# Résumé du protocole d'étude (synopsis), version du 23 novembre 2015

**Sponsor/Sponsor-Investigator**

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**Study Title:**

**Positive Emotions Program for Schizophrenia (PEPS): a randomized controlled study on improving pleasure and motivation in schizophrenia**

**Short Title/Study ID:**

PEPS randomized

**Protocol Version and Date:**

Version 2, September 27th 2015

**Study Category with Rationale**

Other clinical trials, Category A, the health related intervention tested in the clinical trial includes only minimal risks and constraints. In the pilot study.

**Clinical Phase, see Basisformular:**

**Background and Rational:**

Negative symptoms have long been recognized as a central feature of the phenomenology of schizophrenia, dating back to early descriptions by Kraepelin and Bleuler [[1](#_ENREF_1" \o "Foussias, 2014 #1711)]. They negatively affect patients’ longitudinal social and occupational functional outcomes, as well as their long-term recovery [[2-5](#_ENREF_2" \o "Fervaha, 2014 #1709)]. Whereas positive symptoms (hallucinations, delusions) reflect an excess or distortion of normal functions, negative symptoms (flattened affect, alogia, apathy-avolition, anhedonia, inattentiveness) represent the absence or reduction of normal emotions and behaviors. Negative symptoms are classified as primary or secondary. Primary negative symptoms comprise the core features intrinsic to schizophrenia itself. Secondary negative symptoms are transient; they are attributable and temporally related to the effects of such factors as unrelieved positive symptoms, depression, the adverse effects of antipsychotic drugs (akinesia), or the social isolation imposed by the stigma of schizophrenia. Primary and secondary negative symptoms may be similar in clinical expression, despite their contrasting etiologies [[6](#_ENREF_6" \o "Moller, 2007 #1391)]. Often, secondary negative symptoms diminish with the resolution of their causative factors. However the efficacy of drug-based treatments and psychological interventions on primary negative symptoms remains limited [[7-9](#_ENREF_7" \o "Turkington, 2012 #1743)]. Fusar-Poli et al. [[9](#_ENREF_9" \o "Fusar-Poli, 2014 #1098)], in their meta-analysis with 6,503 patients in the treatment arm and 5,815 patients in the placebo arm, showed that most treatments reduced negative symptoms at follow-up relative to placebo: second-generation antipsychotics, effect size −0.579 (−0.755 to −0.404); antidepressants, −0.349 (−0.551 to −0.146); combinations of pharmacological agents, −0.518 (−0.757 to −0.279); glutamatergic medications, −0.289 (−0.478 to −0.1); and psychological interventions, −0.396 (−0.563 to −0.229). However, none of the treatments used reached the threshold for clinically significant improvement. There is a clear clinical need for developing treatments for negative symptoms. The lack of clinically meaningful efficacy of drug or psychological treatments is in line with clinicians’ practical experiences [[8](#_ENREF_8" \o "Erhart, 2006 #1), [9](#_ENREF_9" \o "Fusar-Poli, 2014 #1098)].

Recent literature has distinguished the negative symptoms associated with a diminished capacity to experience (apathy, anhedonia) from those which are associated with a limited capacity for expression (emotional blunting, alogia) [[10-13](#_ENREF_10" \o "Blanchard, 2006 #131)]. The apathy-anhedonia syndrome tends to be associated with a poorer prognosis than the symptoms related to diminished expression, suggesting that it is the more severe facet of the psychopathology [[12](#_ENREF_12" \o "Strauss, 2013 #532)]. This syndrome is also related to the duration of the untreated psychosis, family history of schizophrenia, and the patient’s work status in first-episode schizophrenia [[14](#_ENREF_14" \o "Ergul, 2015 #1229)]. The distinction between diminished experience and limited expression syndromes allows more specific approaches to these problems.

A symptom-specific strategy has been used in the development of specific therapeutic techniques for positive symptoms [[15](#_ENREF_15" \o "Chadwick, 1996 #151), [16](#_ENREF_16" \o "Favrod, 2006 #1934)] and led to the development of more effective interventions, such as the cognitive behavioral therapy (CBT) of delusions or hallucinations [[17](#_ENREF_17" \o "Zimmermann, 2005 #1936)]. More recently, metacognitive training (MCT), which targets associated specific cognitive biases, has appeared to be effective in reducing positive symptoms [[18-20](#_ENREF_18" \o "Kumar, 2014 #1749)]. The symptoms approach has opened the way for the development of new interventions for specific negative symptoms, particularly for anhedonia. Anhedonia has been defined as a reduction in the ability to experience pleasure. Despite its clinical significance, research into anhedonia has produced a paradoxical set of findings, raising questions about its nature. On the one hand, using self-reported measures of trait social and physical anhedonia, individuals with schizophrenia typically report experiencing lower levels of pleasure in their daily lives than non-patients [[21-24](#_ENREF_21" \o "Blanchard, 2001 #1754)]. On the other hand, individuals with schizophrenia have repeatedly reported experiencing levels of pleasant emotions similar to, or even stronger than, non-patient control subjects in laboratory studies using emotionally evocative stimuli [[25-27](#_ENREF_25" \o "Kring, 1999 #20)]. Germans and Kring [[28](#_ENREF_28" \o "Germans, 2000 #1774)] resolved this inconsistency by suggesting that patients do not anticipate that pleasurable activities will indeed be pleasurable, even though they experience pleasant emotions when presented with pleasurable stimuli. This explanation is based on the distinction between appetitive/anticipatory pleasure (i.e., anticipating the potential pleasure of taking part in a future activity) and consummatory pleasure (i.e., the actual level of pleasure experienced directly from participating in an activity). Anticipatory pleasure is linked to motivational processes that promote goal-directed behaviors, while consummatory pleasure is associated with satiety. The Temporal Experience of Pleasure Scale (TEPS) is a trait measure of pleasure [[29](#_ENREF_29" \o "Gard, 2006 #1772)] that distinguishes between ‘momentary pleasure’ and ‘anticipation of future pleasant activities.’ A TEPS score study, comparing subjects with schizophrenia to controls, indicated that patients did not differ from controls on the consummatory scale, however, they reported significantly less anticipatory pleasure than controls [[30](#_ENREF_30" \o "Gard, 2007 #875)]. These results were replicated by the French version of TEPS. Bringing out this new way of conceptualizing anhedonia in schizophrenia permits a redefinition and calibration of the symptom complex as a target for treatment. If persons with schizophrenia show a deficit in their ability to anticipate pleasure, rather than experience pleasure, then cognitive training might well help these individuals anticipate pleasure from foreseeable, future activities. Ideally, treatment would lead to a greater ability to anticipate pleasure, and this in turn would lead to a meaningful increase in spontaneous daily activities. These considerations led us to explore the potential for an intervention training patients who complained of anhedonia, or a lack of desire to engage in activities, in the cognitive skills needed to increase their anticipatory pleasure [[31](#_ENREF_31" \o "Favrod, 2010 #612)]. This first exploratory pilot study included five participants with schizophrenia presenting severe anhedonia and stabilized on atypical antipsychotic medication. They received 10–25 hours of training in anticipatory pleasure. Results showed that the patients improved on the anticipatory scale of TEPS. The patients’ daily activities were also increased according to a time budget. These preliminary data were, of course, interpreted with caution, given the small study sample but they seemed to show a promising path towards the development of new interventions to alleviate anhedonia in schizophrenia.

Recent research has also shown that more specific symptom or syndrome approaches better enabled the identification of specific psychological mechanisms. For example, the endorsement of beliefs regarding low expectations of success and perceptions of limited resources are robustly associated with negative symptoms of diminished experience (avolition, asociality, and anhedonia) but they are not associated with negative symptoms of diminished expressivity (blunted affect, alogia). Similarly, defeatist performance beliefs are slightly related to diminished experience but not at all related to diminished expression [[32](#_ENREF_32" \o "Couture, 2011 #137)]. An impaired ability to envision the future is associated with apathy [[33](#_ENREF_33" \o "Raffard, 2013 #630)]. These results suggest that within the syndrome of diminished capacity to experience, apathy and anhedonia may be the results of the same underlying process that is a diminished capacity to anticipate a particular experience or the achievement of a pleasurable goal [[13](#_ENREF_13" \o "Foussias, 2010 #136)] or a motivational impairment [[34](#_ENREF_34" \o "Strauss, 2014 #1969)].

Further emotional deficits may be present in schizophrenia [[35](#_ENREF_35" \o "Kring, 2013 #885)] and should be taken into account in the development of new interventions [[36](#_ENREF_36" \o "Strauss, 2013 #757), [37](#_ENREF_37" \o "Favrod, 2014 #245)]. Strauss [[36](#_ENREF_36" \o "Strauss, 2013 #757)] suggested maximizing positive emotional experiences by using techniques developed in the field of affective science [[38](#_ENREF_38" \o "Quoidbach, 2010 #827), [39](#_ENREF_39" \o "Bryant, 2007 #883)] to increase the frequency and duration of positive emotional experiences. Five techniques have been found to specifically and reliably increase the frequency, intensity and duration of positive emotions, including anticipating the enjoyment. The others were behavioral display (expressing emotions via nonverbal behaviors); being ‘in the moment’ (directing controlled attention toward positive experiences when they occur—savoring); communicating and celebrating positive experiences with others; and recalling previously pleasurable events. Patients reported lower levels of pleasure in savoring past, present, and future events than did normal controls, and stated that they had low expectations of their self-efficacy [[40](#_ENREF_40" \o "Cassar, 2013 #1116)]. Individuals with schizophrenia also manifested a lesser ability to maintain positive emotions [[41-43](#_ENREF_41" \o "Ursu, 2011 #963)]. Even though observable, outward signs of emotional expression were lessened in schizophrenia, studies indicated that sufferers continued to display very subtle facial muscle movements (as measured by electromyogram) similar to, and in accordance with, their responses [[44](#_ENREF_44" \o "Kring, 2008 #1072)]. Finally, to the best of our knowledge, it appears that communicating and celebrating positive events with others has not been studied in schizophrenia patients. However, one study showed that impaired perspective-taking—a component of cognitive empathy—was associated with poor capacity and community functioning, even after taking into account the influences of neurocognitive deficits and psychopathology [[45](#_ENREF_45" \o "Smith, 2012 #2004)].

***Positive Emotions Program for Schizophrenia (PEPS)***

With this as a background, Jérôme Favrod and Alexandra Nguyen conceived an intervention they named the ‘**Positive Emotions Program for Schizophrenia’ (PEPS), which aims to reduce anhedonia and apathy.** The program teaches skills to help overcome defeatist thinking [[46](#_ENREF_46" \o "Grant, 2009 #123), [47](#_ENREF_47" \o "Rector, 2004 #46)] and to increase the anticipation and maintenance of positive emotions [[35](#_ENREF_35" \o "Kring, 2013 #885), [37](#_ENREF_37" \o "Favrod, 2014 #245)]. PEPS involves eight one-hour group sessions, administered using visual and audio materials as part of a PowerPoint presentation of slides projected onto a screen. Each session includes a number of the following steps. Part one begins with a welcome, followed by a five-minute relaxation-meditation exercise. In part two, the group leaders go over the homework task given during the previous session. Part three involves an exercise in challenging specific defeatist thoughts, which are presented using the program’s two fictitious heroes—Jill and Jack. Jill, for example, expresses such defeatist thinking as “I can’t relax; I’m useless.” The participant’s role is to challenge her belief, initially by assigning different reasons to why Jill has difficulty relaxing. They learn to find out the reasons which might be linked to the program’s hero, but also to other people or to Jill’s environment. They subsequently try to develop an alternative, more positive way of thinking. Subsequently, and according to the session’s theme, participants learn and practice a new skill to improve their anticipation or maintenance of pleasure. The session ends with group leaders setting the homework task that the participants must accomplish for the next session.

The skills taught include savoring a pleasant experience, expressing emotions by increasing behavioral expression, making the most of, or capitalizing on, positive moments, and anticipating pleasant moments. Savoring an agreeable experience involves becoming aware of that pleasure or of the positive emotions the participant feels at a given moment [[39](#_ENREF_39" \o "Bryant, 2007 #883)]. For example, participants are asked to look at a picture of pleasant countryside or listen to soothing music, and hence become aware of the pleasurable experience of doing this and thus appreciate it. Increasing behavioral expression of emotions involves using facial expressions or gestures to accompany that positive emotion. The participants are asked to imitate pictures of actors expressing a positive emotion and to become aware of the sensations this produces. Making the most of positive moments entails communicating and celebrating positive events with others. For example, participants are invited to describe positive events to one another through role-play. Anticipating pleasant moments involves imagining the sensations produced by a positive future event. This strategy is meant to guide the participants through different positive feelings and emotions. It can engage their different senses, for example, by imagining they are eating a fruit, or by anticipating the emotion produced and the physical sensations experienced upon the completion of a pleasurable physical or social activity. A simple homework task is assigned to be done between each session. For example, this could be, choosing an image or an object that provokes a positive emotion or feeling in the participant, who must then bring it back and present it to the group. The pedagogical concept underpinning the program was built according to Kolb and Kolb's model [[48](#_ENREF_48" \o "Kolb, 2009 #897)] of experiential learning. Each learning activity involves: 1) concrete experience, during which the participant completes a concrete task; 2) reflective observation, during which the participant reflects on his/her experience, his/her past—the participant communicates about the completion of the task; 3) abstract conceptualization, during which the participant interprets events—theoretical links are created or introduced by a third party; and 4) active experimentation, during which the participant anticipates a new means of trying out the task, in light of the skills acquired in the preceding phase, and then executes them. The program uses a collaborative, egalitarian approach. Group facilitators participate in sessions just as the participants do, by doing the exercises, sharing their experiences, and carrying out the given tasks.

Patients participate in eight one-hour PEPS sessions at a rate of one per week.

*PEPS Pilot Study*

A pre and post-test pilot study, accepted by your Commission (Protocole 127/14) has shown that PEPS is both a feasible intervention and is associated with an apparently specific reduction of anhedonia and apathy. Depression was also significantly and clinically reduced. However, these findings are limited by the absence of control group and the fact that the rater was not blind to the treatment objectives [[49](#_ENREF_49" \o "Favrod, 2015 #1813)].

**Objective(s):**

The pilot study described above confirms the feasibility of PEPS. The reduction of apathy and anhedonia accompanying PEPS makes it an interesting candidate for further investigation. The goal of the study proposed herein is to establish whether PEPS is clinically effective by using a randomized, controlled and assessor-blind trial. A combination of PEPS plus treatment as usual (PEPS+TAU) will be compared to TAU alone. Sixty participants diagnosed with a schizophrenia spectrum disorder will undergo either intervention for eight weeks. Testing will evaluate individuals’ current psychopathology and ability to savor pleasure and will be performed at the time of inclusion, at the end of the eight-week intervention and at six month follow-up. The study is registered on clinicaltrials.gov <https://clinicaltrials.gov/ct2/show/NCT02593058> and will be recorded on kofam.ch.

### *Hypotheses*

### This trial’s main hypothesis is that eight one-hour sessions of PEPS will lead to a reduction of the composite score of apathy-avolition and anhedonia-asociality scores on the Scale for the Assessment of Negative Symptoms (SANS) compared to the control group. Our secondary hypotheses are that PEPS will increase the capacity to savor pleasure, anticipatory pleasure, and consummatory pleasure, as well as reduce depression. The study will also monitor the sustainability of the potential benefits at a six-month follow-up.

**Outcome (if applicable, see Basisformular): Primary Outcome, secondary Outcome**

Primary outcome : As recommended, the primary outcome is a composite score of apathy/avolition and anhedonia/asociality of the SANS, because these two variables are highly correlated and consistently load on one factor.

Secondary outcome : capacity to savor pleasure, anticipatory pleasure, and consummatory pleasure, as well as depression

**Study Design, see Basisformular: RCT of Treatment as Usal (TAU) + PEPS vs TAU only.**

**Inclusion/Exclusion Criteria, see Basisformular:**

Inclusion criteria for patients are as follows:

1) a psychotic disorder according to ICD 10 (F20 or F25), diagnoses having been established by experienced clinicians;

2) presenting a score of at least 2 on the overall SANS anhedonia scale;

3) age between 18 and 65 years old;

4) French-speaking;

5) sufficient clinical stability to be able to provide informed consent.

Exclusion criteria:

1) evidence of organic brain disease, clinically significant concurrent medical illness, or learning disability;

2) no understanding of the study protocol as assessed with a decisional capacity instrument [[50](#_ENREF_50" \o "Jeste, 2007 #1076)].

**Measurements and Procedures:**

As part of their standardized interviews at the pre- and post-tests, participants will be assessed using the following form by a psychologist trained in its administration:

* Collection of socio-demographic and clinical data: age, sex, psychiatric diagnosis, duration of illness, living arrangements (e.g., nursing home, with family), treatment, etc. These data will be collected at base-line assessment and reassessed for living arrangements and treatment at six-month follow-up.

The following scales will be administrated at baseline assessment, post-test, and six-month follow-up by a psychologist trained in their administration:

* *The Scale for the Assessment of Negative Symptoms* (SANS) [[51](#_ENREF_51" \o "Lecrubier, 1987 #1111)]. This scale measures schizophrenia’s deficit symptoms within the framework of schizophrenic disorders. It comprises 25 items, scored from 0 to 5. A definition of each item, including examples, facilitates a better understanding of the scale’s content. The rating system is ordinal, from 0 (absent) to 5 (severe). The twenty-five items are grouped into five components: 1) withdrawal or emotional poverty; 2) alogia (lack of speech); 3) avolition and apathy (lack of energy, lack of initiative); 4) anhedonia and social withdrawal (loss of interests); 5) attention. The scale was translated into French with acceptable validity [[52](#_ENREF_52" \o "Dollfus, 1995 #1065), [53](#_ENREF_53" \o "Lecrubier, 1987 #1071)]. The total scores for the avolition-apathy and anhedonia-social withdrawal components will be used as the main outcome variables.

*The Calgary Depression Scale for Schizophrenia (CDSS)* [[54](#_ENREF_54" \o "Addington, 1993 #1135)] includes nine items: depression, hopelessness, self-depreciation, guilty ideas of reference, pathological guilt, morning depression, early wakening, suicide, and observed depression. This scale has been validated in French [[55](#_ENREF_55" \o "Reine, 2000 #918)]. The rater will be kept blind to the participation arm’s random assignation.

*The Angus & Simpson scale [[56](#_ENREF_56" \o "Simpson, 1970 #2706)] a* rating scale for extrapyramidal side-effects is used at the first assessment point.

*The Psychotic Symptom Rating Scales* (PSYRATS) [[57](#_ENREF_57" \o "Favrod, 2012 #620)] is used at the first assessment point.

The following self-report scales will be administrated at baseline assessment, post-test and six-month follow-up by a psychologist trained in their administration:

* *The Savoring Belief Inventory (SBI)* is a self-reported scale for measuring beliefs about one's capacity for savoring things. The scale has twenty four items, including a positive scale (twelve items) and a negative scale (twelve items). The scale has good validity and a high test-re-test reliability [[58](#_ENREF_58" \o "Bryant, 2003 #882)]. It measures a person's thinking regarding his/her capacity to savor positive experiences, in terms of past experiences, current experiences, and future anticipation. The total SBI score will be used as a secondary outcome variable.
* *The Temporal Experience of Pleasure Scale (TEPS)* contains eighteen items included in two sub-scales: anticipatory pleasure (ten items) and consummatory pleasure (eight items) [[59](#_ENREF_59" \o "Gard, 2006 #18)]. Items targeting anticipatory pleasure reflect the pleasure felt when anticipating a positive or pleasant stimulus. Items measuring consummatory pleasure refer to the direct pleasure experienced upon exposure to a stimulus. Items can be general or specific. The response to items falls on a six-point Likert scale from 1 (very false for me) to 6 (very true for me). This scale has been validated in French [[60](#_ENREF_60" \o "Favrod, 2009 #22)]. The total TEPS score will be used as a secondary outcome variable.
* *The Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS)* [[61](#_ENREF_61" \o "Gooding, 2014 #919), [62](#_ENREF_62" \o "Gooding, 2014 #920)] is designed to assess one's ability to experience pleasure in the interpersonal domain. It is a seventeen-item self-reported measure that consists of seven anticipatory and ten consummatory items. The ACIPS is scored on a six-point Likert scale, ranging from 1 (very false for me) to 6 (very true for me). The format is therefore quite similar to that of TEPS. The difference between the two scales lies mainly in terms of the items’ content. The total ACIPS score will be used as a secondary outcome variable.

The average time needed to complete the scales and the clinical interview with the participants is one hour and a half at T0 and one hour at the other assessment points.

* *The Social Functioning Scale (SFS)* [[63](#_ENREF_63" \o "Birchwood, 1990 #2115)] is constructed to assess those areas of functioning that are crucial to the community maintenance of individuals with schizophrenia. This is a reliable, valid, sensitive instrument and responsive to change. This last scale will be completed by the case-manager of the participant at baseline assessment and six-month follow-up.

**Study Product/Intervention according to KlinV, if applicable:**

The version v1.1 of PEPS, as described in the pilot study section of this application, will also be used for the RCT. It has been improved in a version v1.2 to make its format more attractive and using original illustrations. In particular, the two fictitious heroes—Jill and Jack—who will now be represented using cartoons.

Participants will receive eight one-hour sessions of PEPS at a rate of one per week.

Session List:

* Session 1: defeatist thinking
* Session 2: savoring pleasant moments (I)
* Session 3: accentuating the behavioral expression of emotions
* Session 4: making the most of pleasant moments by sharing them with others
* Session 5: savoring pleasant moments (II)
* Session 6: anticipating pleasant moments (I)
* Session 7: anticipating pleasant moments (II)
* Session 8: review of all skills.

Participants will conduct the review exercises themselves, during the last session. The trainers themselves will receive six hours of training and two one-hour supervisions during the RCT, as in the pilot study. The trainers are health and social care providers (nurses and social workers). PEPS can be freely downloaded at : <http://www.seretablir.net/outils-interventions/peps/>

**Comparator(s) (if applicable):**

TAU only was chosen as a control condition for a number of reasons. First, in the Canton de Vaud or in Gruyère areas, TAU is multi-facetted and thus assures the ethicality of our procedure. TAU consists of psychiatric management by a clinical team composed of at least one psychiatrist and a social worker and/or a psychiatric nurse with additional access to community treatment or hospital admission. Treatment involves antipsychotic medication, regular office-based or community contact with the clinical team for treatment monitoring, and socialization groups, therapy, and psychoeducational groups. No attempts have been made to standardize this treatment as TAU is tailored to the patient’s specific needs.

**Number of Participants with Rationale (if no Power Analysis conducted):**

For the sample size calculation, α was set at .05. A β was set conservatively at .95 in order to avoid a false negative error. An international expert of the SNF recommended us to use a composite index of the apathy/avolition and anhedonia/asociality scales of the SANS. From the results of the pilot study, the Cohen’s *d* for this composite score is 0.882, or the partial eta - η2 is 0.429. As the participants in the pilot study were not masked from the assessor and because trials in which raters are aware of group allocation tend to have an inflated effect size [[64](#_ENREF_64" \o "Jauhar, 2014 #1548)], we decided to have this effect size to .21.5. Using an a priori computation for an ANCOVA, the proposed trial requires a total sample size of fifty participants for the two arms. In order to avoid a type II error, this sample would be increased to sixty. With a drop-out rate of sixteen per cent we estimate that we should include seventy patients and screen about one hundred potential participants.

**Randomization**

A research manager who is not involved in the clinical part of the trial will randomize participants by blocks of ten, twelve or fourteen patients. The size of the blocks will depend on the speed at which recruitment occurs in order to minimize the time between the baseline assessment and allocation in the treatment arms.

**Independence of raters**

The independence of the raters will be controlled for as follows. At baseline, participants will be randomized following their initial evaluation. Participants will be informed when they give their consent, and again when their appointments for the post-test and follow-up meetings are scheduled. It is extremely important they do not reveal their treatment group allocation to the raters. The raters will not work in the places where the intervention takes place and will not be present during group sessions in order to avoid encounters with participants. Raters will not participate in clinical meetings or group facilitator supervision. Meetings with the raters will be organized by the research coordinator by site (HorizonSud and the Section of social psychiatry). To check whether masking of the participants‘allocation from the raters has been successful, raters will answer a brief questionnaire at the end of post-test and follow-up assessment periods. This questionnaire will measure their guesses about the participants’ treatment allocations and identify potential cues which might unmask them. Our research group is familiar with this procedure [[19](#_ENREF_19" \o "Favrod, 2014 #619)].

**Study Duration:**

The study will last three years.

**Study Schedule:**

The study will start in November 2015 and will be finished in December 2018.

Recruitment : November 2015

Intervention : January 2016 – January 2018

Analyse des données Analysis of data : July – December 2018

**Investigators and sponsors:**

Jérôme Favrod is a clinical nurse specialist at the « Section de psychiatrie sociale du Service de psychiatrie communautaire du Département de psychiatrie du CHUV » (Place Chaudron 18, CH-1003 Lausanne) and a full HES professor at the « Institut et haute école de la santé la Source, Haute école spécialisée de Suisse occidentale » (Avenue Vinet 30, CH-1004 Lausanne). Phone: + 4179 447 31 57, emails: [jerome.favrod@chuv.ch](mailto:jerome.favrod@chuv.ch) et [j.favrod@ecolelasource.ch](mailto:j.favrod@ecolelasource.ch)

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The project is supported by the « Division Sciences humaines et sociales du Fonds national suisse de la recherche scientifique ».

**Study Centre(s):**

The study will be conducted in partnership with the persons and following centers:

* Alban Ismailaj, Organisation de soins à domicile de SISP SA, Avenue des Oiseaux 13, 1018 Lausanne,
* Armando Brana, Fondation HorizonSud, Route de la Rotonde 25, case postale 41, 1633 Marsens
* Abel Ringuet à la Fondation Pro-Home, appartements FOND-VERT, Chemin de l’église 8 1182 Gilly
* Gwennaïg Tamic, EMS « Les Myosotis » Sarl, rue de Venengy 16, 1174 Monterod
* Favrod Jérôme & Charles Bonsack, Section de psychiatrie sociale, Service de psychiatrie communautaire du Département de psychiatrie du Centre Hospitalier du CHUV, Lausanne.

**Statistical Analysis incl. Power Analysis**

Between-group differences in post- and pre-test values will be examined using an analysis of covariance (ANCOVA) for each outcome variable. Differences between pre-test and post-test, as well as pre-test and follow-up scores, will be treated as dependent variables; treatment condition will be treated as a fixed factor; and pre-treatment scores will be treated as covariates. Between-subjects Cohen’s *d* effect sizes will be calculated at post-test and follow-up. For within-subjects Cohen’s *d* will be calculated between pre- and post-test, and pre-test and follow-up, in correcting for dependence among means. This will enable direct comparisons with the effect sizes from other studies.

**GCP Statement:**

This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP or ISO EN 14155 (as far as applicable) as well as all national legal and regulatory requirements.

**Explanation for the Inclusion of vulnerable Subjects (if applicable):**

After initial screening, eligible patients will be asked to participate in the study. Each patient included will be informed about: the aims of the study; the extent and nature of their participation, including randomization; the nature of the control and experimental interventions; the intake assessment; and the six-month follow-up evaluation. The patients included will also be informed about data confidentiality and their right to withdraw from the study at any time. Once the participant has given his/her consent, their understanding of the study protocol will be verified using the University of California, San Diego Brief Assessment of Capacity to Consent (UBACC)—a decisional capacity instrument [[50](#_ENREF_50" \o "Jeste, 2007 #1076)]. Our research group is familiar with this instrument, and in cases of failure to clearly understand the study, patients will not be included. Finally, each patient will sign the informed consent form [[19](#_ENREF_19" \o "Favrod, 2014 #619)].

**Recruitment Procedure (if applicable : Advice/Flyer have to be submitted ; if applicable, please indicate the Localisation / Medium (which Newspaper)**

Patients will be recruited among the population of out-patients treated at the HorizonSud Foundation in the canton of Fribourg and at the Social psychiatry section of the Community Psychiatry Service, Department of Psychiatry, University Hospital Center of Lausanne. Horizonsud is a social foundation offering sheltered accommodation and work to psychiatric patients from the south of the canton of Fribourg (the Gruyère, Glâne and Veveyse areas). The foundation takes care of two hundred and fifty patients. The Social psychiatry section treats patients aged from eighteen to sixty five. The four hundred or so patients likely to fulfil the diagnostic criteria for recruitment to the proposed study are treated in the rehabilitation unit and work closely with the canton of Vaud’s sheltered accommodation services. Both teams are trained and used to dealing with ethical issues, randomization, masking participants’ conditions from raters and other research procedures. Potential participants will be identified using systematic screening alongside the patients’ case managers and medical doctors. An appointment will be organized between the patient, the case manager and the research coordinator in order to explain the study, provide information and obtain informed consent. The participants will have a few days of reflection to give their consent. This strategy was applied successfully during the pilot study and enabled the recruitment of thirty seven subjects over a nine-month period.

**Study Procedure/Flowchart with Timelines: Study specific Examinations have to be clearly identified**



At T0, T1 and T2, the participants will go through a clinical assessment of negative symptoms and depression. At T0 and T2 participants are assessed on social functioning. At T0, participants will be assessed for their extrapyramidal side-effects and psychotic symptoms.

**Risks/ Inconveniences, which are Study specific:**

Participants can leave the study if they wish without consequence. Participants might not appreciate the intervention. In this case, we would be interested to know the reasons of the judgment to the extent that the participant agrees to entrust us. If the investigators observe negative effects of the intervention, this will be interrupted and the effects reported to the Commission cantonale d’éthique de la recherche sur l’être humain.

**Coverage of Damages:** Insurance (yes/no)?

In case of damage to participants, the CHUV will respond to these as sponsor in accordance with legal procedures.

**Storage of Data-and Samples for Future Research Aims: yes/no?,**The data will be coded at the first clinical interview so that the participants cannot be identified. All information when combined that allow to restore the identity of the person will be made unrecognizable and the coding key will be permanently destroyed at the end of the study. The informed consent forms will be preserved by Nataly Viens Python, Doyenne de la recherche à l’Institut et Haute Ecole de la Santé la Source, Lausanne. The data will be saved in a ".sav" file to be treated with SPSS. Informed consents and the encryption key will be kept locked up. Collected data will be preserved for ten years before being destroyed. The data of participants who withdraw consent will be destroyed if the participants ask them to be destroyed..

**Ethical Considerations:**

1. To improve the quality of life for people with schizophrenia, it is necessary to develop interventions that target anhedonia and apathy. An improvement in these symptoms could also increase patient autonomy.  
2. Participants randomize in the active group are invited to attend eight hours of training and two hours of evaluation. They can leave the study at any time. They potentially have the opportunity to learn skills that can improve their well-being. Participants who are randomized in the control group will received the intervention at the end of the study if the intervention is effective.  
3. This is a RCT expected to test the efficacy of the intervention and measure its potential impact.

4. TheCommission cantonale d’éthique de la recherche sur l’être humainwill have access to original data for inspection, monitoring and audits.

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Signatures

Le 23 novembre 2015 :

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