

Design of the integrative medical group visits randomized control trial for underserved patients with chronic pain and depression



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ABSTRACT

Background: Given the public health crisis of opioid overprescribing for pain, there is a need for evidence-based non pharmacological treatment options that effectively reduce pain and depression. We aim to examine the effectiveness of the Integrative Medical Group Visits (IMGV) model in reducing chronic pain and depressive symptoms, as well as increasing pain self-management.

Methods: This paper details the study design and implementation of an ongoing randomized controlled trial of the IMGV model as compared to primary care visits. The research aims to determine if the IMGV model is effective in achieving: a) a reduction in self-reported pain and depressive symptoms and 2) an improvement in the self-management of pain, through increasing pain self-efficacy and reducing use of self-reported pain medication. We intend to recruit 154 participants to be randomized in our intervention, the IMGV model (n = 77) and to usual care (n = 77).

Conclusions: Usual care of chronic pain through pharmacological treatment has mixed evidence of efficacy and may not improve quality of life or functional status. We aim to conduct a randomized controlled trial to evaluate the effectiveness of the IMGV model as compared to usual care in reducing self-reported pain and depressive symptoms as well as increasing pain management skills.

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1. Introduction

In the United States, 56% of adults experience chronic musculoskeletal pain in any given year [1,2]. During one-on-one clinical visits, Primary Care Providers (PCPs) often treat chronic pain through pharmacological treatment (e.g. through prescriptions, anti-inflammatories and opioids) despite mixed evidence of efficacy and increased risk of potentially dangerous side effects, including addiction and death [3–7]. Even when these treatments are effective in reducing pain, they may not improve mental and functional status or quality of life [8], and may actually increase risk of depression [9,10]. Evidence indicates that non-pharmacological treatments (such as mindfulness,

yoga, massage) are potentially as effective as pharmacological treatments for chronic pain, without significant adverse effects [11–13]. Given the public health crisis of opioid overprescribing for pain, and recent CDC guidelines that recommend non-opioid therapy as the preferred method to treat chronic pain [14], there is a critical need for evidence-based non-pharmacological treatment options that effectively reduce pain and address patient well-being affected by pain.

The impact of chronic pain is particularly severe in low-income minority populations, who receive less patient education, as well as less medication, surgery, and specialty referrals [15–18]. Reduced use of non-pharmacological options by low income minorities is attributed to limited coverage of these therapies by insurance, lack of access, not being offered these therapies as an option by their provider, or structural barriers. [16–23] Fig. 1 illustrates individual, interpersonal, social, community, and provider/medical system wide factors related to

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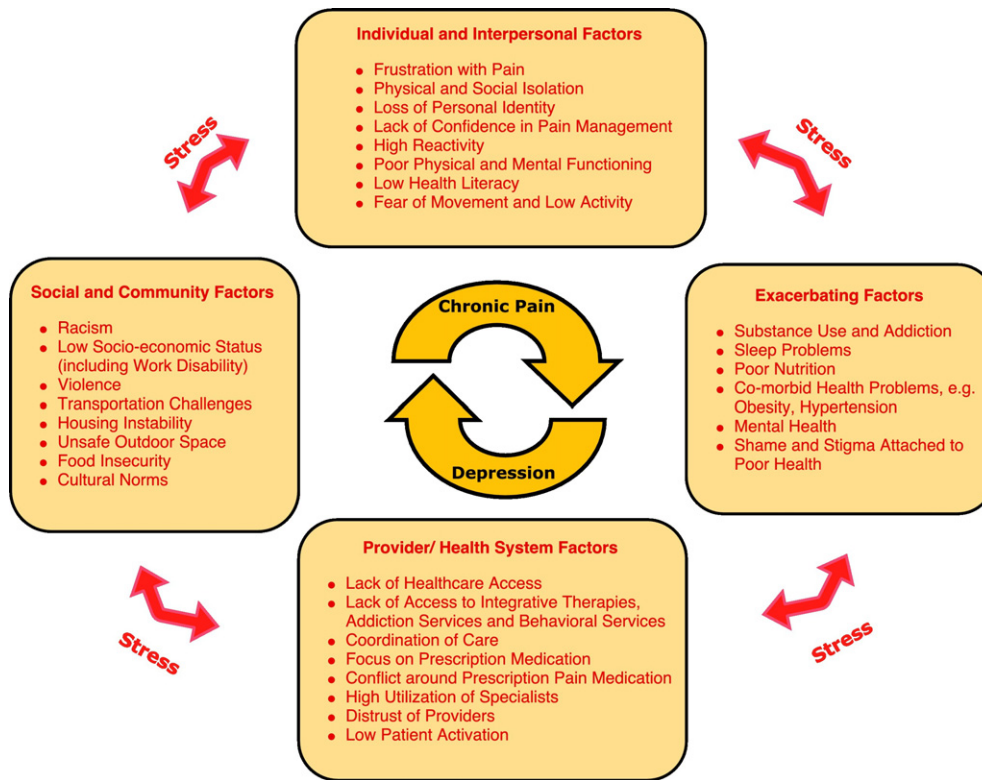


Fig. 1. Factors related to chronic pain and depression.

chronic pain and depression in this patient population based on previous research [24].

In order to improve gaps in the care of chronic pain and expand access to integrative therapies, we developed the Integrative Medical Group Visit (IMGV). The IMGV brings together elements of medical group visits, Principles of Mindfulness Based Stress Reduction (PMBSR), Evidence Based Integrative Medicine (EBIM) and other self-management techniques [22,25–28]. For the last five years, the IMGV has been an innovative model for patients with chronic pain and depression in primary care clinics in Boston. Preliminary results demonstrate statistically significant reductions in pain and depression and an improvement in patient health well-being and quality of life [22].

To address current barriers to effective pain care, particularly for underserved populations, we are studying the IMGV model in a primary care setting multisite randomized controlled trial (RCT). In the RCT, we compare [1] a standardized 10 session IMGV; and [2] Primary Care Provider (PCP) visits including medications and provider's advice (usual care). Our primary outcomes are reductions in chronic pain and depressive symptoms, increased pain self-efficacy and reduced self-reported pain medication use.

In this paper, we: 1) explain the components and theory behind the IMGV, 2) explain the trial design and procedures, 3) establish the outcome measures and 4) discuss the limitations of the design.

2. Materials and methods

2.1. The fusion of care models for chronic pain and associated conditions

In George Engel's biopsychosocial model, chronic pain has interrelated causes and manifestations including: physical (e.g., intensity and symptoms related to pain, "fight or flight" response), psychological (e.g., depression, stress management, poor coping), and social (e.g., relationship stresses, social isolation, work disability). Chronic pain has been associated with multiple chronic conditions and symptoms including depression, stress, somatization, poor coping, fatigue, obesity, and

sleep disorders [29–32]. Psychosocial factors, such as passive coping and loneliness are associated with an increased risk for disabling pain, while social support and active coping with positive self-efficacy are linked with a better prognosis [33].

In addition to the complex etiology of chronic pain, both clinicians and patients face multiple barriers in the treatment of chronic pain in primary care. Clinician-identified barriers include: poor patient self-management, patient non-compliance, time restraints, lack of access, and poor communication [34]. Patient co-morbidities (e.g., depression, anxiety, obesity, sleep disorders, and addictions) further complicate both the severity of pain as well as adherence and effect of the treatment modalities [35]. In the US, clinicians rely heavily on prescription medication to treat pain [4]. In this context, patients report moderate relief and low patient satisfaction with their care [36,37].

We built the IMGV to address physical, psychological, and social needs of participants in the context of barriers to care and different dimension of chronic pain. The IMGV combines principles, practices, and formats from multiple theory-driven interventions: Principles of Mindfulness Based Stress Reduction (PMBSR) [25,26], Evidence Based Integrative Medicine (EBIM) [12,38] and medical group visits [27,28] (see Fig. 2, which diagrams how each element corresponds to the needs of this patient population). To enrich the in-person group visits, social support, and track mind body therapies, we developed two technology components. The first element is a website, containing the IMGV curriculum content and other self-management tools, titled Our Whole Lives (OWL). The second is an interactive Embodied Conversational Agent (ECA) to provide patients with an alternate way to access these tools. The evidence for each component is described below.

Mindfulness Based Stress Reduction (MBSR), a mind-body intervention conducted in a group setting, addresses chronic health conditions and co-morbidities. [39–42] The core curriculum of MBSR consists of eight weekly sessions taught by a trained instructor and one silent retreat day. The major techniques include sitting and walking meditation, body scans, and mindful yoga. A recent systematic review identified 21 randomized controlled trials of MBSR; eleven of these studies showed

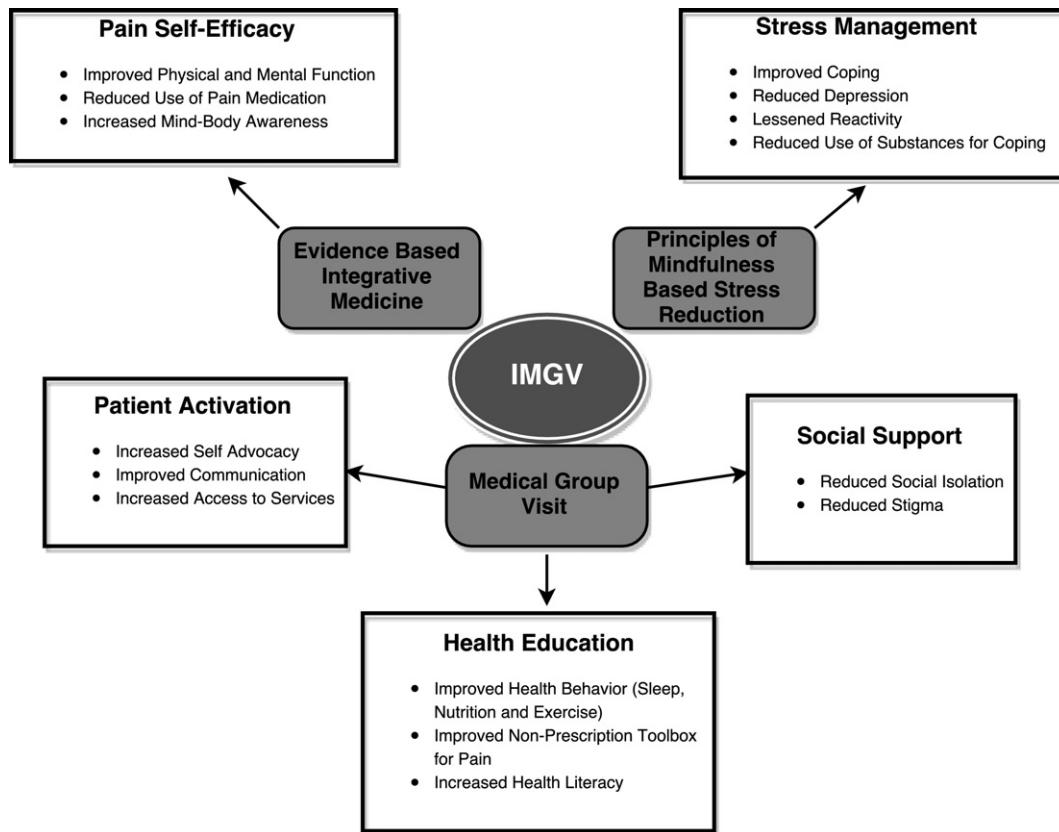


Fig. 2. Components of the IMGV and associated targets for chronic pain treatment.

improvement in mental health measures compared to wait-list or standard care controls, as well as improved pain scores for patients with chronic pain. Patients with two or more co-morbid conditions had the greatest improvement in pain [43]. For the IMGV curriculum, we used the basic eight session structure as well as modified versions of the MBSR techniques that were appropriate to the literacy level and background of this patient population.

Evidence Based Integrative Medicine (EBIM) techniques, such as massage and acupuncture/acupressure, have demonstrated health improvements in patients with chronic pain [12,38,44]. Massage is beneficial for the use of chronic non-malignant pain, especially when used for low back pain. [38,45] A meta-analysis of 29 RCTs indicates that acupuncture/acupressure can effectively treat chronic pain [12]. We have drawn from multiple evidence-based practices that show promise for chronic pain and have integrated them into the IMGV curriculum.

Most medical group visit models include individual time for a medical evaluation between the provider and patient, teaching time (didactic and interactive), time for patient self-management, and time to connect and socialize. Groups range from four to 20 patients with one to two facilitators, and meet at regular intervals – from weekly to monthly – for 1–4 h. The clinician's assessment may be conducted in an adjacent private examining space, and clinicians charge for the visit using established patient reimbursement codes [46–48]. Group visits treat an increasing number of chronic illnesses [46–51]. These visits result in greater improvement in health status indicators including health-related quality of life, disability delays, patient satisfaction, patient trust in their physician, coordination of care, and culturally competent care as compared to usual care [52–56]. Group visits enhance the provider/patient relationship and provide social support from a group of similar patients [28,46,57].

E-Health technologies such as websites have the potential to address health disparities [58] and allow patients to tailor their treatment to

their needs, socialize, and access self-management resources. Currently, there is limited evidence on the use of health technology to improve pain in low literacy populations.

However, there is evidence on the use of an Embodied Conversational Agents (ECA) in low income minority populations. An ECA, an automated character, has been used successfully for a number of healthcare applications such as providing information before hospital discharge to reduce hospital readmissions [59] and promoting physical activity [60]. The use of ECAs has potential for promoting health behavior change outside the time spent in healthcare visits.

For the first year of our study, the IMGV was piloted in six groups across the planned sites (two intervention groups per site). Our process included a plan, do, act, and study (PDAS) [61] cycle that centered upon the insights from pilot groups, group visit facilitators, and patient advisors. This process resulted in improvements and a refinement of the IMGV program. After the pilot groups, we held focus groups to gather qualitative feedback, which suggested that the IMGV model increased self-monitoring, self-regulation, mindfulness, self efficacy, patient-to-patient support, and coping strategies in a supportive network [22,24].

2.2. Advisory groups

Two advisory groups provided feedback throughout the initial study design and continue to do so as the study moves through the stages of recruitment and enrollment of participants, data collection and analysis. The *Patient Advisory Group (PAG)*, consisting of patients who have experienced the initial pilot IMGV groups, has met on a monthly basis since the first year of the study [62]. These patients provided advice on how to deliver and facilitate the curriculum, Embodied Conversational Agent scripts, Our Whole Lives (OWL) website usability, recruitment processes, outcome measures, and continue to provide guidance when challenges arise. The *Scientific Advisory Group (SAG)* includes clinicians, a statistician, an anthropologist, and experts on chronic pain, addiction,

non-pharmacological treatments, and stress. The SAG meets on a monthly basis and provides consultation on any relevant methodological problems faced by the study at that time. These experts have provided guidance on the original study design, outcome measures, and content to be reviewed with primary care providers for the usual care condition and will provide ongoing data analysis review and feedback as data is collected during the RCT.

2.2.1. Data safety monitoring board (DSMB)

The DSMB meets every six months to review adverse events, as well as current recruitment and enrollment data in order to guarantee patient safety. During each meeting the board reviews study data and makes a determination as to whether the study should continue. Adverse Event reports are sent to the DSMB every two months in between board meetings. Unanticipated, serious events related to the study are reported to the DSMB and the IRB within two days of the Principal Investigator becoming aware of the event.

2.3. Specific aims

The aims of the RCT are to:

Compare the effectiveness of Integrative Medical Group Visits ($n = 77$) with the individual primary care provider (PCP) visits ($n = 77$) for chronic pain management on three outcomes: reducing self-reported pain, reducing depressive symptoms and improved self-management of pain (defined as improved pain self-efficacy and reduced use of pain medication). We hypothesize that pain and depression symptoms will be clinically and statistically superior for patients randomized to the IMGV as compared to those randomized to usual care. Our secondary hypothesis is that participants randomized to the IMGV will have higher pain self-efficacy scores and a reduction in self-reported pain medication use as compared to patients randomized to the control group.

2.4. Trial design

We will use a comparative effectiveness randomized controlled trial study design to compare the IMGV to PCP visits for chronic pain and depression. The length of the intervention for participants is a total of 21 weeks, divided into a nine-week treatment phase and a 12 week maintenance phase (please refer to Fig. 3 for an illustration of study flow). Patients will be randomized into either the IMGV group or usual care. The study's primary outcomes are changes in pain (Brief Pain Inventory) [63,64], depression (Patient Health Questionnaire 9) [65] and pain self-efficacy (Pain Self-Efficacy Scale) [66]. Information will be gathered at baseline, after the end of the treatment phase (nine weeks) and maintenance phase (21 weeks).

2.5. Study sites

The RCT will be conducted at three affiliated sites in the Boston HealthNet system: Boston Medical Center (BMC) and two BMC affiliated federally qualified community health centers, Codman Square Health Center (CSHC) and DotHouse Health (DH). BMC is a large academic medical center safety net hospital, with 70% of the patient population belonging to medically underserved communities and 30% non-English speakers. Both CSHC and DH are community-based, outpatient health care and multi-service centers located in the Dorchester neighborhood of Boston, MA.

2.6. Inclusion and exclusion criteria

The inclusion criteria and exclusion criteria are listed in Table 1.

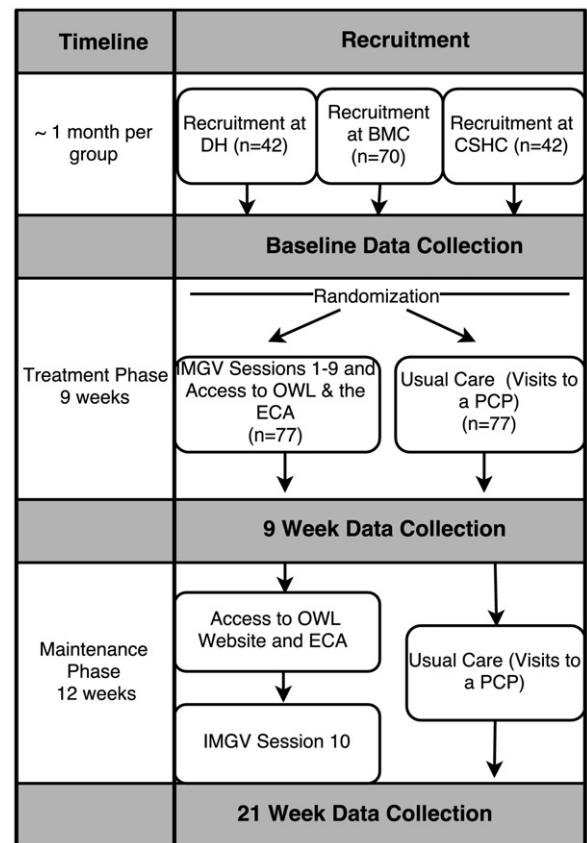


Fig. 3. Study flow for the IMGV RCT.

2.7. Recruitment and enrollment procedures

We will use five strategies to recruit patients:

1. Generating lists of patients ≥ 18 , using ICD-9/ICD-10 diagnosis codes for chronic pain, depression, and other co-morbidities (e.g. rheumatoid arthritis, fibromyalgia, joint/hip/back pain, neuropathy) in the electronic medical records (EMR) of study sites. The resulting lists will be sent to assigned providers for verification of which patients should *not* be contacted due to the exclusion criteria or other concerns. The study team will then send approved patients a recruitment letter by mail.
2. Flyers to be placed in the family medicine and adult medicine departments of the three study sites as well as behavioral health, physical therapy, rheumatology, general internal medicine and neurology departments. Patients may self-refer to be screened for study enrollment.
3. Meetings with the PCPs at all study sites to inform them about the study and our inclusion/exclusion criteria. If a PCP identifies a potentially eligible patient and would like to refer them to the study they can provide the patient with a study pamphlet in a medical encounter, directing him/her to contact the study staff. With patient permission, the PCP's may also pass on the name and phone number of the patient to study staff who will then contacts the patient by phone to determine interest and eligibility.
4. We will provide information about the study on the community health center websites and in appropriate BMC internal weekly emails to employees at the study sites. We also created a BUMC-sponsored website (<https://www.ourwholelives.org/bmc2/for-providers/>) with information about the study for patients and physicians.
5. Through direct referral or "warm hand-offs" at clinics. The clinic leadership will notify clinic staff of study staff availability for referral on

Table 1
Inclusion and exclusion criteria.

Inclusion criteria	Rationale
Age 18 or older	The study intervention is designed for adults and would not be appropriate for younger participants.
Chronic musculoskeletal pain greater or equal to 4 on a 0–10 scale for at least 12 weeks	Pain threshold that meets the criteria for chronic lower back pain according to the National Institutes of Health Task force on Research Standards for lower back pain [67].
A score of 5 or higher on the PHQ-9 depression scale	Meets criteria for mild depressive symptoms. This threshold will allow us to see a significant change throughout the study time period.
English fluency to understand the treatment protocol and answer survey questions	Fully informed consent and valid data collection.
Has a primary care provider in the site where that cohort of the IMGV is being held	If the participant is randomized to the control condition, they should have at least one provider available at the relevant site who is responsible for their care.
Exclusion criteria	Rationale
Symptoms of psychosis	Condition poses a possible risk to safety of the participant, other participants in the group and could preclude compliance with the intervention.
Symptoms of mania	Condition poses a possible risk to safety of the participant, other participants in the group and could preclude compliance with the intervention.
Has previously participated in an IMGV visit (such as the pilot groups)	Could bias or confound treatment effect.
Begun a new pain treatment in the past month or plans to begin any new pain treatments in the next 3 months	Could bias or confound treatment effect.
Has a significant health condition, such as cancer, that affects ability to participate in the IMGV.	Condition could preclude compliance with the intervention.
Pregnant or planning to become pregnant in the next 3 months	Poses an unknown risk to the safety of the participant and the fetus. Also, could be a barrier in study compliance and could bias or confound treatment effect.
Alcohol dependent based on a score 2 on the T-ACE [68]	Condition poses a possible risk to safety of the participant, other participants in the group and could preclude compliance with the intervention.
Involved in a workman's compensation or personal injury claim	Legal concerns could bias participant's incentive to improve, seek care or report outcomes.
Suicidal	Condition poses a possible risk to safety of the participant, other participants in the group and could preclude compliance with the intervention.
No way to access the internet during study period	Barrier to full study participation in using all possible study tools.
Other severe disabling chronic medical or psychiatric co-morbidities as determined by the principal investigator on a case by case basis	Condition poses a possible risk to safety of the participant, other participants in the group and could preclude compliance with the intervention.

pre-scheduled days; clinic staff will be encouraged to notify the study staff of scheduled appointments with potentially eligible participants for screening purposes.

The screening and enrollment will occur in several steps: screening for eligibility, informed consent, baseline data collection and randomization. Eligibility screening will take place either by phone or in person with a trained Research Assistant (RA). The RA will administer verbal consent before proceeding with screening questions, including consent to review medical records. If there is any uncertainty about eligibility based on the patient's responses, the study staff will gather information from the patient's PCP and the patient's medical record. If both these steps are not conclusive, the principal investigator will contact the

patient directly. If the patient is screened eligible, a baseline interview will be scheduled with a research assistant. During this meeting the research assistant will review the informed consent form with the patient and ensure that any questions or concerns about the study are answered. The RA will then administer the baseline survey. After randomization, the research assistant will orient the participant to their assigned study condition, providing them with materials and scheduling their nine and 21 week data collection appointments.

2.8. Randomization

At the end of baseline assessment, the patient will be randomized into intervention or control condition via StudyTRAX, an online HIPAA compliant database. All participants are randomized within the two treatment conditions using permuted blocks of sizes 2, 4, and 6 that are specific to both the site and cohort - i.e. first group at BMC.

2.9. Intervention condition

The intervention condition consists of three elements: the Integrative Medical Group Visits (IMGV), the Embodied Conversational Agent (ECA) and the Our Whole Lives website (OWL). The full participant manual, distributed to all intervention participants is available in the supplementary material.

2.9.1. Integrative medical group visits - structure and curriculum

Groups will be led by a facilitator (prescribing clinician trained in integrative medicine) and a co-facilitator (non-prescriber trained in MBSR or yoga). The clinician will meet each participant randomized to the intervention group prior to the first session. During this meeting, the clinician will review the patient's medical history, problem list and medications. This meeting also serves as a secondary screening to assess if the patient could pose any risk to the safety of other participants in the group.

Participants randomized to the intervention group will attend nine consecutive weekly group visits that occur after the baseline data collection and clinician meeting. They will also attend a tenth maintenance group that occurs 12 weeks after the last treatment group visit. In order to create a sense of safety for each patient within the group, a critical part of the facilitator's role is to establish "ground rules of group behavior" at the first session. These include honoring the contribution of each member and keeping the information shared during the group confidential ("what gets said in the group stays in the group"). Aside from this discussion, participants will also sign a HIPAA confidentiality agreement at the first group meeting.

The IMGV model uses principles of adult learning and engagement to allow for experience and knowledge sharing. This collective experience is intended to empower and motivate participants to create an individualized treatment plan for their pain. Sessions will follow the same structure each week. Prior to the start of each group, the clinician will supervise participants taking and recording their own weight, blood pressure, and pulse. Monitoring vital signs on a weekly basis empowers participants to take an active part in their own healthcare. Patients will also complete an intake form that includes: a pain scale, access to a healthcare provider in the past week, visits to the Emergency Department or urgent care, home practice of pain management tools, daily cigarette use, change in medications (since the last visit) and note any questions for the facilitator. The clinician will use the forms to prioritize which patients to approach for individual time during and after the group, as well as to monitor patient health. During one on one time with the clinician, prescriptions will be refilled, appropriate referrals or labs ordered, and other primary care services are provided. Each patient visit will be documented in the electronic medical record.

Once the group begins, there is a mindfulness centering activity (i.e. awareness of breath meditation), a group check-in, home practice review, and a clinician facilitated discussion on chronic disease

Table 2
The IMGV curriculum.

Session #	Curriculum topics per session	Experiential activities
1	Group orientation: Introduction to IMGV model & mindfulness themes; Confidentiality & ground rules; Vitals tutorial; Introduction to meditation	Awareness of breath meditation (AOB)
2	Our reactions to stress: Stress and your body; Healthy & unhealthy ways of responding to stress; Upstream downstream parable; Role of stress and chronic pain	Opening AOB meditation; Raisin eating exercise; Body scan
3	The importance of healthy sleep: How sleep affects health; Ways to establish a healthy sleeping pattern; Gratitude journaling & promoting positive thoughts; Triangle of Awareness & the mind/body connection; Nine-dots exercise	Opening AOB meditation; Body scan
4	Food and movement as medicine: Healthy eating plate; Reading nutrition labels; Serving sizes; Bringing awareness to pleasant events	Opening AOB meditation; Mindful chair-yoga sequence
5	Our bodies' response to pain: Acute vs. chronic pain; Cycle of chronic pain; Non-pharmacological pain treatment options; Breathing exercise (STOP); Bringing awareness to unpleasant events; Mid-point group evaluation	Opening AOB meditation, Acupressure
6	Our bodies and inflammation: Acute vs. chronic inflammation; Methods for decreasing inflammation in the body; Foods & inflammation: Omega 3 fatty acids, trans and Omega-6 fats, simple carbohydrates	Opening AOB meditation; Sitting meditation
7	Approaches to depression and challenging communications; Bringing awareness to difficult communications; Ways to cope with depression & mind-body approaches; Foods & supplements: Omega-3s, B Vitamins; Importance of Vitamin D	Opening AOB meditation; Loving-kindness meditation
8	Understanding the role of food: Effects of Sugar, fiber and protein on the body; glycemic index; whole vs. processed foods; finding sugar on nutrition labels; Healthy sources of fiber & protein; Mindful eating; Introduction to SMART goal development	Opening AOB meditation; Choice of chair yoga or sitting meditation
9	Goal-Setting & Wellness Review: Setting SMART goals; Tips for continued health & well-being; Wellness review; Resources post-group; Closing ceremony & certificates	Opening loving-kindness meditation; Self-care massage
10	Maintenance Session (12 weeks after session nine): Setting new goals; HOOT mindfulness technique; Review of mind-body practices	Opening sitting meditation with choiceless awareness; Fence visualization meditation

management, such as prevention and management of pain and associated conditions. Based on PAG feedback, throughout the curriculum we emphasized healthy eating and mindfulness content (see Table 2 for a full list of all curriculum topics). In each session, participants will be introduced to a different integrative medicine activity such as self-massage and acupressure. These are designed to have patients experience firsthand evidence-based IM therapies for chronic pain, discuss

the risks and benefits, and how to access them in their communities. At the conclusion of each group, a healthy meal is served, creating an opportunity to model healthy nutrition and unstructured time to build community. All food to be served at the IMGV is based on healthy eating principles and specific anti-inflammatory foods included in curriculum. The meal is also an opportunity for facilitators to speak to patients individually.

Individuals randomized to IMGV will continue to receive routine medical care, including pain medications, from their PCPs. The IMGV physician facilitator and group coordinator will communicate with the participants' PCPs (via electronic medical record or phone) throughout the intervention to provide updates on the activities and progress of the patients.

2.9.2. Embodied conversational agent (ECA)

The ECA is a female automated character that emulates the conversational behavior of an empathic coach. She introduces herself as "Gabby" and will review the content discussed in the IMGV. Gabby provides participants with a menu of the mind-body activities from the IMGV curriculum, assisting them to practice their mind-body homework (mindful eating, meditations, body scan, yoga, etc.). There are also multiple modules with nutrition advice. The ECA encourages the participant to set goals for home practice, provides guidance on PMBSR and information on integrative medicine practices. The Gabby character is based on an ECA system developed from similar research, feedback from beta testing with our patient advisory group and patient pilots [69]. Scripts were tested by study staff and pilot groups before use in the RCT. Access to the ECA is provided via a Dell Venue 8 Pro refurbished tablets, distributed to all intervention participants in the first session of the group.

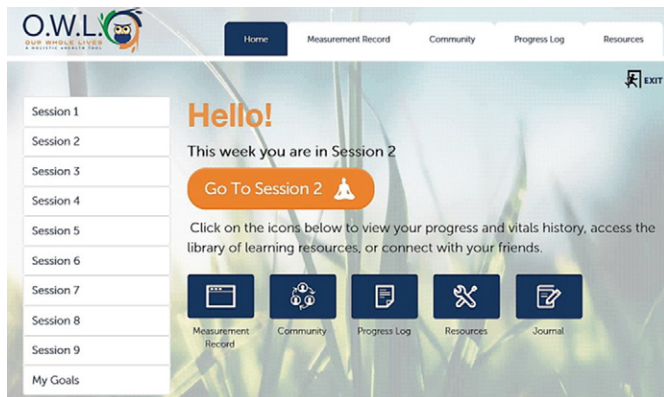


2.9.3. Our Whole Lives (OWL) website

The third component of the intervention is the online toolkit Our Whole Lives (OWL). This website provides interactive monitoring through self-directed learning and goal setting as well as social support through interaction on community forums. Within the group visit session every week, study staff will demonstrate the patients the content available on OWL for that week.

When logging in, the system prompts the patient to enter their pain and depression levels. One page also contains a vital signs tracker, where patients can observe change over time in weight, blood pressure, pulse and pain as recorded during the IMGV session. The website mirrors all the content taught in the IMGV including: the patient manual, journaling space, home practice assignments (e.g., yoga), all meditations, and body scans with a tracker. It also includes recommended goals for home practice, such as, "Practice body scan once a day for at least 6 days." As the participant completes additional mind-body activities, they earn a new puzzle piece. Participants are rewarded with a complete image after finishing all of the mind body activities in a session. The website also displays videos of experiential activities practiced in class and recorded videos of providers discussing the relevant health topic for that week.

The patient will have the ability to select self-care practice options based on his/her own preferences and symptoms. Patients are encouraged to participate by commenting on each video, audio, or other experiential, and tracking their progress (monitored by research staff and clinicians). All materials are divided according to the session covered in the group that week. Independent of session materials, OWL includes local resources for accessing Integrative Medicine Services, nutrition resources and recipes, poems, and other support services including utilities assistance, housing, and intimate partner violence resources. Participants will have an individualized login and can access the website either through their home computer, through a study provided tablet or through their own mobile phone. Additional images of the website are available in the supplementary material.



Participants will be called weekly and reminded of the different options available for home practice as well as the assignments for the next week. We will recommend daily home practice of roughly 20 min (average duration of one home practice on either OWL or the ECA). They can choose to use either the ECA or OWL, or preferably a combination of both. The ECA can be a more accessible tool for patients without a reliable internet service at home, given it does not require a wireless internet connection.

2.9.4. Maintenance phase

After the nine week treatment phase is concluded, the intervention participants will enter a 12 weeks maintenance phase. During this time all intervention participants will retain the study tablet and continue to have access to the ECA and the OWL website, but will not attend group visits. At the end of the 21 weeks there will be one final group visit where participants will review the goals set in session nine and each participant will receive a certificate of completion.

2.10. Usual care/PCP condition

Usual care for this study is defined as the continued treatment with a primary care provider throughout the 21 weeks of the intervention. In order to increase consistency of care provided, we will hold clinical grand rounds or scheduled presentations at clinical meetings in Boston Medical Center and the two Community Health Centers on the most recent evidenced-based guidelines in chronic pain management using the website TOPCARE (<http://mytopcare.org/>). In addition, we will hold orientation meetings for all PCPs about the study procedures, risks and benefits to patients, and data collection methods.

This comparison group was selected because regular contact with a PCP is the most common option of care available for patients who attend BMC and affiliated CHCs. Even if the participant sees specialty care for the source of his/her chronic pain and depression, the most common insurance plans at all three health care centers require patients to see their PCPs before being referred. Using the PCP visit as a control

condition allows for the capture of patient outcomes as they occur in actual patient visits, documented in the electronic medical record (EMR) and self-reported data. After the completion of all IMGV groups, patients randomized to the control group will be given access to the IMGV in a non-study context if desired. Three groups will be held, one at each site.

2.11. Fidelity

Prior to conducting the pilot groups, facilitators participated in a three day training introducing them to study design, curriculum, best practices for running each individual session and were offered guided practice of the PMBSR experiential activities. Three additional one day trainings occurred during the pilot year. Dr. Gardiner and Dr. Gergen-Barnett mentored facilitators via direct observation of group visits, one on one meetings, and phone calls. Study staff will assess adherence to the intervention components at each group visit session through a fidelity checklist (available in supplementary material). Study staff and facilitators will participate in a monthly call to review any ongoing issues and to ensure consistency in implementation of study protocol across all sites and cohorts.

2.12. Data collection

Data collection will occur at baseline, at nine weeks, and after 21 weeks in person or by phone with a trained RA. All data will be entered directly into StudyTRAX at the time of collection. At baseline we will collect the following socio-demographic measures: age, sex, race, ethnicity, language spoken at home, level of education, work status, annual household income, sexual orientation, and health literacy (REALM-R) [70]. We will also collect information on preference for and expectations of condition assignment (IMGV or usual primary care) and on experience with computer use.

All measures used as part of the standardized assessments are reported below in Table 3.

2.12.1. Chart review

Information downloaded from participant's electronic medical record three months after study completion will include all patient diagnoses, medications, emergency department (ED), visits, urgent care, hospital admissions, primary care appointments and use of specialty care appointments related to chronic pain treatment or integrative medicine appointments three months prior to the first IMGV session until three months after the study has concluded.

2.12.2. Technology (OWL and the ECA)

We also will collect data from the OWL website. We will track frequency and duration of use of the home practice tools available on the website and record any comments from the community forums. Data from the website will be collected after 21 weeks. We will record data from the ECA use as well, including the amount of time spent interacting with Gabby, which home practices are used, and participant-inputted information, for example, their weekly mood and home practice goals. Data from the tablets regarding ECA use will be collected at nine weeks and at 21 weeks. At the follow up surveys, the intervention participants will be asked qualitative questions about their experience with the ECA and OWL.

2.12.3. Compensation

Participants in both groups will receive \$100 in gift cards for participating in the study, divided into two \$50 installments distributed at nine and 12 weeks. Participants will also be reimbursed for any parking or other transportation expenses, if requested, to defray the cost of attendance to the interviews or group visits.

Table 3
Content of assessments and purpose.

Outcome tool	Measures	Description of scale	Assessed at:
Primary outcomes			
Brief Pain Inventory (BPI)	Assesses pain severity and interference.	Pain severity measured as a composite score of 4 items each with a 0–10 scale. Pain interference measured as a composite score of 7 items each with a 0–10 scale. Higher scores indicate higher levels of pain [63,64].	Baseline, 9 weeks and 21 weeks
Patient Health Questionnaire (PHQ-9)	Measures severity of depressive symptoms.	Sum of 9 items each with a 0–3 scale. Higher scores indicate higher levels of depression. Cutpoints of 5, 10, and 15 represent mild, moderate, and severe levels of depressive, anxiety, and somatic symptoms, respectively [65,71].	Screening, Baseline, 9 weeks and 21 weeks
Secondary outcomes			
Pain self-efficacy questionnaire (PSEQ)	Used to assess the confidence in performing activities while in pain.	Sum of 10 items each with a 0–6 scale. Higher scores indicate higher levels of confidence [66].	Baseline, 9 weeks and 21 weeks
Self-reported pain medication use	Records medications used for pain by participants in the past seven days and compares use to medications prescribed.	Records current pain medications with mg/pill, daily dosage and whether or not it is listed in the patient's medical record [72].	Baseline, 9 weeks and 21 weeks
Exploratory outcomes			
Duke-UNC functional social support (FSSQ)	Designed to measure functional social support in a family medicine environment.	Composite of 8 items each with a 1–5 scale. Higher scores indicate higher levels of social support [73].	Baseline, 9 weeks and 21 weeks
Patient activation measure (PAM)	Measures patient's knowledge, skill, and confidence for self-managing health and healthcare.	Sum of 13 items each with a 0–4 scale. Higher scores indicate higher levels of patient activation [74,75].	Baseline, 9 weeks and 21 weeks
Pittsburgh sleep quality index (PSQI)	Quality and pattern of sleep.	Sum of 7 component scores each with varying scales. Higher scores indicate lower quality of sleep [76].	Baseline, 9 weeks and 21 weeks
Short form 12 health survey (SF-12)	Mental and physical functioning and overall health-related quality of life.	Measured with 2 component scores for mental and physical health. Each score has a 0–100 scale. Higher scores indicate higher mental and physical functioning [77].	Baseline, 9 weeks and 21 weeks
Other non-pharmacological treatments	Used to assess lifetime use of pain treatments by patients	Records yes or no responses to other treatments participants have ever tried for chronic pain, it includes both integrative options such as massage and acupuncture, but also conventional treatment options such as trigger point injections and surgery.	Baseline, 9 weeks and 21 weeks
Stress related measures			
Stress management	Includes common stress management techniques patients have tried in the past year.	Records yes or no responses to different stress management methods, including deep breathing, meditation, smoking cigarettes or marijuana, etc.	Baseline, 9 weeks and 21 weeks
Perceived stress scale (PSS-4)	Measures the degree to which situations in one's life are perceived as stressful in the past month.	Sum of 4 items each with a 0–4 scale. Items 2 and 3 are reverse scored. Higher scores indicate higher levels of perceived stress [78,79].	Baseline, 9 weeks and 21 weeks
Health behavior			
Nutrition questionnaire	Used to track eating habits and vitamin/supplement intake.	Records number of servings for different food groups, yes or no responses to vitamins and supplements participants currently use, use of nutrition facts labels and whether or not participants receive benefits from food assistance programs [80].	Baseline, 9 week and 21 week
Exercise history	Used to track different forms of physical activity.	Records yes or no responses to different types of exercises, as well as frequency and duration of exercise for the past week [81].	Baseline, 9 week and 21 week
Alcohol and tobacco use	Used to track alcohol and tobacco use.	Records current smoking status, cigarettes smoked per day, current alcohol use and use of illegal drugs or use of prescription medication for non-medical reasons [82,83].	Baseline, 9 week and 21 week
Common opioid misuse measure (COMM)	Used to assess risk of substance abuse for chronic pain patients prescribed opioids.	Sum of 16 items each with a 0–4 scale. Higher scores indicate higher risk of substance abuse. A score of 13 as a threshold value has been previously validated in this population [84–86].	Baseline, 9 week and 21 week

2.12.4. Adverse events (AE)

Adverse Events will be tracked both as data to inform study results and also to ensure patient safety and well-being. AE's will be collected by RAs at the nine week and 21-week follow-ups and as reported incidentally by study participants during the group visit sessions or reminder calls about study appointments. They are defined as reporting pain in a new location, worsening in depression symptoms resulting in psychiatric hospitalization or suicide attempt, an ED visit, hospitalization, or other injury. They will also evaluate on expectedness, relatedness to study procedure, severity and seriousness. Every AE will be reviewed with the PI to ensure the proper categorization and actions are taken. A copy of the AE form is included in the supplementary material.

2.12.5. Midterm evaluation

In order to address any patient concerns while the IMGV groups are occurring, midterm evaluations will be distributed to all intervention participants during session four. We will ask about what has gone well in the groups, any changes participants would like to see and any health changes participants have noticed in their lives.

2.12.6. Policies and procedures

Standard Operating Procedures will be used to implement the group visits, recruitment, screening, enrollment, data collection and adverse events. These include steps to be taken by research staff to increase attendance at the group visits and throughout data collection, protocols for when suicidal ideation or intimate partner violence is reported in the group or in a survey, protocols for consistent data collection, as well as other materials relevant to the day to day running of the study. Our BMC team will meet weekly to review any outstanding issues that have come up in the previous week and ensure consistency moving forward. All protocols are available in the supplementary material.

2.13. Data analysis

Our statistician will be blinded to the participant's assignment. To avoid bias as much as possible, the information on a patient's randomization status is not visible when an RA is collecting follow up data.

Recruitment and retention data, as well as data for each outcome measure will be described with descriptive statistics including means,

medians, and standard deviations for continuous variables and frequencies and percentages for dichotomous and categorical variables. Intention-to-treat (ITT) and Per Protocol (PP) analyses will be performed for all efficacy analyses with the ITT analysis considered as the primary method. The ITT analysis will include all patients in the analysis regardless of adherence. We will also use a multiple imputation approach for missing post baseline data. A per-protocol (PP) analysis will include only those subjects who are considered to be “adherent” to therapy: attending at least 50% and 70% of the recommended sessions for the IMGV arm and at least one PCP visit during the study period for the primary care arm. Any participants found to have violated the inclusion/exclusion criteria will also be excluded from the per-protocol analysis. Participants included in safety analyses will include those attending at least one group visit or one primary care visit.

2.13.1. Preliminary analyses

First, we will assess whether randomization of patients was successful. The two treatment groups will be compared by baseline demographics and clinical characteristics using two-sample *t*-tests or chi-square tests of independence as appropriate and using a $\alpha = 0.05$ level of significance. Variables that have statistically significant differences across treatment groups may be potential confounders and will be adjusted for in all subsequent analyses.

2.13.2. Analysis of pain reduction and depression

The primary hypothesis is participants randomized to the IMGV will have a greater reduction in pain scores and depression levels as compared to participants randomized to the control group. The Brief Pain Inventory (BPI) [63] is used to assess pain severity and pain interference. The Patient Health Questionnaire (PHQ-9) [65] is used to measure severity of depression. Both BPI and PHQ-9 scores are continuous variables. In order to assess changes in pain and depression over the study period for both the intervention and control groups, four difference scores will be calculated for each treatment group. These include difference from baseline to nine weeks and baseline to 21 weeks for each participant's BPI and PHQ-9 score. Two-sample *t*-tests or Mann Whitney *U* tests will compare mean difference scores for all outcomes between the intervention and control groups.

Mixed effects generalized linear regression models, with an indicator for treatment assignment as the predictor of interest, will be used to adjust for potential confounders and assess effect modification. Depending on initial diagnostics, we will determine the most appropriate model to use (linear, Poisson, negative binomial, etc.) and use an unstructured correlation matrix to model. After the initial fit, we will assess whether we can use a simpler correlation matrix. We will determine the need to use a hierarchically formed model to account for correlation within study site, in addition to correlation induced from repeated measures within subjects. The following variables will be considered as effect modifiers for the relationship between treatment group and the outcomes of pain and depression: study site, OWL and ECA use, adherence to home care assignments, and preference/expectation of intervention or control group. A multiplicative interaction term between treatment and the possible effect modifier of interest will be included in a regression model. If a significant interaction occurs, we will examine whether it is quantitative or qualitative in nature. Statistical summaries and sensitivity analyses will be used to describe any missing data in the study, including a comparison of patient baseline characteristics and outcomes with and without missing data.

2.13.3. Analysis of pain self-efficacy and pain medication utilization

The secondary hypothesis states that participants randomized to the IMGV will have higher pain self-efficacy scores and a reduction in self-reported pain medication use as compared to patients randomized to the control group. For pain self-efficacy scores two-sample *t*-tests or Mann Whitney *U* tests will be used to compare the intervention and the control groups. Difference scores will be calculated similarly to the

primary outcome measures. We will use the same modeling strategy as outlined for the primary outcomes. We anticipate using mixed effects generalized linear models, potentially with an additional adjustment for study site and an indicator of intervention or control group.

2.13.4. Exploratory analyses

We will also treat health-related quality of life, sleep quality, perceived stress, eating habits, physical activity, stress management, social support, patient activation, alcohol and tobacco use and a patient's COMM score as continuous or categorical variables and analyze these outcomes in a similar manner to what is mentioned above. Using the Bonferroni correction all analyses will be adjusted for multiple testing.

2.14. Sample size

For primary outcomes, pain and depression, we assume a two-sided alpha error = 0.05 and an estimated 20% drop-out rate from baseline to 9-weeks. Clinically significant changes in pain and depression would be at least 1.5 points for pain and 4 points for depression. From our pilot data, we assume a standard deviation of 2.5 and 4.54 for the mean pain and depression change scores, respectively. Additionally, we assume an intra-class cluster coefficient (ICC) of 0.05 between individuals at the same study site. Based upon these assumptions, a sample size of 62 patients, after dropout, per treatment group across all sites will have 80% power to detect a 1.5 difference in pain and a sample size of 31 per treatment group will have 80% power to detect a 4.0 difference in depression. An initial sample size of 154 participants (77 in each arm) will provide adequate power to detect important clinical differences between the two groups. This study is powered to examine pain and depression scores. Any subgroup analyses cannot make the claim of efficacy for this intervention.

3. Discussion

The IMGV model has the potential to reduce pain and depressive symptoms while increasing patients' ability to manage their chronic conditions. If it is found to be efficacious in the randomized controlled trial, it will be a unique platform to deliver healthcare to chronic pain patients in a group context while also providing training in PMBSR and allowing the participants to experience evidence-based integrative medicine. Additional tools to encourage home practice, such as the OWL website and ECA, will be available at any time and allow for greater customization of pain management based on the patient's symptoms and health concerns. Using a diverse group of patients with different varieties of chronic musculoskeletal pain is an innovative and pragmatic of care delivery in primary care settings where physician time is an ever more limited resource.

Limitations to patient participation in this group include inconvenience of timing and limited internet access. The IMGV visits will be scheduled during the work day. In order to minimize this loss, we will provide medical notes for a patient's employers in order to justify that this time is spent for medical treatment. Another limitation is limited internet access or lack of experience with technology as a barrier to the use of the OWL website and the ECA. However, many low income individuals use their smart phone for internet access [87], and we have adapted the website to be mobile phone accessible. The group visit coordinator will also review the online content every session and how to access it at home.

Throughout this intervention we will be gathering data through validated measurements for social support and perceived stress, recording qualitative data from participants, tracking participant's use technology as part of the intervention, and comparing self-report data to data available in electronic medical records. We expect to use this information to evaluate both pain relief and reduction of depressive symptoms as well as how the different aspects of the study affect these outcomes, for example if group support allows for change in health behavior. One

limitation for the electronic medical record data is that any patient visits outside of the BMC system are not visible to study staff, which may result in an underestimate of clinical visits.

The IMGV model is currently a unique model for pain and depression treatment that focuses on providing access to integrative medicine and self-management techniques in a group setting for a low income population. Positive findings of the effectiveness could allow for dissemination to other health care settings with the use of these tools for chronic disease management. Further studies of feasibility, implementation dissemination for the IMGV protocol are needed to confirm sustainability across different settings and use in different patient populations.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.cct.2016.12.013>.

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