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Ensemble programme for early intervention in informal caregivers of psychiatric adult patients: a protocol for a randomized controlled trial

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Complete List of Authors:	Rexhaj, Shyhrete; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. Monteiro, Shadya; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. Golay, Philippe; CHUV, Community Psychiatry Service, Department of Psychiatry, Lausanne Coloni-Terrapon, Claire; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. Wenger, Daniel; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. Favrod, J; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
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Ensemble programme for early intervention in informal caregivers of psychiatric adult patients: a protocol for a randomized controlled trial

Ensemble RCT

Trial registration:

ClinicalTrials.gov: NCT04020497

Insert Table 1 here: items from the World Health Organization Trial Registration Data Set

Protocol version

28 August 2019, version 2, Project ID-2019-01181

The key revisions to version 1 of the protocol were linked with ethics concerns regarding added value for qualitative data and the specification for their collection and analysis. Information concerning timepoint data collection and time needed to complete the questionnaires was also detailed in the participants' information sheets.

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Authors

- Shyhrete Rexhaj (SR), La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Shadya Monteiro (SM). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Philippe Golay (PG). Community Psychiatry Service, Department of Psychiatry, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland.
- Claire Coloni-Terrapon (CCT). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Daniel Wenger (DW). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Jérôme Favrod (JF). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.

Shyhrete Rexhaj [Corresponding Author]

Authors` contributions

SR and JF designed the study and are grant holders. DW, SM and CCT collected the data and provided the intervention. SR and JF developed the intervention. SR and SM delivered the study material (for example, the recruitment process, programme figures and web information). SR provided training support for the intervention and data collection during the study. SR led the study but was replaced by JF during maternity leave. PG, JF and SR developed the statistical plan and provided statistical support for the study. SR and SM wrote the first version of the paper. All authors contributed to a critical review and approve the final paper.

Trial sponsor, committee and data manager:

La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.

Shyhrete Rexhaj, s.rexhaj@ecolelasource.ch; Telephone: +41 21 556 44 35

The project manager (SR) will be involved in the analysis and interpretation of data, writing of the report, and the decision to submit the report for publication.

The finding source FOPH had no role in the design of this study and will have no responsibility during its execution.

La Source is the only coordinated centre and serves all recruited participants, even those from other French-speaking areas of Switzerland. Lead investigators SR and JF will review the process of the study if necessary. SR, as the principal investigator, is responsible for ethical considerations (providing an annual risk report to the ethics committee, providing information on serious adverse events, and announcing any change in the protocol if necessary) and for the study procedures (management of the team and responsible for the data file and budget administration). Noémie Laverne, who was not involved in the execution of the project, is responsible for randomization even for participants who were randomly by computer, as the computer system requires oversight.

The data manager Anne-Laure Kauffman maintains the trial IT system using the REDCap platform and will audit all procedures of the study once a year.

Acknowledgements

We thank Prof. Charles Bonsack and Prof. Claude Leclerc for their valuable value in the development of the intervention. We thank Dr Engelhorn for a donation in the first step of the programme development. We also thank members of ÎLOT (The association of informal caregivers for mental disorders, in Vaud state, Switzerland).

Abstract:

Introduction: Informal caregivers play a major role in the support and maintenance of community patients with severe psychiatric disorders. A pilot study showed that an individualized brief intervention such as the Ensemble programme leads to significant improvements in psychological health state and optimism. **Methods and analysis:** This randomized clinical trial (RCT) aims to compare the efficacy of using Ensemble in improving informal caregivers' psychological health states and the ability to play an active role in their situations with that of support as usual (SAU). Improvements on the psychological health global index will be measured three times (T0-pre, T1-post and T3 two-month follow) with standardized questionnaires (the Global Severity Index of Brief Inventory Symptoms, the Life Orientation Test-Revised, the 36-item Medical Outcome Study Short-Form Health Survey and the French Zarit Burden Interview). Differences between groups in post- and pre-test values will be examined using an analysis of covariance (ANCOVA) for each outcome variable. The severity of illness measured by the Social and Occupational Functioning Assessment Scale (SOFAS) will also be collected at T0 and T2 to compare eventual patient improvements. At the end of the programme, the experiences of the 20 patients participating in the Ensemble programme will be evaluated qualitatively.

Ethics and dissemination: The research protocol received full authorization from the Human Research Ethics Committee of the Vaud State, Switzerland. The principal paper will concern the results of the experimental design used to test the Ensemble programme. The research team will prioritize open access publications.

Strengths and limitations of this study

- This is the first randomized controlled trial in Switzerland to test *Ensemble*, an active individualized programme for the informal caregivers of people suffering from a psychiatric disorder in comparison to controls.
- The *Ensemble* programme is brief (5 sessions, once a week), tailored and offers different practical tools for informal caregivers to improve their health, quality of life and ability to cope with the patient's illness.
- The intervention provider endorses a facilitator role to improve informal caregivers' empowerment.
- Tailored early interventions are recommended because actual support given in practice lacks consideration of the informal caregivers' specific needs and should not depend on only the patient's treatment.
- No comparison with an active intervention (as a psychoeducation programme) presents a limitation.

Introduction

Care in the community has greatly improved the conditions of people with severe and persistent mental disorders. In this context, informal caregivers are significant partners, and appropriate support must be provided (1, 2). Although family and informal caregiver play a vital role in the early detection of mental health disorders and facilitating access to care, it is not easy for health professionals to develop such partnerships (3). Several studies have underscored the importance of supporting informal caregivers in their capacities to integrate their new caregiver's role (4-6). Moller-Leimkuhler (2006) demonstrated that informal caregivers need emotional support as soon as the diagnosis is made (7). Emotional support is essential in the moratorium stage of recovery (8, 9). When a patient's close informal caregiver first learns about a diagnosed psychiatric disorder, he or she might feel a range of emotions and might exhibit varied reactions linked to this stage (e.g., revolt, confusion, hopelessness, denial). In the second stage of recovery, relatives develop a greater awareness of the disorder, although this awareness can raise significant fears about the future. Feelings such as guilt, avoidance or a desire to give up can emerge (8, 9). It is therefore critical to intervene early during the first two stages of recovery to promote the health of informal caregivers and to reorient them away from unsuccessful coping strategies that might be harmful in the long term (8-10). Informal caregivers often feel helpless, lack confidence regarding how to help the sufferer, and experience shock when faced with a close relative suffering psychologically (11, 12). They can experience significant distress since they lack support and practical tools for managing the situation (4). Feelings of helplessness and uncertainty can be compounded by a lack of knowledge of the disorder and not knowing how to help the patient (13). Informal caregivers could become isolated due to the harmful effects of stigmatization, which can also have negative impacts on their health (14). Indeed, informal caregivers of people with severe psychiatric disorders can experience serious situations with potential negative consequences for their quality of life, their own health and the health of the patient (15-17). In order to help them developing effective coping strategies, interventions must be contextualized, culturally adopted and specified to the informal caregiver's role in order to fill individualized needs (18, 19). These diverse issues are crucial for understanding how to better support informal caregivers. The results of a meta-analysis of patients suffering from schizophrenia spectrum disorders showed that most programmes include information about the disease and focus on the development of communication and coping skills to reduce the negative effects on caregivers (20). Interventions for bipolar disorder are mainly based on the "vulnerability-stress model" and include information about how this illness impacts relatives, as well as training sessions on communication skills and problem-solving techniques (21). Interventions tested in a study of depressive disorders included theoretical input on aetiology, and they focused on the causes of depression, depressive symptoms, treatment and the development of coping strategies (22). Previous studies have also identified that informal

caregivers need tailored knowledge of the patient's illness, clarification of their roles and responsibilities, better control over their own lives and effective collaboration with health professionals (5, 6, 23-27). Additionally, scientific data recommend adjusting caregivers' support according to the phase and severity of illness, as well as the caregiver's sociodemographic characteristics (26). Most of the interventions published in the literature have focused on the ill family member and his or her support but not on the specific needs of informal caregivers as the core intervention. Lobban and colleagues (2013) presented an individualized programme that is self-managed and specific for relatives of people with recent-onset psychosis (11). To reduce the gap between scientific recommendations and actual practice, a tailored intervention called *Ensemble* (Together in English) was developed and tested in a pilot study (3, 28). The results of this pilot study showed that informal caregivers experience many difficulties and unmet needs regarding their caregiver role, as well as painful emotions, while having many social resources that are not specific to their individual needs. The participants had several difficulties in essential areas of life, such as family, children, romantic relationships and mental health. Regarding the primary outcome, the participants showed significant improvements in psychological health status as measured by the Global Severity Index (GSI), based on the Brief Symptom Inventory (BSI) scale (28). After five sessions, the 21 participants' psychological health statuses were improved compared with their pretest scores (pretest mean of the GSI score 0.72 vs. posttest GSI score mean 0.53). These findings emphasize that informal caregivers are at greater risk of developing psychological problems than those in non-clinical populations; for example, their mean GSI score pretest (0.72) was higher than that of a healthy British community sample (0.44) (29) and lower than that of a British psychiatric outpatient sample (1.65) (30). Informal caregivers were also more optimistic regarding their future at the end of the programme as a secondary outcome (mean pretest 15.52 vs. mean posttest 17.43).

The goal of the current study is to determine whether the *Ensemble* programme is clinically effective using a randomized, controlled, and assessor-blinded trial. A combination of *Ensemble* plus support as usual (SAU) will be compared to SAU alone.

This trial's main hypothesis is that five one-hour sessions of the Ensemble programme will lead to an improved psychological health state, as evaluated with the GSI score on the BSI scale, compared to those of the control group. The secondary hypothesis is that the Ensemble programme will increase optimism levels as measured on the LOT-R scale, improve quality of life as measured by the SF-36 scale and decrease the burden score on the Zarit scale. The study will also monitor the sustainability of the potential benefits at follow-up (two months after completing the Ensemble programme). Qualitative data through 20 semi-oriented interviews will provide information on outcomes concerning the experience and the added value of the programme for participants at the end of the study.

Methods: Participants, interventions, and outcomes

Study setting

The study is being conducted in four cantons of French-speaking Switzerland. Informal caregivers providing close support to persons with psychiatric disorders are the target population. "Informal caregiver", "caregiver" and "family caregiver" are terms used to describe family members, friends or significant others who provide this close support. In this area, no systematic or standardized individualized intervention for informal caregivers is implemented. Several sites in these four cantons are informed, and different partners actively support this project (a detailed list can be obtained from the authors) to reflect generalization issues. The main study site is La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. However, the research assessments and the meeting intervention can take place at the participants' homes or in other locations defined as appropriate by the participants and intervention providers. The research members will travel up to 3 hours one-way for these meetings and assessments.

Eligibility criteria

The study is open to informal caregivers of adult psychiatric patients with a burden score of at least 20 on the French Zarit Burden Interview (ZBI) version scale (31). This 22-item scale uses a five-point scale (0 = "never"; 4 = "nearly always") to assess the subjective burden (emotional, physical and financial) of an informal caregiver of an individual with a loss of autonomy. The total score can range from 0 to 88. A score less than or equal to 20 indicates a low burden; a score between 21 and 40 indicates a light burden; a score between 41 and 60 indicates a moderate burden; and a score greater than 60 indicates a severe burden. The inclusion criteria for informal caregivers are as follows: being at least 18 years old; living in French-speaking Switzerland; speaking French; and having an adult relative suffering from a psychiatric disorder (with or without an established diagnosis). One hundred sixty participants will be included in this study (n=80 for Ensemble+SAU; n=80 for SAU).

Recruitment

Participants will be recruited from the following family associations in French-speaking Switzerland: l'Îlot (VD), AFS Berne-Neuchâtel (NE), A3 Jura (JU) and APF (FR). Participants will also be recruited at "l'Espace Proches", which is a nonprofit association created in 2014 and a member of the Department of Health and Social Welfare (DSAS) and the Pallium Foundation. The services of this association are run by health and social professionals and focused on informing, orienting and supporting informal caregivers or relatives. Public mental health services will also be used to recruit participants. Meetings with the presidents of each association and professionals working in mental health services will be organized to present the project. Regular information about the research will be provided at these sites. A recruitment strategy aimed at general practitioners, local newspapers, schools and social and cultural centres, as well as social networks such as Facebook, will be deployed

to ensure equivalent treatment among informal caregivers who are isolated or not in contact with any association. Informal caregivers who are willing to participate will choose either to call the research coordinator or give their authorization to be contacted.

Interventions

Ensemble programme

Ensemble is a brief individualized intervention designed to promote the well-being of informal caregivers who experience the effects of their patients' psychiatric disorders. It is a five-session programme led by a nurse (who had two days of specific training), addressed to the informal caregiver and delivered independent of the patient's treatment. Figure 1 below demonstrates the objectives of the Ensemble programme and its process. The five sessions are described and allow the participant to take a step back on her/his informal caregiver's role.

Insert Figure 1 here

Clinical tools

Three clinical tools are used to specifically assess the needs, difficulties, painful emotions and social networks of the informal caregivers (Table 2). These clinical tools are systematic, structured, and easy to administer. The three clinical tools selected in the Ensemble programme are 1) the Difficulties and Needs Self-Assessment Tool, 2) the Painful Emotions Tool and 3) the Social Network Tool (3, 28, 32, 33).

Insert Table 2 here

Support as usual (SAU)

SAU was chosen as a control condition. Informal caregivers must often manage situations in different ways. SAU consists of informal support given by various structures. The patient's clinical team can provide support to the informal caregiver. Specific psychoeducation programmes tailored to the patient's illness (such as "Profamille" for schizophrenia) are also implemented in the French-speaking Switzerland context. Peer support depends on the voluntary work of family associations. Some general professional services such as "l'Espace Proches" focus on informing and orienting informal caregivers or relatives in the state of Vaud. No attempts have been made to standardize this treatment as SAU that depends on informal caregivers' needs, knowledge of the health system, and their capacity to be in contact with the patient's psychiatric team.

Outcomes

Quantitative data gathered through various standard instruments will inform the main and secondary outcomes. Table 3 summarizes the expected results.

Insert Table 3 here

Qualitative data will also inform some secondary outcomes. Content analysis will focus on not only informal caregivers' experiences but also their capacity to manage the situation. To narrate their experiences and construct meaning through heuristic narrative processes (34), the analysis of the categorization devices used by the participants will provide us with comprehensive insight into the types of experiences during the programme, different capacities and unmet needs.

Sample size

The sample size was estimated using the results of the pilot study regarding the main outcome of the expected BSI Global Index. For the sample size calculation, α was set at .05 with a power of β =.80. The effect size of the expected difference between the two groups was equal to Cohen's d= .470. Using an a priori computation for ANCOVA, the proposed trial required a total sample size of 144 participants for the two arms, 72 in each arm. In the pilot study, one of 22 participants dropped out, resulting in a dropout rate of approximately 5%; to increase security in the proposed study, a drop-up rate of 10% will be considered, corresponding to a dropout number of 22 participants, so the present study will recruit 160 participants. Between-group differences in pre- and posttest values will be examined using analysis of covariance (ANCOVA).

Participant timeline and RCT process

Figure 2 shows the clear and synthetic timeline of participant interactions and this RCT process.

Insert Figure 2 here

Allocation

The Research Electronic Data Capture (REDCap) platform will be used to randomize the participants. REDCap is a secure, web-based application designed to support data capture for research studies. It developed a module that allows a defined randomization model be implemented within the project. The randomization by group/site model was defined. A randomization table was created by the data manager and imported to the project database to structure the allocation. REDCap will randomize the participants according to this table, which is not available to the research team. A total of 180 assignments in the allocation table were included to accommodate possible drop-outs and additional enrolment of participants.

A person not involved in the execution of the project will confirm that the eligibility data are complete in order to proceed with the randomization. She/he will then inform the intervention provider of the allocated arm.

The intervention provider will inform the participants whether they are in the intervention arm, but the assessor will not be informed of hers/his treatment group allocation.

The role of the assessor is to ensure the connexion to the REDCap platform that holds the research questionnaires. The assessor responds to eventual questions about item understandings during the assessment. The assessor is blind and reminds the participant not to communicate hers/his treatment group allocation at the beginning of every encounter at T1 and T2. The assessor will also collaborate with one of the investigators at the end of the study to collect qualitative data.

The research assistants will alternatively play the role of either the assessor or the intervention provider to diversify their work and develop specific competences related to each role. To maintain blindness of assessment, several conditions have been set: one assistant researcher will take the role of assessor for the first five participants before providing the intervention for the next five. Another assistant researcher will do the opposite and so on. If a leak of allocation occurs, this information will be noted, and analyses concerning the eventual impacts will be conducted. However, all standardized questionnaires are basically self-administered.

The interventions will take place in a building other than the assistants' office. The supervision between interventions will be individualized and organized by one of the two lead investigators.

Data collection, management and analysis

Study data will be collected and managed using REDCap electronic data capture tools hosted at HES-SO Fribourg. REDCap provides 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Primary outcome:

The BSI aims to assess psychological symptoms and psychological distress. It includes 53 items organized into 9 primary and clinically relevant symptom dimensions: 1) somatization; 2) obsessive-compulsive; 3) interpersonal sensitivity; 4) depression; 5) anxiety; 6) hostility; 7) phobic anxiety; 8) paranoid ideation; and 9) psychoticism (35). This scale also has three global distress indices: the GSI, the Positive Symptom Distress Index (PSDI) and the Positive Symptom Total (PST). The BSI scale has been used in a variety of clinical and counselling settings as a screening tool for mental disorders and as a method of measuring symptom reduction (36-39). It has also been used to assess the psychological health status of informal caregivers (28, 40, 41). The GSI of the BSI scale was used as one of the main outcome measures in the pilot study and represents the mean of the nine primary symptom dimensions and is more sensitive than the two other global indices (35). Higher GSI scores indicate a greater effect on informal caregivers' psychological health. The validation of the French BSI scale indicated good internal consistency for the GSI score (α=0.91) (42).

Secondary outcomes:

The French ZBI includes 22 items to assess the subjective burden (emotional, physical and financial) of an informal caregiver of an individual with a loss of autonomy (31). The total score can range from 0 to 88. A score less than or equal to 20 indicates a low burden; a score between 21 and 40 indicates a light burden; a score between 41 and 60 indicates a moderate burden; and a score greater than 60 indicates a severe burden. This questionnaire has been mainly used for chronic illnesses such as dementia, palliative care or mental disorders (43-45).

The Life Orientation Test – Revised (LOT-R) developed by Scheier, Carver and Bridges (46) measures an individual's optimism regarding a given situation. This self-administered scale measures the adaptive strategies correlated with well-being and is used to evaluate optimism versus pessimism. The LOT-R has been translated and validated in French, with good psychometric proprieties (internal consistency α=0.76) (47). The scale includes 10 items: three items measure optimism, three others measure pessimism, and four items function as fillers. The participants respond to each item on a 5-point Likert scale ranging from zero (strongly disagree) to four (strongly agree); the four filler items are not included in the total score calculation. Higher scores suggest more optimism. Optimism has been shown to be negatively correlated with distress (48, 49) and to positively influence quality of life (50). Among informal caregivers in particular, optimism promotes engagement in supportive programmes (51), whereas pessimism leads to the use of avoidance strategies, which can predict informal caregiver burden (52).

The 36-item Medical Outcome Study Short-Form Health Survey (SF-36) developed by Ware and Sherbourne (53) measures some health indicators related to quality of life. It includes 36 items and is used in clinical and general population settings to evaluate eight health dimensions: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. Two global scores – 1) a Physical Component Score (PCS) and 2) the Mental Component Score (MCS) – are obtained by grouping the eight dimensions, and these two synthetic variables allow different populations to be compared. The French version of the SF-36 was validated by obtaining Cronbach's (reliability) coefficients ranging from 0.76 to 0.92 (54-57). In clinical settings, this type of measure can also help professionals orient informal caregivers towards a targeted intervention (58, 59).

The different standard measures will be used in the three standard evaluations (T0=pretest; T1=posttest at an average of 2 months and T2=follow-up at an average of 4-5 months). A research assistant trained to answer technical questions will be present during the questionnaire's completion.

Sociodemographic data will be collected at T0: sex, age, education level, professional activity, the nature of their relationship with the patient, whether they live with the patient, the number of close contacts and previous requests for help. Information about the patient will complete the sociodemographic data: the patient's sex, age, diagnosis according to the caregivers, and the duration and severity of the patient's illness. The Social and Occupational Functioning Assessment Scale (SOFAS) will be used to measure the severity of the patient's illness. The SOFAS will also be administered at T2 to compare eventual improvements by the patient according to the informal caregiver.

The Satisfaction Scale concerning the Ensemble programme was developed and used in the pilot study (28). This scale will be used only in the posttest evaluation of the intervention group to show the participants' satisfaction.

The qualitative data will be collected through semi-directive interviews. They will aim to provide significant information regarding participant experiences in the programme (capacities to manage painful emotions and difficulties worked on during the programme and to have and increase awareness of the informal caregiver's role). Concerns about the programme's eventual improvement will also be recorded.

Semi-directive interviews will be conducted at the end of the study with twenty selected participants to explore their experiences participating in the Ensemble programme. These participants will be selected at the end of the intervention for each randomization group. Two groups of participants will be included in this phase: those who have benefited greatly from the program (G1; n=10) and those who have benefited less (G2; n=10). This stratification of the sample will allow us to better understand the added value of the Ensemble programme and to identify areas for improvement. The process for this step occurs in two phases: 1) the participant receives information at the time of recruitment and agrees to participate (not only in the project itself but also to the semi-directive interview) and 2) the research team contacts the participants who have consented. Detailed information and conditions will then be given. The participants will have time to read the conditions and think about their participation in this research step. At the time of the interview, before starting the interview and its audio recording, a few minutes will be dedicated to potential questions about the information and consent form or other interrogations. Qualitative data collection will thus constitute both an autonomous inquiry and an opportunity to enrich data obtained through standardized questionnaires (60). Participants will also be able to express their views about possible improvements to the programme during these interviews.

The questionnaires will be checked at the end of each assessment meeting for the presence of missing data and to reach agreement about how to complete these missing data.

Table 4 presents the plan to retain participants and the completed list of the collected data.

Insert Table 4 here

Analysis

Primary analyses will be conducted on an intent-to-treat basis. To ensure the statistical analyses, a researcher responsible for the analysis will be involved. He/she will double control the final quantitative data before analyses and check the different tests. The following analyses are planned: between-group differences in pre- and posttest values will be examined using an analysis of covariance (ANCOVA) for each outcome variable for the quantitative data. Differences between pretest and posttest scores, as well as between pretest and follow-up scores, will be treated as dependent variables; treatment conditions will be treated as a fixed factor, and pretreatment scores will be treated as covariates. Between-subjects Cohen's d effect sizes will be calculated at posttest and follow-up. For within subjects, Cohen's d will be calculated between the pre- and posttest and between the pretest and follow-up, correcting for dependence among means.

The content analysis of the qualitative data will focus on informal caregivers' experiences, as well as their capacity to manage situations. The aim of this analysis is to provide us with a participant's comprehensive insight into the types of experiences during the programme, their different capacities and unmet needs.

Monitoring

Data will be accessible to the investigators and the research assistants during the project. The REDCap platform will control this accessibility. Relevant data will be accessible by a login password to only staff members of this project depending on their responsibilities. For example, an assistant scientific researcher involved in the randomization phase will only access these data. The data set will be controlled by investigators and transferred to SPSS software before the final analyses. The investigators using the REDCap platform will ensure the traceability of the data and present all the aspects to the audit trial member.

A person external to the project and the institution will audit the data and the project process once a year. She/he will perform the following functions:

- Consent checks (100%);
- Verification of raw data (1st participant all data; for the other participants several randomly selected data);

- Verification of CRF completeness and consistency: data consistency, data reconciliation, data cleaning, generation of subsequent queries, data derivation, data set formatting prior to statistical analysis, table shells, depersonalization, and anonymization;

Ethics and dissemination

The research protocol received full authorization from the Human Research Ethics Committee of the Vaud State, Switzerland. Participants will be informed about the study and their rights and sign a written informed consent form. All data will be archived for 10 years after study termination or premature termination of the study. The data pertaining to the hypothesis will be mostly published in open access journals. After priority publications, metadata following FAIR recommendations will be accessible on the FORSbase platform to allow other researchers to access these data, to proceed with other secondary analyses and to enrich research. This trusted platform offers the possibility of archiving and ensuring the long-term visibility and preservation of the data. Access to the data files will be granted only to researchers external to the project who meet the criteria required by FORSbase.

Adverse event management

Informal caregivers could present painful emotions and could need care for their own health conditions at the beginning of the project and during it. Ethical recommendations allow for those experiencing such adverse events to be enrolled, as they present significant symptoms that are not immediately life-threatening (61). The principal investigators will be informed within 24 hours and will assess the severity of the event as mild, moderate or severe. Mild complications are tolerable, moderate complications interfere with daily activities, and severe complications render daily activities impossible. If a severe adverse event occurs according to Art. 63 (61), the research project will be interrupted and the ethics committee will be notified about the circumstances within 15 days according to HRO Art. 212 (61). Only one severe adverse event not related to the research project occurred during the pilot study. The participant decided merely to stop the project to have time for individual care related to advanced cancer. The informed consent materials and information sheets given to participants are available in French and English through the following website: https://www.seretablir.net/ensemble/

Declaration of interests

The authors declare that they have no competing interests.

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Table 1: WHO Trial registration Data Set of Ensemble RCT

Data Category	Information
Primary Registry and Trial Identifying Number	ClinicalTrials.gov: NCT04020497
Date of Registration in Primary Registry	July 16, 2019
Secondary Identifying Numbers	The Federal Office of Public Health's (FOPH) portal for human research in Switzerland NCT04020497 | SNCTP000003434
Source(s) of Monetary or Material Support	Swiss National Science Foundation (SNF) 10001C_185422
Primary Sponsor	Shyhrete Rexhaj
Secondary Sponsor(s)	Jérôme Favrod
Contact for Public Queries	Shyhrete Rexhaj, s.rexhaj@ecolelasource.ch; +41 21 556 44 35; Avenue Vinet 30; 1004 Lausanne, Vaud, Switzerland
Contact for Scientific Queries	Shyhrete Rexhaj, PhD, Professor associate
Public Title	Programme Ensemble: an early intervention for informal caregivers in psychiatry
Scientific Title	Ensemble programme an early intervention for informal caregivers of psychiatric adult patients: a protocol for a randomized controlled trial Ensemble RCT
Countries of Recruitment	Switzerland
Health Condition(s) or Problem(s) Studied	Psychological Distress, quality of life
Intervention(s)	Support as usual (SAU) Informal caregivers often have to manage the situation in various ways. SAU alone consists of informal support by the patient's clinical team. There are specific psychoeducational programs depending on the patient's illness (such as "Profamille" for schizophrenia) or peer-support depending to the voluntary work of the families' associations. Some general professional services focused on informal caregivers or relatives in order to inform and orient them if they need are available in the study area. No attempts have been made to standardize this treatment.
	Ensemble programme plus support as usual (SAU) The five-session Ensemble program provides targeted support to informal caregivers. It addresses informal caregiver's specific unmet needs, emotions and social resources in order to adapt care activities to each participant.
Key Inclusion and Exclusion Criteria	Inclusion Criteria: Being at least 18 years old; living in the French-speaking Switzerland cantons (commonly referred to as "Romandie") speaking French; having an adult relative suffering from a psychiatric disorder (with or without an established diagnosis); and having the capacity to agree to participate in the project
	Exclusion Criteria: Less than 20 on the Zarit score.
Study Type	Interventional
	Allocation: randomized; intervention model: parallel assignment; masking: assessor blind
	Primary purpose: health prevention and promotion
Date of First Enrollment	October 2019
Sample Size	160
Recruitment Status	Recruiting
Primary Outcome(s)	Psychological state change on the Global Severity Index (GSI): Timepoint: Baseline; at post-test, at 2 months follow
Key Secondary Outcomes	Optimism change on the Life Orientation Test-Revised (LOT-R) Timepoint: Baseline; at post-test, at 2 months follow Quality of life change on the Mental Component Score (MCS) Timepoint: Baseline; at post-test, at 2 months follow Burden level change on the Zarit Burden Interview (ZBI) Timepoint: Baseline; at post-test, at 2 months follow Standardized severity of the patient's illness changes on the Social an Occupational Functioning Assessment Scale (SOFAS) Timepoint: Baseline; at 2 months follow Qualitative participants' experiences concerning Ensemble benefits
Ethics Review	Approved; 28 August 2019; La Commission cantonale d'éthique de la recherche sur l'être humain (CER-VD)
Completion date	30 April, 2023

Table 2. Clinical tools

Clinical tools	Description
The Difficulties and Needs Self-Assessment Tool (ELADEB)	The ELADEB includes two independent scales, one focusing on difficulties and the other focusing on support for unmet needs. Twenty-one areas of life that enable identification of priority problems and orientation of support according to the level of emergency are assessed. These 21 areas of life are organized into 4 life dimensions: life conditions, daily pragmatic activities, relationships and health.
The Painful Emotions Tool	It uses pictures that reflect painful emotions such as guilt, judgment from others, loneliness, sadness, distress, despair, anxiety, helplessness, anger, confusion and shame. The participant selects the painful emotions that are present in his/her life. The tool also assesses the frequency of the emotions. Consequently, the support provided is targeted to the caregiver's most painful emotions.
The Social Network Tool	It uses a network map that specifies the social resources available to the caregiver. This tool provides a graphic representation aimed at identifying the informal caregiver's primary, secondary and tertiary environment.

Table 3: Expected quantitative results

Outcome	Question	Data	Analysis	Expected result
Main	Is the psychological state improved?	*Global Severity Index on the Brief Symptom Inventory*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically significantly improved compared to SAU
Secondary	Is optimism improved?	*Life Orientation Test – Revised*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically significantly improved compared to SAU
	Is quality of life improved?	*36-item Medical Outcome Study Short-Form Health Survey - Mental Component Score*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically significantly improved compared to SAU
	Is the burden reduced?	*Zarit Burden Interview*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically showed significant reduction compared to SAU
	Is the patient's social and occupational function improved?	*Social and Occupational Functioning Assessment Scale*	ANCOVA of T0-T2, T0 as dependent, treatment condition as fixed factor	Experimental group statistically reported improvements for patients compared to SAU

SAU = Support as usual

Table 4. Ensemble risk reduction protocol schedule of assessments and procedures

Procedures/assessments	CRF (Yes/No)	Staff member	Time (min)	-1 Screening/ consent	T0 Baseline/ randomization	1st and 2nd Month Ensemble vs support as usual	T1 Post-test	T2 Follow-up 4-months
Oral and written information	No	Research collaborator	20	√				
Consent	No	Research collaborator	30	√				
Eligibility criteria assessment	Yes	Research collaborator	10		√			
Sociodemographic questionnaire	Yes	Assessor			√			
The French Zarit Burden Interview (ZBI)	Yes	Assessor			√		√	√
Randomization - Computer-generated	Yes	A specific randomization coordinator	10		√			
The Brief Symptom Inventory (BSI)	Yes	Assessor			√		√	√
The Life Orientation Test – Revised (LOT-R)	Yes	Assessor			√		√	√
The 36-item Medical Outcome Study Short-Form Health Survey (SF-36)	Yes	Assessor			√		√	√
The Social and Occupational Functioning Assessment Scale (SOFAS)	Yes	Assessor			√			√
Qualitative data by 20 semi-directed interviews with participants in intervention	No	Two research collaborators						√
Treatment group	Yes	Intervention provider	360			√		
All groups, being in touch and continuing information	No	Intervention provider	30			√		
Supervision of intervention provider	No	Study coordinator	According to need			Continuously		
Termination of the study		Study coordinator	According to need			Continuously		
Serious adverse event form		Study coordinator	According to need			Continuously		
Progress notes	No	All team members	According to need			Continuously		

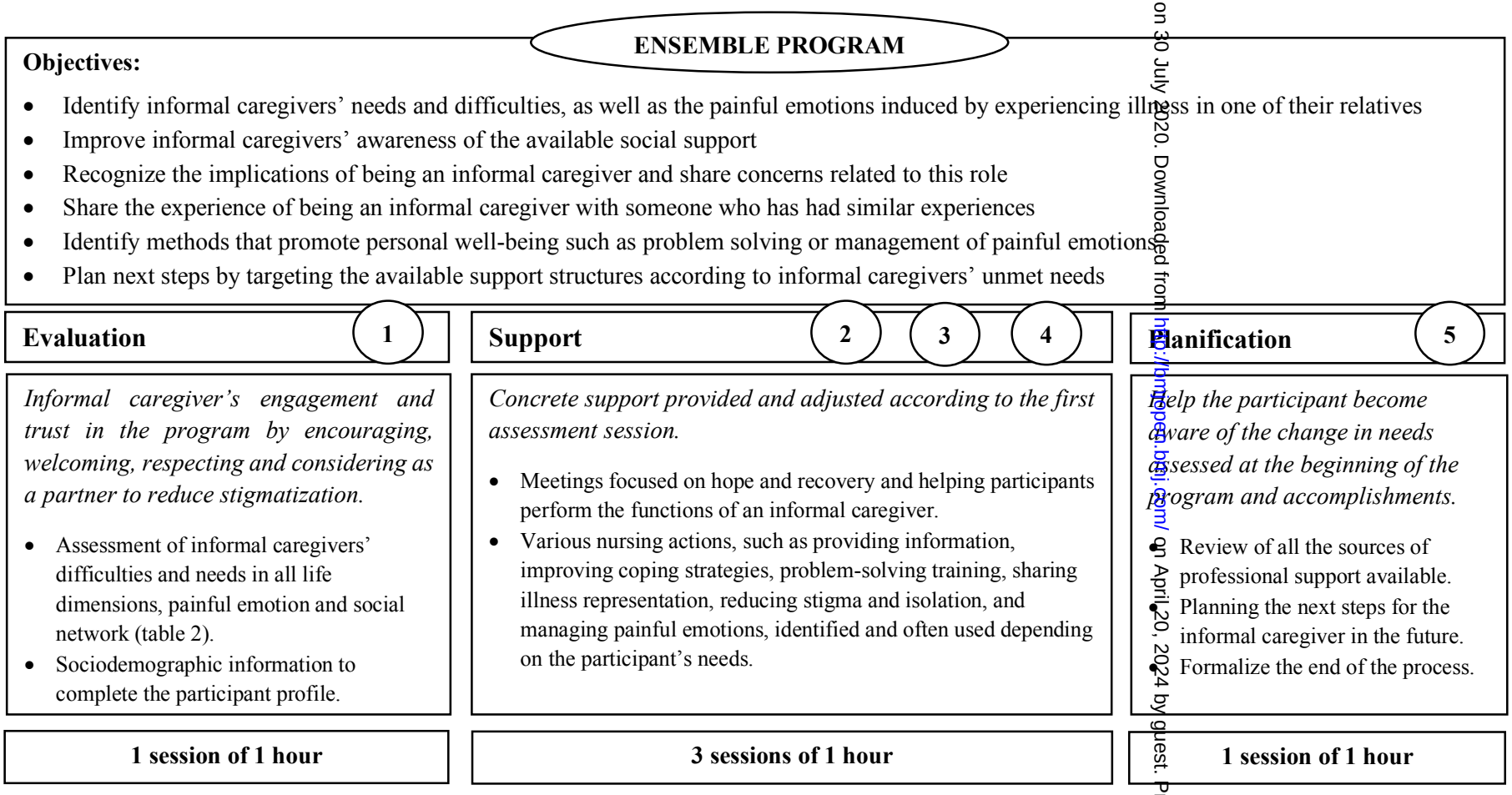

Figure 1. Ensemble program and process

Figure 2. RCT Flowchart

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	1
Protocol version	#3	Date and version identifier	1
Funding	#4	Sources and types of financial, material, and other support	1
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1-2
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	2
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	2
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	2

Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and	6

		individuals who will perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	7
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	7
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7-8
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended	8

		(see Figure)	
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	8
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	8
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8-9

Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8-9
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8-9
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	9-11
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values).	12

		Reference to where details of data management procedures can be found, if not in the protocol	
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	12
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	
Methods: Monitoring			12
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	12
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	12
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial	12

		conduct	
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	12-13
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	13
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	13
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	13
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	13
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	13
Declaration of	#28	Financial and other competing interests for principal	13

interests		investigators for the overall trial and each study site	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	13
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	13
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	13
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	13
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	13
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	13
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

BMJ Open

Ensemble programme for early intervention in informal caregivers of psychiatric adult patients: a protocol for a randomized controlled trial

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Complete List of Authors:	Rexhaj, Shyhrete; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. Monteiro, Shadya; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. Golay, Philippe; CHUV, Community Psychiatry Service, Department of Psychiatry, Lausanne Coloni-Terrapon, Claire; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. Wenger, Daniel; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. Favrod, J; HES-SO, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
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Ensemble programme for early intervention in informal caregivers of psychiatric adult patients: a protocol for a randomized controlled trial

Ensemble RCT

Trial registration:

ClinicalTrials.gov: NCT04020497

Insert Table 1 here: items from the World Health Organization Trial Registration Data Set

Protocol version

28 August 2019, version 2, Project ID-2019-01181

The key revisions to version 1 of the protocol were linked with ethics concerns regarding added value for qualitative data and the specification for their collection and analysis. Information concerning timepoint data collection and time needed to complete the questionnaires was also detailed in the participants' information sheets.

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Authors

- Shyhrete Rexhaj (SR), La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Shadya Monteiro (SM). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Philippe Golay (PG). Community Psychiatry Service, Department of Psychiatry, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland.
- Claire Coloni-Terrapon (CCT). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Daniel Wenger (DW). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Jérôme Favrod (JF). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.

Shyhrete Rexhaj [Corresponding Author]
s.rexhaj@ecolelasource.ch

Authors` contributions

SR and JF designed the study and are grant holders. DW, SM and CCT collected the data and provided the intervention. SR and JF developed the intervention. SR and SM delivered the study material (for example, the recruitment process, programme figures and web information). SR provided training support for the intervention and data collection during the study. SR led the study but was replaced by JF during maternity leave. PG, JF and SR developed the statistical plan and provided statistical support for the study. SR and SM wrote the first version of the paper. All authors contributed to a critical review and approve the final paper.

Trial sponsor, committee and data manager:

La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.

Shyhrete Rexhaj, s.rexhaj@ecolelasource.ch; Telephone: +41 21 556 44 35

The project manager (SR) will be involved in the analysis and interpretation of data, writing of the report, and the decision to submit the report for publication.

The finding source FOPH had no role in the design of this study and will have no responsibility during its execution.

La Source is the only coordinated centre and serves all recruited participants, even those from other French-speaking areas of Switzerland. Lead investigators SR and JF will review the process of the study if necessary. SR, as the principal investigator, is responsible for ethical considerations (providing an annual risk report to the ethics committee, providing information on serious adverse events, and announcing any change in the protocol if necessary) and for the study procedures (management of the team and responsible for the data file and budget administration). Noémie Laverne, who was not involved in the execution of the project, is responsible for randomization even for participants who were randomly by computer, as the computer system requires oversight.

The data manager Anne-Laure Kauffman maintains the trial IT system using the REDCap platform and will audit all procedures of the study once a year.

Acknowledgements

We thank Prof. Charles Bonsack and Prof. Claude Leclerc for their valuable value in the development of the intervention. We thank Dr Engelhorn for a donation in the first step of the programme development. We also thank members of ÎLOT (The association of informal caregivers for mental disorders, in Vaud state, Switzerland).

Abstract:

Introduction: Informal caregivers play a major role in the support and maintenance of community patients with severe psychiatric disorders. A pilot study showed that an individualized brief intervention such as the Ensemble programme leads to significant improvements in psychological health state and optimism. **Methods and analysis:** This randomized clinical trial (RCT) aims to compare the efficacy of using Ensemble in improving informal caregivers' psychological health states and the ability to play an active role in their situations with that of support as usual (SAU). Improvements on the psychological health global index will be measured three times (T0-pre, T1-post and T3 two-month follow) with standardized questionnaires (the Global Severity Index of Brief Inventory Symptoms, the Life Orientation Test-Revised, the 36-item Medical Outcome Study Short-Form Health Survey and the French Zarit Burden Interview). Differences between groups in post- and pre-test values will be examined using an analysis of covariance (ANCOVA) for each outcome variable. The severity of illness measured by the Social and Occupational Functioning Assessment Scale (SOFAS) will also be collected at T0 and T2 to compare eventual patient improvements. At the end of the programme, the experiences of the 20 patients participating in the Ensemble programme will be evaluated qualitatively.

Ethics and dissemination: The research protocol received full authorization from the Human Research Ethics Committee of the Vaud State, Switzerland. The principal paper will concern the results of the experimental design used to test the Ensemble programme. The research team will prioritize open access publications.

Strengths and limitations of this study

- This is the first randomized controlled trial in Switzerland to test *Ensemble*, an active individualized programme for the informal caregivers of people suffering from a psychiatric disorder in comparison to controls.
- The *Ensemble* programme is brief (5 sessions, once a week), tailored and offers different practical tools for informal caregivers to improve their health, quality of life and ability to cope with the patient's illness.
- The intervention provider endorses a facilitator role to improve informal caregivers' empowerment.
- Tailored early interventions are recommended because actual support given in practice lacks consideration of the informal caregivers' specific needs and should not depend on only the patient's treatment.

- No comparison with an active intervention (as a psychoeducation programme) presents a limitation.

Introduction

Care in the community has greatly improved the conditions of people with severe and persistent mental disorders. In this context, informal caregivers are significant partners, and appropriate support must be provided (1, 2). Although family and informal caregiver play a vital role in the early detection of mental health disorders and facilitating access to care, it is not easy for health professionals to develop such partnerships (3). Several studies have underscored the importance of supporting informal caregivers in their capacities to integrate their new caregiver's role (4-6). Moller-Leimkuhler (2006) demonstrated that informal caregivers need emotional support as soon as the diagnosis is made (7). Emotional support is essential in the moratorium stage of recovery (8, 9). When a patient's close informal caregiver first learns about a diagnosed psychiatric disorder, he or she might feel a range of emotions and might exhibit varied reactions linked to this stage (e.g., revolt, confusion, hopelessness, denial). In the second stage of recovery, relatives develop a greater awareness of the disorder, although this awareness can raise significant fears about the future. Feelings such as guilt, avoidance or a desire to give up can emerge (8, 9). It is therefore critical to intervene early during the first two stages of recovery to promote the health of informal caregivers and to reorient them away from unsuccessful coping strategies that might be harmful in the long term (8-10). Informal caregivers often feel helpless, lack confidence regarding how to help the sufferer, and experience shock when faced with a close relative suffering psychologically (11, 12). They can experience significant distress since they lack support and practical tools for managing the situation (4). Feelings of helplessness and uncertainty can be compounded by a lack of knowledge of the disorder and not knowing how to help the patient (13). Informal caregivers could become isolated due to the harmful effects of stigmatization, which can also have negative impacts on their health (14). Indeed, informal caregivers of people with severe psychiatric disorders can experience serious situations with potential negative consequences for their quality of life, their own health and the health of the patient (15-17). In order to help them developing effective coping strategies, interventions must be contextualized, culturally adopted and specified to the informal caregiver's role in order to fill individualized needs (18, 19). These diverse issues are crucial for understanding how to better support informal caregivers. The results of a meta-analysis of patients suffering from schizophrenia spectrum disorders showed that most programmes include information about the disease and focus on the development of communication and coping skills to reduce the negative effects on caregivers (20). Interventions for bipolar disorder are mainly based on the "vulnerability-stress model" and include information about how this illness impacts relatives, as well as training sessions on communication skills and problem-solving techniques (21). Interventions tested in a study of depressive disorders included theoretical

input on aetiology, and they focused on the causes of depression, depressive symptoms, treatment and the development of coping strategies (22). Previous studies have also identified that informal caregivers need tailored knowledge of the patient's illness, clarification of their roles and responsibilities, better control over their own lives and effective collaboration with health professionals (5, 6, 23-27). Additionally, scientific data recommend adjusting caregivers' support according to the phase and severity of illness, as well as the caregiver's sociodemographic characteristics (26). Most of the interventions published in the literature have focused on the ill family member and his or her support but not on the specific needs of informal caregivers as the core intervention. Lobban and colleagues (2013) presented an individualized programme that is self-managed and specific for relatives of people with recent-onset psychosis (11). To reduce the gap between scientific recommendations and actual practice, a tailored intervention called *Ensemble* (Together in English) was developed and tested in a pilot study (3, 28). The results of this pilot study showed that informal caregivers experience many difficulties and unmet needs regarding their caregiver role, as well as painful emotions, while having many social resources that are not specific to their individual needs. The participants had several difficulties in essential areas of life, such as family, children, romantic relationships and mental health. The needs of each caregiver differ between the participants which confirm the necessity of individualized support (29). Comparing Ensemble to psychoeducational programs or counselling programme would involve tailoring the support to the need of each participant. The support sessions offer different practical exercises and tools (problem solving, positive communication and assertiveness, involvement as an informed caregiver, emotional support…), which need to be adapted to each participant.

Regarding the primary outcome of the Ensemble pilot study, the participants showed significant improvements in psychological health status as measured by the Global Severity Index (GSI), based on the Brief Symptom Inventory (BSI) scale (28). After five sessions, the 21 participants' psychological health statuses were improved compared with their pretest scores (pretest mean of the GSI score 0.72 vs. posttest GSI score mean 0.53). These findings emphasize that informal caregivers are at greater risk of developing psychological problems than those in non-clinical populations; for example, their mean GSI score pretest (0.72) was higher than that of a healthy British community sample (0.44) (30) and lower than that of a British psychiatric outpatient sample (1.65) (31). Informal caregivers were also more optimistic regarding their future at the end of the programme as a secondary outcome (mean pretest 15.52 vs. mean posttest 17.43).

The goal of the current study is to determine whether the *Ensemble* programme is clinically effective using a randomized, controlled, and assessor-blinded trial. A combination of *Ensemble* plus support as usual (SAU) will be compared to SAU alone.

This trial's main hypothesis is that five one-hour sessions of the Ensemble programme will lead to an

improved psychological health state, as evaluated with the GSI score on the BSI scale, compared to those of the control group. The secondary hypothesis is that the Ensemble programme will increase optimism levels as measured on the LOT-R scale, improve quality of life as measured by the SF-36 scale and decrease the burden score on the Zarit scale. The study will also monitor the sustainability of the potential benefits at follow-up (two months after completing the Ensemble programme). Qualitative data through 20 semi-oriented interviews will provide information on outcomes concerning the experience and the added value of the programme for participants at the end of the study.

A study summary according to the World Health Organization Trial Registration Data Set items is presented in Table 1.

Insert Table 1 here

Methods: Participants, interventions, and outcomes

Study setting

The study is being conducted in four cantons of French-speaking Switzerland. Informal caregivers providing close support to persons with psychiatric disorders are the target population. "Informal caregiver", "caregiver" and "family caregiver" are terms used to describe family members, friends or significant others who provide this close support. In this area, no systematic or standardized individualized intervention for informal caregivers is implemented. Several sites in these four cantons are informed, and different partners actively support this project (a detailed list can be obtained from the authors) to reflect generalization issues. The main study site is La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. However, the research assessments and the meeting intervention can take place at the participants' homes or in other locations defined as appropriate by the participants and intervention providers. The research members will travel up to 3 hours one-way for these meetings and assessments.

Eligibility criteria

The study is open to informal caregivers of adult psychiatric patients with a burden score of at least 20 on the French Zarit Burden Interview (ZBI) version scale (32). This 22-item scale uses a five-point scale (0 = "never"; 4 = "nearly always") to assess the subjective burden (emotional, physical and financial) of an informal caregiver of an individual with a loss of autonomy. The total score can range from 0 to 88. A score less than or equal to 20 indicates a low burden; a score between 21 and 40 indicates a light burden; a score between 41 and 60 indicates a moderate burden; and a score greater than 60 indicates a severe burden. The inclusion criteria for informal caregivers are as follows: being at least 18 years old; living in French-speaking Switzerland; speaking French; and having an adult

relative suffering from a psychiatric disorder (with or without an established diagnosis). One hundred sixty participants will be included in this study (n=80 for Ensemble+SAU; n=80 for SAU). In this study, a self-report identification as informal caregivers is selected to offer support to all informal caregivers according to their needs independently of their direct implication in caregiving to patient.

Recruitment

Participants will be recruited from the following family associations in French-speaking Switzerland: l'Îlot (VD), AFS Berne-Neuchâtel (NE), A3 Jura (JU) and APF (FR). Participants will also be recruited at "l'Espace Proches", which is a nonprofit association created in 2014 and a member of the Department of Health and Social Welfare (DSAS) and the Pallium Foundation. The services of this association are run by health and social professionals and focused on informing, orienting and supporting informal caregivers or relatives. Public mental health services will also be used to recruit participants. Meetings with the presidents of each association and professionals working in mental health services will be organized to present the project. Regular information about the research will be provided at these sites. A recruitment strategy aimed at general practitioners, local newspapers, schools and social and cultural centres, as well as social networks such as Facebook, will be deployed to ensure equivalent treatment among informal caregivers who are isolated or not in contact with any association. Informal caregivers who are willing to participate will choose either to call the research coordinator or give their authorization to be contacted.

Patient and Public Involvement

No patient involved

Interventions

Ensemble programme

Ensemble is a brief individualized intervention designed to promote the well-being of informal caregivers who experience the effects of their patients' psychiatric disorders. It is a five-session programme led by a nurse (who had two days of specific training), addressed to the informal caregiver and delivered independent of the patient's treatment. Figure 1 below demonstrates the objectives of the Ensemble programme and its process. The five sessions are described and allow the participant to take a step back on her/his informal caregiver's role.

Insert Figure 1 here

Clinical tools

Three clinical tools are used to specifically assess the needs, difficulties, painful emotions and social networks of the informal caregivers (Table 2). These clinical tools are systematic, structured, and easy to administer. The three clinical tools selected in the Ensemble programme are 1) the Difficulties and Needs Self-Assessment Tool, 2) the Painful Emotions Tool and 3) the Social Network Tool (3, 28, 33, 34).

Insert Table 2 here

Support as usual (SAU)

SAU was chosen as a control condition. Informal caregivers must often manage situations in different ways. SAU consists of informal support given by various structures. The patient's clinical team can provide support to the informal caregiver. Specific psychoeducation programmes tailored to the patient's illness (such as "Profamille" for schizophrenia) are also implemented in the French-speaking Switzerland context. Peer support depends on the voluntary work of family associations. Some general professional services such as "l'Espace Proches" focus on informing and orienting informal caregivers or relatives in the state of Vaud. No attempts have been made to standardize this treatment as SAU that depends on informal caregivers' needs, knowledge of the health system, and their capacity to be in contact with the patient's psychiatric team.

Ensemble programme's implantation

Three nurses are trained to deliver the programme. The training took to days and is organised in four sessions.

Session 1: issues concerning support for family caregivers, theoretical foundations of the Ensemble program, professional posture and informal caregivers' health considerations.

Session 2: Ensemble Program: tailored support, structured and individualized process, assessment of difficulties and needs, painful emotions and social resources, practical training to use the clinical tools with a vignette designed from the pilot phase, issues concerning the awareness of the informal caregiver's role.

Session 3: Practical exercises of the support tools - problem solving, positive communication and assertiveness, and involvement as an informed caregiver.

Sessions 4: Practical exercises of the support tools - emotional support, isolation and peer support, and referral to appropriate structures.

In addition to this training, nurses received a manual protocol and are supervised for every clinical situation. To ensure the standardisation on delivery, two supervisions moments are planned: the first after the first meeting between the nurse and the participants and the second before their last meeting. The place for delivery of the sessions are in a private and quiet room located to the nursing school, or in a clinical local or in the participant's home. Sometime if the participant prefers the delivery could

take place in the "tea-room or hotel" but this option is retained only if the other options are not suitable for the participant.

Outcomes

Quantitative data gathered through various standard instruments will inform the main and secondary outcomes. Table 3 summarizes the expected results.

Insert Table 3 here

Qualitative data will also inform some secondary outcomes. Content analysis will focus on not only informal caregivers' experiences but also their capacity to manage the situation. To narrate their experiences and construct meaning through heuristic narrative processes (35), the analysis of the categorization devices used by the participants will provide us with comprehensive insight into the types of experiences during the programme, different capacities and unmet needs.

Sample size

The sample size was estimated using the results of the pilot study regarding the main outcome of the expected BSI Global Index. For the sample size calculation, α was set at .05 with a power of β =.80. The effect size of the expected difference between the two groups was equal to Cohen's d= .470. Using an a priori computation for ANCOVA, the proposed trial required a total sample size of 144 participants for the two arms, 72 in each arm. In the pilot study, one of 22 participants dropped out, resulting in a dropout rate of approximately 5%; to increase security in the proposed study, a drop-up rate of 10% will be considered, corresponding to a dropout number of 22 participants, so the present study will recruit 160 participants. Between-group differences in pre- and posttest values will be examined using analysis of covariance (ANCOVA).

Participant timeline and RCT process

Figure 2 shows the clear and synthetic timeline of participant interactions and this RCT process.

Insert Figure 2 here

Allocation

The Research Electronic Data Capture (REDCap) platform will be used to randomize the participants. REDCap is a secure, web-based application designed to support data capture for research studies. It developed a module that allows a defined randomization model be implemented within the project. The randomization by group/site model was defined. A randomization table was created by the data manager and imported to the project database to structure the allocation. REDCap will randomize the participants according to this table, which is not available to the research team. A total of 180

assignments in the allocation table were included to accommodate possible drop-outs and additional enrolment of participants.

A person not involved in the execution of the project will confirm that the eligibility data are complete in order to proceed with the randomization. She/he will then inform the intervention provider of the allocated arm.

The intervention provider will inform the participants whether they are in the intervention arm, but the assessor will not be informed of hers/his treatment group allocation.

The role of the assessor is to ensure the connexion to the REDCap platform that holds the research questionnaires. The assessor responds to eventual questions about item understandings during the assessment. The assessor is blind and reminds the participant not to communicate hers/his treatment group allocation at the beginning of every encounter at T1 and T2. The assessor will also collaborate with one of the investigators at the end of the study to collect qualitative data.

The research assistants will alternatively play the role of either the assessor or the intervention provider to diversify their work and develop specific competences related to each role. To maintain blindness of assessment, several conditions have been set: one assistant researcher will take the role of assessor for the first five participants before providing the intervention for the next five. Another assistant researcher will do the opposite and so on. If a leak of allocation occurs, this information will be noted, and analyses concerning the eventual impacts will be conducted. However, all standardized questionnaires are basically self-administered.

The interventions will take place in a building other than the assistants' office. The supervision between interventions will be individualized and organized by one of the two lead investigators.

Data collection, management and analysis

Study data will be collected and managed using REDCap electronic data capture tools hosted at HES-SO Fribourg. REDCap provides 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Primary outcome:

The BSI aims to assess psychological symptoms and psychological distress. It includes 53 items organized into 9 primary and clinically relevant symptom dimensions: 1) somatization; 2) obsessive-compulsive; 3) interpersonal sensitivity; 4) depression; 5) anxiety; 6) hostility; 7) phobic anxiety; 8) paranoid ideation; and 9) psychoticism (36). This scale also has three global distress indices: the GSI, the Positive Symptom Distress Index (PSDI) and the Positive Symptom Total (PST). The BSI scale has been used in a variety of clinical and counselling settings as a screening tool for mental disorders and as a method of measuring symptom reduction (37-40). It has also been used to assess the

psychological health status of informal caregivers (28, 41, 42). The GSI of the BSI scale was used as one of the main outcome measures in the pilot study and represents the mean of the nine primary symptom dimensions and is more sensitive than the two other global indices (36). Higher GSI scores indicate a greater effect on informal caregivers' psychological health. The validation of the French BSI scale indicated good internal consistency for the GSI score (α=0.91) (43).

Secondary outcomes:

The French ZBI includes 22 items to assess the subjective burden (emotional, physical and financial) of an informal caregiver of an individual with a loss of autonomy (32). The total score can range from 0 to 88. A score less than or equal to 20 indicates a low burden; a score between 21 and 40 indicates a light burden; a score between 41 and 60 indicates a moderate burden; and a score greater than 60 indicates a severe burden. This questionnaire has been mainly used for chronic illnesses such as dementia, palliative care or mental disorders (44-46).

The Life Orientation Test – Revised (LOT-R) developed by Scheier, Carver and Bridges (47) measures an individual's optimism regarding a given situation. This self-administered scale measures the adaptive strategies correlated with well-being and is used to evaluate optimism versus pessimism. The LOT-R has been translated and validated in French, with good psychometric proprieties (internal consistency α=0.76) (48). The scale includes 10 items: three items measure optimism, three others measure pessimism, and four items function as fillers. The participants respond to each item on a 5-point Likert scale ranging from zero (strongly disagree) to four (strongly agree); the four filler items are not included in the total score calculation. Higher scores suggest more optimism. Optimism has been shown to be negatively correlated with distress (49, 50) and to positively influence quality of life (51). Among informal caregivers in particular, optimism promotes engagement in supportive programmes (52), whereas pessimism leads to the use of avoidance strategies, which can predict informal caregiver burden (53).

The 36-item Medical Outcome Study Short-Form Health Survey (SF-36) developed by Ware and Sherbourne (54) measures some health indicators related to quality of life. It includes 36 items and is used in clinical and general population settings to evaluate eight health dimensions: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. Two global scores – 1) a Physical Component Score (PCS) and 2) the Mental Component Score (MCS) – are obtained by grouping the eight dimensions, and these two synthetic variables allow different populations to be compared. The French version of the SF-36 was validated by obtaining Cronbach's (reliability) coefficients ranging from 0.76 to 0.92 (55-58). In clinical settings, this type of measure can also help professionals orient informal caregivers towards a targeted intervention (59, 60).

The different standard measures will be used in the three standard evaluations (T0=pretest; T1=posttest at an average of 2 months and T2=follow-up at an average of 4-5 months). A research assistant trained to answer technical questions will be present during the questionnaire's completion.

The Social and Occupational Functioning Assessment Scale (SOFAS) developed by Goldman, Skodol and Lavet (61) is used in order to reflect the severity of the patient's illness in the professional and social functioning. This scale does not consider the psychiatric symptoms' severity. It is a continuous scale (0–100) which present 10 functioning level, each level is described by a short text. A higher level (91 to 100) shows a more superior social and occupational functioning. This scale is validated in French (coefficients ranging from 0,61 à 0,91) and largely used in clinical context and different research projects (62-64). The SOFAS will be administered at T2 to compare eventual improvements by the patient according to the informal caregiver and explore differences in informal caregivers' outcomes.

Sociodemographic data will be collected at T0: sex, age, education level, professional activity, the nature of their relationship with the patient, whether they live with the patient, the number of close contacts and previous requests for help. Information about the patient will complete the sociodemographic data: the patient's sex, age, diagnosis according to the caregivers and its duration. No medical data about the patient will be collected which limits the medical diagnosis specification. However, analyses by diagnostic group according to the informal caregiver and the SOFAS level will be done in order to explore differences between groups.

The Satisfaction Scale concerning the Ensemble programme was developed and used in the pilot study (28). This scale will be used only in the posttest evaluation of the intervention group to show the participants' satisfaction.

The aim of the qualitative part of this project is to conduct a qualitative open and exploratory study. Qualitative data will be collected through semi-directive interviews. They will aim to provide significant information regarding participant experiences in the programme (capacities to manage painful emotions and difficulties worked on during the programme and to have and increase awareness of the informal caregiver's role). Participants will be able to express their views about both advantages and disadvantages of the intervention, and the impacts in the quality of life.

Semi-directive interviews will be conducted at the end of the study with twenty selected participants to explore their experiences participating in the Ensemble programme. These participants will be selected at the end of the intervention in the intervention arm. Two groups of participants will be included in this phase: those who have benefited greatly from the program (G1; n=10) and those who have benefited less (G2; n=10). At the end of the quantitative part for all participants, the 80 subjects will be separated in two groups: those who have a better score and those who have a poorer score in

the main outcome (BSI score) in T1 compare to T0. Then for each group ten participants will randomly be selected and be contacted for participating in the qualitative study.

This stratification of the sample will allow us to better understand the added value of the Ensemble programme and to identify areas for improvement. The process for this step occurs in two phases: 1) the participant receives information at the time of recruitment and agrees to participate (not only in the project itself but also to the semi-directive interview) and 2) the research team contacts the participants who have consented. Detailed information and conditions will then be given. The participants will have time to read the conditions and think about their participation in this research step. At the time of the interview, before starting the interview and its audio recording, a few minutes will be dedicated to potential questions about the information and consent form or other interrogations. Qualitative data collection will thus constitute both an autonomous inquiry and an opportunity to enrich data obtained through standardized questionnaires (65). Participants will be able to express their views about both advantages and disadvantages of the intervention, and the impacts in the quality of life. In order to ensure that the participant feels free in sharing her/his experiences and challenges, a researcher not involved in the project realisation will conduct these qualitative interviews.

Finally, all standardized questionnaires will be checked at the end of each assessment meeting for the presence of missing data and to reach agreement about how to complete these missing data.

Table 4 presents the plan to retain participants and the completed list of the collected data.

Insert Table 4 here

Analysis

Primary analyses will be conducted on an intent-to-treat basis. To ensure the statistical analyses, a researcher responsible for the analysis will be involved. He/she will double control the final quantitative data before analyses and check the different tests. The following analyses are planned: between-group differences in pre- and posttest values will be examined using an analysis of covariance (ANCOVA) for each outcome variable for the quantitative data. Differences between pretest and posttest scores, as well as between pretest and follow-up scores, will be treated as dependent variables; treatment conditions will be treated as a fixed factor, and pretreatment scores will be treated as covariates. Between-subjects Cohen's d effect sizes will be calculated at posttest and follow-up. For within subjects, Cohen's d will be calculated between the pre- and posttest and between the pretest and follow-up, correcting for dependence among means.

The content analysis of the qualitative data will focus on informal caregivers' experiences in general, as well as their capacity to manage situations. The aim of this analysis is to provide us with a

participant's comprehensive insight into the types of experiences (positive or negative) during the programme, their different capacities and unmet needs. The interview guide (Table 5) permits to better show all elements that will be explored during the qualitative study. A content analysis will be provided for each part of the follow-up questions.

Insert Table 5 here

Monitoring

Data will be accessible to the investigators and the research assistants during the project. The REDCap platform will control this accessibility. Relevant data will be accessible by a login password to only staff members of this project depending on their responsibilities. For example, an assistant scientific researcher involved in the randomization phase will only access these data. The data set will be controlled by investigators and transferred to SPSS software before the final analyses. The investigators using the REDCap platform will ensure the traceability of the data and present all the aspects to the audit trial member.

A person external to the project and the institution will audit the data and the project process once a year. She/he will perform the following functions:

- Consent checks (100%);
- Verification of raw data (1st participant all data; for the other participants several randomly selected data);
- Verification of CRF completeness and consistency: data consistency, data reconciliation, data cleaning, generation of subsequent queries, data derivation, data set formatting prior to statistical analysis, table shells, depersonalization, and anonymization;

Ethics and dissemination

The research protocol received full authorization from the Human Research Ethics Committee of the Vaud State, Switzerland. Participants will be informed about the study and their rights and sign a written informed consent form (see supplementary file: Information et consent_Ensemble). All data will be archived for 10 years after study termination or premature termination of the study. The data pertaining to the hypothesis will be mostly published in open access journals. After priority publications, metadata following FAIR recommendations will be accessible on the FORSbase platform to allow other researchers to access these data, to proceed with other secondary analyses and

to enrich research. This trusted platform offers the possibility of archiving and ensuring the long-term visibility and preservation of the data. Access to the data files will be granted only to researchers external to the project who meet the criteria required by FORSbase.

Adverse event management

Informal caregivers could present painful emotions and could need care for their own health conditions at the beginning of the project and during it. Ethical recommendations allow for those experiencing such adverse events to be enrolled, as they present significant symptoms that are not immediately life-threatening (66). The principal investigators will be informed within 24 hours and will assess the severity of the event as mild, moderate or severe. Mild complications are tolerable, moderate complications interfere with daily activities, and severe complications render daily activities impossible. If a severe adverse event occurs according to Art. 63 (66), the research project will be interrupted and the ethics committee will be notified about the circumstances within 15 days according to HRO Art. 212 (66). Only one severe adverse event not related to the research project occurred during the pilot study. The participant decided merely to stop the project to have time for individual care related to advanced cancer. The informed consent materials and information sheets given to participants are available in French and English through the following website: https://www.seretablir.net/ensemble/

Declaration of interests

The authors declare that they have no competing interests.

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Table 1: WHO Trial registration Data Set of Ensemble RCT

Data Category	Information
Primary Registry and Trial Identifying Number	ClinicalTrials.gov: NCT04020497
Date of Registration in Primary Registry	July 16, 2019
Secondary Identifying Numbers	The Federal Office of Public Health's (FOPH) portal for human research in Switzerland NCT04020497 | SNCTP000003434
Source(s) of Monetary or Material Support	Swiss National Science Foundation (SNF) 10001C_185422
Primary Sponsor	Shyhrete Rexhaj
Secondary Sponsor(s)	Jérôme Favrod
Contact for Public Queries	Shyhrete Rexhaj, s.rexhaj@ecolelasource.ch; +41 21 556 44 35; Avenue Vinet 30; 1004 Lausanne, Vaud, Switzerland
Contact for Scientific Queries	Shyhrete Rexhaj, PhD, Professor associate
Public Title	Programme Ensemble: an early intervention for informal caregivers in psychiatry
Scientific Title	Ensemble programme an early intervention for informal caregivers of psychiatric adult patients: a protocol for a randomized controlled trial Ensemble RCT
Countries of Recruitment	Switzerland
Health Condition(s) or Problem(s) Studied	Psychological Distress, quality of life
Intervention(s)	Support as usual (SAU) Informal caregivers often have to manage the situation in various ways. SAU alone consists of informal support by the patient's clinical team. There are specific psychoeducational programs depending on the patient's illness (such as "Profamille" for schizophrenia) or peer-support depending to the voluntary work of the families' associations. Some general professional services focused on informal caregivers or relatives in order to inform and orient them if they need are available in the study area. No attempts have been made to standardize this treatment.
	Ensemble programme plus support as usual (SAU) The five-session Ensemble program provides targeted support to informal caregivers. It addresses informal caregiver's specific unmet needs, emotions and social resources in order to adapt care activities to each participant.
Key Inclusion and Exclusion Criteria	Inclusion Criteria: Being at least 18 years old; living in the French-speaking Switzerland cantons (commonly referred to as "Romandie") speaking French; having an adult relative suffering from a psychiatric disorder (with or without an established diagnosis); and having the capacity to agree to participate in the project
	Exclusion Criteria: Less than 20 on the Zarit score.
Study Type	Interventional
	Allocation: randomized; intervention model: parallel assignment; masking: assessor blind
	Primary purpose: health prevention and promotion
Date of First Enrollment	October 2019
Sample Size	160
Recruitment Status	Recruiting
Primary Outcome(s)	Psychological state change on the Global Severity Index (GSI): Timepoint: Baseline; at post-test, at 2 months follow
Key Secondary Outcomes	Optimism change on the Life Orientation Test-Revised (LOT-R) Timepoint: Baseline; at post-test, at 2 months follow Quality of life change on the Mental Component Score (MCS) Timepoint: Baseline; at post-test, at 2 months follow Burden level change on the Zarit Burden Interview (ZBI) Timepoint: Baseline; at post-test, at 2 months follow Standardized severity of the patient's illness changes on the Social an Occupational Functioning Assessment Scale (SOFAS) Timepoint: Baseline; at 2 months follow Qualitative participants' experiences concerning Ensemble benefits
Ethics Review	Approved; 28 August 2019; La Commission cantonale d'éthique de la recherche sur l'être humain (CER-VD)
Completion date	30 April, 2023

Table 2. Clinical tools

Clinical tools	Description
The Difficulties and Needs Self-Assessment Tool (ELADEB)	The ELADEB includes two independent scales, one focusing on difficulties and the other focusing on support for unmet needs. Twenty-one areas of life that enable identification of priority problems and orientation of support according to the level of emergency are assessed. These 21 areas of life are organized into 4 life dimensions: life conditions, daily pragmatic activities, relationships and health.
The Painful Emotions Tool	It uses pictures that reflect painful emotions such as guilt, judgment from others, loneliness, sadness, distress, despair, anxiety, helplessness, anger, confusion and shame. The participant selects the painful emotions that are present in his/her life. The tool also assesses the frequency of the emotions. Consequently, the support provided is targeted to the caregiver's most painful emotions.
The Social Network Tool	It uses a network map that specifies the social resources available to the caregiver. This tool provides a graphic representation aimed at identifying the informal caregiver's primary, secondary and tertiary environment.

Table 3: Expected quantitative results

Outcome	Question	Data	Analysis	Expected result
Main	Is the psychological state improved?	*Global Severity Index on the Brief Symptom Inventory*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically significantly improved compared to SAU
Secondary	Is optimism improved?	*Life Orientation Test – Revised*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically significantly improved compared to SAU
	Is quality of life improved?	*36-item Medical Outcome Study Short-Form Health Survey - Mental Component Score*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically significantly improved compared to SAU
	Is the burden reduced?	*Zarit Burden Interview*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically showed significant reduction compared to SAU
	Is the patient's social and occupational function improved?	*Social and Occupational Functioning Assessment Scale*	ANCOVA of T0-T2, T0 as dependent, treatment condition as fixed factor	Experimental group statistically reported improvements for patients compared to SAU

SAU = Support as usual

Table 4. Ensemble risk reduction protocol schedule of assessments and procedures

Procedures/assessments	CRF (Yes/No)	Staff member	Time (min)	-1 Screening/ consent	T0 Baseline/ randomization	1st and 2nd Month Ensemble vs support as usual	T1 Post-test	T2 Follow-up 4-months
Oral and written information	No	Research collaborator	20	√				
Consent	No	Research collaborator	30	√				
Eligibility criteria assessment	Yes	Research collaborator	10		√			
Sociodemographic questionnaire	Yes	Assessor			√			
The French Zarit Burden Interview (ZBI)	Yes	Assessor			√		√	√
Randomization - Computer-generated	Yes	A specific randomization coordinator	10		√			
The Brief Symptom Inventory (BSI)	Yes	Assessor			√		√	√
The Life Orientation Test – Revised (LOT-R)	Yes	Assessor			√		√	√
The 36-item Medical Outcome Study Short-Form Health Survey (SF-36)	Yes	Assessor			√		√	√
The Social and Occupational Functioning Assessment Scale (SOFAS)	Yes	Assessor			√			√
Qualitative data by 20 semi-directed interviews with participants in intervention	No	Two research collaborators						√
Treatment group	Yes	Intervention provider	360			√		
All groups, being in touch and continuing information	No	Intervention provider	30			√		
Supervision of intervention provider	No	Study coordinator	According to need			Continuously		
Termination of the study		Study coordinator	According to need			Continuously		
Serious adverse event form		Study coordinator	According to need			Continuously		
Progress notes	No	All team members	According to need			Continuously		

Table 5: Interview guide for the qualitative open and exploratory study relative to caregiver's experiences during the Ensemble programme

Introduction	
Acknowledgments and facilitator presentation: First, I would like to thank you for accepting this interview. It will allow us to explore your experience during the Ensemble programme. I would like you to share with me your experience, feelings, advantages and disadvantages that occurred during your participation in this programme. I am, **Name and Surname.** I am speaking as a researcher. I was not involved in the Ensemble project until now. I work at La Source, School of nursing, University of Applied sciences and Arts Western Switzerland, in Lausanne. I am very pleased to meet you this morning/afternoon. Purpose of the interview: As the project investigators have already told you, the purpose of this interview is to understand, in a qualitative way, your Ensemble programme experience. Interview procedure: The interview should last about 1hour maximum. Confidentiality: I guarantee you that the content of our exchange will only be used for scientific research purposes and that your identity will remain confidential. The analyses will focus on the content of this interview and the results of the questionnaires that you have filled in during the first step of the project. There will be no way to identify your personal data is coded. Audio recording: If it is ok with you, as written in the consent sheet/form, I would like to record the interview, in order to make our note-taking easier and so allow me to focus on our conversation. The recordings will not be in any case diffused nor shared outside the project's team. Participant's comfort: Is everything ok for you? Do you have any question before we start?	
Interview	**Objectives**
Interview opening question: **Can you describe me your experience during the Ensemble programme?**	To understand the Ensemble programme experience of the participant in general.
Questions to ask in order to sustain and revive the speech of the participant: How would you qualify the help that you have received during the Ensemble programme? What advantages for you and your relative, have you identified in this programme? What disadvantages for you and your relative, have you identified in this programme? Which contents/exercises have helped you to better manage your situation or your caregiver role? On the contrary, which contents/exercises have you found pointless? What do you think of the term « caregiver »? Has the Ensemble programme eventually contributed to better assimilate this notion or on the contrary, to reject it? Explain. What remarks or suggestions would you give to improve the support that you have received? Is your situation different after the intervention compared to your situation before? Yes/No; How different is your situation? If Yes, do you attribute this difference to your participation in the Ensemble programme? Which elements of the programme seem to have played a part in this change of your situation/life? Which elements of the programme seem to have helped to initiate that change? Is your relative health state different after this intervention (compared to what it was before)? Yes/No; How different is the state of health of your relative? Do you think that this improvement/change is related to the support that you have received? Yes/No; If Yes, how do you explain this relation between improvement/change and the Ensemble programme Which impacts have you noticed in your quality of life? Could you tell me a major situation that you might have experienced during the Ensemble programme? What was useful during the accompaniment? What more would you have liked? What do you considerate as not enough nor not useful? How would you qualify the relationship that you have had with the intervention provider of the Ensemble programme?	To identify: i) the eventual benefits and disadvantages of the Ensemble programme for the caregiver and his/her relative, ii) the contribution of the contents and practical exercises of the programme in the capacity to manage painful emotions and resolve difficulties during the programme, or in the future, iii) the contribution of the programme on the empowerment in the caregiving role or for the person independently of this role, iiii) indications in order to improve the programme. To observe the eventual process of change (quality of life, situation…) that the programme might have generated. To get concrete illustrations of these changes and information on the accompaniment of the intervention provider.
Conclusion	
In the end, what « word » would you choose to qualify/describe your experience as a participant in this programme? Would you like to add anything?	To propose a review and offer possibility to add anything.

Figure 1. Ensemble program and process

Figure 2. RCT Flowchart

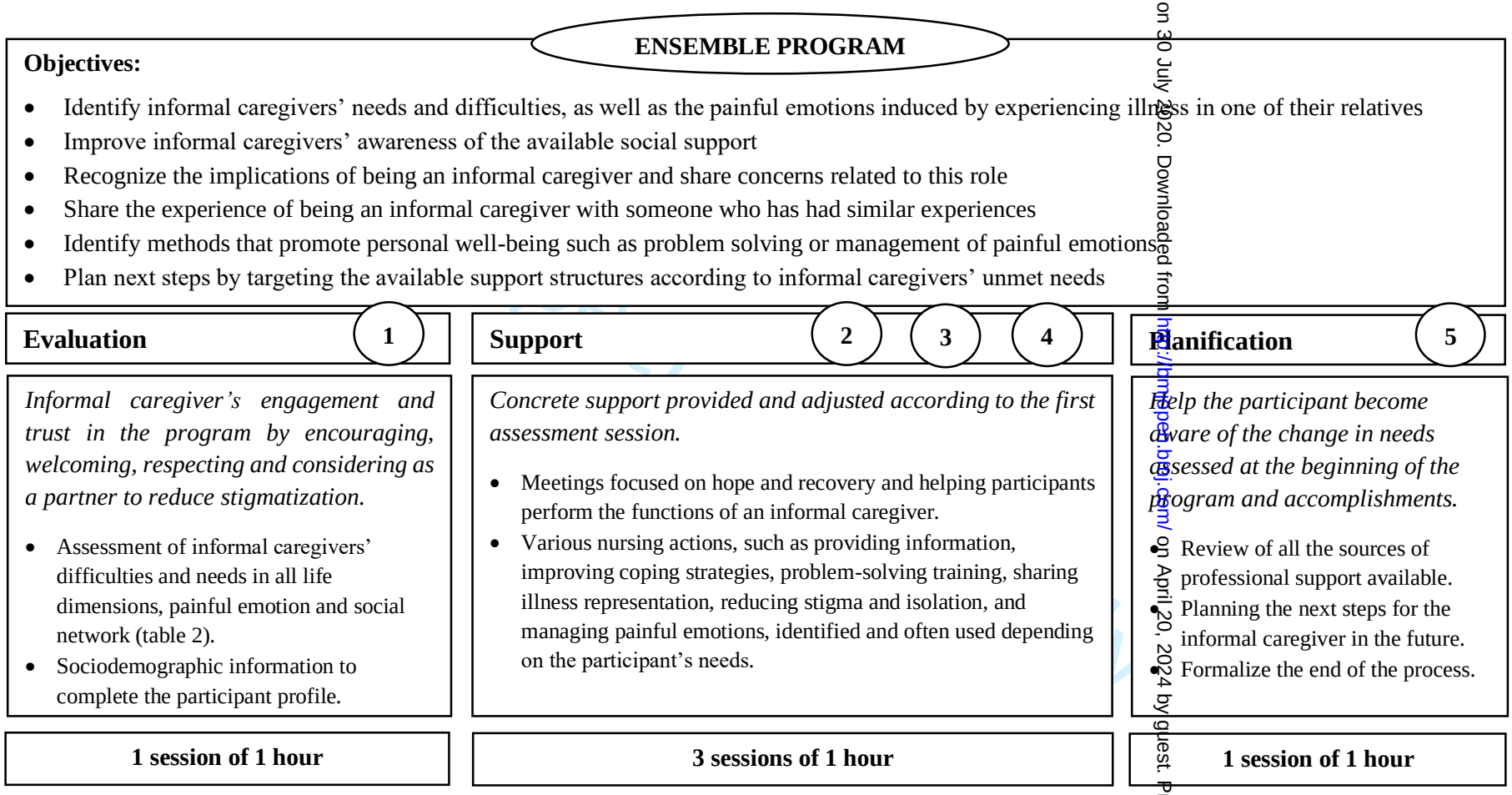

Figure 1. Ensemble program and process

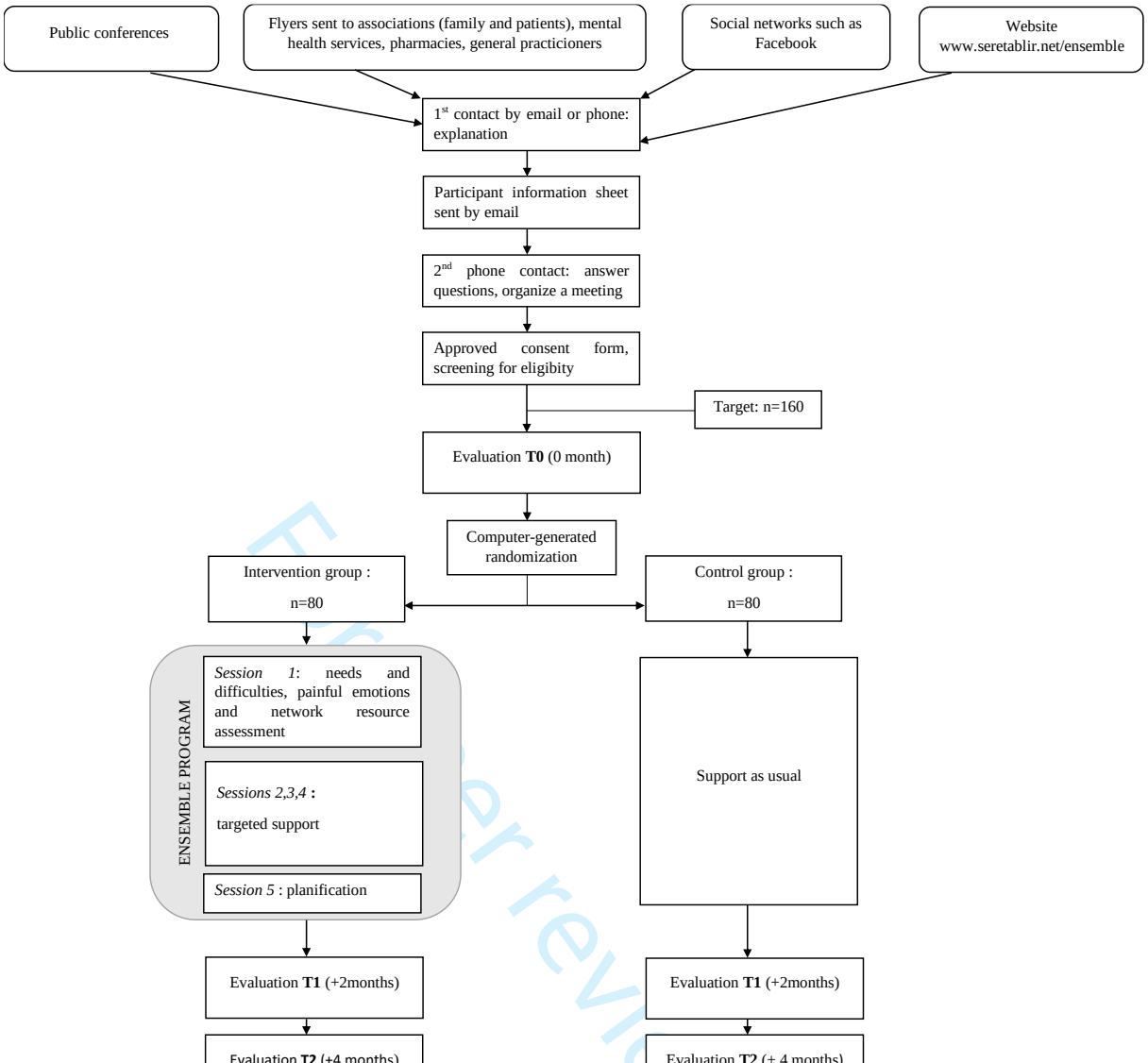

Figure 2. RCT Flowchart

Santé mentale et psychiatrie
Laboratoire d'Enseignement et de Recherche

Title of the study

Ensemble Programme an early intervention for informal caregivers of psychiatric patients: a randomized controlled trial

This study is conducted by: Rexhaj Shyhrete and Favrod Jérôme, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne

Dear Sir/Madam,

We invite you to participate to our research project. This information sheet describes the research project.

Detailed information

1. Objectives of the study

This study concerns the difficulties to maintain an optimal psychologic health state and a good quality of life for the informal caregivers providing support to persons with severe psychiatric disorders. The possible difficulties that can impact negatively the health of informal caregivers are generally linked to a high level of burden. An early intervention, Ensemble program, allowing to promote their health state, was therefore developed. The primary outcomes indicate a significative improvement of their psychological state of health. This brief intervention includes five sessions conducted by a healthcare practitioner as nurses or psychologists and allows the informal caregiver to take a step back on his/her supporting role. The first session helps the informal caregiver to observe his/her needs, difficulties, painful emotions and social network resources.
The professional provides during the next three sessions adjusted and tailored support according to the first assessment session. The last session allows to review what has been done and to plan the next steps according the informal caregiver needs. This study must allow us to know if the Ensemble program improves informal caregivers' psychological health state, quality of life, optimism and reduce their burden induced by the psychiatric disorder of the person they are supporting. The study will also allow to assess the durability of the potential advantages of Ensemble with a two months follow-up set. This study will allow us to assess the clinic efficacity and potential feasibility of the Ensemble program. This study outcomes will provide essential information on the way of providing adjusted and efficient support to informal caregivers.

2. Selection of people being able to participate in the study

The study is open to every informal caregiver who provides close support to persons with psychiatric disorders. The following criteria must be met: 1) being an informal caregiver providing support to a person with psychiatric disorder and having a burden score of at least 20 on the French Zarit Burden Interview (ZBI) which indicates a lower burden (Hébert, Bravo and Girouard, 1993), 2) being at least 18 years old and 3) speaking French.

3. General Information about the study

This research project follows a first pilot study conducted in an adult psychiatric service from the CHUV in collaboration with l'Ilot (association of informal caregivers of psychiatric disorders) and with La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland. The pilot study helped to construct and to validate the acceptability of the Ensemble program with 21 informal caregivers. The preliminary outcomes were promising, therefore we decided to test the efficacity of the program with a larger number of informal caregivers living in the Switzerland French speaking area. This project runs for 4 years starting from September 2019. We hope being able to recruit 160 informal caregivers' volunteers.
To test the effects of the Ensemble program, you will be randomly assigned into two groups: either intervention group or control group. In the intervention group you will begin rapidly the Ensemble program. However, if you are assigned into the control group, you will be able to benefit from the Ensemble program once the study is finished. Study participants fill in research questionnaires three times: (1) at the beginning of the project, (2) two months later and (3) four/five months later, in order to compare the informal caregivers following the Ensemble program at the beginning of the project and the informal caregivers who need to wait. You will meet

a research assistant to help you fill in the different questionnaires. This assistant does not know if you have received the Ensemble program at the beginning of the project or if you will receive it after. At the end of the project, a group of 20 participants will also be randomly selected in order to participate to individual interviews to evaluate qualitatively the effects of the Ensemble program.

Your involvement in the project lasts approximately five months: four times one hour to fill in approved consent form and research questionnaires and five times one hour to receive the Ensemble program. If you are in the intervention group, you will begin the Ensemble program after filling in the research questionnaires. The program can take up to two months. The five sessions will be planned between you and the professional once a week or one every two weeks. The program sessions can be held at any place of your choosing, at your place, at one of our facilities in La Source, School of Nursing Sciences in Lausanne or at another consultation location in l'Espace Proches facility for example. This will allow a calm and confidential space for the individual. If a session cannot happen (moving obligation, impossibility to come, etc.), the intervention could exceptionally be given by visio-conference. We need to proceed that way because the time between two meetings cannot be more than ten days.
However, if you are in the control group, you will fill in the research questionnaires three times 1) at the beginning of the project, 2) two months later and 3) at the end. Then, you will be able to benefit from the Ensemble program of five support sessions with a professional.

The research questionnaires allow us to assess your current psychological health state (the BSI Global Index Score), your quality of life (the 36-item Medical Outcome Study Short-Form Health Survey), your optimism (Life Orientation Test-Revised (French version)) and your burden (Zarit Burden Interview (French version)). The social and occupational functioning of the person that you are providing support to (the Social and Occupational Functioning Assessment Scale (SOFAS)) will also be assessed.

At the end of the study, 20 participants will be selected and interviewed in an individual interview to explore their experience of the Ensemble program. Two groups of participants will be included in this phase, those who have benefited greatly from the program (G1; n=10) and those who have less benefited (G2; n=10). This selection will allow us to better understand the added value of the Ensemble program and to identify areas for improvement. The interviews will be recorded with an omnidirectional microphone (Marantz audio MP3 format) and will be transcribed on Microsoft Word. We need the recordings to ensure the interviews' transcription. Your recording will be destroyed after transcription. If you approve, we will contact you for this qualitative evaluation at the end of the study. Further information will be given in due course. You will have time to examine the conditions and will be free to refuse even if you have had already approved at the beginning of the project. Furthermore, video recordings can also be realized to help the professional who is meeting you in the Ensemble program, develop his/her skills. These recordings will be accessible by the professional him/herself and his/her supervisor (Shyhrete Rexhaj or Jérôme Favrod). Some of these recordings will also be used as specific analyses to enrich pedagogy and develop the different professional skills of the Ensemble program.

If you agree to participate to this process, you will be given detailed information about the pedagogic aims of theses video recordings. If you approve, the professional who will follow you during the Ensemble program, will give you further information. You will have time to examine these conditions and will be free to refuse even if you already have signed the approved consent at the beginning of the project.

All these research data and your personal data will be given to the manager research team of this project who will safely keep them. The team will contact you, following your approved consent, during the different steps of the project.
We conduct this study in respect of the swiss legislation prescriptions. We follow all the international recognized guidelines. The cantonal ethics Committee have controlled and authorized the study. You will find a study description on the Federal Office of Public Health website: https://www.kofam.ch/fr/portail-snctp/recherche/74009/etude/47320; NCT04020497 | SNCTP000003434.

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4. Conduct for the participants

The table below allows you to visualize the moments of measures and the duration of the Ensemble program participation either you are in the control or intervention group.

		Intervention group	Control group
Beginning of the project	Filling in the standard questionnaires with a research assistant (1H)	√	√
	Ensemble program (5x1h per week or up to every two weeks)	√	
Two months later	Filling in the standard questionnaires with a research assistant (1H)	√	√
Four/five months later:	Filling in the standard questionnaires with a research assistant (1H)	√	√
	Participation to an individual interview only 20 participants (up to 1H30)	√	
End of the study			
	Ensemble program (5x1h per week or up to every two weeks)		√

5. Benefits for the participants

This project allows you to benefit freely from the Ensemble program. In case of positives Ensemble program outcomes are confirmed, the support that you will get during the project will help you to step back from your informal caregiver role and find solutions to better cope with your relative psychiatric disorder. The study outcomes could prove significant later, to the informal caregivers that live a similar experience as your own.

6. Participants rights

Your participation is entirely free. If you choose not to participate or if you come back from your decision during the study, you will not have to justify your decision. This will change nothing to your usual support. You can ask all the questions linked to the study at any time. You may contact one of the persons indicated at the end of this information sheet, to do so.

7. Participants obligations

As a study participant, you will have to:

- Fill in the research questionnaires
- Participate to the planned Ensemble program meetings with a professional

8. Risks and constraints for the participants

As the intervention is a complement to usual support, risks are low. However, assessing your individual needs, painful emotions and social network as you take a step back, can generate pain. The planned meetings will be adjusted following your needs and should not provoke supplementary risks.

Also, the randomly repartition (intervention or control group) requires that participants of control group be more patient than the participants of intervention group to benefit from the support offered in Ensemble program set.

9. Others treatment possibilities

You are under no obligation to participate to the study. If you decide not to take part in it, it will be possible to be advised on the other possibilities of informal caregiver support.

10. Discoveries during the study

Any appearing discovery during the study relevant to your health will be transmitted.

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11. Data confidentiality

We respect all legal dispositions relating to the data protection. Your personal and your data relating to your well-being and your quality of life are protected and used coded. Only a limited number of people can consult your data under a non-coded way and will exclusively use it to fulfill their duties within the scope of the study. Coding means that all data allowing to identify you (for example name, date of birth, etc.) are replaced with a code (ex: name and first name will be replaced by initials with a combination of letters as factices initials) that have no link to your true initials (for example 'AAA', 'BBB'). The code stays permanently in our institution. People who do not know the code cannot linked these data to you. In a publication, data will be anonymised. Your name will not appear of the internet or any publication. Sometimes, scientific journals ask for individual data (raw data). In this case, individual data will be coded and will not allow to identify you as a person. All involved persons in this study are bounded by professional secrecy. All guidelines relating to data protection are respected. You have the right to consult your data at any time.

During its course, the study can be inspected. The ethical commission who has controlled and authorised this study can conduct inspections. Investigators might communicate your personal data for the needs of these inspections. All people are bounded by professional secrecy.

During the project, your data will be inserted into a secured software named REDCap. Only staff members of this project will have access to these data. At the end of the project, your data will be coded and will be stored in a secured platform named FORS.

12. Withdraw from the study

You can withdraw at any time. The personal and relevant data of your wellbeing and quality of life will be coded and analyzed as the other participants and then fully anonymized.

13. Participants compensation

If you participate to this study, you will not receive any compensation.

14. Compensation of incurred damages

In the event of study-related damage or injuries, the liability of the institution Institut et Haute Ecole de la Santé, La Source provides compensation.

15. Funding of the study

This study is financed by the Swiss National Science Foundation.

16. Contact persons

In case of any doubts, concerns or emergencies during or after the study, you can contact at any time one of the following persons:

Rexhaj Shyhrete, HES Associate professor, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Av. Vinet 30 1004 Lausanne/079 103 18 16

Favrod Jérôme, HES Full Professor La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Av. Vinet 30 1004 Lausanne/ 079 447 31 57

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Written consent declaration for the participation of a research project

Read with caution this form. Do not hesitate to ask any questions if you do not understand anything or if you need precisions.

Study BASEC number: (After submission to the competent ethics commission)*:*	
Study title*:* (Scientific title and usual title)	**Ensemble Programme an early intervention for informal caregivers of psychiatric patients: a randomized controlled trial** **Programme Ensemble: clinical trial to test its effect**
Leader institution:	La Source, School of Nursing Sciences, Avenue Vinet 30, 1004 Lausanne
Localization of the study:	French-speaking Switzerland
Monitoring managers and investigators of the project on the site:	Rexhaj Shyhrete Favrod Jérôme
Participant: (PRINT NAME and FIRST NAME): Date of birth:	☐ woman ☐ man

- I declare having been informed, by the responsible investigator and/or his/her research coworker undersigned, orally and in writing, of the objectives and conduct of the study.
- I take part in this study voluntarily and I accept the content of this above-mentioned study information sheet that I was given. I have had enough time to take my decision.
- I received satisfactory answers to the questions that I have asked about my participation to the study. I keep this information sheet and receive a copy of my written consent declaration.
- I have been informed of the other possible support for informal caregivers.
- I accept that the competent specialist of the sponsor of the study and Ethics Commission can consult my draw data to proceed to controls, in the case where the confidentiality of these data are strictly assured.
- I will be informed of any discoveries with a direct impact on my health.
- I know that my personal data and the data relating to my well-being and my quality of life can be transmitted for research purposes in this project set only and under a coded form.
- I can whenever and without justification withdraw my consent to participate in this study, without any negative repercussion on my informal caregiver situation and the situation of the person I take care of. Data collected until my withdraw will be analyzed.
- I am informed that the liability of the institution Institut et Haute Ecole de la Santé, La Source provides compensation in case of any damages that could incur in this project.

Location, date	Participant signature

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Putting an X in the Yes box, I agree to participate to a qualitative interview for research purposes.

Yes: ☐ **No :** ☐

Putting an X in the Yes box, I agree to participate to the video recordings useful for the supervisions.

Yes : ☐ **No :** ☐

Putting an X in the Yes box, I agree to participate to the video recordings useful for the pedagogy research

Yes : ☐ **No :** ☐

Investigator/research coworker confirmation : Hereby, I confirm having explained to the participant the nature, the importance and the scope of the study. I declare satisfying all legal obligations relating to this project. If I should notice, whenever during the project realization, susceptible elements of influencing on the consent of the participant to take part in the project, I engage to inform him/her immediately.

Location, date	PRINT NAME and FIRST NAME of the investigator/research coworker assuring the information to the participants. Investigator/research coworker signature

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	1
Protocol version	#3	Date and version identifier	1
Funding	#4	Sources and types of financial, material, and other support	1
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1-2
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	2
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	2
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	2

Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and	6

		individuals who will perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	7
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	7
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7-8
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended	8

		(see Figure)	
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	8
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	8
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8-9

Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8-9
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8-9
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	9-11
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values).	12

		Reference to where details of data management procedures can be found, if not in the protocol	
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	12
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	
Methods: Monitoring			12
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	12
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	12
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial	12

		conduct	
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	12-13
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	13
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	13
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	13
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	13
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	13
Declaration of	#28	Financial and other competing interests for principal	13

interests		investigators for the overall trial and each study site	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	13
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	13
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	13
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	13
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	13
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	13
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-

BMJ Open

Ensemble programme for early intervention in informal caregivers of psychiatric adult patients: a protocol for a randomized controlled trial

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Ensemble programme for early intervention in informal caregivers of psychiatric adult patients: a protocol for a randomized controlled trial

Ensemble RCT

Trial registration:

ClinicalTrials.gov: NCT04020497

Protocol version

28 August 2019, version 2, Project ID-2019-01181

The key revisions to version 1 of the protocol were linked with ethics concerns regarding added value for qualitative data and the specification for their collection and analysis. Information concerning timepoint data collection and time needed to complete the questionnaires was also detailed in the participants' information sheets.

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Authors

- Shyhrete Rexhaj (SR), La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Shadya Monteiro (SM). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Philippe Golay (PG). Community Psychiatry Service, Department of Psychiatry, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland.
- Claire Coloni-Terrapon (CCT). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Daniel Wenger (DW). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.
- Jérôme Favrod (JF). La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.

Shyhrete Rexhaj [Corresponding Author]

s.rexhaj@ecolelasource.ch

Authors` contributions

SR and JF designed the study and are grant holders. DW, SM and CCT collected the data and provided the intervention. SR and JF developed the intervention. SR and SM delivered the study material (for example, the recruitment process, programme figures and web information). SR provided training support for the intervention and data collection during the study. SR led the study but was replaced by JF during maternity leave. PG, JF and SR developed the statistical plan and provided statistical support for the study. SR and SM wrote the first version of the paper. All authors contributed to a critical review and approve the final paper.

Trial sponsor, committee and data manager:

La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne.

Shyhrete Rexhaj, s.rexhaj@ecolelasource.ch; Telephone: +41 21 556 44 35

The project manager (SR) will be involved in the analysis and interpretation of data, writing of the report, and the decision to submit the report for publication.

The finding source FOPH had no role in the design of this study and will have no responsibility during its execution.

La Source is the only coordinated centre and serves all recruited participants, even those from other French-speaking areas of Switzerland. Lead investigators SR and JF will review the process of the study if necessary. SR, as the principal investigator, is responsible for ethical considerations (providing an annual risk report to the ethics committee, providing information on serious adverse events, and announcing any change in the protocol if necessary) and for the study procedures (management of the team and responsible for the data file and budget administration). Noémie Laverne, who was not involved in the execution of the project, is responsible for randomization even for participants who were randomly by computer, as the computer system requires oversight.

The data manager Anne-Laure Kauffman maintains the trial IT system using the REDCap platform and will audit all procedures of the study once a year.

Acknowledgements

We thank Prof. Charles Bonsack and Prof. Claude Leclerc for their valuable value in the development of the intervention. We thank Dr Engelhorn for a donation in the first step of the programme development. We also thank members of ÎLOT (The association of informal caregivers for mental disorders, in Vaud state, Switzerland).

Abstract:

Introduction: Informal caregivers play a major role in the support and maintenance of community patients with severe psychiatric disorders. A pilot study showed that an individualized brief intervention such as the Ensemble programme leads to significant improvements in psychological health state and optimism. **Methods and analysis:** This randomized clinical trial (RCT) aims to compare the efficacy of using Ensemble in improving informal caregivers' psychological health states and the ability to play an active role in their situations with that of support as usual (SAU). Improvements on the psychological health global index will be measured three times (T0-pre, T1-post and T3 two-month follow) with standardized questionnaires (the Global Severity Index of Brief Inventory Symptoms, the Life Orientation Test-Revised, the 36-item Medical Outcome Study Short-Form Health Survey and the French Zarit Burden Interview). Differences between groups in post- and pre-test values will be examined using an analysis of covariance (ANCOVA) for each outcome variable. The severity of illness measured by the Social and Occupational Functioning Assessment Scale (SOFAS) will also be collected at T0 and T2 to compare eventual patient improvements. At the end of the programme, the experiences of the 20 patients participating in the Ensemble programme will be evaluated qualitatively.

Ethics and dissemination: The research protocol received full authorization from the Human Research Ethics Committee of the Vaud State, Switzerland. The principal paper will concern the results of the experimental design used to test the Ensemble programme. The research team will prioritize open access publications.

Strengths and limitations of this study

- This is the first randomized controlled trial in Switzerland to test *Ensemble*, an active individualized programme for the informal caregivers of people suffering from a psychiatric disorder in comparison to controls.
- The *Ensemble* programme is brief (5 sessions, once a week), tailored and offers different practical tools for informal caregivers to improve their health, quality of life and ability to cope with the patient's illness.
- The intervention provider endorses a facilitator role to improve informal caregivers' empowerment.
- Tailored early interventions are recommended because actual support given in practice lacks consideration of the informal caregivers' specific needs and should not depend on only the patient's treatment.
- No comparison with an active intervention (as a psychoeducation programme) presents a limitation.

Introduction

Care in the community has greatly improved the conditions of people with severe and persistent mental disorders. In this context, informal caregivers are significant partners, and appropriate support must be provided (1, 2). Although family and informal caregiver play a vital role in the early detection of mental health disorders and facilitating access to care, it is not easy for health professionals to develop such partnerships (3). Several studies have underscored the importance of supporting informal caregivers in their capacities to integrate their new caregiver's role (4-6). Moller-Leimkuhler (2006) demonstrated that informal caregivers need emotional support as soon as the diagnosis is made (7). Emotional support is essential in the moratorium stage of recovery (8, 9). When a patient's close informal caregiver first learns about a diagnosed psychiatric disorder, he or she might feel a range of emotions and might exhibit varied reactions linked to this stage (e.g., revolt, confusion, hopelessness, denial). In the second stage of recovery, relatives develop a greater awareness of the disorder, although this awareness can raise significant fears about the future. Feelings such as guilt, avoidance or a desire to give up can emerge (8, 9). It is therefore critical to intervene early during the first two stages of recovery to promote the health of informal caregivers and to reorient them away from unsuccessful coping strategies that might be harmful in the long term (8-10). Informal caregivers often feel helpless, lack confidence regarding how to help the sufferer, and experience shock when faced with a close relative suffering psychologically (11, 12). They can experience significant distress since they lack support and practical tools for managing the situation (4). Feelings of helplessness and uncertainty can be compounded by a lack of knowledge of the disorder and not knowing how to help the patient (13). Informal caregivers could become isolated due to the harmful effects of stigmatization, which can also have negative impacts on their health (14). Indeed, informal caregivers of people with severe psychiatric disorders can experience serious situations with potential negative consequences for their quality of life, their own health and the health of the patient (15-17). In order to help them developing effective coping strategies, interventions must be contextualized, culturally adopted and specified to the informal caregiver's role in order to fill individualized needs (18, 19). These diverse issues are crucial for understanding how to better support informal caregivers. The results of a meta-analysis of patients suffering from schizophrenia spectrum disorders showed that most programmes include information about the disease and focus on the development of communication and coping skills to reduce the negative effects on caregivers (20). Interventions for bipolar disorder are mainly based on the "vulnerability-stress model" and include information about how this illness impacts relatives, as well as training sessions on communication skills and problem-solving techniques (21). Interventions tested in a study of depressive disorders included theoretical input on aetiology, and they focused on the causes of depression, depressive symptoms, treatment and the development of coping strategies (22). Previous studies have also identified that informal caregivers need tailored knowledge of the patient's illness, clarification of their roles and

responsibilities, better control over their own lives and effective collaboration with health professionals (5, 6, 23-27). Additionally, scientific data recommend adjusting caregivers' support according to the phase and severity of illness, as well as the caregiver's sociodemographic characteristics (26). Most of the interventions published in the literature have focused on the ill family member and his or her support but not on the specific needs of informal caregivers as the core intervention. Lobban and colleagues (2013) presented an individualized programme that is self-managed and specific for relatives of people with recent-onset psychosis (11). To reduce the gap between scientific recommendations and actual practice, a tailored intervention called *Ensemble* (Together in English) was developed and tested in a pilot study (3, 28). The results of this pilot study showed that informal caregivers experience many difficulties and unmet needs regarding their caregiver role, as well as painful emotions, while having many social resources that are not specific to their individual needs. The participants had several difficulties in essential areas of life, such as family, children, romantic relationships and mental health. The needs of each caregiver differ between the participants which confirm the necessity of individualized support (29). Comparing Ensemble to psychoeducational programs or counselling programme would involve tailoring the support to the need of each participant. The support sessions offer different practical exercises and tools (problem solving, positive communication and assertiveness, involvement as an informed caregiver, emotional support…), which need to be adapted to each participant.

Regarding the primary outcome of the Ensemble pilot study, the participants showed significant improvements in psychological health status as measured by the Global Severity Index (GSI), based on the Brief Symptom Inventory (BSI) scale (28). After five sessions, the 21 participants' psychological health statuses were improved compared with their pretest scores (pretest mean of the GSI score 0.72 vs. posttest GSI score mean 0.53). These findings emphasize that informal caregivers are at greater risk of developing psychological problems than those in non-clinical populations; for example, their mean GSI score pretest (0.72) was higher than that of a healthy British community sample (0.44) (30) and lower than that of a British psychiatric outpatient sample (1.65) (31). Informal caregivers were also more optimistic regarding their future at the end of the programme as a secondary outcome (mean pretest 15.52 vs. mean posttest 17.43).

The goal of the current study is to determine whether the *Ensemble* programme is clinically effective using a randomized, controlled, and assessor-blinded trial. A combination of *Ensemble* plus support as usual (SAU) will be compared to SAU alone.

This trial's main hypothesis is that five one-hour sessions of the Ensemble programme will lead to an improved psychological health state, as evaluated with the GSI score on the BSI scale, compared to those of the control group. The secondary hypothesis is that the Ensemble programme will increase optimism levels as measured on the LOT-R scale, improve quality of life as measured by the SF-36

scale and decrease the burden score on the Zarit scale. The study will also monitor the sustainability of the potential benefits at follow-up (two months after completing the Ensemble programme). Qualitative data through 20 semi-oriented interviews will provide information on outcomes concerning the experience and the added value of the programme for participants at the end of the study.

A study summary according to the World Health Organization Trial Registration Data Set items is presented in Table 1.

Insert Table 1 here

Methods: Participants, interventions, and outcomes

Study setting

The study is being conducted in four cantons of French-speaking Switzerland. Informal caregivers providing close support to persons with psychiatric disorders are the target population. "Informal caregiver", "caregiver" and "family caregiver" are terms used to describe family members, friends or significant others who provide this close support. In this area, no systematic or standardized individualized intervention for informal caregivers is implemented. Several sites in these four cantons are informed, and different partners actively support this project (a detailed list can be obtained from the authors) to reflect generalization issues. The main study site is La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne. However, the research assessments and the meeting intervention can take place at the participants' homes or in other locations defined as appropriate by the participants and intervention providers. The research members will travel up to 3 hours one-way for these meetings and assessments.

Eligibility criteria

The study is open to informal caregivers of adult psychiatric patients with a burden score of at least 20 on the French Zarit Burden Interview (ZBI) version scale (32). This 22-item scale uses a five-point scale (0 = "never"; 4 = "nearly always") to assess the subjective burden (emotional, physical and financial) of an informal caregiver of an individual with a loss of autonomy. The total score can range from 0 to 88. A score less than or equal to 20 indicates a low burden; a score between 21 and 40 indicates a light burden; a score between 41 and 60 indicates a moderate burden; and a score greater than 60 indicates a severe burden. The inclusion criteria for informal caregivers are as follows: being at least 18 years old; living in French-speaking Switzerland; speaking French; and having an adult relative suffering from a psychiatric disorder (with or without an established diagnosis). One hundred sixty participants will be included in this study (n=80 for Ensemble+SAU; n=80 for SAU). In this study, a self-report identification as informal caregivers is selected to offer support to all informal caregivers according to their needs independently of their direct implication in caregiving to patient.

Recruitment

Participants will be recruited from the following family associations in French-speaking Switzerland: l'Îlot (VD), AFS Berne-Neuchâtel (NE), A3 Jura (JU) and APF (FR). Participants will also be recruited at "l'Espace Proches", which is a nonprofit association created in 2014 and a member of the Department of Health and Social Welfare (DSAS) and the Pallium Foundation. The services of this association are run by health and social professionals and focused on informing, orienting and supporting informal caregivers or relatives. Public mental health services will also be used to recruit participants. Meetings with the presidents of each association and professionals working in mental health services will be organized to present the project. Regular information about the research will be provided at these sites. A recruitment strategy aimed at general practitioners, local newspapers, schools and social and cultural centres, as well as social networks such as Facebook, will be deployed to ensure equivalent treatment among informal caregivers who are isolated or not in contact with any association. Informal caregivers who are willing to participate will choose either to call the research coordinator or give their authorization to be contacted.

Patient and Public Involvement

No patient involved

Interventions

Ensemble programme

Ensemble is a brief individualized intervention designed to promote the well-being of informal caregivers who experience the effects of their patients' psychiatric disorders. It is a five-session programme led by a nurse (who had two days of specific training), addressed to the informal caregiver and delivered independent of the patient's treatment. Figure 1 below demonstrates the objectives of the Ensemble programme and its process. The five sessions are described and allow the participant to take a step back on her/his informal caregiver's role.

Insert Figure 1 here

Clinical tools

Three clinical tools are used to specifically assess the needs, difficulties, painful emotions and social networks of the informal caregivers (Table 2). These clinical tools are systematic, structured, and easy to administer. The three clinical tools selected in the Ensemble programme are 1) the Difficulties and Needs Self-Assessment Tool, 2) the Painful Emotions Tool and 3) the Social Network Tool (3, 28, 33, 34).

Insert Table 2 here

Support as usual (SAU)

SAU was chosen as a control condition. Informal caregivers must often manage situations in different ways. SAU consists of informal support given by various structures. The patient's clinical team can provide support to the informal caregiver. Specific psychoeducation programmes tailored to the patient's illness (such as "Profamille" for schizophrenia) are also implemented in the French-speaking Switzerland context. Peer support depends on the voluntary work of family associations. Some general professional services such as "l'Espace Proches" focus on informing and orienting informal caregivers or relatives in the state of Vaud. No attempts have been made to standardize this treatment as SAU that depends on informal caregivers' needs, knowledge of the health system, and their capacity to be in contact with the patient's psychiatric team.

Ensemble programme's implementation

Three nurses are trained to deliver the programme. The training took two days and is organised in four sessions.

Session 1: issues concerning support for family caregivers, theoretical foundations of the Ensemble program, professional posture and informal caregivers' health considerations.

Session 2: Ensemble Program: tailored support, structured and individualized process, assessment of difficulties and needs, painful emotions and social resources, practical training to use the clinical tools with a vignette designed from the pilot phase, issues concerning the awareness of the informal caregiver's role.

Session 3: Practical exercises of the support tools - problem solving, positive communication and assertiveness, and involvement as an informed caregiver.

Sessions 4: Practical exercises of the support tools - emotional support, isolation and peer support, and referral to appropriate structures.

In addition to this training, nurses received a manual protocol and are supervised for every clinical situation. To ensure the standardisation on delivery, two supervisions moments are planned: the first after the first meeting between the nurse and the participants and the second before their last meeting. The place for delivery of the sessions are in a private and quiet room located to the nursing school, or in a clinical local or in the participant's home. Sometime if the participant prefers the delivery could take place in the "tea-room or hotel" but this option is retained only if the other options are not suitable for the participant.

Outcomes

Quantitative data gathered through various standard instruments will inform the main and secondary outcomes. Table 3 summarizes the expected results.

Insert Table 3 here

Qualitative data will also inform some secondary outcomes. Content analysis will focus on not only informal caregivers' experiences but also their capacity to manage the situation. To narrate their experiences and construct meaning through heuristic narrative processes (35), the analysis of the categorization devices used by the participants will provide us with comprehensive insight into the types of experiences during the programme, different capacities and unmet needs.

Sample size

The sample size was estimated using the results of the pilot study regarding the main outcome of the expected BSI Global Index. For the sample size calculation, α was set at .05 with a power of β =.80. The effect size of the expected difference between the two groups was equal to Cohen's d= .470. Using an a priori computation for ANCOVA, the proposed trial required a total sample size of 144 participants for the two arms, 72 in each arm. In the pilot study, one of 22 participants dropped out, resulting in a dropout rate of approximately 5%; to increase security in the proposed study, a drop-up rate of 10% will be considered, corresponding to a dropout number of 22 participants, so the present study will recruit 160 participants. Between-group differences in pre- and posttest values will be examined using analysis of covariance (ANCOVA).

Participant timeline and RCT process

Figure 2 shows the clear and synthetic timeline of participant interactions and this RCT process.

Insert Figure 2 here

Allocation

The Research Electronic Data Capture (REDCap) platform will be used to randomize the participants. REDCap is a secure, web-based application designed to support data capture for research studies. It developed a module that allows a defined randomization model be implemented within the project. The randomization by group/site model was defined. A randomization table was created by the data manager and imported to the project database to structure the allocation. REDCap will randomize the participants according to this table, which is not available to the research team. A total of 180 assignments in the allocation table were included to accommodate possible drop-outs and additional enrolment of participants.

A person not involved in the execution of the project will confirm that the eligibility data are complete in order to proceed with the randomization. She/he will then inform the intervention provider of the allocated arm.

The intervention provider will inform the participants whether they are in the intervention arm, but the assessor will not be informed of hers/his treatment group allocation.

The role of the assessor is to ensure the connexion to the REDCap platform that holds the research questionnaires. The assessor responds to eventual questions about item understandings during the assessment. The assessor is blind and reminds the participant not to communicate hers/his treatment group allocation at the beginning of every encounter at T1 and T2. The assessor will also collaborate with one of the investigators at the end of the study to collect qualitative data.

The research assistants will alternatively play the role of either the assessor or the intervention provider to diversify their work and develop specific competences related to each role. To maintain blindness of assessment, several conditions have been set: one assistant researcher will take the role of assessor for the first five participants before providing the intervention for the next five. Another assistant researcher will do the opposite and so on. If a leak of allocation occurs, this information will be noted, and analyses concerning the eventual impacts will be conducted. However, all standardized questionnaires are basically self-administered.

The interventions will take place in a building other than the assistants' office. The supervision between interventions will be individualized and organized by one of the two lead investigators.

Data collection, management and analysis

Study data will be collected and managed using REDCap electronic data capture tools hosted at HES-SO Fribourg. REDCap provides 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Primary outcome:

The BSI aims to assess psychological symptoms and psychological distress. It includes 53 items organized into 9 primary and clinically relevant symptom dimensions: 1) somatization; 2) obsessive-compulsive; 3) interpersonal sensitivity; 4) depression; 5) anxiety; 6) hostility; 7) phobic anxiety; 8) paranoid ideation; and 9) psychoticism (36). This scale also has three global distress indices: the GSI, the Positive Symptom Distress Index (PSDI) and the Positive Symptom Total (PST). The BSI scale has been used in a variety of clinical and counselling settings as a screening tool for mental disorders and as a method of measuring symptom reduction (37-40). It has also been used to assess the psychological health status of informal caregivers (28, 41, 42). The GSI of the BSI scale was used as one of the main outcome measures in the pilot study and represents the mean of the nine primary symptom dimensions and is more sensitive than the two other global indices (36). Higher GSI scores indicate a greater effect on informal caregivers' psychological health. The validation of the French BSI scale indicated good internal consistency for the GSI score (α=0.91) (43).

Secondary outcomes:

The French ZBI includes 22 items to assess the subjective burden (emotional, physical and financial) of an informal caregiver of an individual with a loss of autonomy (32). The total score can range from 0 to 88. A score less than or equal to 20 indicates a low burden; a score between 21 and 40 indicates a light burden; a score between 41 and 60 indicates a moderate burden; and a score greater than 60 indicates a severe burden. This questionnaire has been mainly used for chronic illnesses such as dementia, palliative care or mental disorders (44-46).

The Life Orientation Test – Revised (LOT-R) developed by Scheier, Carver and Bridges (47) measures an individual's optimism regarding a given situation. This self-administered scale measures the adaptive strategies correlated with well-being and is used to evaluate optimism versus pessimism. The LOT-R has been translated and validated in French, with good psychometric proprieties (internal consistency α=0.76) (48). The scale includes 10 items: three items measure optimism, three others measure pessimism, and four items function as fillers. The participants respond to each item on a 5-point Likert scale ranging from zero (strongly disagree) to four (strongly agree); the four filler items are not included in the total score calculation. Higher scores suggest more optimism. Optimism has been shown to be negatively correlated with distress (49, 50) and to positively influence quality of life (51). Among informal caregivers in particular, optimism promotes engagement in supportive programmes (52), whereas pessimism leads to the use of avoidance strategies, which can predict informal caregiver burden (53).

The 36-item Medical Outcome Study Short-Form Health Survey (SF-36) developed by Ware and Sherbourne (54) measures some health indicators related to quality of life. It includes 36 items and is used in clinical and general population settings to evaluate eight health dimensions: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue, and general health perceptions. Two global scores – 1) a Physical Component Score (PCS) and 2) the Mental Component Score (MCS) – are obtained by grouping the eight dimensions, and these two synthetic variables allow different populations to be compared. The French version of the SF-36 was validated by obtaining Cronbach's (reliability) coefficients ranging from 0.76 to 0.92 (55-58). In clinical settings, this type of measure can also help professionals orient informal caregivers towards a targeted intervention (59, 60).

The different standard measures will be used in the three standard evaluations (T0=pretest; T1=posttest at an average of 2 months and T2=follow-up at an average of 4-5 months). A research assistant trained to answer technical questions will be present during the questionnaire's completion.

The Social and Occupational Functioning Assessment Scale (SOFAS) developed by Goldman, Skodol and Lavet (61) is used in order to reflect the severity of the patient's illness in the professional and social functioning. This scale does not consider the psychiatric symptoms' severity. It is a continuous

scale (0–100) which present 10 functioning level, each level is described by a short text. A higher level (91 to 100) shows a more superior social and occupational functioning. This scale is validated in French (coefficients ranging from 0,61 à 0,91) and largely used in clinical context and different research projects (62-64). The SOFAS will be administered at T2 to compare eventual improvements by the patient according to the informal caregiver and explore differences in informal caregivers' outcomes.

Sociodemographic data will be collected at T0: sex, age, education level, professional activity, the nature of their relationship with the patient, whether they live with the patient, the number of close contacts and previous requests for help. Information about the patient will complete the sociodemographic data: the patient's sex, age, diagnosis according to the caregivers and its duration. No medical data about the patient will be collected which limits the medical diagnosis specification. However, analyses by diagnostic group according to the informal caregiver and the SOFAS level will be done in order to explore differences between groups.

The Satisfaction Scale concerning the Ensemble programme was developed and used in the pilot study (28). This scale will be used only in the posttest evaluation of the intervention group to show the participants' satisfaction.

The aim of the qualitative part of this project is to conduct a qualitative open and exploratory study. Qualitative data will be collected through semi-directive interviews. They will aim to provide significant information regarding participant experiences in the programme (capacities to manage painful emotions and difficulties worked on during the programme and to have and increase awareness of the informal caregiver's role). Participants will be able to express their views about both advantages and disadvantages of the intervention, and the impacts in the quality of life.

Semi-directive interviews will be conducted at the end of the study with twenty selected participants to explore their experiences participating in the Ensemble programme. These participants will be selected at the end of the intervention in the intervention arm. Two groups of participants will be included in this phase: those who have benefited greatly from the program (G1; n=10) and those who have benefited less (G2; n=10). At the end of the quantitative part for all participants, the 80 subjects will be separated in two groups: those who have a better score and those who have a poorer score in the main outcome (BSI score) in T1 compare to T0. Then for each group ten participants will randomly be selected and be contacted for participating in the qualitative study.

This stratification of the sample will allow us to better understand the added value of the Ensemble programme and to identify areas for improvement. The process for this step occurs in two phases: 1) the participant receives information at the time of recruitment and agrees to participate (not only in the project itself but also to the semi-directive interview) and 2) the research team contacts the participants who have consented. Detailed information and conditions will then be given. The

participants will have time to read the conditions and think about their participation in this research step. At the time of the interview, before starting the interview and its audio recording, a few minutes will be dedicated to potential questions about the information and consent form or other interrogations. Qualitative data collection will thus constitute both an autonomous inquiry and an opportunity to enrich data obtained through standardized questionnaires (65). Participants will be able to express their views about both advantages and disadvantages of the intervention, and the impacts in the quality of life. In order to ensure that the participant feels free in sharing her/his experiences and challenges, a researcher not involved in the project realisation will conduct these qualitative interviews.

Finally, all standardized questionnaires will be checked at the end of each assessment meeting for the presence of missing data and to reach agreement about how to complete these missing data.

Table 4 presents the plan to retain participants and the completed list of the collected data.

Insert Table 4 here

Analysis

Primary analyses will be conducted on an intent-to-treat basis. To ensure the statistical analyses, a researcher responsible for the analysis will be involved. He/she will double control the final quantitative data before analyses and check the different tests. The following analyses are planned: between-group differences in pre- and posttest values will be examined using an analysis of covariance (ANCOVA) for each outcome variable for the quantitative data. Differences between pretest and posttest scores, as well as between pretest and follow-up scores, will be treated as dependent variables; treatment conditions will be treated as a fixed factor, and pretreatment scores will be treated as covariates. Between-subjects Cohen's d effect sizes will be calculated at posttest and follow-up. For within subjects, Cohen's d will be calculated between the pre- and posttest and between the pretest and follow-up, correcting for dependence among means.

The content analysis of the qualitative data will focus on informal caregivers' experiences in general, as well as their capacity to manage situations. The aim of this analysis is to provide us with a participant's comprehensive insight into the types of experiences (positive or negative) during the programme, their different capacities and unmet needs. The interview guide (Table 5) permits to better show all elements that will be explored during the qualitative study. A content analysis will be provided for each part of the follow-up questions.

Insert Table 5 here

Monitoring

Data will be accessible to the investigators and the research assistants during the project. The REDCap platform will control this accessibility. Relevant data will be accessible by a login password to only staff members of this project depending on their responsibilities. For example, an assistant scientific researcher involved in the randomization phase will only access these data. The data set will be controlled by investigators and transferred to SPSS software before the final analyses. The investigators using the REDCap platform will ensure the traceability of the data and present all the aspects to the audit trial member.

A person external to the project and the institution will audit the data and the project process once a year. She/he will perform the following functions:

- Consent checks (100%);
- Verification of raw data (1st participant all data; for the other participants several randomly selected data);
- Verification of CRF completeness and consistency: data consistency, data reconciliation, data cleaning, generation of subsequent queries, data derivation, data set formatting prior to statistical analysis, table shells, depersonalization, and anonymization;

Ethics and dissemination

The research protocol received full authorization from the Human Research Ethics Committee of the Vaud State, Switzerland. Participants will be informed about the study and their rights and sign a written informed consent form (see supplementary file: Information et consent_Ensemble). All data will be archived for 10 years after study termination or premature termination of the study. The data pertaining to the hypothesis will be mostly published in open access journals. After priority publications, metadata following FAIR recommendations will be accessible on the FORSbase platform to allow other researchers to access these data, to proceed with other secondary analyses and to enrich research. This trusted platform offers the possibility of archiving and ensuring the long-term visibility and preservation of the data. Access to the data files will be granted only to researchers external to the project who meet the criteria required by FORSbase.

Adverse event management

Informal caregivers could present painful emotions and could need care for their own health conditions at the beginning of the project and during it. Ethical recommendations allow for those experiencing such adverse events to be enrolled, as they present significant symptoms that are not

immediately life-threatening (66). The principal investigators will be informed within 24 hours and will assess the severity of the event as mild, moderate or severe. Mild complications are tolerable, moderate complications interfere with daily activities, and severe complications render daily activities impossible. If a severe adverse event occurs according to Art. 63 (66), the research project will be interrupted and the ethics committee will be notified about the circumstances within 15 days according to HRO Art. 212 (66). Only one severe adverse event not related to the research project occurred during the pilot study. The participant decided merely to stop the project to have time for individual care related to advanced cancer. The informed consent materials and information sheets given to participants are available in French and English through the following website: https://www.seretablir.net/ensemble/

Declaration of interests

The authors declare that they have no competing interests.

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Table 1: WHO Trial registration Data Set of Ensemble RCT

Data Category	Information
Primary Registry and Trial Identifying Number	ClinicalTrials.gov: NCT04020497
Date of Registration in Primary Registry	July 16, 2019
Secondary Identifying Numbers	The Federal Office of Public Health's (FOPH) portal for human research in Switzerland NCT04020497 | SNCTP000003434
Source(s) of Monetary or Material Support	Swiss National Science Foundation (SNF) 10001C_185422
Primary Sponsor	Shyhrete Rexhaj
Secondary Sponsor(s)	Jérôme Favrod
Contact for Public Queries	Shyhrete Rexhaj, s.rexhaj@ecolelasource.ch; +41 21 556 44 35; Avenue Vinet 30; 1004 Lausanne, Vaud, Switzerland
Contact for Scientific Queries	Shyhrete Rexhaj, PhD, Professor associate
Public Title	Programme Ensemble: an early intervention for informal caregivers in psychiatry
Scientific Title	Ensemble programme an early intervention for informal caregivers of psychiatric adult patients: a protocol for a randomized controlled trial Ensemble RCT
Countries of Recruitment	Switzerland
Health Condition(s) or Problem(s) Studied	Psychological Distress, quality of life
Intervention(s)	Support as usual (SAU) Informal caregivers often have to manage the situation in various ways. SAU alone consists of informal support by the patient's clinical team. There are specific psychoeducational programs depending on the patient's illness (such as "Profamille" for schizophrenia) or peer-support depending to the voluntary work of the families' associations. Some general professional services focused on informal caregivers or relatives in order to inform and orient them if they need are available in the study area. No attempts have been made to standardize this treatment.
	Ensemble programme plus support as usual (SAU) The five-session Ensemble program provides targeted support to informal caregivers. It addresses informal caregiver's specific unmet needs, emotions and social resources in order to adapt care activities to each participant.
Key Inclusion and Exclusion Criteria	Inclusion Criteria: Being at least 18 years old; living in the French-speaking Switzerland cantons (commonly referred to as "Romandie") speaking French; having an adult relative suffering from a psychiatric disorder (with or without an established diagnosis); and having the capacity to agree to participate in the project
	Exclusion Criteria: Less than 20 on the Zarit score.
Study Type	Interventional
	Allocation: randomized; intervention model: parallel assignment; masking: assessor blind
	Primary purpose: health prevention and promotion
Date of First Enrollment	October 2019
Sample Size	160
Recruitment Status	Recruiting
Primary Outcome(s)	Psychological state change on the Global Severity Index (GSI): Timepoint: Baseline; at post-test, at 2 months follow
Key Secondary Outcomes	Optimism change on the Life Orientation Test-Revised (LOT-R) Timepoint: Baseline; at post-test, at 2 months follow Quality of life change on the Mental Component Score (MCS) Timepoint: Baseline; at post-test, at 2 months follow Burden level change on the Zarit Burden Interview (ZBI) Timepoint: Baseline; at post-test, at 2 months follow Standardized severity of the patient's illness changes on the Social an Occupational Functioning Assessment Scale (SOFAS) Timepoint: Baseline; at 2 months follow Qualitative participants' experiences concerning Ensemble benefits
Ethics Review	Approved; 28 August 2019; La Commission cantonale d'éthique de la recherche sur l'être humain (CER-VD)
Completion date	30 April, 2023

Table 2. Clinical tools

Clinical tools	Description
The Difficulties and Needs Self-Assessment Tool (ELADEB)	The ELADEB includes two independent scales, one focusing on difficulties and the other focusing on support for unmet needs. Twenty-one areas of life that enable identification of priority problems and orientation of support according to the level of emergency are assessed. These 21 areas of life are organized into 4 life dimensions: life conditions, daily pragmatic activities, relationships and health.
The Painful Emotions Tool	It uses pictures that reflect painful emotions such as guilt, judgment from others, loneliness, sadness, distress, despair, anxiety, helplessness, anger, confusion and shame. The participant selects the painful emotions that are present in his/her life. The tool also assesses the frequency of the emotions. Consequently, the support provided is targeted to the caregiver's most painful emotions.
The Social Network Tool	It uses a network map that specifies the social resources available to the caregiver. This tool provides a graphic representation aimed at identifying the informal caregiver's primary, secondary and tertiary environment.

Table 3: Expected quantitative results

Outcome	Question	Data	Analysis	Expected result
Main	Is the psychological state improved?	*Global Severity Index on the Brief Symptom Inventory*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically significantly improved compared to SAU
Secondary	Is optimism improved?	*Life Orientation Test – Revised*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically significantly improved compared to SAU
	Is quality of life improved?	*36-item Medical Outcome Study Short-Form Health Survey - Mental Component Score*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically significantly improved compared to SAU
	Is the burden reduced?	*Zarit Burden Interview*	ANCOVA of T1-T0, T2-T0, T0 as dependent, treatment condition as fixed factor	Experimental group statistically and clinically showed significant reduction compared to SAU
	Is the patient's social and occupational function improved?	*Social and Occupational Functioning Assessment Scale*	ANCOVA of T0-T2, T0 as dependent, treatment condition as fixed factor	Experimental group statistically reported improvements for patients compared to SAU

SAU = Support as usual

Table 4. Ensemble risk reduction protocol schedule of assessments and procedures

Procedures/assessments	CRF (Yes/No)	Staff member	Time (min)	-1 Screening/ consent	T0 Baseline/ randomization	1st and 2nd Month Ensemble vs support as usual	T1 Post-test	T2 Follow-up 4-months
Oral and written information	No	Research collaborator	20	√				
Consent	No	Research collaborator	30	√				
Eligibility criteria assessment	Yes	Research collaborator	10		√			
Sociodemographic questionnaire	Yes	Assessor			√			
The French Zarit Burden Interview (ZBI)	Yes	Assessor			√		√	√
Randomization - Computer-generated	Yes	A specific randomization coordinator	10		√			
The Brief Symptom Inventory (BSI)	Yes	Assessor			√		√	√
The Life Orientation Test – Revised (LOT-R)	Yes	Assessor			√		√	√
The 36-item Medical Outcome Study Short-Form Health Survey (SF-36)	Yes	Assessor			√		√	√
The Social and Occupational Functioning Assessment Scale (SOFAS)	Yes	Assessor			√			√
Qualitative data by 20 semi-directed interviews with participants in intervention	No	Two research collaborators						√
Treatment group	Yes	Intervention provider	360			√		
All groups, being in touch and continuing information	No	Intervention provider	30			√		
Supervision of intervention provider	No	Study coordinator	According to need			Continuously		
Termination of the study		Study coordinator	According to need			Continuously		
Serious adverse event form		Study coordinator	According to need			Continuously		
Progress notes	No	All team members	According to need			Continuously		

Table 5: Interview guide for the qualitative open and exploratory study relative to caregiver's experiences during the Ensemble programme

Introduction	
Acknowledgments and facilitator presentation: First, I would like to thank you for accepting this interview. It will allow us to explore your experience during the Ensemble programme. I would like you to share with me your experience, feelings, advantages and disadvantages that occurred during your participation in this programme. I am, **Name and Surname.** I am speaking as a researcher. I was not involved in the Ensemble project until now. I work at La Source, School of nursing, University of Applied sciences and Arts Western Switzerland, in Lausanne. I am very pleased to meet you this morning/afternoon. Purpose of the interview: As the project investigators have already told you, the purpose of this interview is to understand, in a qualitative way, your Ensemble programme experience. Interview procedure: The interview should last about 1hour maximum. Confidentiality: I guarantee you that the content of our exchange will only be used for scientific research purposes and that your identity will remain confidential. The analyses will focus on the content of this interview and the results of the questionnaires that you have filled in during the first step of the project. There will be no way to identify your personal data is coded. Audio recording: If it is ok with you, as written in the consent sheet/form, I would like to record the interview, in order to make our note-taking easier and so allow me to focus on our conversation. The recordings will not be in any case diffused nor shared outside the project's team. Participant's comfort: Is everything ok for you? Do you have any question before we start?	
Interview	**Objectives**
Interview opening question: **Can you describe me your experience during the Ensemble programme?**	To understand the Ensemble programme experience of the participant in general.
Questions to ask in order to sustain and revive the speech of the participant: How would you qualify the help that you have received during the Ensemble programme? What advantages for you and your relative, have you identified in this programme? What disadvantages for you and your relative, have you identified in this programme? Which contents/exercises have helped you to better manage your situation or your caregiver role? On the contrary, which contents/exercises have you found pointless? What do you think of the term « caregiver »? Has the Ensemble programme eventually contributed to better assimilate this notion or on the contrary, to reject it? Explain. What remarks or suggestions would you give to improve the support that you have received? Is your situation different after the intervention compared to your situation before? Yes/No; How different is your situation? If Yes, do you attribute this difference to your participation in the Ensemble programme? Which elements of the programme seem to have played a part in this change of your situation/life? Which elements of the programme seem to have helped to initiate that change? Is your relative health state different after this intervention (compared to what it was before)? Yes/No; How different is the state of health of your relative? Do you think that this improvement/change is related to the support that you have received? Yes/No; If Yes, how do you explain this relation between improvement/change and the Ensemble programme Which impacts have you noticed in your quality of life? Could you tell me a major situation that you might have experienced during the Ensemble programme? What was useful during the accompaniment? What more would you have liked? What do you considerate as not enough nor not useful? How would you qualify the relationship that you have had with the intervention provider of the Ensemble programme?	To identify: i) the eventual benefits and disadvantages of the Ensemble programme for the caregiver and his/her relative, ii) the contribution of the contents and practical exercises of the programme in the capacity to manage painful emotions and resolve difficulties during the programme, or in the future, iii) the contribution of the programme on the empowerment in the caregiving role or for the person independently of this role, iiii) indications in order to improve the programme. To observe the eventual process of change (quality of life, situation…) that the programme might have generated. To get concrete illustrations of these changes and information on the accompaniment of the intervention provider.
Conclusion	
In the end, what « word » would you choose to qualify/describe your experience as a participant in this programme? Would you like to add anything?	To propose a review and offer possibility to add anything.

Figure 1. Ensemble program and process

Figure 2. RCT Flowchart

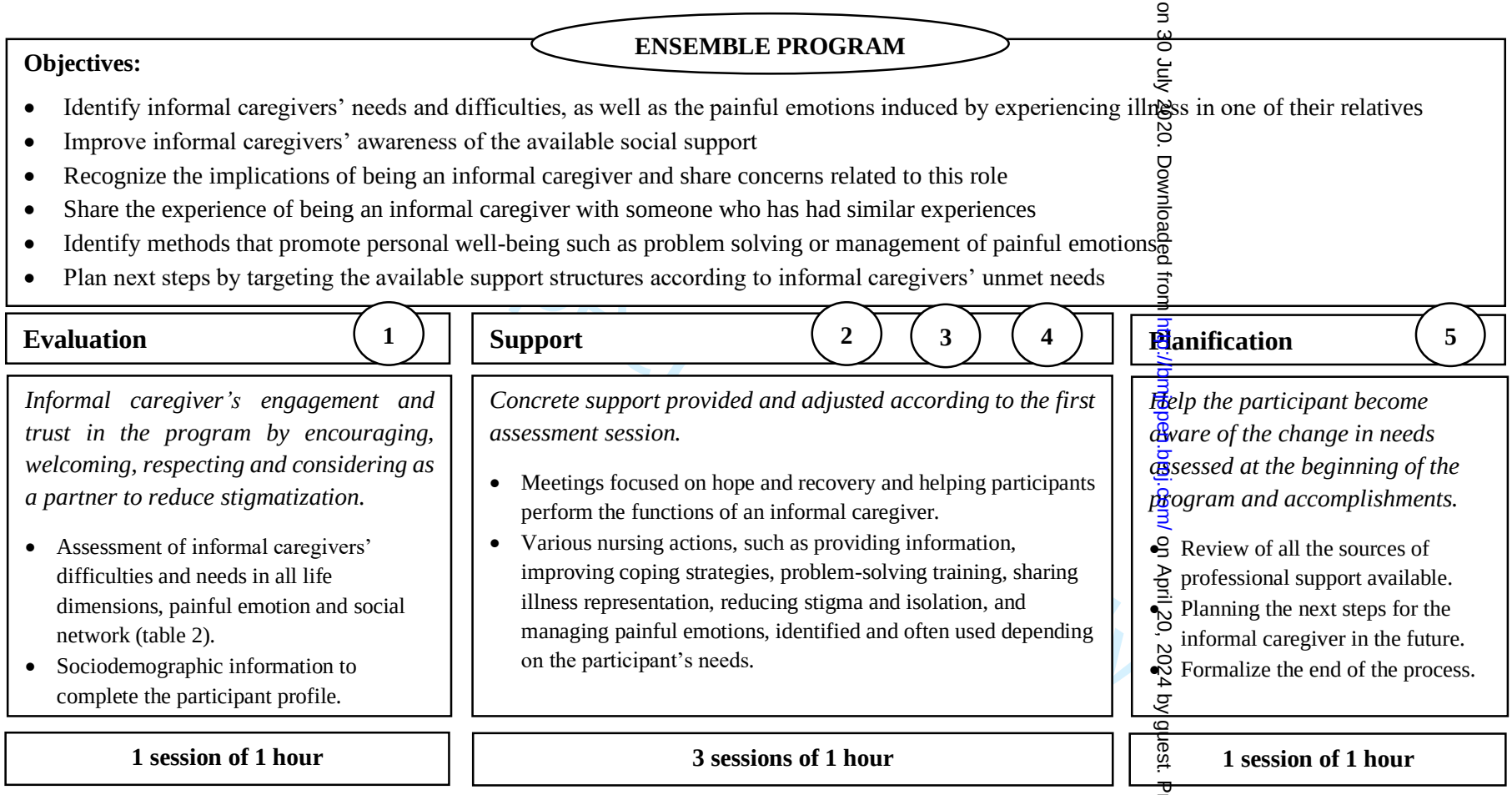

Figure 1. Ensemble program and process

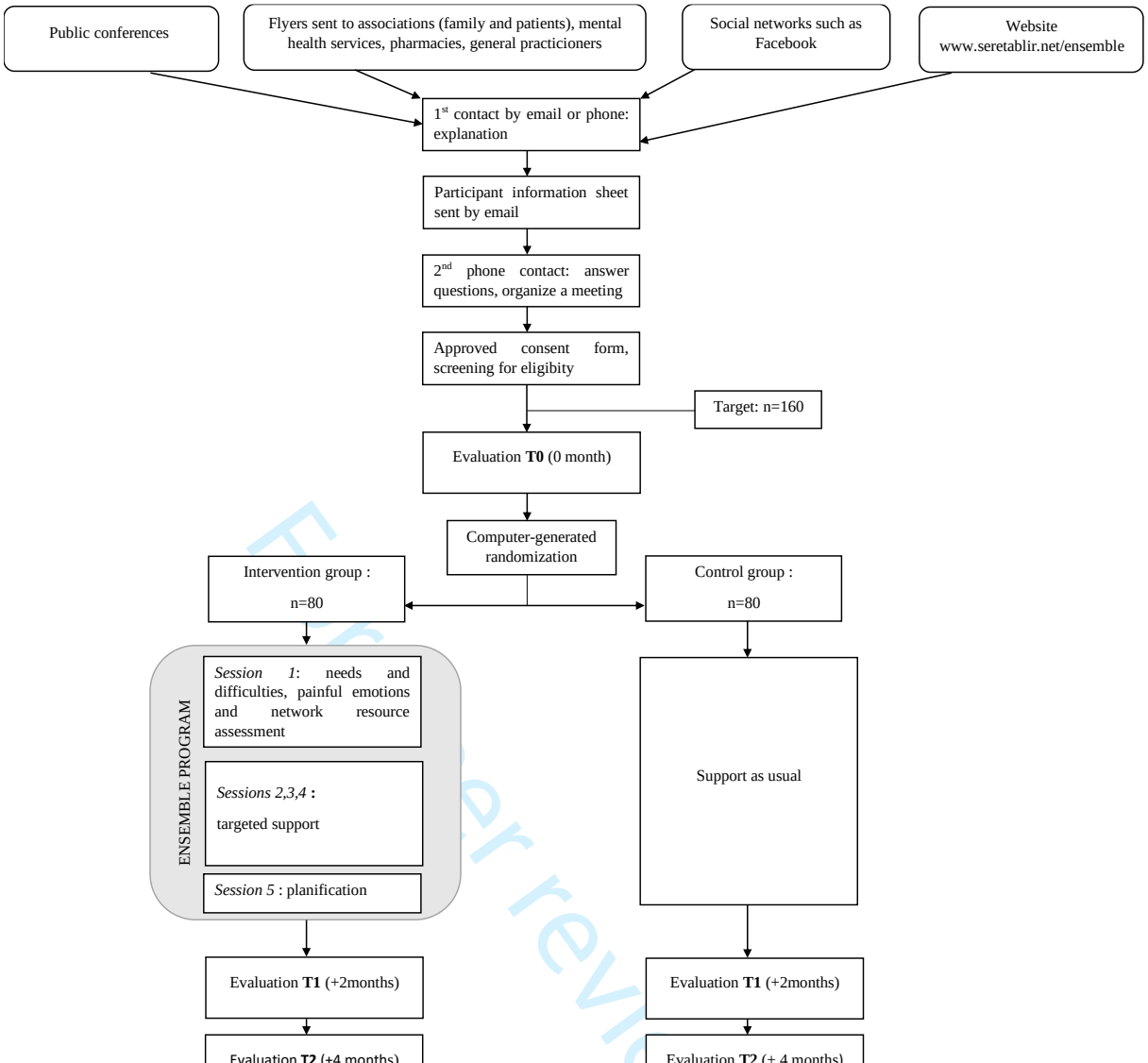

Figure 2. RCT Flowchart

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Title of the study

Ensemble Programme an early intervention for informal caregivers of psychiatric patients: a randomized controlled trial

This study is conducted by: Rexhaj Shyhrete and Favrod Jérôme, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Lausanne

Dear Sir/Madam,

We invite you to participate to our research project. This information sheet describes the research project.

Detailed information

1. Objectives of the study

This study concerns the difficulties to maintain an optimal psychologic health state and a good quality of life for the informal caregivers providing support to persons with severe psychiatric disorders. The possible difficulties that can impact negatively the health of informal caregivers are generally linked to a high level of burden. An early intervention, Ensemble program, allowing to promote their health state, was therefore developed. The primary outcomes indicate a significative improvement of their psychological state of health. This brief intervention includes five sessions conducted by a healthcare practitioner as nurses or psychologists and allows the informal caregiver to take a step back on his/her supporting role. The first session helps the informal caregiver to observe his/her needs, difficulties, painful emotions and social network resources.
The professional provides during the next three sessions adjusted and tailored support according to the first assessment session. The last session allows to review what has been done and to plan the next steps according the informal caregiver needs. This study must allow us to know if the Ensemble program improves informal caregivers' psychological health state, quality of life, optimism and reduce their burden induced by the psychiatric disorder of the person they are supporting. The study will also allow to assess the durability of the potential advantages of Ensemble with a two months follow-up set. This study will allow us to assess the clinic efficacity and potential feasibility of the Ensemble program. This study outcomes will provide essential information on the way of providing adjusted and efficient support to informal caregivers.

2. Selection of people being able to participate in the study

The study is open to every informal caregiver who provides close support to persons with psychiatric disorders. The following criteria must be met: 1) being an informal caregiver providing support to a person with psychiatric disorder and having a burden score of at least 20 on the French Zarit Burden Interview (ZBI) which indicates a lower burden (Hébert, Bravo and Girouard, 1993), 2) being at least 18 years old and 3) speaking French.

3. General Information about the study

This research project follows a first pilot study conducted in an adult psychiatric service from the CHUV in collaboration with l'Ilot (association of informal caregivers of psychiatric disorders) and with La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland. The pilot study helped to construct and to validate the acceptability of the Ensemble program with 21 informal caregivers. The preliminary outcomes were promising, therefore we decided to test the efficacity of the program with a larger number of informal caregivers living in the Switzerland French speaking area. This project runs for 4 years starting from September 2019. We hope being able to recruit 160 informal caregivers' volunteers.
To test the effects of the Ensemble program, you will be randomly assigned into two groups: either intervention group or control group. In the intervention group you will begin rapidly the Ensemble program. However, if you are assigned into the control group, you will be able to benefit from the Ensemble program once the study is finished. Study participants fill in research questionnaires three times: (1) at the beginning of the project, (2) two months later and (3) four/five months later, in order to compare the informal caregivers following the Ensemble program at the beginning of the project and the informal caregivers who need to wait. You will meet

a research assistant to help you fill in the different questionnaires. This assistant does not know if you have received the Ensemble program at the beginning of the project or if you will receive it after. At the end of the project, a group of 20 participants will also be randomly selected in order to participate to individual interviews to evaluate qualitatively the effects of the Ensemble program.

Your involvement in the project lasts approximately five months: four times one hour to fill in approved consent form and research questionnaires and five times one hour to receive the Ensemble program. If you are in the intervention group, you will begin the Ensemble program after filling in the research questionnaires. The program can take up to two months. The five sessions will be planned between you and the professional once a week or one every two weeks. The program sessions can be held at any place of your choosing, at your place, at one of our facilities in La Source, School of Nursing Sciences in Lausanne or at another consultation location in l'Espace Proches facility for example. This will allow a calm and confidential space for the individual. If a session cannot happen (moving obligation, impossibility to come, etc.), the intervention could exceptionally be given by visio-conference. We need to proceed that way because the time between two meetings cannot be more than ten days.
However, if you are in the control group, you will fill in the research questionnaires three times 1) at the beginning of the project, 2) two months later and 3) at the end. Then, you will be able to benefit from the Ensemble program of five support sessions with a professional.

The research questionnaires allow us to assess your current psychological health state (the BSI Global Index Score), your quality of life (the 36-item Medical Outcome Study Short-Form Health Survey), your optimism (Life Orientation Test-Revised (French version)) and your burden (Zarit Burden Interview (French version)). The social and occupational functioning of the person that you are providing support to (the Social and Occupational Functioning Assessment Scale (SOFAS)) will also be assessed.

At the end of the study, 20 participants will be selected and interviewed in an individual interview to explore their experience of the Ensemble program. Two groups of participants will be included in this phase, those who have benefited greatly from the program (G1; n=10) and those who have less benefited (G2; n=10). This selection will allow us to better understand the added value of the Ensemble program and to identify areas for improvement. The interviews will be recorded with an omnidirectional microphone (Marantz audio MP3 format) and will be transcribed on Microsoft Word. We need the recordings to ensure the interviews' transcription. Your recording will be destroyed after transcription. If you approve, we will contact you for this qualitative evaluation at the end of the study. Further information will be given in due course. You will have time to examine the conditions and will be free to refuse even if you have had already approved at the beginning of the project. Furthermore, video recordings can also be realized to help the professional who is meeting you in the Ensemble program, develop his/her skills. These recordings will be accessible by the professional him/herself and his/her supervisor (Shyhrete Rexhaj or Jérôme Favrod). Some of these recordings will also be used as specific analyses to enrich pedagogy and develop the different professional skills of the Ensemble program.

If you agree to participate to this process, you will be given detailed information about the pedagogic aims of theses video recordings. If you approve, the professional who will follow you during the Ensemble program, will give you further information. You will have time to examine these conditions and will be free to refuse even if you already have signed the approved consent at the beginning of the project.

All these research data and your personal data will be given to the manager research team of this project who will safely keep them. The team will contact you, following your approved consent, during the different steps of the project.
We conduct this study in respect of the swiss legislation prescriptions. We follow all the international recognized guidelines. The cantonal ethics Committee have controlled and authorized the study. You will find a study description on the Federal Office of Public Health website: https://www.kofam.ch/fr/portail-snctp/recherche/74009/etude/47320; NCT04020497 | SNCTP000003434.

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4. Conduct for the participants

The table below allows you to visualize the moments of measures and the duration of the Ensemble program participation either you are in the control or intervention group.

		Intervention group	Control group
Beginning of the project	Filling in the standard questionnaires with a research assistant (1H)	√	√
	Ensemble program (5x1h per week or up to every two weeks)	√	
Two months later	Filling in the standard questionnaires with a research assistant (1H)	√	√
Four/five months later:	Filling in the standard questionnaires with a research assistant (1H)	√	√
	Participation to an individual interview only 20 participants (up to 1H30)	√	
End of the study			
	Ensemble program (5x1h per week or up to every two weeks)		√

5. Benefits for the participants

This project allows you to benefit freely from the Ensemble program. In case of positives Ensemble program outcomes are confirmed, the support that you will get during the project will help you to step back from your informal caregiver role and find solutions to better cope with your relative psychiatric disorder. The study outcomes could prove significant later, to the informal caregivers that live a similar experience as your own.

6. Participants rights

Your participation is entirely free. If you choose not to participate or if you come back from your decision during the study, you will not have to justify your decision. This will change nothing to your usual support. You can ask all the questions linked to the study at any time. You may contact one of the persons indicated at the end of this information sheet, to do so.

7. Participants obligations

As a study participant, you will have to:

- Fill in the research questionnaires
- Participate to the planned Ensemble program meetings with a professional

8. Risks and constraints for the participants

As the intervention is a complement to usual support, risks are low. However, assessing your individual needs, painful emotions and social network as you take a step back, can generate pain. The planned meetings will be adjusted following your needs and should not provoke supplementary risks.

Also, the randomly repartition (intervention or control group) requires that participants of control group be more patient than the participants of intervention group to benefit from the support offered in Ensemble program set.

9. Others treatment possibilities

You are under no obligation to participate to the study. If you decide not to take part in it, it will be possible to be advised on the other possibilities of informal caregiver support.

10. Discoveries during the study

Any appearing discovery during the study relevant to your health will be transmitted.

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11. Data confidentiality

We respect all legal dispositions relating to the data protection. Your personal and your data relating to your well-being and your quality of life are protected and used coded. Only a limited number of people can consult your data under a non-coded way and will exclusively use it to fulfill their duties within the scope of the study. Coding means that all data allowing to identify you (for example name, date of birth, etc.) are replaced with a code (ex: name and first name will be replaced by initials with a combination of letters as factices initials) that have no link to your true initials (for example 'AAA', 'BBB'). The code stays permanently in our institution. People who do not know the code cannot linked these data to you. In a publication, data will be anonymised. Your name will not appear of the internet or any publication. Sometimes, scientific journals ask for individual data (raw data). In this case, individual data will be coded and will not allow to identify you as a person. All involved persons in this study are bounded by professional secrecy. All guidelines relating to data protection are respected. You have the right to consult your data at any time.

During its course, the study can be inspected. The ethical commission who has controlled and authorised this study can conduct inspections. Investigators might communicate your personal data for the needs of these inspections. All people are bounded by professional secrecy.

During the project, your data will be inserted into a secured software named REDCap. Only staff members of this project will have access to these data. At the end of the project, your data will be coded and will be stored in a secured platform named FORS.

12. Withdraw from the study

You can withdraw at any time. The personal and relevant data of your wellbeing and quality of life will be coded and analyzed as the other participants and then fully anonymized.

13. Participants compensation

If you participate to this study, you will not receive any compensation.

14. Compensation of incurred damages

In the event of study-related damage or injuries, the liability of the institution Institut et Haute Ecole de la Santé, La Source provides compensation.

15. Funding of the study

This study is financed by the Swiss National Science Foundation.

16. Contact persons

In case of any doubts, concerns or emergencies during or after the study, you can contact at any time one of the following persons:

Rexhaj Shyhrete, HES Associate professor, La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Av. Vinet 30 1004 Lausanne/079 103 18 16

Favrod Jérôme, HES Full Professor La Source, School of Nursing Sciences, HES-SO University of Applied Sciences Western Switzerland, Av. Vinet 30 1004 Lausanne/ 079 447 31 57

Santé mentale et psychiatrie
Laboratoire d'Enseignement et de Recherche

Written consent declaration for the participation of a research project

Read with caution this form. Do not hesitate to ask any questions if you do not understand anything or if you need precisions.

Study BASEC number: (After submission to the competent ethics commission)*:*	
Study title*:* (Scientific title and usual title)	**Ensemble Programme an early intervention for informal caregivers of psychiatric patients: a randomized controlled trial** **Programme Ensemble: clinical trial to test its effect**
Leader institution:	La Source, School of Nursing Sciences, Avenue Vinet 30, 1004 Lausanne
Localization of the study:	French-speaking Switzerland
Monitoring managers and investigators of the project on the site:	Rexhaj Shyhrete Favrod Jérôme
Participant: (PRINT NAME and FIRST NAME): Date of birth:	☐ woman ☐ man

- I declare having been informed, by the responsible investigator and/or his/her research coworker undersigned, orally and in writing, of the objectives and conduct of the study.
- I take part in this study voluntarily and I accept the content of this above-mentioned study information sheet that I was given. I have had enough time to take my decision.
- I received satisfactory answers to the questions that I have asked about my participation to the study. I keep this information sheet and receive a copy of my written consent declaration.
- I have been informed of the other possible support for informal caregivers.
- I accept that the competent specialist of the sponsor of the study and Ethics Commission can consult my draw data to proceed to controls, in the case where the confidentiality of these data are strictly assured.
- I will be informed of any discoveries with a direct impact on my health.
- I know that my personal data and the data relating to my well-being and my quality of life can be transmitted for research purposes in this project set only and under a coded form.
- I can whenever and without justification withdraw my consent to participate in this study, without any negative repercussion on my informal caregiver situation and the situation of the person I take care of. Data collected until my withdraw will be analyzed.
- I am informed that the liability of the institution Institut et Haute Ecole de la Santé, La Source provides compensation in case of any damages that could incur in this project.

Location, date	Participant signature

Santé mentale et psychiatrie
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Putting an X in the Yes box, I agree to participate to a qualitative interview for research purposes.

Yes: ☐ **No :** ☐

Putting an X in the Yes box, I agree to participate to the video recordings useful for the supervisions.

Yes : ☐ **No :** ☐

Putting an X in the Yes box, I agree to participate to the video recordings useful for the pedagogy research

Yes : ☐ **No :** ☐

Investigator/research coworker confirmation : Hereby, I confirm having explained to the participant the nature, the importance and the scope of the study. I declare satisfying all legal obligations relating to this project. If I should notice, whenever during the project realization, susceptible elements of influencing on the consent of the participant to take part in the project, I engage to inform him/her immediately.

Location, date	PRINT NAME and FIRST NAME of the investigator/research coworker assuring the information to the participants. Investigator/research coworker signature

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1

Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	1
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	1
Protocol version	#3	Date and version identifier	1
Funding	#4	Sources and types of financial, material, and other support	1
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1-2
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	2
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	2
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	2

Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-5
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	4-5
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and	6

		individuals who will perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	7
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	7
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	7-8
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended	8

		(see Figure)	
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	8
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	8
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8-9

Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8-9
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	8-9
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	9-11
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values).	12

		Reference to where details of data management procedures can be found, if not in the protocol	
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	12
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	12
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	
Methods: Monitoring			12
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	12
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	12
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial	12

		conduct	
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	12-13
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	13
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	13
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	13
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	13
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	13
Declaration of	#28	Financial and other competing interests for principal	13

interests		investigators for the overall trial and each study site	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	13
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	13
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	13
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	13
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	13
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	13
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	-