Study Protocol and Statistical Analysis Plan

Unique Protocol ID: 17611615

Brief Title: Mindfulness Meditation and Qigong for Colorectal Cancer Survivors

Official Title: Starting from the Mind or the Body in Mind-Body Intervention? A Randomized Controlled Trial on Comparative Effectiveness of Mindfulness Meditation and Qigong on Psychophysiological Outcomes in Colorectal Cancer Patients

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Research impact and objectives

Long-term impact

Colorectal cancer is the most prevalent form of cancer in Hong Kong[1]. Patients often suffer from physical symptoms such as fatigue, insomnia, constipation and diarrhea[2]. The physiological changes and emotional fluctuations can further lead to sleep disturbance[3] and loss of a sense of bodily control[4]. Depression and anxiety have prevalence ranging from 11%–69% while rates remain high five years post-diagnosis[5]. Such physical and psychological symptoms relate closely to the dysregulation of circadian and cortisol rhythm [6] which may further predict poor quality of life and survival in colorectal cancer patients[7].

Popular Practices Remain Understudied

To cope with physical and psychological concerns, cancer survivors turn to various mind-body practices adjuvant to the usual medical or pharmacological treatment for their holistic benefits and reduced side-effects[8, 9]. It has long been known that mind-body practices simultaneously cultivate the mind and body for overall health improvement and the treatment of chronic conditions[10]. Evidence for the effectiveness of highly popular local mind-body practices for cancer, like qigong or mindfulness meditation practices, are accumulating but limited by methodological flaws[11, 12].

Understanding the Two Approaches to Mind-body Practices

Most mind-body practices fall into two distinct categories: mind-based practices (i.e.mindfulness meditation, imagery), and body-based practices (i.e.qigong, taichi, yoga). These practices are typically studied independently; comparative effectiveness research was seldom conducted within or across two categories[13]. Others recognize their similar therapeutic components (e.g.breath regulation) and therapeutic goals (e.g.tranquility), leading to studies documenting interventions with mixed qigong and mindfulness meditation components[14].

Qigong and mindfulness meditation practices thus represent two very distinct forms of mindbody practices which contrasted dynamic (resembling physical exercise) with static (still) practices though both attend to the mind, body and breath. Qigong is even connoted as a type of "mindful physical exercise" highlighting the similar underpinnings in introspection and mental cultivation qigong shares with mindfulness meditation[15]. A meta-analysis on qigong and taichi further found that it was the mental component of qigong rather than the physical exercise aspect contribute more on moderating the effects on anxiety or depression[16]. Interestingly, qigong relies on physical exertion to arrive at mental changes while mindfulness meditation begins directly at mental level but can also impact physical health. The current study therefore, not only aims to provide evidence for the psychophysiological effectiveness of qigong and mindfulness meditation for colorectal cancer patients, but also to elucidate how the different entry-points of these two mind-body approaches differ in outcomes, balance the dysfunctional bodily stress response through the Hypothalamic-Pituitary-Adrenal (HPA) system and affect practice compliance in cancer patients.

Theoretical contributions

Despite the growing family of mind-body practices, few studies juxtaposed their differential outcomes, magnitude and pace of change and post-intervention compliance. Limitation of single-intervention controlled studies was pointed out in a systematic review of mindfulness meditation[17]. This limitation contrasts the swift progression of psychosocial cancer research this decade where many studies were designed to compare amongst two or more related interventions to identify the uniqueness of interventional approaches[18]. Therefore, using a comparative randomized-controlled trial, this study is set out to further establish mind-body practices in psychosocial oncology by exploring the contrasting approaches with which qigong and mindfulness meditation exert their influences.

Current knowledge on mind-body practices tells very little about these contrasting "dynamic moving bodily" versus "static mindful" approaches. This study will measure both physiological and psychological outcomes which offer a comprehensive understanding on the mental and bodily changes before, during, after each approach and their maintenance.

In Traditional Chinese medicine, both movement-based and mind-based mind-body practices are known to have homeostatic functions to balance dysfunctional bodily systems. Examining the effects of mind-body practices on circadian cortisol rhythm may shed light on the homeostatic effect of mind-body practices on the dysregulation of the HPA system.

Clinical contributions

The clinical popularity of qigong and mindfulness meditation among local cancer survivors calls for a need for more established evidence on their benefits. Better understanding on culturally popular interventions, in particular, the common and unique effectiveness of different approaches are crucial, as patients and qualified healthcare professionals can select or provide practices which will produce maximum benefits, satisfaction, adherence, and sustainability. This study envisions bringing forth evidence-based mind-body practices which are easily learned, can be self-practiced and incorporated into patients' lifestyles.

Objectives

1. **Primary objective 1** is to study the effectiveness of Baduanjin qigong and Mindfulness mediation for Chinese colorectal cancer (CRC) patients as compared to a no-intervention control independently on:

(1) cancer-related symptoms and symptom distress

(2) mental health

(3) quality of life

(4) biomarkers

(5) mindfulness level

2. **Primary objective 2** is to examine the commonalities and differential effectiveness between two interventions on:

(1) outcome variables

(2) magnitude of change

(3) pace of change

(4) extended compliance

3. **Secondary objective** is to examine the associations between psychological, physical and psychophysical markers and how those relationships change across the time points.

Background of the research

The Reciprocity of the Mind and Body in Cancer

Colorectal cancer impairs patients on multiple levels of well-being. While most physical symptoms can be managed by medication, psychosocial stressors may arise and persist to complicate survival and reduce quality of life of survivors[19]. Patients, especially those who requiring colostomy, suffer from psychosocial trauma including depression, the fear of relapse, altered self-image, loss of social functioning and connections[20]. Local statistics further indicated a high prevalence of elevated depressive symptoms (21.8%)[21].

In recent years, research studies have emerged to suggest reciprocity between physical symptomatology and psychosocial stress of cancer patients. Evidence in psychoimmunology suggested that, for example, among those who are struggling with cancer, many who suffered from depressive symptoms reported sleep disturbance as well; and that sleep disturbance is a risk factor to depression and disease progression among cancer patients[22]. Other cancer studies have also clearly demonstrated mutually damaging effects of the body and mind[23]. Survival studies further highlight this connection where depression, anxiety, quality of life and other psychosocial factors predict survival among colorectal cancer patients[24]. Patients with high preoperative quality of life were 34.2% were more likely to survive 1 year after[25]. Given the psychological and prognostic importance of these factors, the need for psychosocial support which targets the reciprocal mind and body in colorectal cancer patients is warranted.

Benefits of Mindfulness meditation and Qigong for Cancer Patients

Evidence of Mind-body approaches for Cancer

In view of the reciprocal suffering of the body and mind, there is an imminent need for effective interventions that would help people with cancer cope. For this reason, psychosocial interventions for cancer patients have been rapidly developing, and were put into rigorous empirical testing, over the past two decades. Evidence-based intervention strategies have been developed, such as cognitive-behavioral therapies, psycho-education interventions[26], social support groups[27, 28], and mindfulness-based stress reduction programs[12, 29, 30].

A large number of research studies have demonstrated that mind-body intervention, in its various forms, have a beneficial effect on various aspects of psychological and physical functioning among people with cancer[29-31]. Mind-body practices like relaxation training, meditation, qigong, yoga, taichi and biofeedback, do not only improve functioning, reduce treatment- related nausea, vomiting, and physical pain, but also improve mood and quality of life[9, 32]. Although the mechanism of change of mind-body practices are not well known, one theory is that there is a relaxation response whereby autonomic activity is controlled and causes a decrease of sympathetic activation[33].

The focus of this present study on Mindfulness Meditation and Qigong (Baduanjin) is due to an increasing popularity of practising these approaches among local cancer patients. This is coupled with marked evidence pertaining to safety, feasibility and effectiveness on various aspects of health in cancer patients.

Mindfulness meditation

Mindfulness as a clinical practice refers to the intentional, accepting and non-judgmental focus of one's attention on the emotions, thoughts and sensations occurring in the present moment[34]. The well-known Mindfulness-based Stress Reduction, for instance, stemmed from the Buddhist view of universal suffering, the practice focuses on the development of mindful-awareness, non-judgmental mindset, and self-acceptance.

One of the reasons why mindfulness-based intervention have been applied to cancer care is that there is a psychogenic basis for cancer. Immunological study yielded evidence to support the notion that cancer may be exacerbated or caused by stress, negative emotions, and sleep disturbance[22]. Secondly, the here-and-now orientation of mindfulness[30] moderate the sources of stress for people with cancer concerns about the past, such as the attribution of cancer causations, or regrets about past life decisions; while other sources of stress concerns about the future, such as enduring the suffering of pain, loss, and grief towards one's own death. During meditation, the sense of time becomes plastic and each moment may serve as a timeless refuge from the inexorable demands of life as someone living with cancer[30]. A large number of research studies have demonstrated that mindfulness-based interventions have a beneficial effect on various aspects of psychological and physical functioning among people with cancer[29, 31]. In a randomized controlled study, participants in the mindful mediation program resulted in less mood disturbance, tension, depressive symptoms, anger, problem in concentration, and more vigor at post-intervention when compared the control[35]. Participants also reported fewer stress symptoms, gastrointestinal symptoms, and sleep disturbance. Gains were sustainable after 6months. Mindfulness mediation for cancer patients was also able to alter cortisol and immune patterns consistent with less stress and mood disturbance and decrease blood pressure in a 1-year follow up[36]. Locally, although study on the effectiveness of mindfulness on cancer patients is rare, results from studies on the effects of mindfulness on chronic pain, psychiatric symptoms and functioning are promising [37, 38].

Qigong

Qigong consists of a mild form of muscular activity accompanied by an introspective and proprioceptive focus and an awareness of the flow of one's intrinsic energy. According to Traditional Chinese Medicine, qigong aims at cultivating and enhancing qi which refers to the energy that can sustain health and well-being[39]. It also employs breath-centering techniques and fosters anatomic alignment through disciplined body movement[40]. Among the existing mindful exercises, Baduanjin qigong is one of the most popular forms which is formally recognized and recommended by General Administration of Sport of China. With only eight movements, it requires relatively less cognitive and physical effort[41] compared with tahichi and other forms of qigong. As such, the undemanding nature of Baduanjin qigong makes it a feasible intervention for a wide range of population, even for those who are less able due to old age and illness. Tsang and colleagues have carried out extensive research on the effect of Baduanjin qigong and have found promising results in its ability to improve depressive symptoms among elderly who suffered from chronic medical conditions[42]. Given its practicality and potential health benefits, qigong is also a popular mind-body therapy for cancer patients[43]. In support for its positive effect on cancer patients, a recent systematic review of 13

randomized control trials in this area[44] has concluded that, practicing qigong can help to improve cancer-specific quality of life, fatigue, immune function and cortisol level. This is largely in line with the result of a previous systematic review[11], particularly on its ability to boost immune function. In addition, Baduanjin qigong has been found to alleviate sleep disturbance[45], which is another common problem experienced by cancer patients.

Need for Comparative Study of the Two Main Approaches in Mind-Body Practices

The foregoing brief review suggests that mind-body practices like meditation and qigong benefit both physical and mental health albeit via different entry points. As discussed in earlier sections (Long-term impact), qigong and mindfulness meditation practices represent two very distinct approaches of mind-body practices. Although riding on the common component of focusing on breath, Chinese medical philosophies contrasted dynamic with static practices. Mind-based practices such as mindfulness meditation, relaxation or imagery are typically connoted as techniques to cultivate the mind's ability to influence bodily function and symptoms[32], by means of focused-awareness training; while movement-based practices like qigong and yoga represent another category of health practice capitalizing on movement and attention to foster such mind-body connection via the physical body, by means of mild-moderate physical exercise with inner-directed focus.

The review above is also suggestive of how most existing research on qigong and mindfulness meditation has thus far studied their effects independently, which calls for a need to provide comparative intervention research to elucidate how such contrasting approaches in mindbody practices affect the psychosocial and physiological benefits as well as compliance on patients.

Diurnal Cortisol rhythm and Cancer

The hypothalamic-pituitary-adrenal (HPA) axis activity is responsible for the body's reaction to stress and immune regulation. The dysfunction of the HPA axis in cancer patients reflected by the distortion of the diurnal cortisol rhythm is further associated with tumor characteristics and even survival[7, 46, 47]. Salivary cortisol is a neuroendocrine indicator of HPA axis. It is an established and reliable physiological marker for stress-related improvements after mindfulness and qigong practices[10, 48]. Yet, the limited handful of studies on mindfulness and qigong showed little consensus to establish its effects on cortisol patterns or levels[44, 48]. Meanwhile, a local study found a positive decreasing trend of cortisol after Baduanjin qigong with depressed elders with chronic medical illnesses[49]. Given the important implications of salivary cortisol on cancer, understanding the changes in cortisol profiles after qigong and meditation can further elucidate the linkage between mind-body practices with patients' total well-being.

Study Hypotheses

1. Baduanjin qigong is more effective than no-intervention control in (i)reducing cancer-related symptoms and symptom distress, (ii)improving mental health, (iii)enhancing quality of life, (iv)positively altering biomarkers, (v)enhancing mindfulness level.

- 2. Mindfulness meditation is more effective than no-intervention control in similar areas and directionality as the above (i) to (v).
- 3. There would be commonalities and differences between Baduanjin qigong and Mindfulness meditation in a)type of outcome variables, b)magnitude of change, c)time when significant outcomes emerge, d)frequency and length of self-practice and long-term compliance.
- 4. The associations among physical and psychological variables as well as psychophysiological biomarkers and the changes of such associations across the time points are exploratory.

Research Plan and Methodology

Research design

This study will utilize a 3-arm randomized controlled trial design with waitlist control. A conceptual model is provided in Appendix A. Upon recruitment, participants will be screened according to the inclusion and exclusion criteria (Appendix B). Baseline data will then be collected. Subsequently, eligible participants will be randomly assigned into one of the 8-week (i)Baduanjin qigong group, (ii)Mindfulness meditation group, and (iii)Waitlist Control group. The Waitlist Control group will continue to receive routine medical care and will have the option to attend either of the interventions after the study is completed. Participants from all 3 arms will be assessed on 4 time points (i)baseline prior randomization, (ii)mid-intervention (4th week), (iii)post intervention (8th week), (iii)6 months post-intervention. Participants will complete the study in 8 months.

Sample size determination, Participant eligibility and Recruitment

To achieve a statistical power of 0.8 with medium effect size (f2 = 0.25) and significance level of 0.05 in repeated measures MANOVA under the proposed 3-group, 4-time point design, a sample size of 126 is needed. Assuming an attrition rate of about 33.5%, based on prior trials on cancer patients using qigong[8], recruitment of 189 participants (63 per arm) is required. The study population will consist of 189 Chinese-speaking patients aged between 18 and 74, diagnosed with colorectal cancer. Participants will be recruited via posters and newsletters put up at hospital and community organizations servicing cancer patients including Hong Kong Anticancer society. Recruitment will also be done via referral from oncologists. Screening will be conducted after recruitment by a trained research assistant or by the referring medical professional based on the inclusion and exclusion criteria listed in Appendix B.

Intervention groups

Both intervention groups will consist of 8 weekly 90-minute sessions, with a total of 12 contact hours. Interventions will be held in groups of about 10 participants led by 2 trainers qualified for the respective intervention form, one of whom will also be a mental health professional.

a) *The Baduanjin qigong Intervention*[61] consist of eight sequential forms of movements which is practiced with guidance on rhythmic breathing and mindful awareness (see Appendix C for details). Each cycle of the eight movements requires 10 to 15 minutes for completion. Four

cycles will be practiced in each session with short breaks arranged between them. In addition to the in-session practices, participants are encouraged to practice Baduanjin qigong for at least 20 minutes each day and keep a record of their daily practice in a log book.

(b) *The Mindfulness meditation Intervention* which has been used by co-Is (C.L.W.Chan and Ng.S.M.) in previous studies is developed based on the core components of the established Mindfulness-Based Stress Reduction and the Mindful Self-Compassion program with adaptation for local practice[57, 62]. The focus of the group is to nurture mindful awareness, acceptance, and self-compassion. The group sessions are composed of a combination of mindfulness-based practice, relaxation, and yoga exercise (Appendix D). The basic philosophy of this intervention is the emphasis of the nurturing of self-kindness attitude, and non-attachment attitude towards inter-personal connectedness and letting go of self-criticism, need for control, and defensive separation in times of adversity. Short breaks will be arranged between each practice. Adjuvant to the in-session practices, participants are recommended to practice the mindful techniques every day for at least 20 minutes while keeping a record of their practice.

(c) Waitlist control group members will continue with routine care and can join either the Baduanjin or Mindful intervention after the 6-month post-intervention assessment.

Ethics

This study will be reviewed by the HKU/HA Institutional Review Board. Written informed consent will be obtained from all participants. To ensure confidentiality, codes will be used to replace names. All data collected will be kept in locked spaces and destroyed 3 years after the study ends. The study will also be registered with the Hong Kong clinical trial registry.

Measurements

Assessments pertain to areas of (i)cancer-related symptoms and symptom distress, (ii)mental health, (iii)quality of life, (iv)biomarkers, (v)mindfulness, (vi)compliance, and (vii)demographic and clinical details. Self-rated scales and salivary cortisol are administered by participants themselves while blood pressure would be measured by the trained research assistant blinded to the randomization. Measurements are taken at all time points except demographic and clinical details.

Cancer-related symptom, symptom distress and quality of life

(a) Sleep quality. Quality of sleep will be indexed by the Pittsburgh Sleep Quality Index (PSQI)[63]. The PSQI is a self-report questionnaire that assesses multiple dimensions of sleep over past one month. The 19-item scale generates 7 'component' scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The sum of the seven component scores yields one global score of subjective sleep. The Chinese version of the PSQI was validated by the team and will be used[64].

- (b) Cancer-related symptom distress. Cancer-related symptoms distresses are measured by the Chinese version of Memorial Symptom Assessment Scale (MSAS)[65]. The scoring of the 32-item MSAS yields a MSAS Global Distress Index (10 items) measuring of overall symptom distress; the Physical Symptom Subscale score (12 items); the Psychological Symptom Subscale score (6 items), a Total MSAS score.
- (c) Health-related Quality of life. This will be assessed using the Chinese (HK) Short form-12 (SF-12)[66]. With 12 items, the scale results a physical and a mental health summary.

Mental Health

- (d) Anxiety and depressive symptoms. Anxiety and depressive symptoms will be captured by the Cantonese/Chinese version of the Hospital Anxiety and Depression Scale (HADS)[67]. The 14-item scale consists of two subscales (anxiety and depression) with seven items in each. The items are scored on a 4-point Likert-type scale (0–3).
- (e) Perceived stress. Perceived stress levels will be assessed by the Chinese Perceived Stress Scale[68]. Using a 5-point Likert scale (0-4), the scale consists of 10 items about the degree to which life events are appraised as stressful.

Biomarkers

- (f) Salivary cortisol. Salivary cortisol collection will be conducted by participants themselves. Saliva samples will be collected at 5 prescribed times (awakening, 45 minutes postawakening, 12:00pm, 5:00pm and 9:00pm) using the collection device, Salivette, which includes a cotton swab to place under the tongue. Smoking, eating and drinking should be avoided and refrained one hour prior to saliva collection. Samples collected will be kept frozen at -20°C.Daily condition measures with salivary cortisol-Measures on participants' health behaviors and activities on the day of saliva collection will be collected along with cortisol. These include (i)sleep quantity that day (hours of sleep at night and nap hours), (ii)subjective sleep quality rated on a scale of 1-10, (iii)smoking habit and the number of cigarettes that day (iv)alcohol/coffee drinking habit and the approximate amount that day, and (v)subjective evaluation of stress levels on the day of collection rated on a scale of 1-10. All the above measures will affect the diurnal cortisol rhythm and must be considered in analysis.
- (g) Blood pressure and heart rate. Following recommended procedures by the Canadian Medical Association[69], blood pressure and heart rates would be measured twice from each arm with a five minute rest intervals between measurements. The four collected readings will be averaged.
- (h) Mindfulness. The Chinese Five Facet Mindfulness Questionnaire (Short form) will be used upon permission. It has 5 domains, observing, describing, acting with awareness, nonjudging to inner experience and nonreacting to inner experience[70]. The 5-point Likert scale has 20 items.

- (i) Compliance. Participants will record their daily duration of qigong or mindfulness meditation practice over the course of the study. This will provide information on the frequency and intensity of practice, and maintenance of self-practice habits after the intervention period.
- (j) Demographics. Participants socio-demographic, such as age, gender, education level, employment status and marital status, as well as clinical profile, including cancer diagnosis, staging, treatment and medication record, onset of mood disturbances if any, critical events around the time of onset, physical exercise habits, complementary treatment used, and psychosocial support service utilization, will be documented based on self-report.

Data analyses

1. Effectiveness of Baduanjin qigong and Mindfulness meditation (Objective 1 & hypotheses 1&2)

Analysis of variance and chi-square independence tests will be carried out using SPSS to compare the demographic profile of the three groups. The study will use latent growth modeling (LGM) in Mplus 7 [71] to explore the effectiveness of the two mind-body interventions over the four assessment time points, between the respective experimental and waitlist control groups. Traditional analytic techniques such as ANOVA or MANOVA adopt traditional deletion or substitution methods and may not yield precise estimates in the presence of missing data. LGM flexibly analyzes the overall population trajectories using nonlinear modeling such as quadratic growth and the between-person variation in outcome variables, thus allows analysis of all available data via full information maximum likelihood under missing-at-random assumption. This matches the standard intent-to-treat analytic approach of clinical trials with missing data. The level of statistical significance is set at p=0.05, with p-values greater than 0.05 but smaller than 0.10 taken as marginal significance. All models are estimated using the robust maximum likelihood estimator.

2. Commonalities and Differential effectiveness for Baduanjin qigong and Mindfulness meditation (Objective 2 and hypothesis 3).

To examine the commonalities and differential effectiveness for Baduanjin qigong and Mindfulness meditation, treatment effects of the two interventions are directly compared in multigroup conditional growth models. The linear slope factors of the outcomes are contrasted across the two intervention groups via computing the difference in the intercepts of the slope factors between two groups using Model Constraint option. Demographic and clinical characteristics that differed significantly across the three groups in the preliminary analysis are entered as covariates. Influential confounding variables such as clinical prognosis or frequency, intensity and duration of maintenance (compliance) of practice will be controlled.

3. The Mind-body correlations reflected in symptoms and psychophysiological markers (Objective 3 and hypothesis 4).

Employing baseline data from both the experimental and control groups, correlation analyses will be used to understand the relationship between the parameters reflected on the mind and body which include diurnal cortisol patterns, subjective stress and assessments on the psychological symptoms, sleep patterns, health-related quality of life. Changes of those associations across time can be analyzed by latent growth modeling using Mplus.

4. Analysis of salivary cortisol data (for all objectives and hypotheses)

Saliva samples will be centrifuged at 3000rpm for 15 minutes at room temperature. Cortisol levels will be determined with an enzyme-linked immunoabsorbent assay kit (EIA, Salimetrics, Inc) in the HKU Clinical Oncology Lab. The assay sensitivity is 0.193 nmol/l and the intra-assay and inter-assay coefficients of variation are 3% and 10% respectively. Due to the skewed distribution of salivary cortisol data, natural logarithm will be used to transform the raw cortisol data to yield an unskewed distribution for analysis. The mean cortisol level will average the 5 collected across the day and total cortisol level is measured by the area under the curve.

To explore individual trajectories of changes in cortisol level over time and also the complex relationships between different variables, a two-level individual growth curve model using Mplus software will be adopted as cortisol measures at 5 daily time points are nested within participants. This method is a variant of multiple regression modeling appropriate for the nested structure of our data.

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Appendix A: Conceptual model of the proposed study



Appendix B: Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
 Diagnosis of primary colorectal cancer of any stages 0 to III An expected survival length of 12 months or longer 0.5 to 5 years following completion of main treatment for colorectal cancer Ages 18 or higher Chinese speaking 	 Regularly practicing baduanjin qigong, other forms of qigong, taichi, meditation, mindfulness practices or yoga once a week or more Having participated in the above trainings in the past 6 months Severe cachexia, dizziness, bone pain, nausea or significant orthopedic problem or other contraindications for mild to moderate physical exertion Diagnosis of major medical or psychiatric disorder besides cancer (including but not limited to severe cardiovascular disease, epilepsy, uncontrolled diabetes, untreated hypothyroidism, delirium or dementia) Recurrence of colorectal cancer or other cancers





Appendix D: Main components of the Mindfulness Meditation Program

- 1. Introduction to Mindfulness
- 2. Practising mindfulness meditation
- 3. Practising loving-kindness meditation
- 4. Developing self-love through mindfulness meditation
- 5. Exploring meaning in life through mindfulness application
- **6.** Bringing in difficult emotions
- 7. Practising self-kindness and gratitude as way of coping wrong difficult emotions and difficult situations in life
- 8. Transferring mindfulness meditation as a way of living