E., Figueira, I., & Ventura, P. (2009). Does Cognitive Behavioral Therapy Change the Brain? A Systematic Review of Neuroimaging in Anxiety Disorders. *The Journal of Neuropsychiatry and Clinical Neurosciences, 21*(2), 114-125. doi: doi:10.1176/jnp.2009.21.2.114

Prins, M. A., Verhaak, P. F., van der Meer, K., Penninx, B. W., & Bensing, J. M. (2009). Primary care patients with anxiety and depression: need for care from the patient's perspective. *J Affect Disord, 119*(1-3), 163-171. doi: 10.1016/j.jad.2009.03.019

Prochaska, J. O., Norcross, J. C., & DiClemente, C. C. (2013). Applying the stages of change. *Psychotherapy in Australia, 19*(2), 10-15.

Prochaska, J. O., Velicer, W. F., Rossi, J. S., Goldstein, M. G., Marcus, B. H., Rakowski, W., . . . et al. (1994). Stages of change and decisional balance for 12 problem behaviors. *Health Psychol, 13*(1), 39-46.

Proudfoot, J., Klein, B., Barak, A., Carlbring, P., Cuijpers, P., Lange, A., . . . Andersson, G. (2011). Establishing guidelines for executing and reporting Internet intervention research. *Cogn Behav Ther, 40*(2), 82-97. doi: 10.1080/16506073.2011.573807

Proudfoot, J., Ryden, C., Everitt, B., Shapiro, D. A., Goldberg, D., Mann, A., . . . Gray, J. A. (2004). Clinical efficacy of computerised cognitive-behavioural therapy for anxiety and depression in primary care: randomised controlled trial. *Br J Psychiatry, 185*, 46-54.

Reiser, R. A., & Dempsey, J. V. (2007). *Trends and Issues in Instructional Design and Technology* (2nd ed.). Saddle River, NJ: Pearson Education.

Richards, D., & Richardson, T. (2012). Computer-based psychological treatments for depression: A systematic review and meta-analysis. *Clinical Psychology Review, 32*(4), 329-342. doi: http://dx.doi.org/10.1016/j.cpr.2012.02.004

Rickwood, D. J., Deane, F. P., & Wilson, C. J. (2007). When and how do young people seek professional help for mental health problems? *Med J Aust, 187*(7 Suppl), S35-39.

Ritterband, L. M., Thorndike, F. P., Cox, D. J., Kovatchev, B. P., & Gonder-Frederick, L. A. (2009). A Behavior Change Model for Internet Interventions. *Ann Behav Med, 38*(1), 18-27. doi: 10.1007/s12160-009-9133-4

Sanchez-Meca, J., Rosa-Alcazar, A. I., Marin-Martinez, F., & Gomez-Conesa, A. (2010). Psychological treatment of panic disorder with or without agoraphobia: a meta-analysis. *Clinical Psychology Review, 30*(1), 37-50. doi: 10.1016/j.cpr.2009.08.011

Sareen, J., Cox, B. J., Afifi, T. O., Clara, I., & Yu, B. N. (2005). Perceived need for mental health treatment in a nationally representative Canadian sample. *Can J Psychiatry, 50*(10), 643-651.

Schmidt, N. B., Lerew, D. R., & Trakowski, J. H. (1997). Body vigilance in panic disorder: Evaluating attention to bodily perturbations. *Journal of Consulting and Clinical Psychology, 65*(2), 214-220. doi: Doi 10.1037/0022-006x.65.2.214

Schulz, K. F., Altman, D. G., & Moher, D. (2010). CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann Intern Med, 152*(11), 726-732. doi: 10.7326/0003-4819-152-11-201006010-00232

Shah, A. (1992). The burden of psychiatric disorder in primary care. *International Review of Psychiatry, 4*(3-4), 243-250. doi: doi:10.3109/09540269209066324

Sherbourne, C. D., & Stewart, A. L. (1991). The Mos Social Support Survey. *Social Science & Medicine, 32*(6), 705-714. doi: Doi 10.1016/0277-9536(91)90150-B

Silfvernagel, K., Gren-Landell, M., Emanuelsson, M., Carlbring, P., & Andersson, G. (2015). Individually tailored internet-based cognitive behavior therapy for adolescents with anxiety disorders: A pilot effectiveness study. *Internet Interventions, 2*(3), 297-302. doi: http://dx.doi.org/10.1016/j.invent.2015.07.002

Simpson, S. G., & Reid, C. L. (2014). Therapeutic alliance in videoconferencing psychotherapy: a review. *Aust J Rural Health, 22*(6), 280-299. doi: 10.1111/ajr.12149

Spek, V., Cuijpers, P., Nykicek, I., Riper, H., Keyzer, J., & Pop, V. (2007). Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. *Psychol Med, 37*(3), 319-328. doi: Doi 10.1017/S0033291706008944

Ștefănescu, F. (2014). Cele mai frecvente tulburări psihice în România - anxietatea, depresia și tulburările psihosomatice [Press release]

Stein, M. B., Roy-Byrne, P. P., Craske, M. G., Campbell-Sills, L., Lang, A. J., Golinelli, D., . . . Sherbourne, C. D. (2011). Quality of and patient satisfaction with primary health care for anxiety disorders. *J Clin Psychiatry, 72*(7), 970-976. doi: 10.4088/JCP.09m05626blu

Steketee, G., & Chambless, D. L. (1992). Methodological issues in prediction of treatment outcome. *Clinical Psychology Review, 12*(4), 387-400. http://dx.doi.org/10.1016/0272-7358(92)90123-P

Strain, J. J. (1982). Needs for psychiatry in the general hospital. *Hosp Community Psychiatry, 33*(12), 996-1001.

Straube, T., Glauer, M., Dilger, S., Mentzel, H. J., & Miltner, W. H. (2006). Effects of cognitive-behavioral therapy on brain activation in specific phobia. *Neuroimage, 29*(1), 125-135. doi: 10.1016/j.neuroimage.2005.07.007

Stubbings, D. R., Rees, C. S., Roberts, L. D., & Kane, R. T. (2013). Comparing in-person to videoconference-based cognitive behavioral therapy for mood and anxiety disorders: randomized controlled trial. *J Med Internet Res, 15*(11), e258. doi: 10.2196/jmir.2564

Sucala, M., Schnur, J. B., Constantino, M. J., Miller, S. J., Brackman, E. H., & Montgomery, G. H. (2012). The Therapeutic Relationship in E-Therapy for Mental Health: A Systematic Review. *J Med Internet Res, 14*(4), 175-187. doi: ARTN e110 DOI 10.2196/jmir.2084

Sussman, L. K., Robins, L. N., & Earls, F. (1987). Treatment-seeking for depression by black and white Americans. *Social Science & Medicine, 24*(3), 187-196.

Théberge-Lapointe, N., Marchand, A., Langlois, F., Gosselin, P., & Watts, S. (2015). Efficacy of a cognitive-behavioural therapy administered by videoconference for generalized anxiety disorder. *Revue*

Européenne de Psychologie Appliquée/European Review of Applied Psychology, 65(1), 9-17. doi: http://dx.doi.org/10.1016/j.erap.2014.10.001

Titov, N., Andrews, G., Choi, I., Schwencke, G., & Johnston, L. (2009). Randomized controlled trial of web-based treatment of social phobia without clinician guidance. *Australian and New Zealand Journal of Psychiatry, 43*(10), 913-919. doi: Doi 10.1080/00048670903179160

Titov, N., Andrews, G., Kemp, A., & Robinson, E. (2010). Characteristics of Adults with Anxiety or Depression Treated at an Internet Clinic: Comparison with a National Survey and an Outpatient Clinic. *PLoS One, 5*(5). doi: ARTN e10885 DOI 10.1371/journal.pone.0010885

Tracey, T. J., & Kokotovic, A. M. (1989). Factor structure of the Working Alliance Inventory. *Psychological Assessment: A Journal of Consulting and Clinical Psychology, 1*(3), 207.

Turner, E. H., Matthewes, A. M., Linardatos, E., Tell, R. A., & Rosenthal, R. (2008). Selective publication of antidepressant trials and its influence on apparent efficacy. *New England Journal of Medicine, 358*, 252-260.

Üstün, T. B., & Sartorius, N. (1995). *Mental illness in general health care: an international study*: John Wiley & Sons.

Vernmark, K., Lenndin, J., Bjarehed, J., Carlsson, M., Karlsson, J., Oberg, J., . . . Andersson, G. (2010). Internet administered guided self-help versus individualized e-mail therapy: A randomized trial of two versions of CBT for major depression. *Behav Res Ther, 48*(5), 368-376. doi: 10.1016/j.brat.2010.01.005

Wang, P. S., Berglund, P., Olfson, M., Pincus, H. A., Wells, K. B., & Kessler, R. C. (2005). Failure and delay in initial treatment contact after first onset of mental disorders in the national comorbidity survey replication. *Arch Gen Psychiatry, 62*(6), 603-613. doi: DOI 10.1001/archpsyc.62.6.603

Wang, P. S., Lane, M., Olfson, M., Pincus, H. A., Wells, K. B., & Kessler, R. C. (2005). Twelve-month use of mental health services in the United States: results from the National Comorbidity Survey Replication. *Arch Gen Psychiatry, 62*(6), 629-640. doi: 10.1001/archpsyc.62.6.629

Warmerdam, L., Van Straten, A., Twisk, J., & Cuijpers, P. (2013). Predicting outcome of Internet-based treatment for depressive symptoms. *Psychotherapy Research, 23*(5), 559-567. doi: 10.1080/10503307.2013.807377

Weisberg, R. B., Beard, C., Moitra, E., Dyck, I., & Keller, M. B. (2014). ADEQUACY OF TREATMENT RECEIVED BY PRIMARY CARE PATIENTS WITH ANXIETY DISORDERS. *Depression and Anxiety, 31*(5), 443-450. doi: 10.1002/da.22209

White, J., Jones, R., & McGarry, E. (2000). Cognitive behavioural computer therapy for the anxiety disorders: A pilot study. *Journal of Mental Health, 9*(5), 505-516.

WHO. (2008). The World Health Report 2008. Primary Health Care - Now More Than Ever. Geneva: World Health Organization.

WHO. (2011). Mental health atlas 2011. Geneva, Switzerland.

WHO&Wonca. (2008). News from WHO and Wonca: new report calls for mental health to be better integrated into primary care. *Mental Health in Family Medicine, 5*(2), 125-125.

Wittchen, H. U., Jacobi, F., Rehm, J., Gustavsson, A., Svensson, M., Jonsson, B., . . . Steinhausen, H. C. (2011). The size and burden of mental disorders and other disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol, 21*(9), 655-679. doi: 10.1016/j.euroneuro.2011.07.018

Yuen, E. K., Herbert, J. D., Forman, E. M., Goetter, E. M., Juarascio, A. S., Rabin, S., . . . Bouchard, S. (2013). Acceptance based behavior therapy for social anxiety disorder through videoconferencing. *Journal of Anxiety Disorders, 27*(4), 389-397. doi: http://dx.doi.org/10.1016/j.janxdis.2013.03.002

Zimmerman, M., & Mattia, J. I. (2001). The Psychiatric Diagnostic Screening Questionnaire: Development, reliability and validity. *Comprehensive Psychiatry, 42*(3), 175-189. doi: DOI 10.1053/comp.2001.23126