

Measuring Success of Meditation, Curcumin Supplementation and Sunlight Exposure among Office Workers with Mild Depression

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Abstract

Background: Globally, major depression is the primary cause of disability, where a large part of cases is reported among the working-class.

Methods: We conducted comparative cross-sectional study with 8-week observation includes mindfulness meditation, curcumin supplementation and sunlight exposure (MCS program) among mildly depressed office workers of both sexes - 34 in observed group (OG) and 34 in control group (CT). At baseline, day 30, and day 60, participants were compared in terms of (a) vitamin D, (b) brain-derived neurotrophic factor (BDNF), (c) interleukin-6 (IL-6), and (d) depression scores using PHQ-9. ELISA were performed for all serum samples.

Results: The rates of increase of vitamin D in both day 0, 30 and day 30, 60 intervals were significantly higher in OG ($p < 0.05$). BDNF levels varied extensively between the groups. IL-6 means were significantly lower in OG at day 30 than in CG ($p < 0.05$). Depression scores rate of change demonstrated appreciable fall in day 0, 30 interval and stayed down to day 60 in OG. Significantly, lower depression scores were observed for OG at both day 30 and day 60 ($p < 0.05$).

Conclusion: MCS program resulted in significant decreases in depression scores and some of its related biomarkers, thus can be a sustainable and cost-effective approach to alleviating psychological depression among the working-class.

Keywords: 25-hydroxyvitamin D; brain-derived neurotrophic factor; interleukin-6; major depression; working-class; mindfulness meditation; curcumin; sunlight exposure.

Introduction

By 2030, major depression will become the number one leading cause of disability globally, according to WHO.¹ Today, it is the second leading

cause of disability and of global burden of disease, troubling more than 150 million individuals.^{2,3} Without treatment, depression has the potential to take a chronic course, be recurring, and be linked with increasing disability over time.^{4,5} This critical public-

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health problem often occurs alongside other long-lasting diseases and can exacerbate health outcomes especially in people who are in the workforce.^{6,7} As working is a substantial part of a person's life, the environment of the workplace is where psychological burden can accumulate. Among all medical illnesses, depression may have the greatest negative impact on time management and productivity and is one of the major causes of absenteeism and presenteeism.^{8,9} Both medicinal treatments and psychotherapy treatments have been found to be the most economical choices for organizations.¹⁰ Ever-increasing numbers of organizations are creatively addressing the issue of depression in their places of business.

Department of Mental Health found that the prevalence of depression among all Thais was 2.4%, signifying that 1.5 million individuals had depression. 58.5% of the depressed individuals were at risk of committing suicide.¹¹ Between all regions of Thailand, Bangkok scored the greatest prevalence of individuals with depressive occurrence at 4.1% where 28.8% was found in female employees, notably greater than the national rate.^{11,12}

Workplaces have been recommended as a supreme location for psychotherapy interventions in several regards. Firstly, 60% of the global population is employed in some industries, and the majority of those people's waking hours are spent at the workplace – ideal for influencing a large number of individuals in a reliable and controllable approach.¹⁰ Secondly, an unfavourable psychosocial work atmosphere is well-known as a risk factor for mental disorders, suggesting that work-based programs can be multi-modal and at the same time reducing risk factors while improving employees' coping skills and resilience.¹⁰ Thirdly, the expenditure of interventions could be shared by both the private and health sectors.¹⁰ A meta-analytic review shows that prevention or treatment programs focused on individuals with subthreshold depression have real potential.¹³

Major depression, a multi-factorial disorder, has been intensively linked to the increase of a pro-inflammatory cytokine, interleukin-6 (IL-6). During depression episodes, increased serum IL-6 levels are observed, indicating a worsening of a person's depression.¹⁴ The cytokine is involved in the management of numerous physiological pathways, predominantly in the immune system, metabolism, sleep regulation, and mood

disorders.¹⁵⁻¹⁷ As depression symptoms intensify, inverse correlation has been shown with brain-derived neurotrophic factor (BDNF) as well as vitamin D levels. Moreover, IL-6 is an independent predictor of BDNF.¹⁴

25-hydroxy vitamin D (25-(OH)D) elevation is naturally achieved by sunlight exposure (SE), it is theorized to repress cellular inflammation.¹⁸ 25-(OH)D is inversely and independently connected with serum IL-6.^{18,19} On its own, 25-(OH)D may have the action of suppressing the production of IL-6.²⁰ In addition, natural light exposure has been shown to improve depressive symptoms which could be the result of the increase in 25-(OH)D production.¹⁸

Only a handful of depression intervention programs, however, have been performed on the working-class. Thus, our study consisted of 3 components: mindfulness meditation + curcumin supplementation + sunlight exposure (MCS) given to mildly depressed office workers conducted with a control group (CG) and an observed group (OG). In past studies, the 3 attributes have all been shown to alleviate scores, symptoms, and/or biomarkers attached to depression. The primary outcome of this study is the difference of change of value in depression scores over time represented by the difference of slopes between groups. We also evaluated the slope's changes in 25-(OH)D, BDNF, and IL-6 level as secondary outcomes.

Materials and Methods

Research Design

Our study was an 8-week comparative cross-sectional study with a control group (CG) carried out amongst two real-estate companies nine kilometers apart from each other in the middle of Bangkok. Employees of both companies had similar job tasks and daily routines. For logistical and contamination prevention purposes, one company comprised OG and the other CG.

At the preliminary phase, all consenting employees from the two companies were screened using standard tests, Thai version of Patient Health Questionnaire 2 and 9 (PHQ-2 and PHQ-9). Upon completion, we observed a total of 61 employees (54.46%) in company A and 42 employees (48.28%) in company B with mild depression (PHQ-9 score of 7-12).²³ PHQ-2 and PHQ-9 are professionally translated into Thai and standard in depression

evaluation. In the screening process, voluntary participation was achieved via posters posted on bulletin boards and a meeting where information sheets, purpose of study, methodology, and consent forms were clarified for each company at a time. Consented participants were screened once more for exclusion and inclusion criteria by an expert.

This experiment included office workers between 25-59 years of age working full-time in 2 real-estate companies with mild depression. Individuals with cancer, cardiovascular disease, hypertension, liver disease, history of psychiatric illnesses, and taking psychiatric medications were excluded. Per protocol, we also excluded people who had been taking vitamin D and/or curcumin supplementation (CS) prior the study for more than 2 weeks, who were suffering from alcohol addiction, who were pregnant or breast feeding, who just lost a loved one in the past 6 months. The suitable sample size of participants was confirmed by calculation result of G*Power 3 software version 3.1.9.2 where the input effect size of Cohen's *d* was 1.70.²²

Ethical approval was obtained from the Chulalongkorn University Ethics Committee (ID number: 176.2/62). The methodology was explained. Signed informed consent were voluntarily obtained from every participant. Resignation from the program was permissible at any time.

Intervention

Participants in OG underwent an 8-week program involving curcumin supplementation (CS) of 2 capsules after breakfast and dinner (1000 mg of curcumin), sunlight exposure (SE) in sky garden at 4:30 pm for 10-15 minutes 4 times a week, and 20 minutes of sitting mindfulness meditation (MM) in a meeting hall on same days as the sunbathing. Men and women were asked to wear short sleeves tops and shorts for being in the sun. During MM sessions, participants were asked to sit comfortably on floor with or without a provided cushion or on chair and to close eyes and focus on their breathing. Whenever other thoughts enter their minds, participants were asked to lightly and non-judgmentally refocus their minds on the breathing.²¹ A 5-minute session of question and answer was available for participants to ask about uncertain things that should have happened during each session to the licensed meditation instructor.

For every session, sunlight intensities were measured by a standard calibrated digital lux meter

version LX-1010B.²² There was a total of 24 meeting sessions, each participant was allowed to miss 4 sessions. The fifth time a participant missed a session, he/she had to compensate by doing SE and MM in their own time. CG did not participate in the treatment and lived normal daily lives. Retention rate was 96%.

Data Collection Procedures

For both the OG and CG groups, blood was drawn, general questionnaires were administered, and PHQ-9 were self-administered on day 0, day 30 and day 60 of the MCS program at the two companies meeting halls.

Blood tests

Day 0, day 30 and day 60 of follow-up serum blood tests were measured for BDNF ELISA, IL-6 ELISA, and 25-OH (D). Two licensed medical technicians drew blood from participants at both locations before the intervention began.

Blood (6 ml) was drawn and transferred into lithium heparin tubes, centrifuged at 3000 rpm for 10 min to obtain serum, and stored at -20 degree Celsius. 1 ml each of which was used for BDNF, IL-6, and 25-OH (D) immune fluorescent analysis. The medical technician collected blood samples in an air-tight, temperature-controlled container and transported to Chiang Mai University Biochemistry laboratory for analysis. A sandwich enzyme-linked immunosorbent assay (sandwich ELISA) was applied for quantitation of BDNF (Catalogue No. SEA011Hu) and IL-6 (Catalogue No. SEA079Hu). Competitive inhibition enzyme-linked immunosorbent assay (cELISA) was applied for 25-OH (D) (Catalogue No. CEA920Ge) according to the manufacturer's guidelines (Cloud-Clone Corp., Uscn Life Science Inc., Wuhan, P.R. China).²⁶

Depression evaluation

Thai PHQ-2 and PHQ-9 are standard self-evaluated questionnaires which were used to screen and follow-up on people with high risk of depressive symptoms, translated into Thai version by Lotrakul²³.

Curcumin Acquisition

The curcumin supplementation given to OG were Curcuma Longa L. extract obtained from The Government Pharmaceutical Organization – the same one of a study done by Chuengsamarn et al in 2012.²⁴ Each capsule contained 250 mg of curcuminoids with

product number of 110211750411. The supplement received Good Manufacturing Product and Certification of Analysis number of 040000012169. It passed appearance test and identification test. The curcumin capsules consisted of 103.40% curcuminoids concentration, water content of 1.08%, and disintegration time of 8.0 minutes (Thai FDA number of 1A 1/60(H)).

Statistical analysis

A descriptive statistic was made to assess the similarity of participants characteristic at the baseline. Analysis of several factors were done to reveal confounding effects, including sociodemographic factors using bivariate analysis. Differences in vitamin D, BDNF, IL-6 and depression scores between study times for each group were conducted by using fixed effects regression methods in SAS version 9.2 (SAS

Institute, Cary, NC). Comparison of demographic data between OG and CG were analyzed by Mann-Whitney U-test in SPSS version 17. P-values of < 0.05 were deemed significant.

Results

Sociodemographic Characteristics

There was 50% male and 50% female in CG, and 77% female and 23% male in OG. Weight mean of CG was 65.20 ± 10.98 SD slightly higher than OG (61.03 ± 9.22 SD), but without statistical significance ($p > 0.05$). The average height was higher in CG (163.40 ± 9.17 SD) than in OG (158.97 ± 6.82 SD) ($p < 0.05$). There were no significant differences of sleep quality(De0_SQ), physical activity(De0_PAL), income satisfaction(De0_IS), alcohol drinking(De0_AD), and sunlight exposure(De0_SEL).

Table 1: Sociodemographic characteristics

Variable	Abbreviation	Treated group	Control group	p-value
Sex				
Male	—	N=23 (77%)	N=15 (50%)	
Female	—	N=7 (23%)	N=15 (50%)	
Weight	—	61.03 ± 9.22	65.20 ± 10.98	0.12
Height	—	158.97 ± 6.82	163.40 ± 9.17	0.03 *
Day0: Sleep quality	De0_SQ	30.13 ± 8.22	26.73 ± 5.98	0.07
Day0: Physical activity	De0_PAL			0.83
Score 1 (No exercise)		40	26.7	
Score 2 (Exercise 1-4 times/week)		46.7	70	
Score 3 (Exercise 5-7 times/week)		13.3	3.3	
Day0: Income Satisfaction	De0_IS			0.052
Score 1 (Not satisfied)		3.3	20	
Score 2 (Satisfied)		96.7	80	
Day0: Alcohol drinking	De0_AD			0.19
Score 1 (Do not drink)		30	46.7	
Score 2 (Drink)		70	53.3	
Day0: Sunlight exposure level	De0_SEL			0.84
Score 1 (No exposure)		3.3	0	
Score 2 (5 mins or less per day)		36.7	40	
Score 3 (6-30 mins per day)		53.3	53.3	
Score 4 (31 mins or more per day)		3.3	6.7	

Vitamin D

Data shows no difference in vitamin D at baseline (day 0). From SAS output, the slope (rate of increase) from day 0, day 30 in OG is higher (by 0.1633) than in

CG. Specifically, in [day 0, day 30] interval, the slope is $0.2297 + 0.1633 = 0.3930$ for OG, and 0.2297 for CG.

Similar difference in slopes hold true. [day 30, day 60] slope of OG also exceeds CG [day 30, day

60] slope of CG by the same amount (0.16). The slope for OG is 0.90 and for CG is 0.74 in [day 30, day 60]. We conclude that the rate of increase in vitamin D is consistently higher for OG versus CG over the range of study (Figure 1).

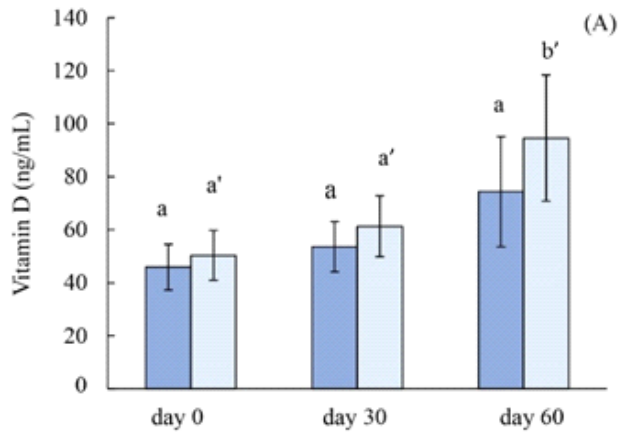


Figure 1: Means (\pm SD) vitamin D of CG (dark blue) and of OG (pale blue) at each study time. Significant values are indicated with difference in letters ($p < 0.05$). Asterisks indicate significant difference between CG and OG ($p < 0.05$).

BDNF

Time profiles are different between OG and CG. First, the means of BDNF differs at baseline: 3876 for CG and $3876 + 1395 = 5271$ for OG. Second, the slopes from [day 0, day 30] differ: 86.59 for CG and $86.59 - 157.18 = -70.59$ for OG. Finally, the slopes from [day 30, day 60] differ as well: $86.59 - 253.28 = -166.69$ for CG and $86.59 - 253.28 - 157.18 + 282.64 = -41.23$ for OG. Therefore, the profiles for the BDNF data vary extensively between the two groups (Figure 2).

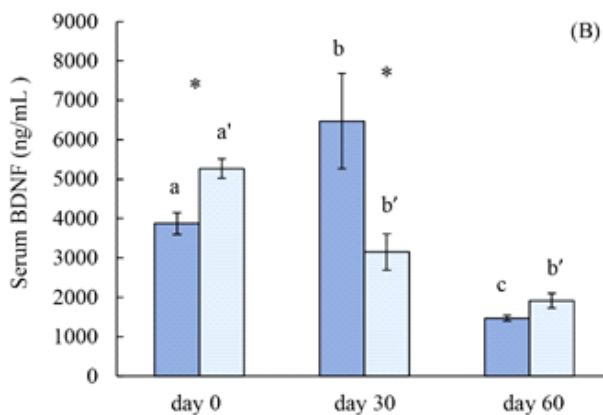


Figure 2: Means (\pm SD) BDNF of CG (dark blue) and of OG (pale blue).

IL-6

IL-6 data shows variability, especially for CG at day 30; suggesting that IL-6 values vary widely in CG (Figure 3). Separate analysis shows very marginal evidence of a difference in means at day 30, but because of the two outliers, this means test is not considered here due to violation of assumptions. The result of this noise is that there is no significant difference in the CG and OG slopes at [day 0, day 30] and no difference in the CG and OG slopes at [day 30, day 60] ($p = 0.1126$ and $p = 0.1247$, respectively) with no difference in means at baseline, as well. The output determines that for both groups, the slope in [day 0, day 30] is 0.2015 and the slope [day 30, day 60] is $0.2015 - 0.3953 = -0.1938$. However, there is a significant difference at day 30 means between the groups.

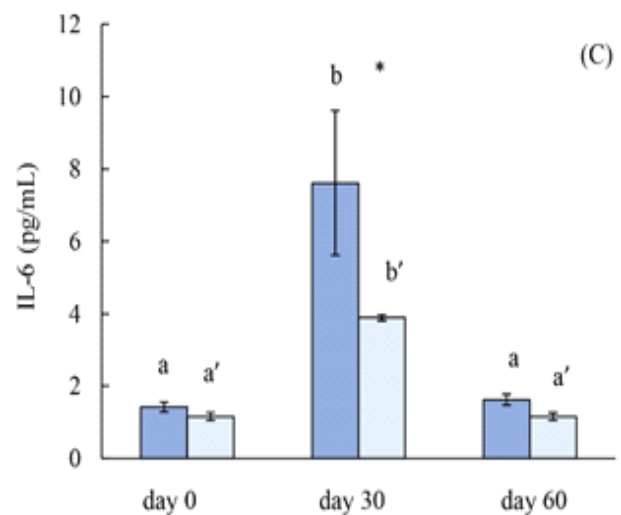


Figure 3: Means (\pm SD) IL-6 of CG (dark blue) and of OG (pale blue).

Depression Scores

Depression scores do not differ at baseline. For CG, the average line segments from [day 0, day 30] and [day 30, day 60] are flat with non-significant slopes ($p = 0.8714$ and $p = 0.5444$, respectively). For OG, the slope of [day 0, day 30] is -0.1151 and of [day 30, day 60] is $-0.1151 + 0.09263 = -0.0225$, and these changes differ significantly from the (flat) control line segments. Depression scores significantly drop in OG at day 30 and stay significantly below CG until day 60 (Figure 4).

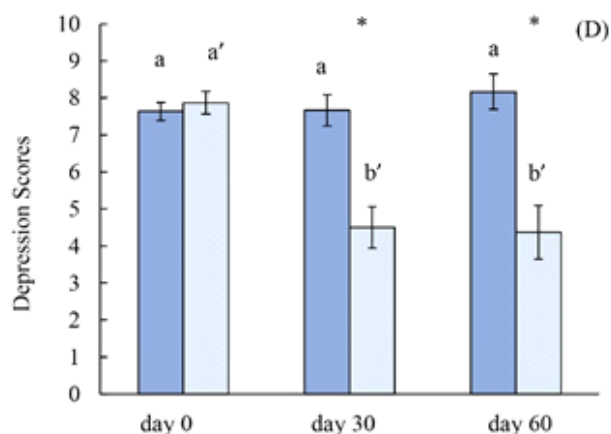


Figure 4: Average (±SD) depression scores of CG (dark blue) and of OG (pale blue).

Discussion

Our results are divided into four outcomes:

Vitamin D

The cause of steady increase of 25-(OH)D in both groups could be that the intervention period was toward the end of the year with more days-off than previous months. Participants usually stayed and worked indoors, but with longer holidays they had more outdoors, thus receiving more SE. Being

consistent with literature, the more sunlight skin exposure one receives the more chance for him/her to produce more vitamin D.²⁵ However, the rate of increase between OG and CG from [day 30, day 60] had a significant difference. The results indicate additional 3 times a week in the sun resulted in greater 25-(OH)D production. Consequently, more 25-(OH)D circulating in their blood could have facilitated with the decrease in depression scores that participants received.

Several hospitals also introduced programs with SE on psychiatric patients which were successful as they lessened their depressive symptoms.²⁶ Studies show that 25-(OH)D levels change seasonally—higher in summers than in winters. SE can stimulate serotonin production helping to brighten mood, reducing anxiety while lacking serotonin can cause stress.²⁷ Less exposure to sun during thick cloud is found to reduce about 50% of ultraviolet (UV). Toxic haze can also reduce UV levels by about 60%.²⁸ Moreover, UVB cannot go through glass; therefore, shaded SE might not provide enough vitamin D.²⁹ Skin tones with more melanin has been shown to absorb more UVB and reduce vitamin D synthesis.³⁰ Participants in MCS were all Thais which helped in terms of having less variations in skin tone.

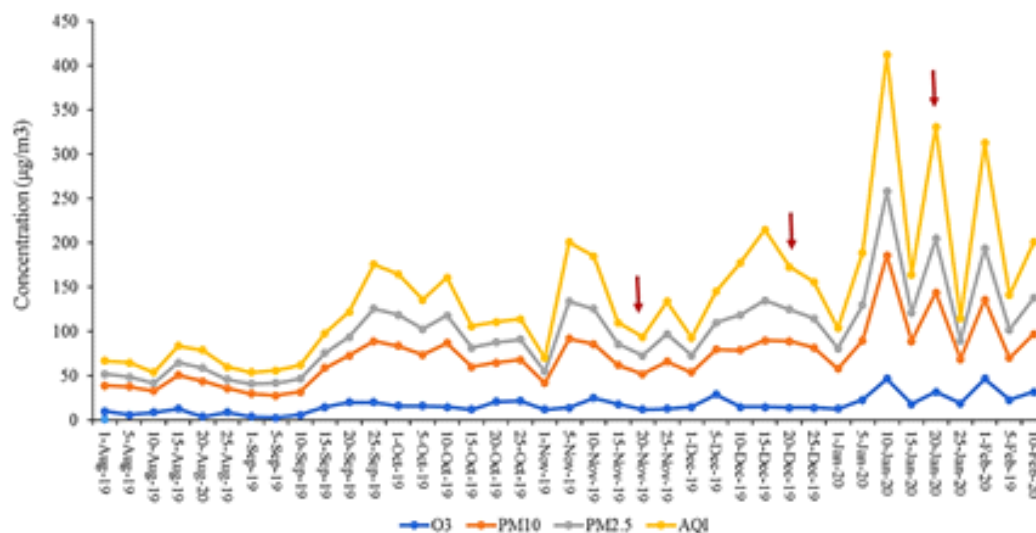


Figure 5: Air Quality Index data, www.pcd.go.th 2019. Red arrows are the three times of blood sample collection.

IL-6

IL-6 values were higher at day 30 compared to day 60 and day 0 in both OG and CG. The perplexing outcome could be the result of air quality index (AQI) which disturbed all participants equally.

Thai government reported in 2019 that there was a haze event towards the end of the year which raised the particulate matters (PM) in Bangkok air (Figure 5). PM10, PM2.5, and AQI have been extensively reported to be linked with increased expression of many pro-inflammatory interleukin

genes, including IL-6. PM 10 was reported to have an IL-6 increase effect on human dermal fibroblasts, peripheral blood mononuclear cells in vitro, and the pulmonary epithelial barrier.³³⁻³⁵ PM2.5 was also reported to facilitate an increase of IL-6 in human osteoarthritis synovial fibroblasts through ASK1 activation.³⁶ During 2013 haze events in China, biomarkers of pro-inflammatory oxidative potential, IL-6, IFN- γ and TNF- α levels were also found to be altered in a dose-dependent manner.³⁷

Nevertheless, day 30 IL-6 of OG was noticeably higher than day 30 IL-6 of CG. The finding could have been the result of the program taking effect on withstanding the increase of inflammatory cytokines including IL-6. Curcumin has been reported extensively that it has IL-6 lowering effects with both dose and duration of treatment.³⁸ The high IL-6 levels found in major depressive disorder (MDD) patients in clinical studies are more obvious in treatment-resistant patients. Thus, to continue with clinical recovery for depression, IL-6 activity suppression is necessary.³⁹ Clinical studies also showed IL-6 antibodies' potential anti-depressive effect.⁴⁰⁻⁴² When the body is inflamed or stressed, it adjusts to produce more inflammatory cytokines, resulting in destruction of molecules in the nervous system causing depression.⁴² Studies revealed that exercise, natural products, light therapy, electroconvulsive therapy, and psychological interventions may normalize IL-6 levels.

BDNF

In both OG and CG, the level of the BDNF steadily decreased from day 0 to day 60. The undesirable finding, could well be the impact of the continual increase in AQI, PM2.5, and PM10 in Bangkok atmosphere from beginning to the end of the program (Figure 5). Not only there were not any increase but also a decrease in BDNF, indicating that air pollution could have been the uncontrollable factor that impacted all members in both groups biologically. In 2014, Bos et al. showed that BDNF of cyclists did not increase as a result of increased physical activity in the city near a busy road where PM10 and PM2.5 were found high, concluding that traffic-related air pollution exposure during exercise may well be the major factor hindering positive influences of exercise on cognition via BDNF inhibition⁴³. All participants either lived in the middle of the city or had to commute to their companies using mass transit exposing themselves

to the increase in PM10 and PM2.5. The surge in the pollution could have been the answer for the decline of BDNF in both groups from day 0 to day 60. Still, day 30 BDNF of CG spiked up which may be the result of unmanageable factors like physical activities which have been reported to increase serum BDNF levels through the action of the ketone body β -hydroxybutyrate.⁴⁴⁻⁴⁶

Depression Scores

Day 30 of OG had a significant decrease in their depression scores while CG had none which could be due to the success use of meditation which helped reduce ruminative thinking and increase simultaneously attentional control as demonstrated by past studies.⁴⁷ MM might cause neuroplastic changes in the structure and function of brain areas responsible in attention management, emotion and self-awareness.⁴⁷ Generally, the content of the mind includes dysfunctional attitudes and negative self-referent ideas.⁴⁸ When depression prone individuals engage in rumination, they ponder in the 'recycles' process of the content of the negative thought, amplifying the opportunities of relapse and the intensity of the depressive episode.⁴⁸ Meditation could have worked by increasing present moment awareness and by welcoming emotions nonjudgmentally.⁴⁸⁻⁵⁰ OG depression score stayed down to the end, while CG score did not change. Corresponding with trials, where mindfulness therapies lessened depressive signs and prevented relapses.^{47,51} Majority of participants verbally expressed lasting improvements. The study results are consistent to past findings where large-scale mindfulness approaches by organizations have been found to be even more effective than small-scale approaches.^{51,52}

Leaders could use mindfulness interventions to improve well-beings of their workforce, where they may have more potential to improve health than individual lifestyle modifications.⁵⁴ Future research should extend to a larger population of workers in a variety of occupational settings, delve deeper into reasons for drop out, and explore if results correlate to healthcare utilization costs or health status which can add value to both the individual and the organization and may be an especially practical reason for organizational sponsorship of the intervention itself.

Limitations and Strengths

The small sample size, the assignment of companies to OG or CG, and the uncontrollable

change in air pollution particulate matters were limitations. Potential strengths of this study include measuring biological confirmation for 3 time points, well compliance of participants, and high retention rate (96%).

Conclusions

This study provides evidence-based program for the increase in vitamin D and the reduction of depression scores and its related biomarkers. MCS could be developed and implemented in clinical practice. It is recommended that future studies include comparisons between active placebo and CG as well as consider time of year especially in cities prone to air pollution when inflammatory markers are involved. When applied together, MM, CS and SE, MCS program could conceivably be an effective tool to help alleviate depressive symptoms in the most venerable and most economically structural group of people, the working class.

Funding: This research was self-funded and received no external funding.

Institutional Review Board Statement: Ethical approval was obtained from the Chulalongkorn University Ethics Committee, Bangkok (ID number: 176.2/62). The study was conducted according to the guidelines of the committee.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the participants to publish this paper. The nature and methodology of the intervention were explained clearly. Resignation from the program was permissible at any time.

Conflicts of Interest: The authors declare no conflict of interest.

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