Non-adherence to telemedicine interventions for drug users: systematic review

Não adesão em intervenções por telemedicina para usuários de drogas: revisão sistemática

ABSTRACT

OBJECTIVE: To estimate rates of non-adherence to telemedicine strategies aimed at treating drug addiction.

METHODS: A systematic review was conducted of randomized controlled trials investigating different telemedicine treatment methods for drug addiction. The following databases were consulted between May 18, 2012 and June 21, 2012: PubMed, PsycINFO, SciELO, Wiley (The Cochrane Library), Embase, Clinical trials and Google Scholar. The Grading of Recommendations Assessment, Development and Evaluation was used to evaluate the quality of the studies. The criteria evaluated were: appropriate sequence of data generation, allocation concealment, blinding, description of losses and exclusions and analysis by intention to treat. There were 274 studies selected, of which 20 were analyzed.

RESULTS: Non-adherence rates varied between 15.0% and 70.0%. The interventions evaluated were of at least three months duration and, although they all used telemedicine as support, treatment methods differed. Regarding the quality of the studies, the values also varied from very poor to high quality. High quality studies showed better adherence rates, as did those using more than one technique of intervention and a limited treatment time. Mono-user studies showed better adherence rates than poly-user studies.

CONCLUSIONS: Rates of non-adherence to treatment involving telemedicine on the part of users of psycho-active substances differed considerably, depending on the country, the intervention method, follow-up time and substances used. Using more than one technique of intervention, short duration of treatment and the type of substance used by patients appear to facilitate adherence.

DESCRIPTORS: Drug Users. Patient Acceptance of Health Care. Patient Dropouts. Telemedicine. Review.
Adherence to treatment for drug addiction is one of the biggest challenges in mental health clinical practice. It is measured by the dropout rate, expressed as a percentage, reflecting the losses in monitored individuals, for whatever reason, over a specific time. Poor adherence to treatment is responsible for many setbacks in treating drug addiction as it leads to reductions in the efficacy of treatment, to socio-economic costs and to high mortality rates. Adherence is related to attitudes and beliefs regarding both the disease and the treatment, to level of knowledge concerning the disease, to personality and family structure characteristics and to the history and severity of the disease, as well as to factors linked to the type of intervention and to the health care professionals, which may or may not facilitate commitment to the therapy, thus increasing motivation to be treated.

Health care professionals monitor these behaviors which include taking medication, attending appointments, accompaniment by the family and keeping in contact with support services, goals to be developed in order for the patient to improve their health. When the patient is more engaged, this is associated with better outcomes, whereas high levels of abandoning the monitoring and control make it difficult to evaluate the results of the interventions. In studies of efficacy, adherence is essential in order to examine issues such as internal and external validity, which are compromised when there are high losses of patients during treatment and monitoring.

Drug addiction interventions using telemedicine, such as counselling via the telephone, internet and text messages aim to minimize the impact of abandoning treatment when offered together with face-to-face contact. 

\footnote{World Health Organization. Adherence to long-term therapies: evidence for action. Geneva; 2003 [cited 2010 Nov 23]. Available from: http://www.who.int/chp/knowledge/publications/adherence_report/en/}
interventions and often represent significant treatment alternatives when used in isolation.\textsuperscript{18,36}

Even when it is easy to collect data, there are still few studies on dropout rates for isolated interventions or interventions in combination with face-to-face telemedicine based interventions.\textsuperscript{38} In addition, little is known about reasons for non-adherence and the specific components that can improve patient engagement in studies using telemedicine based interventions.\textsuperscript{17} Randomized clinical trial with alcohol users showed that 80 of the 136 individuals who participated in an internet intervention completed the six-month monitoring period, representing a dropout rate of approximately 42.0\%.\textsuperscript{3} In face-to-face interventions for drug addiction, generally, 50.0\% of patients abandon treatment before the end of the period.\textsuperscript{12} The rates have been studied from different perspectives. In Brazil, there are still few studies on telemedicine based interventions. The rate of adherence to treatment for drug addiction and the cultural, technological and disease-related factors that influence its effectiveness and the patients' engagement with recommendations made through internet, telephone and text message are unknown.

The aim of this study was to estimate non-adherence rates in drug addiction treatment strategies using telemedicine.

\textbf{METHODS}

Randomized clinical trials meeting the following criteria were selected: a) testing different telemedicine treatment methods in drug users and estimating factors associated with non-adherence rates; b) population aged over 18; c) published in English between 2000 and 2012. Telemedicine is a recent field of study and studies were found from 2000 onwards, hence the start date for the search. The authors searched for publications in English as the majority of publications were in this language.

The following search terms were used “randomized controlled trial”, “drug abuse”, “telemedicine” and its “mesh terms” in Google Scholar, and in the PubMed, PsycINFO, SciELO, Wiley (The Cochrane Library), Embase and Clinical trials databases. The search strategy included Boolean operators combining the limits and filters for each term. The studies found were then evaluated to verify the following characteristics: year of publication, demographic region in which the study was carried out, the psychoactive substance included in the studies, a description of the sample allocation (randomization), blinding of outcomes, description of losses and exclusion, analysis by intention to treat, number of drug addicts (sample size), number of groups in the study, division of participants into control or intervention groups, type of intervention used with the groups, type of control used, stratification of groups by sex, age of the individuals being monitored and length of follow-up, the means used to apply the intervention and the frequency with which it was applied, methods of measuring the results, control and intervention group scores before and after the proposed intervention, relationship of adherence for the control and intervention groups.

There were 274 records recovered. Of these, 253 were excluded after analysis of the title and the abstract (Figure). The remaining 20 articles were analyzed by 2 investigators (LS and LRF) and compared in case of disagreement. Inclusion or exclusion was decided by a third assessor (TM).

In order to analyze the quality of the randomized clinical trials, the GRADE scale was used.\textsuperscript{22} To ensure transparency and simplicity, the GRADE system classifies the quality of evidence into one of four levels, high, moderate, low and very low quality. Studies scoring 5/5 were considered high quality, score of 4/5 and 3/5 were of moderate quality and 2/5 and 1/5 were low and very low quality, respectively. Evidence based on randomized clinical trials begins with high quality evidence, but confidence in the evidence can decrease for a variety of reasons including: limitations of the study, inconsistent results, indirect evaluations, inaccuracy and indications of bias.\textsuperscript{22} Thus, the definitions of quality can be classified as:\textsuperscript{22}

- High quality research: very unlikely that confidence in the estimate of effect changes;
- Moderate quality research: likely to have a significant impact on confidence in the estimate of effect and may change the estimate;
- Low quality research: very likely to have a significant impact on confidence in the estimate of effect and the estimate is likely to change;
- In very low quality research, the estimate of effect is very uncertain.

The clinical relevance of the studies included was evaluated using the United States Preventive Services Task Force (USPSTF) criteria\textsuperscript{24} in accordance with the five questions recommended by the Cochrane Back Review Group.\textsuperscript{43} Each question was classified as positive (+) if the relevant item was met; negative (-) if the item was not found and unclear (u) if the data were not available for analysis. Thus, the relevance of the interventions can be classified as:

- Good (5/5): consistent results, well designed, well conducted study of a representative population that directly evaluates effects on health results;
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- Reasonable (4/5 and 3/5): sufficient evidence to determine effects on health results, although the strength of relevancy is limited by the number, quality, size or consistency of the included study, or generalization for routine practice and the results;
- Limited or poor (2/5 and 1/5): there is insufficient evidence to evaluate the effects on health results due to the limited number of studies, inexplicable inconsistency, important faults in the design or conduct of the study, problems in the evaluation of lack of information on important results.

RESULTS

Of the 20 randomized clinical trials analyzed, the most commonly studied substance was alcohol (13 articles) and the majority of the research was on users of single psycho-active substances (13 articles). The number of patients involved in each study varied between 20 and 230 in the studies with smaller samples and between 358 and 873 in those with large samples. The participants’ ages varied between 24 and 58 years of age.

All of the studies used telemedicine combined with different interventions, such as brief motivational intervention, individual therapy, group therapy, cognitive-behavioral therapy – using strategies for coping, for identifying risky situations and identifying problems associated with use, among others – and preventing relapses. The non-adherence rate varied between 7.4% and 68.8%. The majority of studies followed patients for more than six months and described losses and exclusions; randomization and allocation concealment were adequate in half of the studies, 26.0% blinded the results and 63.0% analyzed according to intention to treat (Table 1).

Regarding the quality of the results analyzed, 50.0% were of moderate to high quality (Table 2). As for clinical relevance, 13 studies had a reasonable level of relevance (Table 3).

DISCUSSION

Lower rates of non-adherence are related to high quality studies evaluated using GRADE. Studies with single users, limited intervention time and which used different techniques to stop drug use appeared to increase rates of adherence. The interventions in the randomized clinical trials evaluated in this systematic review were of at least three months duration and, although all of them used telemedicine as primary or secondary support, the treatment methods differed, which may have affected adherence.

Treating drug addiction is a complex process. In addition to the factors related to treatment methods, coping abilities, motivation, self-efficacy, the users' emotional state and social support influence the process of changing behavior, affecting adherence to treatment for substance abuse. For Brazilian alcoholics, rates of non-adherence to drug addiction treatment depend on the type of intervention, on the result related to abstinence, as they had to avoid consuming alcohol for six months after the intervention.
Table 1. Characteristics and main results of the selected randomized clinical trials, GRADEa score and clinical relevance score. (N = 20)

| Source/Country in which the study was conducted | Substance studied | Sample size | Type of intervention/Method to minimize abandonment/Non-adherence rate | Outcome measured | GRADE totalb – Clinical relevancec |
|-------------------------------------------------|-------------------|-------------|-----------------------------------------------------------------------|------------------|-----------------------------------|
| Agyapong et al (2012)1                             | Alcohol           | N = 54      | SMS/control Not used                                                   | Text messaging support showed improvement in outcomes for patients with depression and comorbidity (alcohol dependence). | 5/5-5/5             |
| Blankers M et al (2011)5                          | Alcohol           | N = 205     | Cognitive behavioral therapy and motivational interviewing online/internet Motivational e-mails, telephone calls to collect data, 15 Euro voucher for every questionnaire completed | Reducing the number of units of alcohol per week in 6 months. | 4/5-5/5             |
| Joseph A et al (2011)28                           | Tobacco           | N = 443     | Prevalence of relapse and telephone /usual care Not used               | The approach increased tobacco abstinence in the short and long term. | 5/5-5/5             |
| McKay J et al (2011)34                           | Alcohol           | N = 252     | Counselling and telephone monitoring/telephone monitoring/usual treatment Not used | Telephone monitoring and counseling decreased % of days of alcohol consumption up to 18 months of intervention. | 5/5-5/5             |
| Postel M et al (2011)38                           | Alcohol           | N = 924     | Internet/waiting list Not used                                        | Gender, educational level, age, initial intake and motivational level were predictors of completing treatment. | 1/5-2/5             |
| Whittaker R et al (2011)48                        | Tobacco           | N = 226     | Video message/control Not used                                        | Efficacy not shown in the tested intervention. Dropout rates were high in both groups. | 5/5-3/5             |
| Fernandes S et al (2010)18                        | Marijuana         | N = 1,744   | Brief, motivational telephone interview/telephone control Not used     | Positive efficacy for stopping marijuana use. | 2/5-3/5             |
| Girard B et al (2010)20                           | Tobacco           | N = 91      | Virtual game Not used                                                  | E-cigarettes led to a significant reduction in nicotine dependence, abstinence and dropout rates. | 5/5-4/5             |
| Zanjani F et al (2010)49                          | Tobacco           | N = 113     | Brief motivational telephone interview/usual care                      | The proposed intervention did not lead to a significant improvement in the results of psychiatric health. | 3/5-5/5             |
| Eberhard S et al (2009)15                         | Tobacco           | N = 344     | Motivational telephone interview (1 session-15 min.) Intervention group received feedback at the beginning 12.5% in 6 months | Alcohol consumption reduced to safe levels. | 1/5-2/5             |
| Kavanagh D & Connelly J (2009)30                  | Alcohol           | N = 204     | Letter and telephone: immediate treatment/delayed treatment Not used   | High levels of adherence to treatment and substantial reduction of alcohol use. | 5/5-4/5             |

Continue
Of the studies evaluated, six were of high quality and the clinical relevance of four of these was good. Considering the impact of non-adherence rates in each of the six best studies, a difference in non-adherence rates can be identified, even in well-designed studies. Agyapong et al. used SMS (an effective technique often used on studies of adherence, as, with the development of new technology, individuals are increasingly more interconnected, due to growing use of this technology), and had the lowest non-adherence rate of the randomized clinical trials. Thus, reminders or messages received during the treatment period

| Study | Country | Substance | N | Intervention | Control | Results |
|-------|---------|-----------|---|-------------|---------|---------|
| Kay-Lambkin F et al (2009) | Australia | Alcohol and marijuana | 97 | Computerized cognitive behavioral therapy/brief intervention | Not used | Marijuana use and hazardous use of substances reduced with computerized therapy |
| Litt M et al (2009) | United States | Alcohol and marijuana | 110 | Individual treatment program (cell phone)/package of cognitive-behavioral therapy | Not used | Intervention decreased the days of alcohol intake and increased use of coping strategies |
| Brendryen H et al (2008) | Norway | Tobacco | 290 | Messages via Internet, e-mail and cellular (SMS) | Not used | Better rates of abstinence from tobacco |
| El-Khorazaty M et al (2007) | United States | Polydrug | 1,070 | Educational intervention and multimodal integrative counseling/usual care | Telephone contacts, current contact information, financial incentives, training of staff in the recruitment and implementation of the study, salary support for staff, quick resolution to the problems that the team could have, continuous monitoring of the study | Well-developed telephone approaches facilitate the approaches between professional and patient |
| Hubbard R et al (2007) | United States | Polydrug | 339 | Telephone group/standard care group | Both groups were reminded to enroll in outpatient and continuing care following; reminded of the dates of the calls | Telephone counseling was well received by pregnant low-income women. The cessation rate was higher among those who received the intervention |
| Parker D et al (2007) | United States | Tobacco | 1,065 | Motivational interview (telephone), incentives, self-help material/incentives and self-help material/joining a monetary incentive program (30 days of abstinence confirmed by screening) | Not used | Intervention by phone showed greater reduction in anxiety and depression, and increased self-efficacy |
| Vridine D et al (2006) | United States | Tobacco | 95 | Telephone/standard care | Not used | Better sleep parameters for both groups and equal levels of lapse and relapse to alcohol |
| Currie S et al (2004) | Canada | Alcohol | 57 | Individual face-to-face treatment (I) X self-help/telephone support (C) | Not used | The use of telemedicine facilitated interaction with customers and decreased costs |
| Hall J & Hubert D (2000) | United States | Polydrug | 230 | Case management/interactive voice response system/control | Not used | |

1: Intervention Group; C: Control Group

a GRADE study quality scale, Guyatt GH et al (2008).
b The complete data for the scale are described in Table 3.
c The complete data for the scale are described in Table 4.
contributed to better adherence. On the other hand, the study by Agyapong et al., when compared to the other good quality ones, had the shortest follow-up time.

Lower rates of non-adherence are also found in shorter treatments, or those with a limited time, irrespective of the use of telemedicine. According to a meta-analysis of data on face-to-face therapy, a short follow-up time is more effective than treatments that have no time limit or even those in which there is a limited, albeit extensive, period. Another important factor in the study by Agyapong et al. is that the treatment was only for alcohol users, and the literature describes how it is easier for users of a single substance to follow treatment and stop taking it than for users of more than one drug. The study using pharmacological treatment for tobacco had a low non-adherence rate, which may be explained by the use of medication that, by increasing rates of quitting, may motivate the patient to adhere more to treatment. Moreover, research conducted with smokers shows that pharmacological treatment is widely studied, with positive results for treating nicotine dependence. It is probable that the use of strategies to prevent relapse with longer follow-up than in the other studies (one year) and the patients’ financial incentive ($25 per follow up conducted) may also have positively influenced adherence results.

The study of users of alcohol alone had a higher non-adherence rate compared with other good quality studies. Alcohol dependence is also associated with high rates of non-adherence in face-to-face treatment. Even with more follow-up, the patients in this study were monitored for longer than in other studies, probably due to the use of a combination of different techniques. Making use of more than one technique, including using telemedicine, is a good alternative for treating drug users, as, when the intervention contains different tools and approaches, there is a greater possibility of the individual being engaged, and the results of the treatment may also be better. The study by Brendryen et al. highlights using the telemedicine

| First author/Year of publication | Proper sequence of data generation | Allocation concealment | Blinding | Description of losses and exclusions | Analysis by intention to treat | Score |
|----------------------------------|----------------------------------|------------------------|----------|--------------------------------------|------------------------------|-------|
| Agyapong et al (2012)            | Yes                              | Yes                    | Yes      | Yes                                  | Yes                          | 5/5   |
| Blankers et al (2011)            | Yes                              | Yes                    | No       | Yes                                  | Yes                          | 4/5   |
| Joseph et al (2011)              | Yes                              | Yes                    | Yes      | Yes                                  | Yes                          | 5/5   |
| McKay et al (2011)               | Yes                              | Yes                    | Yes      | Yes                                  | Yes                          | 5/5   |
| Postel et al (2011)              | No                               | No                     | No       | Yes                                  | No                           | 1/5   |
| Whittaker et al (2011)           | Yes                              | Yes                    | Yes      | Yes                                  | Yes                          | 5/5   |
| Fernandes et al (2010)           | Yes                              | No                     | No       | Yes                                  | No                           | 2/5   |
| Girard et al (2010)              | No                               | No                     | No       | Yes                                  | Yes                          | 2/5   |
| Zanjani et al (2010)             | Yes                              | Yes                    | No       | Yes                                  | Unclear                      | 3/5   |
| Eberhard et al (2009)            | No                               | No                     | No       | No                                   | Yes                          | 1/5   |
| Kavanagh & Connolly (2009)       | Yes                              | Yes                    | Yes      | Yes                                  | Yes                          | 5/5   |
| Kay-Lambkin et al (2009)         | Yes                              | Yes                    | No       | Yes                                  | Yes                          | 4/5   |
| Litt et al (2009)                | No                               | No                     | No       | Yes                                  | Unclear                      | 1/5   |
| Brendryen et al (2008)           | Yes                              | Yes                    | Yes      | Yes                                  | Yes                          | 5/5   |
| El-Khorazaty et al (2007)        | No                               | No                     | No       | Yes                                  | Yes                          | 2/5   |
| Hubbardi et al (2007)            | Yes                              | Yes                    | No       | Yes                                  | Yes                          | 4/5   |
| Parker et al (2007)              | No                               | No                     | No       | Yes                                  | Yes                          | 2/5   |
| Vidrine et al (2006)             | No                               | No                     | No       | Yes                                  | No                           | 1/5   |
| Currie et al (2004)              | No                               | No                     | No       | Yes                                  | No                           | 1/5   |
| Hall & Hubert (2000)             | No                               | No                     | No       | No                                   | No                           | 0/5   |

* GRADE study quality questionnaire, Guyatt GH et al (2008).
Happy Ending technique, consisting of an intense stop smoking program with the help of contact via e-mail, text messages, a helpline for dealing with cravings and a system to prevent relapse. Moreover, it emphasizes how psychological support can be efficaciously provided through modern communication technology with excellent results. The study by Brendryen et al was of high quality and had better results for stopping smoking when technological interventions were used, confirming that well-designed studies have more reliable results.

As the quality of the studies included in this systematic review decreased, there was an increase in non-adherence rates. This shows that in research that is more reliable in estimating effect – represents the effect present in the population and not only in the sample studied – there are better adherence rates. In moderate quality studies, only that of Blankers et al had high rates of non-adherence (41.0% in six months) and the others showed little variation (between 22.0% and 29.0%). Regarding clinical relevance of the moderate quality studies, only that of Blankers et al had reasonable relevance, whereas the others met the criteria evaluated with good clinical relevance. Although the study by Blankers et al was conducted solely with alcohol users, the only intervention technique used was that of online therapy, in which there was no contact with a therapist and the individuals was self-guided by the programs used. The authors themselves highlight the technique as being effective but limited to reduced alcohol consumption.

### Tabela 3. Relevância clínica dos estudos selecionados.

| Source                      | Description of patients | Description of interventions and definition of treatment | Results with clinical relevance | Clinical importance | Benefits x Potential harm | Total |
|-----------------------------|-------------------------|--------------------------------------------------------|--------------------------------|---------------------|---------------------------|-------|
| Agyapong et al (2012)¹      | +                       | +                                                      | +                              | +                   | +                         | 5/5   |
| Blankers et al (2011)⁵      | +                       | +                                                      | +                              | +                   | +                         | 5/5   |
| Joseph et al (2011)²⁸       | +                       | +                                                      | +                              | +                   | +                         | 5/5   |
| McKay et al (2011)¹⁴        | +                       | +                                                      | +                              | +                   | +                         | 5/5   |
| Postel et al (2011)³⁸       | +                       | +                                                      | -                              | -                   | -                         | 2/5   |
| Whittaker et al (2011)¹⁸    | +                       | +                                                      | +                              | -                   | -                         | 3/5   |
| Fernandes et al (2010)¹⁸    | +                       | +                                                      | -                              | +                   | -                         | 3/5   |
| Girard et al (2010)²⁰       | +                       | +                                                      | -                              | +                   | +                         | 4/5   |
| Zanjani et al (2010)⁴⁹      | +                       | +                                                      | +                              | +                   | +                         | 5/5   |
| Eberhard et al (2009)¹⁵     | +                       | +                                                      | -                              | -                   | -                         | 2/5   |
| Kavanagh & Connolly (2009)²⁰| +                       | +                                                      | +                              | +                   | -                         | 4/5   |
| Kay-Lambkin et al (2009)¹²  | +                       | +                                                      | +                              | +                   | +                         | 5/5   |
| Litt et al (2009)¹5         | +                       | +                                                      | -                              | -                   | -                         | 2/5   |
| Brendryen et al (2008)⁶     | +                       | +                                                      | +                              | +                   | +                         | 5/5   |
| El-Khorazaty et al (2007)¹⁶ | +                       | +                                                      | -                              | -                   | -                         | 2/5   |
| Hubbardi et al (2007)¹⁶     | +                       | +                                                      | +                              | +                   | +                         | 5/5   |
| Parker et al (2007)¹⁷       | +                       | +                                                      | -                              | +                   | +                         | 4/5   |
| Vidrine et al (2006)⁴⁷      | +                       | +                                                      | -                              | -                   | -                         | 2/5   |
| Currie et al (2004)¹¹       | +                       | +                                                      | -                              | -                   | -                         | 2/5   |
| Hall & Hubert (2000)¹¹      | -                       | +                                                      | -                              | -                   | -                         | 1/5   |
was conducted solely with smokers, with a six-month follow-up to facilitate adherence.\textsuperscript{16,18,20,37} Hubbard et al\textsuperscript{29} only used groups via telephone with tele-counselors and indicated that in-person clinical monitoring is necessary to keep abstinence.

Studies considered to be of\textsuperscript{16,18,20,37} have high non-adherence rates, which may be explained by difficulty maintaining the effect estimate.\textsuperscript{10} The evaluation of the results for the discussion of adherence to telemedicine were based on the relevance of the studies that, in this case, may be considered of poor reliability. Using a greater number of techniques contributed to higher adherence rates\textsuperscript{16,37} and adherence to interventions may increase in drug users who have made various attempts to stay clean,\textsuperscript{32} irrespective of whether a face-to-face or telemedicine intervention was used.

Among the limitations of this study is the fact that the therapies used in the studies used different telemedicine strategies and had different periods of follow-up, which makes it difficult to compare them. Another limitation is that the studies were on treatments for different types of substances and included users of single substances or poly drug users.

Despite the limitations found, it was possible to observe that certain factors favor non-adherence to treatment for drug addiction using telemedicine. Adherence is better when more than one intervention technique is used and when the treatment time is shorter.

In some countries, the use of telemedicine is of recent date. Treatments that use this tool are still unknown to many patients and professionals, which leads us to believe that this decreases confidence in the possibility of a positive result and leads to non-adherence.

As rates of non-adherence are high, more research is necessary on personal and socioeducational characteristics of patients which affect non-adherence to interventions using telemedicine technology.

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