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Sequential multiple assignment randomised controlled trial protocol for developing an adaptive intervention to improve depressive symptoms among family caregivers of people with dementia

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ABSTRACT

Objectives Family caregivers of people with dementia (FC-of-PWD) suffer from a high level of stress and depressive symptoms, which usually require different interventions at different stages. Although some standalone interventions such as behavioural activation (BA) and mindfulness practice (MP) have been shown to be potentially effective at reducing depressive symptoms, the best sequence and combination of these interventions for caregivers are unknown. This study aims to develop and identify a two-stage adaptive intervention with prespecified rules guiding whether, how or when to offer different interventions initially/over time to reduce depressive symptoms in FG-of-PWD.

Methods A sequential multiple assignment randomised trial design will be adopted. 272 FG-of-PWD with mild to moderate depressive symptoms will be recruited from the community. Four two-stage, embedded adaptive interventions involving BA and MP of different sequences and dosages (eg, 8 weeks of BA followed by booster sessions for responders and 8 weeks of MP for non-responders) will be assigned to the participants following a set of decision rules. The primary outcomes will be depressive symptoms (measured using the Patient Health Questionnaire-9), assessed after the second stage of the intervention. Other outcomes, such as positive aspects of caregiving (measured using the Positive Aspects of Caregiving Scale), sleep quality (measured using the Pittsburgh Sleep Quality Index) and time points will also be assessed. The analyses will follow the intention-to-treat principle. Several process indicators (eg, engagement in meaningful activities and level of mindfulness) will also be assessed. The findings will have strong implications for the further development of psychosocial adaptive interventions to reduce depressive symptoms among FC-of-PWD.

Ethics and dissemination This study has received ethical approval from the Human Research Ethics Committee at The Hong Kong Polytechnic University (HSEARS20211223001). The findings will be presented at academic conferences and submitted to peer-reviewed journals for publication.

Trial registration number NCT05634317.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study adopts a sequential multiple assignment randomised trial design to develop an adaptive intervention to improve depressive symptoms in family caregivers of people with dementia.
⇒ Two evidence-based interventions, namely behavioural activation and mindfulness practice, will be adopted to develop the adaptive intervention for family caregivers of people with dementia.
⇒ The findings can inform us of prespecified rules guiding whether, how or when to offer different interventions initially/over time to reduce depressive symptoms in family caregivers of people with dementia.

INTRODUCTION

Dementia is a public health priority affecting over 50 million individuals worldwide, without breakthroughs in prevention and treatment, the prevalence will keep increasing.[1] Demanding caregiving tasks, difficulty of managing behavioural and psychological symptoms of dementia, and conflicts between caregiving and other social roles (eg, employment, other family responsibilities) can result in high levels of personal stress and a lack of time for leisure and rest.[2] Family caregivers of people with dementia (FC-of-PWD) are, therefore, vulnerable to depression, with a prevalence rate of 30%—50%.[3 4] Unsurprisingly, overburdened caregivers often choose to exit their caregiver role by institutionalising

the care recipient.[5] The impact of the disease on persons suffering from dementia and their caregivers is projected to lead to significant increases in healthcare and long-term care costs.[6] Additionally, those caregivers who do not seek help tend to suffer from a higher risk of developing depression, which is associated with a higher risk of suicidal ideation.[7] In a recent systematic review, two types of interventions, namely behavioural activation (BA) and mindfulness practice (MP), were shown to have significant effects on reducing depressive symptoms in FC-of-PWD.[8]

BA is a psychological intervention aimed at engaging individuals in activities that provide positive reinforcement and improve their mood.[9] Recent evidence indicates that BA is as effective as traditional cognitive behavioural therapy for treating depression in adults, but is more accessible and affordable.[10] In a recent meta-analysis, BA was found to be effective at treating depression (Cohen's d=0.55) in the FC-of-PWD.[11] In particular, in a recent study, an 8-week telephone-delivered psychoeducation intervention with an enhanced BA module had a stronger impact on reducing depressive symptoms among the FC-of-PWD than a psychoeducation programme alone.[12] MP is another psychosocial intervention aimed at increasing an individual's attention and self-awareness in the present moment in a non-judgdemental manner through formal MP such as sitting meditation and informal exercises such as mindful eating.[13] In a recent meta-analysis, MP was also found to be one of the standalone interventions that had a large impact on reducing depressive symptoms in FC-of-PWD.[8] MP could help FC respond in a less reactive way to the stressors from their caregiving, and accept the stressors in a non-judegmental manner.[14] In particular, a systematic review and meta-analysis indicated that MP could significantly reduce depressive symptoms in FC-of-PWD (standardised mean difference (SMD) 0.62, 95% confidence interval (CI) 0.97 to 0.27).[15] The beneficial effects on the caregivers' psychological health could also extend to improving the care-recipients' behavioural and psychological symptoms of dementia.[16]

Psychosocial interventions for the FC-of-PWD are often standardised, one-off programmes lasting for about 4 months.[8] However, dementia caregiving has a trajectory that is persistent, extending over months or years, and progressive.[17] Consequently, the beneficial effect of a one-off standardised intervention is relatively small, particularly if one takes a long-term perspective due to the progressive nature of dementia.[8] Another problem relates to manualised interventions delivered to all caregivers, in that a substantial proportion of dementia caregivers may not respond to that particular psychosocial intervention.[18]

	STUDY PERIOD							
	Enrolment	1st allocation	Post-1st allocation		2nd allocation	Post-2nd allocation		
TIMEPOINT	$-t_1$	0	T1 Baseline	T2 8 weeks		T3 16 weeks	T4 20 weeks	T5 32 weeks
ENROLMENT:								
Eligibility screen	X							
Informed consent	X							
Allocation		X			X			
INTERVENTIONS:								
Mindfulness Practice			—	—		—		
Behavioural Activation			—	—		—		
ASSESSMENTS:								
Socio-demographic data			X					
Depressive symptoms			X	X		X	X	X
Perceived caregiving stress			X	X		X	X	X
Positive Aspect of Caregiving			X	X		X	X	X
Sleep Quality			X	X		X	X	X
Health-related quality of life			X	X		X	X	X

Figure 1 SPIRIT flow diagram of the study. SPIRIT, Standard Protocol Items: Recommendations for Interventional Trials.

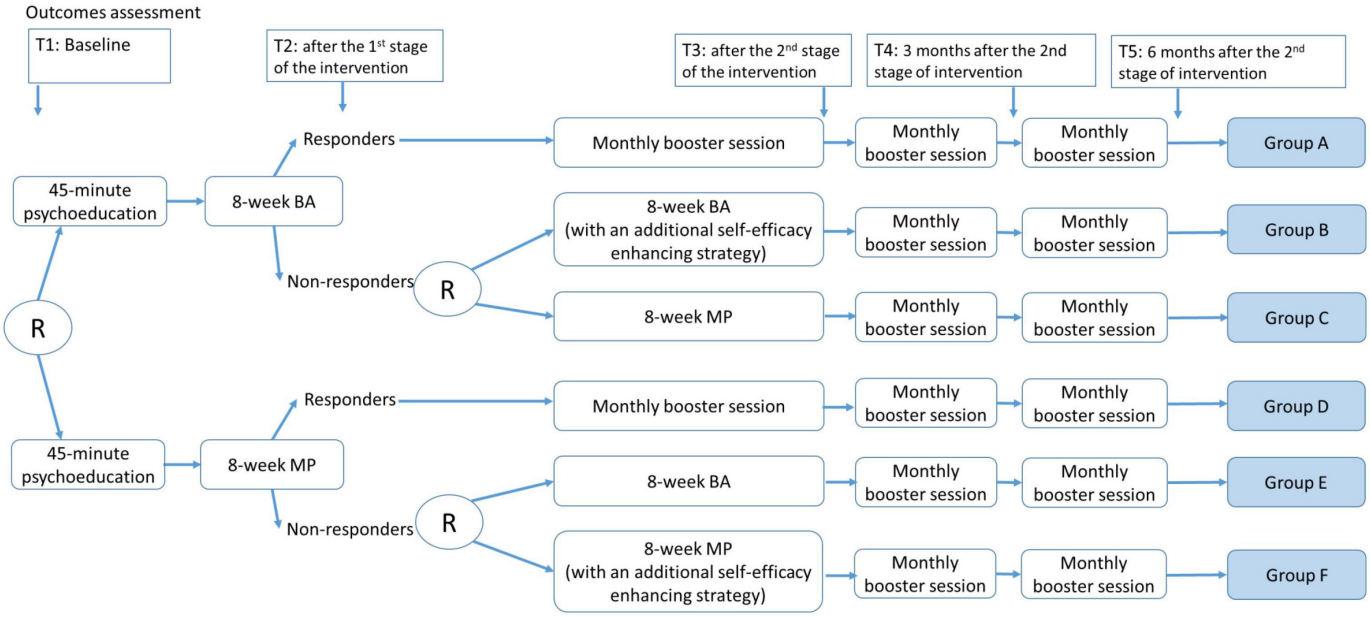

Figure 2 SMART design flow chart. BA, behavioural activation; MP, mindfulness practice; SMART, sequential multiple assignment randomised trial.

An adaptive intervention is a sequence of decision rules specifying whether, how, when and on the basis of which measures, to alter the dosage (such as duration or frequency), type or delivery of treatment at decision stages in the course of delivering care.[19] Given the above limitations in previous studies, we will identify a two-stage adaptive intervention with a prespecified set of decision rules that guide whether, how or when, and based on which measures, to offer different intervention options initially and over time through this proposed study. The ultimate goal of this study is to identify an adaptive intervention protocol that could reduce depressive symptoms to a minimal level in the FC-of-PWD and allow those gains to be maintained over time.

METHODS

Study design

This is a prospective, sequential multiple assignment randomised trial (SMART). The traditional randomised controlled trial (RCT) design allows for the effectiveness of an intervention to be rigorously tested, but provides limited data for developing 'treatment strategies' that may involve a number of different interventions, dosages or components. In contrast to typical RCTs, a SMART design will randomise participants into different sequences of intervention options according to a set of decision rules. The design of SMART allows researchers to investigate the effects of different intervention options and develop an adaptive approach to better meet participants' needs.[19] Therefore, we propose using the SMART design to provide evidence of which intervention to provide initially, how to determine whether or not the first stage of the intervention is working and, if it is not, which intervention to provide next. We also reported this study protocol following the guideline of Standard Protocol Items: Recommendations for Interventional Trials statement (figure 1).[20] This proposed study is a 3-year study lasting from October 2022 to September 2025, including the preparatory phase (October 2022–June 2023) of training research personnel and developing training materials, followed by the implementation phase (June 2023–September 2025).

Objective

The ultimate goal of this study is to identify an adaptive intervention that could reduce depressive symptoms in the FC-of-PWD.

Hypotheses of the study

We hypothesise that different sequences and combinations of the two interventions, BA and MP, will have different effects (figure 2). The following hypotheses have been formulated:

1. The primary hypothesis is that the following embedded adaptive interventions (table 1) will have different effects on depressive symptoms and secondary outcomes (stress, positive aspects of caregiving (PAC), sleep quality and health-related quality of life (HRQoL)) at T3 (immediately after the second stage of the intervention), T4 (3 months after the second stage of the intervention) and T5 (6 months after the second stage of the intervention):
   - Eight-week BA; if no response (defined as a 'less than 50% reduction in Patient Health Questionnaire-9 (PHQ-9) scores indicating a clinically significant improvement'[21]), deliver another 8 weeks of BA with an additional self-efficacy enhancing component (BA and BA); otherwise, provide 2 monthly booster sessions for responders.

- Eight-week BA; if no response, deliver a further 8 weeks of MP (BA and MP); otherwise, provide 2 monthly booster sessions for responders.
- Eight-week MP; if no response, deliver another 8 weeks of MP with an additional self-efficacy enhancing component (MP and MP); otherwise, provide 2 monthly booster sessions for responders.
- Eight-week MP; if no response, deliver a further 8 weeks of BA (MP and BA); otherwise, provide 2 monthly booster sessions for responders.

2. The BA and the MP will have different effects on depressive symptoms and secondary outcomes at T2 (immediately after the first stage of the intervention).
3. For participants who do not respond to the first stage of the intervention, further extending their original first stage of the intervention with an additional self-efficacy enhancing component or switching to an alternative intervention (opposite to the first stage of the intervention, MP or BA) will have a different effect on depressive symptoms and secondary outcomes at T3, T4 and T5.
4. The sequence of the intervention, BA followed by MP or MP followed by BA, will have different effects on depressive symptoms and secondary outcomes at T3, T4 and T5. There will also be two hypotheses to help explain positive changes in the BA and MP:
5. The process indicators of BA (engagement in meaningful, healthful and enjoyable activities) and/or MP (level of mindfulness) will mediate the effect of the interventions on depressive symptoms at T2, T3, T4 and T5.
6. The changes in the process indicators of the BA and/or MP intervention measured at 2, 4 or 6 weeks after the start of the first stage of the intervention will predict the response to the intervention at that stage at T2. (Rationales: to confirm whether the process indicators are a better variable than depressive symptoms for determining the effectiveness of the first stage of the intervention).

Study setting and participants

The target population will be community-dwelling FC-of-PWD recruited from three local non-governmental organisations (NGOs) that provide dementia care services. Inclusion criteria: (1) aged 18 or above; (2) the FC of an individual with a confirmed medical diagnosis of Alzheimer's, vascular or a mixed type of dementia who has been residing in the community; (3) had been providing care for at least 3 months prior to recruitment and (4) the presence of mild-to-moderate depressive symptoms (PHQ-9 score of 5–14). Exclusion criteria: (1) had participated in any structured mind-body intervention, cognitive therapy or structured psychosocial intervention 6 months prior to recruitment, (2) have acute psychiatric and medical comorbidities that are potentially life-threatening or would limit the caregivers' participation or adherence (eg, suicidal ideation, acute psychosis) and (3) had commenced taking antipsychotic medications in the past 2 months.

Sample size

A power analysis was conducted to estimate a sample size sufficient to detect the main effect on depressive symptoms in a SMART design.[19] Two previous studies on dementia caregivers receiving mindfulness and BA had an attrition rate of 9.0% and 8.9%, respectively.[12 22] After considering the effect size and their attrition rates, a conservative effect size of Cohen's d=0.5 and 20% attrition will be adopted for the estimation. A sample size of 136 FC (68 per group) will be needed to achieve 85% power at a two-sided 5% level of significance for the first stage. Taking a conservative non-response rate of 0.5 for both BA and MP in the first stage of the intervention,[22] a total sample of 136/0.5=272, 63 in each subgroup (eg, subgroup B+E, see figure 1) will be needed. To compare the effects between the four embedded adaptive interventions, a total sample of 166 will be needed to identify the best embedded adaptive intervention, considering at least a 95% probability with a medium effect size of 0.5

Table 1 Four embedded adaptive interventions

Embedded adaptive intervention	First stage of the intervention	Status after the first stage of the intervention	Second stage of the intervention	Subgroups (see figure 2)
#1	8 weeks BA	Responder	Booster sessions	A+B
		Non-responder	8 weeks BA (with an additional self-efficacy enhancement component)	
#2	8 weeks BA	Responder	Booster sessions	A+C
		Non-responder	8 weeks MP	
#3	8 weeks MP	Responder	Booster sessions	D+C
		Non-responder	8 weeks MP (with an additional self-efficacy enhancement component)	
#4	8 weeks MP	Responder	Booster sessions	D+F
		Non-responder	8 weeks BA	

BA, behavioural activation; MP, mindfulness practice.

(Cohen's d) and an attrition rate of 20%.[23] After considering sample sizes of 136, 166 and 272 for different stages, we choose a conservative sample size of 272 FC for this study.

Recruitment strategy, randomisation and procedure

A convenience sampling method will be used to recruit participants. An email will be sent to NGOs that provide elderly care services for PWD and their caregivers inviting them to participate in this study. The NGOs will refer potential participants to the research team. A research assistant will then screen them for eligibility. Written informed consent will be obtained from all participants, to whom all aspects of the study will be explained and questions answered. Participants can refuse to take part or withdraw from the study at any time. After screening, those who agree to participate will be interviewed to obtain their health sociodemographic data and will undergo a baseline assessment. Permuted block randomisation will be employed in this study following the allocation concealment mechanism. At all stages, an independent statistician will randomise a list of eligible caregivers via computer-generated random numbers and the caregivers will be informed of their group allocation via a sealed opaque envelope containing information about their group allocation. The researchers/research assistants who perform the assessment and analysis will be blinded to the group allocations.

Interventions

Behavioral activation

The BA will be a modified version of the phone-based BA protocol developed in a prior study for FC-of-PWD.[12] The aim of BA is to reduce activities that maintain or contribute to depressive symptoms and increase or reinforce activities that are meaningful, healthful and enjoyable, to improve mood, through goal setting and activity planning (figure 3). BA, consisting of a total of 16 sessions (30 min each) offered twice a week over 8 weeks, will be delivered by a trained instructor through a videoconference mobile app (table 2). Participants will be asked to review their daily activity patterns and then choose activity goals and review their successes and areas of improvement. They will also be taught how to fill out the daily monitoring record, which will involve noting down their daily activities, and rating the importance and degree of enjoyment associated with each activity. All participants will be encouraged to fill out the form and make sure they feel that it is a doable task. To enhance their adherence, participants can complete the form in a mobile app or in hardcopy, according to their preference. The research assistant will work with the participants to identify and schedule values-based, rewarding engagements and activities, and use components to reduce depressive symptoms and solve the problem of barriers to engaging in meaningful, healthful and enjoyable activities via smartphone.

Mindfulness practice

The MP programme to be used in this study is based on a modified MP that was shown in a prior study to be effective at reducing depressive symptoms in FC-of-PWD.[16] A qualified mindfulness instructor will deliver the programme through a videoconference mobile app. Various MPs will be included (eg, mindful walking, body scanning) and thoughts and feelings will be shared (table 2). The programme is aimed at helping participants to develop mindfulness skills through the formal and informal practice of mindfulness and to disengage from their negative thought patterns (figure 3). To standardise the interventions in this study, the previous approach will be changed from 7 weekly sessions of 120 min each to 16 sessions of 30 min each, held twice a week over 8 weeks. The participants will also be encouraged to perform 30 min of MP every day. All participants will be given an audio (mp3) recording of guided mindfulness activities to enhance their daily practice, and a logbook via a mobile app or in hardcopy (according to their preference) to record the frequency of their self-practice at home and to monitor their compliance rate. Volunteers will provide support via smartphone to answer questions and address difficulties (eg, technical problems or difficulties in the daily practice). All of the volunteers will be postgraduate students in a healthcare-related discipline and will have received 40 hours of training in delivering basic BA and MP skills. If the volunteers are unable to answer the participants' questions, they will refer them to the therapist.

SMART design and procedure

Figure 2 shows details of the randomisation according to the SMART design. In the first stage, the participants will be randomised following an allocation concealment mechanism into either the BA group receiving 16 sessions (30 min each) of BA through their smartphone over 8 weeks, or the MP group receiving 16 sessions (30 min each) of MP through their smartphone over 8 weeks. Before the intervention, the participants will attend a 45 min psychoeducation session on depression, caregiving and MP or BA, to gain a basic understanding of the causes of depressive symptoms and of how the intervention might help them. They will be instructed to not divulge the condition to which they have been assigned. In the second stage, non-responders (those with a reduction in PHQ 9 scores of less than 50%) to the first stage of the intervention will be randomised to either receive the same intervention with an additional self-efficacy enhancing component over 8 weeks, or the alternative intervention (8-week BA or MP). The aim of the self-efficacy enhancing component is to enhance the participants' belief in their ability and competence to perform the interventions (eg, regular MP). The components, which will be developed based on the experience gained from previous studies, will include (1) a daily smartphone reminder of the participants' personal goals for conducting the mindfulness/BA activities, (2) information on the positive effects of BA and MP; and (3) a 10 min

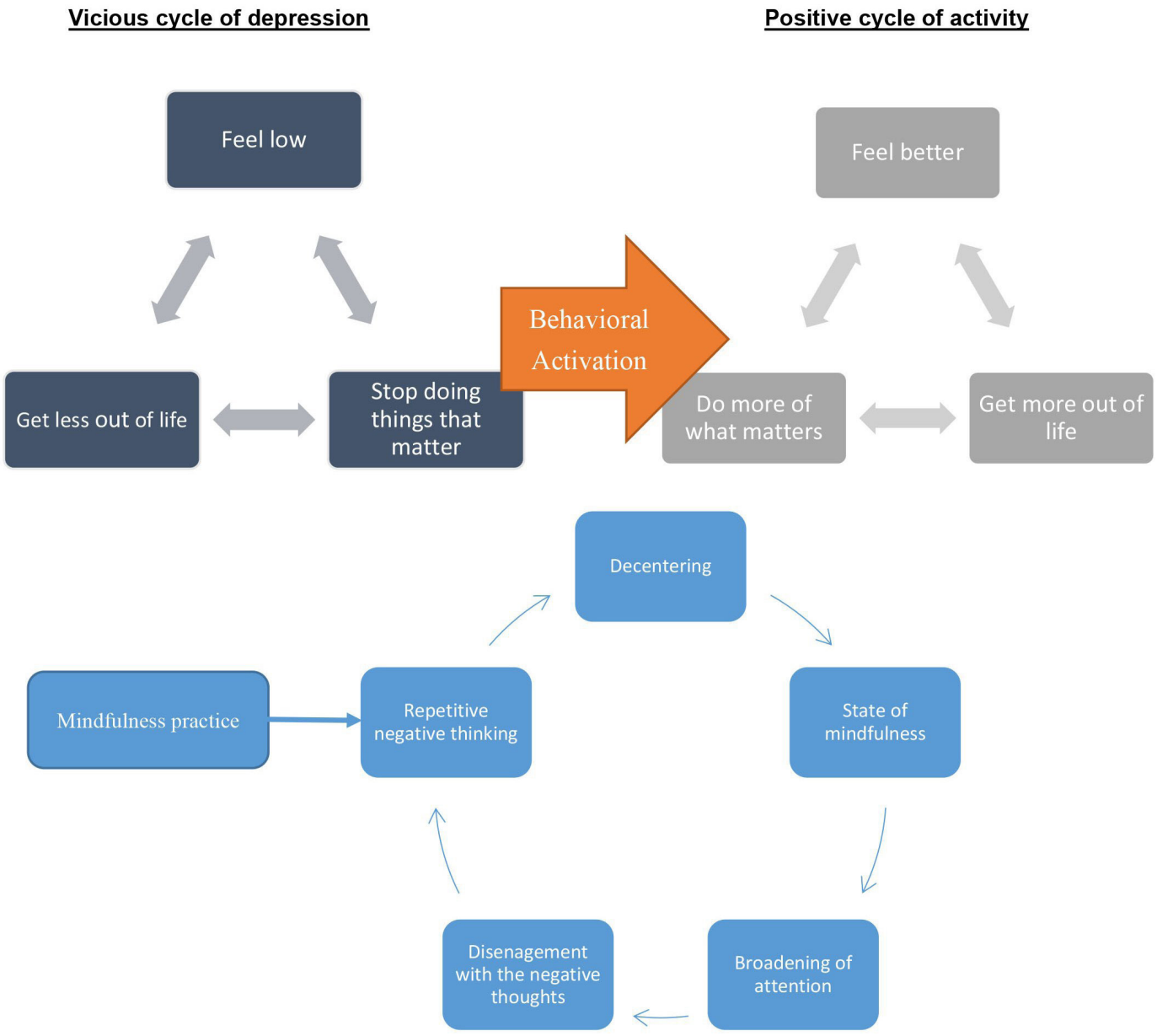

Figure 3 Conceptual model of the behavioural activation and mindfulness programme.

video clip showing two FC-of-PWD as role models for prasticing BA or MP. Responders will receive the 2 monthly booster sessions of the original first stage of the intervention. All participants will receive two booster sessions to maintain treatment gains 2 months before the T4 and T5 follow-up assessments. Responders who received both types of interventions in the earlier stage will select the type of booster that they prefer. Non-responders to the second stage of the intervention will receive mood treatment recommendations from a psychiatrist, and referrals after the completion of the study.

Patient and public involvement

No patients involved.

Outcome assessment

A research assistant blinded to the group allocation will assess all participants for the following outcomes at five time points: T1 (baseline assessment), T2 (immediately after the first stage of the intervention), T3 (immediately after the second stage of the intervention), T4 (3 months after the second stage of the intervention) and T5 (6 months after the second stage of the intervention)

Primary outcome

Depressive symptoms will be measured using the nine-item Chinese version of the PHQ-9. Responses are made on a 4-point Likert scale (0–3), with higher scores indicating more severe depression.[24] The scale demonstrated acceptable levels of internal consistency, with a Cronbach's alpha of 0.86 and a test–retest reliability coefficient of 0.86.[24] Generally, a total score of 20 indicates depressive symptoms that warrant treatment. The primary time point will be the end of the second stage of the intervention (T3).

Table 2 Content of the smartphone-delivered behavioural activation and mindfulness practice programme

Week	Contents	
0	45 min psychoeducation on caregiving and depression 1. Overview of depressive symptoms 2. Cause and how to manage them 3. Caregiving role and demands 4. Impact of the caregiving burden	
1	Behavioural activation (30 min per session, total of 16 sessions)	Mindfulness practice (30 min per session, total of 16 sessions)
	Review the present use of time Use the monitoring form	► Establish the orientation of the class ► The Raisin exercise (eating meditation) ► 12 min body scan ► Feedback and discussion of the exercise
2	Brainstorm pleasant events Schedule pleasant activities	► Practice review ► Exercises on thoughts and feelings ► 12 min body scan ► Brief mindfulness breathing
3	Review scheduling of events Discuss how to improve	► Exercises focusing on unpleasant experiences ► Practising seeing and hearing ► Sitting meditation (awareness of breath and body, and of responses to painful sensations) ► 3 min breathing space ► Mindful stretching and breath meditation
4	Review modifications Consolidate gains on scheduling	► Practice review ► Practising seeing and hearing ► Mindful communication ► 3 min breathing space ► Sitting meditation (awareness of breath, body and sounds, then of how we relate to our experience through the reaction)
5	Review present social support Explore new sources of support	► Practice review ► Mindful walking ► 3 min breathing space ► Sitting meditation (awareness of breath, body and sounds, then of how we relate to our experience through the reaction)
6	Examine communication skills Explore new options	► Practice review ► Sitting meditation ► Exercises on thoughts and alternative viewpoints ► 3 min breathing space (responsive)
7	Review new communications Discuss how to improve	► Practice review ► Sitting meditation with breath, body, sounds ► Activity and mood exercise ► Identifying habitual emotional reactions to difficulties ► 3 min breathing space (responsive)
8	Review modification Consolidate gains on support	► Practice review ► 12 min body scan ► Exercise on looking forward ► Exercise on preparing for the future

Secondary outcomes

Perceived caregiving stress will be assessed using the Chinese version of the Perceived Stress Scale,[25 26] which contains 10 items rated on a 5-point Likert-type scale, from 0 (never) to 4 (very often). The scale showed satisfactory levels of psychometric properties, including internal consistency, with a Cronbach's alpha of 0.85 and a test–retest reliability coefficient of 0.85.[26 27] Higher scores indicate greater perceived stress.

PAC will be assessed using the 11-item Chinese version of this measure (PAC) scale.[28] The PAC scale demonstrated acceptable levels of internal consistency, with a Cronbach's alpha of 0.85, among the FC-of-PWD.[28] Higher scores indicated more positive self-perceptions of caregiving.

Sleep quality will be measured using the nine-item Chinese short version of the Pittsburgh Sleep Quality Index,[29] which assess seven components of sleep quality,

namely sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medications and daytime dysfunction. Higher scores indicate greater levels of insomnia. The tool has demonstrated satisfactory internal consistency, with a Cronbach's alpha of 0.79 and a test–retest reliability coefficient of 0.91 in Chinese populations.[29] Higher scores indicate poorer sleep quality.

HRQoL will be assessed using the Chinese version of the WHO Quality of Life-brief (WHOQOL-brief) scale.[30] It is composedd of 28 items, with each item rated on a 5-point Likert-type scale ranging from 1 (very dissatisfied) to 5 (very satisfied), and with a higher score indicating a better QoL. The internal consistency of the Hong Kong Chinese version of the WHOQOL has been confirmed to be satisfactory, with a Cronbach's alpha of from 0.73 in the environment domain to 0.83 in the psychological domain, and a test–retest reliability coefficient of 0.83.[30]

Process indicators

The information from the logbook, including the frequency (times per week) and duration (minutes each time) of engagement in meaningful, healthful, and enjoyable activities in the past 2 weeks, and the Five Facet Mindfulness Questionnaire (FFMQ), will be assessed biweekly as process indicators until the end of the 8-week intervention at the second stage. FFMQ is a self-reported questionnaire that is commonly used to measure mindful awareness through measuring the five facets of mindfulness: observing, describing, acting with awareness, not being judgemental of inner experience and not reacting to inner experience.[31] The FFMQ demonstrated acceptable levels of internal consistency with a Cronbach's alpha of 0.80 and a test–retest reliability of 0.82.

Sociodemographic data

The following data on both PWD and FC will be collected: (1) age, gender, marital status, living conditions and level of education; (2) health-related information, including medical history (eg, history of depression), activities of daily living, cognitive status and medications and (3) the use of social and caregiving support such as respite care, day-care centres and domestic helpers.

Data processing and analysis

Data will be entered into SPSS V. 28 for Windows. Descriptive statistics will be generated for the demographic data, outcomes and other variables. Similarities in the sociodemographic and baseline outcome variables between the two groups/subgroups will be compared using an independent sample t (two-tailed) or χ^2 test. The analyses will follow the intention-to-treat principle. Participants will be asked to complete outcome questionnaires whether or not they have completed the interventions.

Analysis of hypothesis 1

Linear mixed models will be used to compare the four subgroups: A+B (BA, booster+BA, BA), A+C (BA, booster+BA, MP), D+E (MP, booster, MP, MP), D+F (MP, booster+MP, BA). Since non-responders will be randomised twice while responders will only be randomised once, non-responders and responders will respectively only have a 25% and 50% probability of following the sequence of the interventions they are offered. To account for the underrepresentation of non-responders in the first stage of the intervention compared with the corresponding responders, we will assign a weight of 4 and 2 to non-responders and responders, respectively, as the weights are inversely proportional to the likelihood of being offered a particular sequence of interventions.[32] Adjustment for replication is necessary because subgroup A is used in both embedded adaptive interventions #1 and #2 (table 1), as is subgroup D. To account for this replication of responders, the outcomes and covariates (eg, time) for all responders will be replicated twice.[32] After the mean outcomes and SE are estimated for each of the four embedded adaptive interventions, we will compare those interventions and identify the one that produces the greatest reduction in each primary outcome (depressive symptoms) and other secondary outcomes at T3, T4 and T5.

Analysis of hypotheses 2, 3 and 4

Linear mixed models will be adopted to address the following main effects on depressive symptoms and secondary outcomes:

- Subgroups A+B+C (BA at first stage) versus subgroups D+E+F (MP at first stage) at T2, to determine whether BA or MP is a better intervention option in the first stage of the intervention.
- Subgroup B (BA, BA) versus subgroup C (BA, MP) and subgroup E (MP, BA) versus subgroup F (MP, MP) at T3, T4 and T5, to determine whether it is better to extend the original intervention or to switch to an alternative intervention for the non-responders at the first stage.
- Subgroup C (BA, MP) versus subgroup E (MP, BA) at T3, T4 and T5, to determine whether the sequence of BA and MP or MP and BA more effectively reduces depressive symptoms.

Analysis of hypothesis 5

Path analysis will be adopted to investigate the mediation effects of the process indicators on the link between the BA or MP interventions and depressive symptoms.

Analysis of hypothesis 6

Operating characteristics analysis will be adopted to identify the time point and degree of increase in the process indicators that best predict the intervention response in terms of depressive symptoms at the end of the intervention (T2) using the three data points (2, 4 and 6 weeks after the start of the invention). A cut-off (eg, 20%, 30%, 40% or 50%) of the process indicators at weeks 2, 4 or 6 from baseline will be found to represent the best combination of sensitivity and specificity for predicting response status in terms of depressive symptoms at the end of the 8-week interventions.

DISCUSSION

FC-of-PWD face many challenges since they need to provide assistance in various daily activities, manage the unpredictable behavioural and psychological problems of the PWD, and balance their caregiving tasks with other demands, such as their career and social life. Numerous studies have reported that caring for a PWD is stressful and can lead to depression and other psychological comorbidities. It is hoped that this proposed study will be the first to identify an effective adaptive intervention to reduce depressive symptoms in FC-of-PWD through a SMART design. As such, it will address an internationally significant issue on how to support the FC of community-dwelling PWD and provide scientific evidence on rules relating to extending or intensifying two evidence-based interventions, namely MP/BA, or on switching to a new intervention when caregivers do not respond favourably to the original intervention.

In a recent mindfulness intervention study among the FC-of-PWD, only 42.30% of the participants responded to the mindfulness intervention, reaching the minimal clinically important difference in the assessment.[16] A majority reported that disturbance from the PWD and time constraints are common difficulties in practising mindfulness. In this proposed study, we will adopt a phone-based approach with a flexible schedule for practising mindfulness to facilitate their learning. In practice, we will rely on clinical judgement to determine whether to extend or intensify the original intervention, or switch to a new one when caregivers do not respond to the original intervention. Therefore, the effective clinical management of chronic conditions, such as depressive symptoms, may require a sequence of interventions, depending on the responses to the interventions; hence, multiple intervention decisions can be made over the lifetime of the caregiving role. Ideally, such decisions should be based on adequate empirical evidence. A SMART design could provide such evidence.[19]

As mentioned, FC-of-PWD are heavily engaged in caring tasks. Although BA and MP were shown to be effective at improving the psychological health of the caregivers, the research team anticipates that the caregivers will encounter difficulty in attending a regular face-to-face training programme. Rapid advancements in technology and increasing internet penetration have significantly contributed to the increasing number of programmes for caregivers of PWD that are being delivered through smartphone or online.[33] Therefore, this study will adopt both a face-to-face (psychoeducation session) and smartphone-based (guided practice session) approach to delivering the intervention.[33] Mobile health technologies are helpful in reducing the long distances that FC-of-PWD need to travel to receive support and care. Several recent studies also showed phone-based MP and BA programmes to be feasible and effective at improving the psychological well-being of participants.[12 34] Further research is needed on integrating different psychosocial interventions into a smartphone-based approach with evidence of outcomes. Moreover, to minimise the potential impact of confounding factors (eg, commencement of medication, changes in the PWD's health, a nursing home placement during the study) on the validity of the study, we will collect possible factors found from the literature and measure them at baseline, during the study and at the follow-up, and adjust the factors in the analysis if needed.

Conclusion

The main purpose of this proposed study is to develop and identify an effective two-stage adaptive intervention process that can reduce depressive symptoms among FC-of-PWD using an innovative SMART design. Adaptive intervention is 'a sequence of decision rules that specify whether, how, when, and on the basis of which measures, to alter the dosage, type, or delivery of treatment' at decision stages in the provision of treatment or care.[35] It provides healthcare providers with a chance to operationalise the intervention strategies (eg, switch, increase, step down), resulting in an individualised sequence of treatment for the participants, and maximises the number of participants who could benefit from the intervention.[35] If this study is successful, its findings will have strong implications for the further development of psychosocial adaptive interventions to reduce depressive symptoms among the FC-of-PWD.

Ethics and dissemination

This study received ethical approval from the Human Research Ethics Committee at The Hong Kong Polytechnic University (HSEARS20211223001). A data monitoring committee consisting of an independent clinical psychologist, nurses and a mindfulness therapist will be established to ensure that the participants come to no harm from the intervention. The committee will review the participants' responses (eg, PHQ-9 score) and their experiences of discomfort to determine whether they are in a condition to continue the interventions or require any referrals or support. The findings from this study will be presented at academic conferences and submitted to peer-reviewed journals for publication.

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