PRIMIER

A National Integrative Medicine Database

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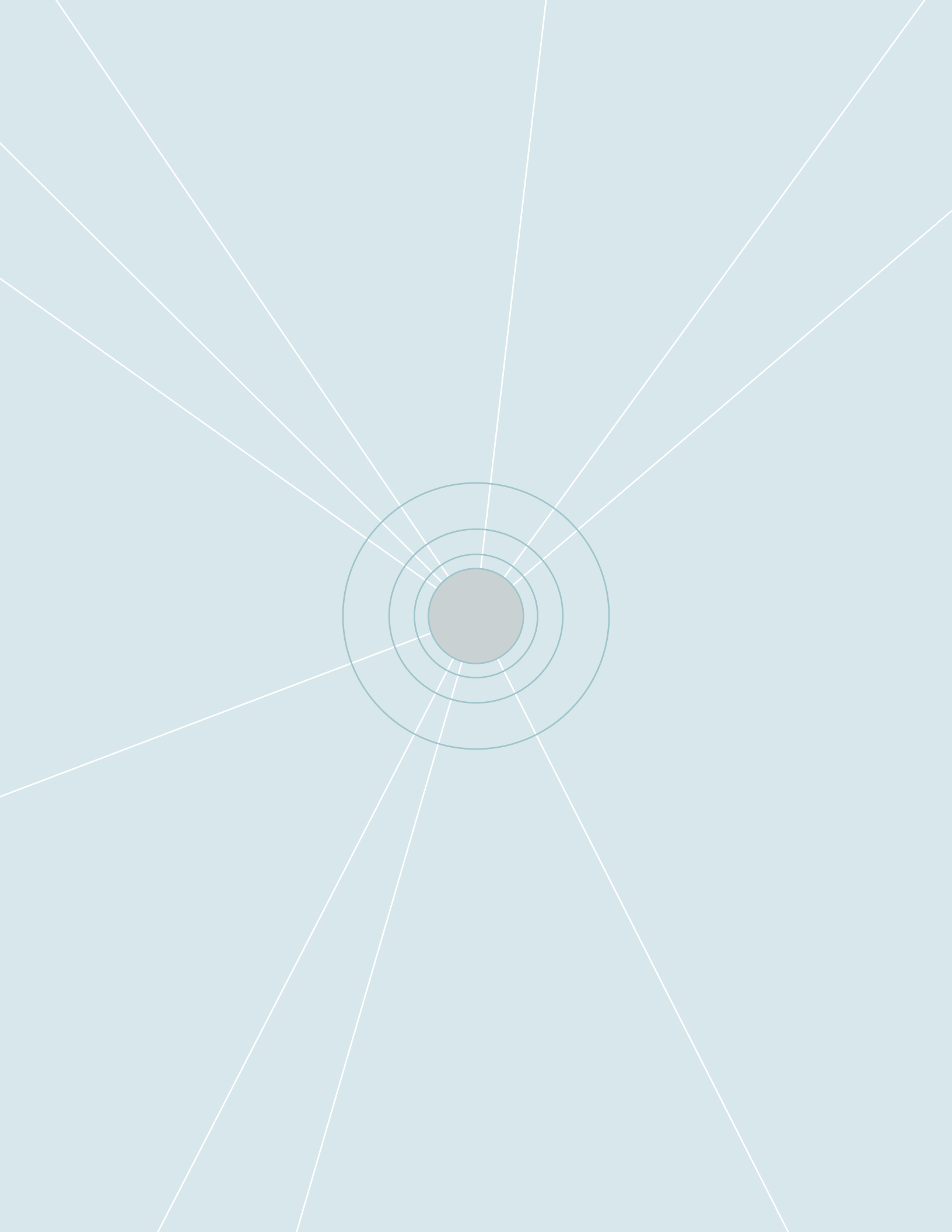


INTRODUCTION

Practice-Based Research Networks (PBRNs) are an increasingly important part of the healthcare research landscape. Drawing on the insight and experience of practicing clinicians to identify and frame research questions whose answers can improve care, PBRNs provide clinical outcome information that is not otherwise available. The Agency for Healthcare Research and Quality (AHRQ), which is charged with producing evidence that makes healthcare safer, of higher quality, more accessible and affordable, notes that: "By linking questions of importance to clinical practice with rigorous research methods, PBRNs produce research findings that are immediately relevant to clinicians and more easily translated into everyday practice."[1]

Understanding the need for Integrative Medicine clinics to conduct this kind of real-world PBRN research, The Bravewell Collaborative *(see Appendix A)* founded BraveNet in 2007. BraveNet is a PBRN that initially consisted of eight Integrative Medicine clinics that had robust patient populations as well as strong research capabilities. Bravewell funded BraveNet — now a registered PBRN with AHRQ — with the intent that it would provide data on Integrative Medicine's use, effectiveness, safety, costs, and patient satisfaction. Since 2007, BraveNet has grown to include 14 member sites. *[See Appendix B and Figure 1.]*

In 2013 the network created and launched **PRIMIER** (*Patients Receiving Integrative Medicine Interventions Effectiveness Registry*), a multi-institution project designed to uniformly collect patient-reported outcomes and extracted electronic health record (EHR) data into a large national registry that would help improve the health and well-being of patients. PRIMIER provides a framework that can be used for quality improvement and evidence-based research, as well as discovering best practices within Integrative Medicine. PRIMIER is listed in the Registry of Registries that is maintained by AHRQ and **ClinicalTrials.gov**. The intent is that PRIMIER will continue to expand over time, including more public as well as private Integrative Medicine centers.

PRIMIER

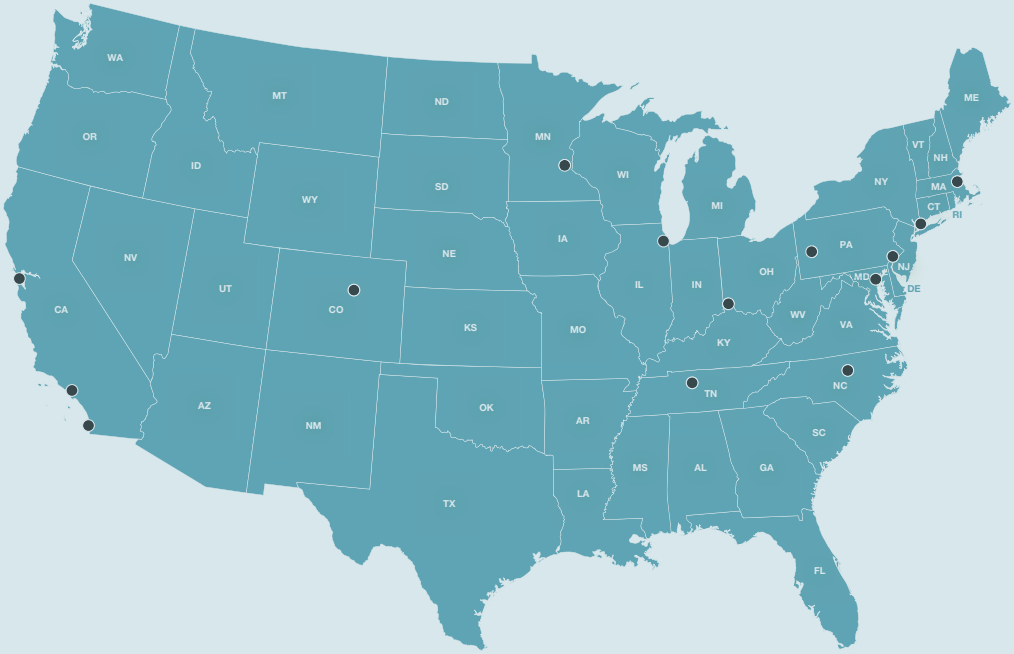
PATIENTS
RECEIVING
INTEGRATIVE
MEDICINE
INTERVENTIONS
EFFECTIVENESS
REGISTRY

Through the collection of prospective patient-reported outcomes on a number of frequently seen medical conditions and by clustering participants at the multiple Integrative Medicine clinical sites into subsets with the same medical condition, researchers are able to compare the impact of various integrative therapies on patient-reported and clinical outcomes. This approach is cost-effective and allows researchers to gather evidence on a much larger scale than would be possible in a typical clinical trial

1 **http://www.ahrq.gov/research/findings/factsheets/primary/pbrn/**. Accessed 14 February 2015.

at a single institution. With more than 1600 patients enrolled in PRIMIER to date, this unique data registry is already providing foundational new knowledge on how Integrative Medicine is being used in real world settings and provides an early glimpse into several important outcomes improved by the provision of Integrative Medicine.

FIGURE 1: Location of BraveNet Member Centers



The intent of this report is to (1) explain what data is being collected in PRIMIER, (2) demonstrate how the database can be used to answer important clinical questions, and (3) inspire other Integrative Medicine centers to join PRIMIER.

PRIMIER OVERVIEW

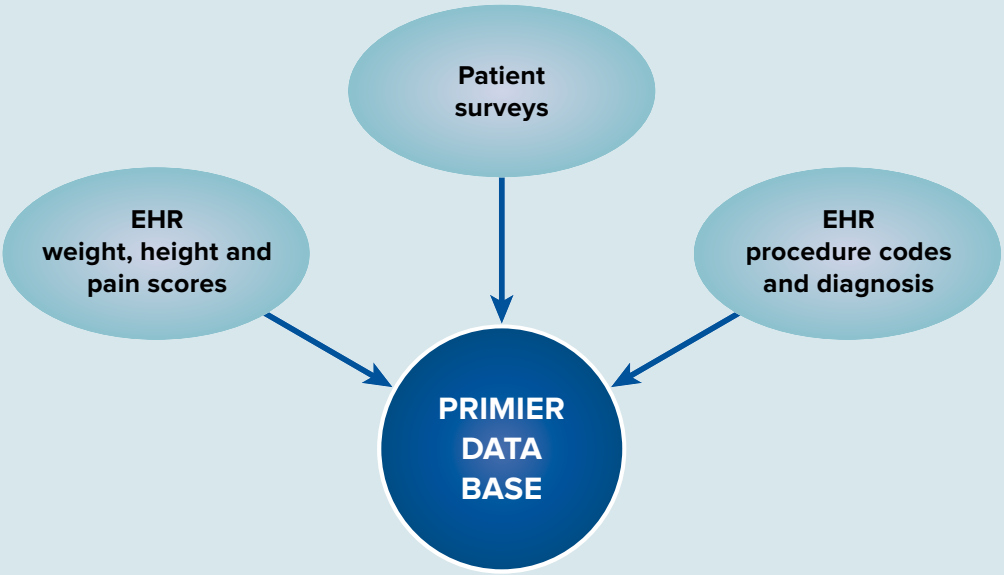
The overarching goal of PRIMIER is to build a national database that will enable PRIMIER researchers to evaluate the change in patient-reported outcomes (e.g., quality of life, mood, stress, and pain) over time for patients receiving Integrative Healthcare.

The database is populated as patients complete an online survey at specified intervals. Over time, it is expected that up to 10,000 patients at the 14 participating clinics will complete questionnaires at baseline and then every two months for six months, and then every six months thereafter for two years.

The online survey utilizes a secure electronic platform called REDCap, which is a research program developed at Vanderbilt University and widely used by thousands of investigators at medical schools across the nation for conducting healthcare research. The encrypted database allows each participating clinic to view its own patient survey data, while the Data Coordinating Center at Albert Einstein College of Medicine has access to the combined data from all of the 14 centers.

Every six months, the patient survey measures are integrated with data extracted from the corresponding electronic health records (EHR) at each center. The EHR data includes dates of clinical visits, procedure codes (CPT), and clinical diagnoses (ICD-9/ICD-10), and if available, weight, height and pain scores. This information is securely aggregated at the Data Coordinating Center where data analyses are performed.

FIGURE 2: Data Collection



PRIMIER is conducted in accordance with current International Conference on Harmonisation guidelines on Good Clinical Practice (ICH E6, the principles of which have their origin in the Declaration of Helsinki), and all other applicable national and local laws and regulations. Institutional Review Boards at each PBRN site and the coordinating center have reviewed and approved the protocol and subsequent amendments.

PROTOCOL SYNOPSIS

PRIMIER is a registry database that, using validated questionnaires, enables prospective cohort surveillance of patients receiving Integrative Medicine interventions at PRIMIER clinics.

Although participants can leave or be withdrawn from the study at any time, the study is designed to collect data on each patient for a two-year period.

To participate, patients must:

- Be a clinical patient in one of the participating Integrative Medicine clinics and willing to participate in the Registry
- Be 18 years of age or older
- Be willing to be contacted in the future by study investigators

Patients who are not being seen by a provider for clinical purposes, but are only involved in an education program or one-time group activity are excluded from study participation.

The primary objective of PRIMIER is to evaluate the change in patient-reported outcomes (e.g., quality of life, mood, stress, and pain) over time. The secondary objective is to evaluate whether patient-reported outcomes differ by baseline characteristics of the participants (e.g., demographics, clinical condition, patient activation measure score, or intervention sought).

THE PRIMIER SURVEY BATTERY

All patients attending a participating Integrative Medicine clinic for clinical services are invited to participate in PRIMIER. Patients who decide to participate access the PRIMIER website and enroll directly into the registry. A paper version is available for patients without computer access or electronic mail.

The opening screen of the initial visit to the survey website is the participant consent form, such that informed consent is given when a patient voluntarily proceeds to enter the PRIMIER site.

When a patient accesses the secure, encrypted REDCap PRIMIER website, they provide demographic information on their age, gender, ethnicity, race, date of birth, name, address, email address, and phone number. *[See Figure 3, page 9.]*

Participants are asked to report their use of Integrative Medicine therapies in the past six months, especially since some therapies can be performed alone or outside the Integrative Medicine centers. Figure 4 depicts the questions and answer options for the Visit Information screen of the PRIMIER survey. *[See page 10.]*

This individually identifiable health information (IIHI) is secure within REDCap and only available to the research staff associated with the patients' enrolling clinic and the database administrative staff of the Coordinating Center at the Albert Einstein College of Medicine.

Essential data elements that capture patient-reported outcomes and measures of clinical activity are obtained at approximately two-month intervals for the first six months, then every six months through the end of year two. This information is then combined with data contained in the participants' electronic health record, which includes information about demographics, diagnosis, treatments received, healthcare utilization, and clinical outcomes.

PRIMIER uses the Patient-Reported Outcome Measurement Information System (PROMIS®), created with funding from the National Institutes of Health; the Perceived Stress Score (PSS-4) developed at Carnegie Mellon University; and the Patient Activation Measure (PAM) developed by researchers at the University of Oregon.

FIGURE 3: PRIMIER Survey Instrument — Demographics

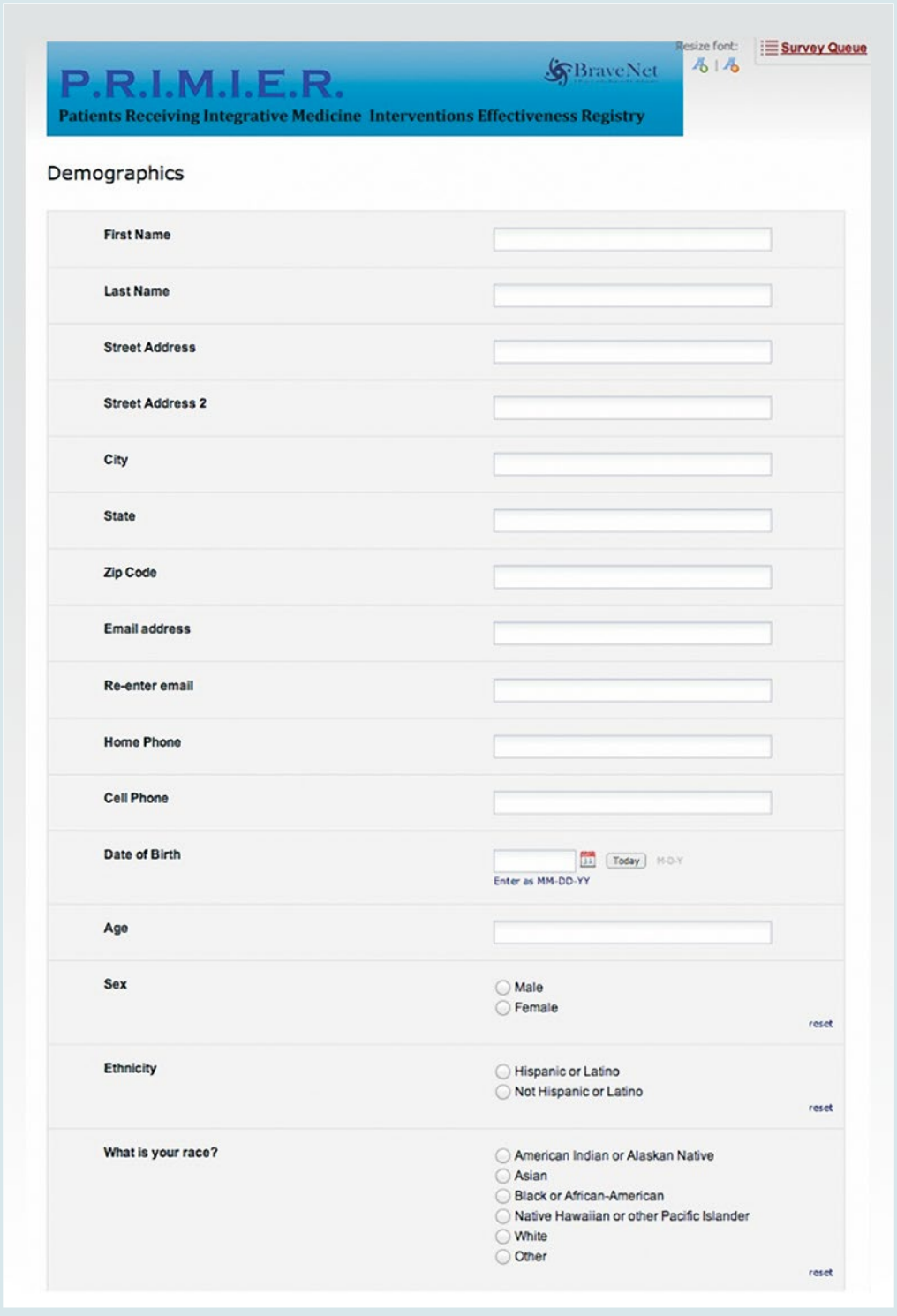
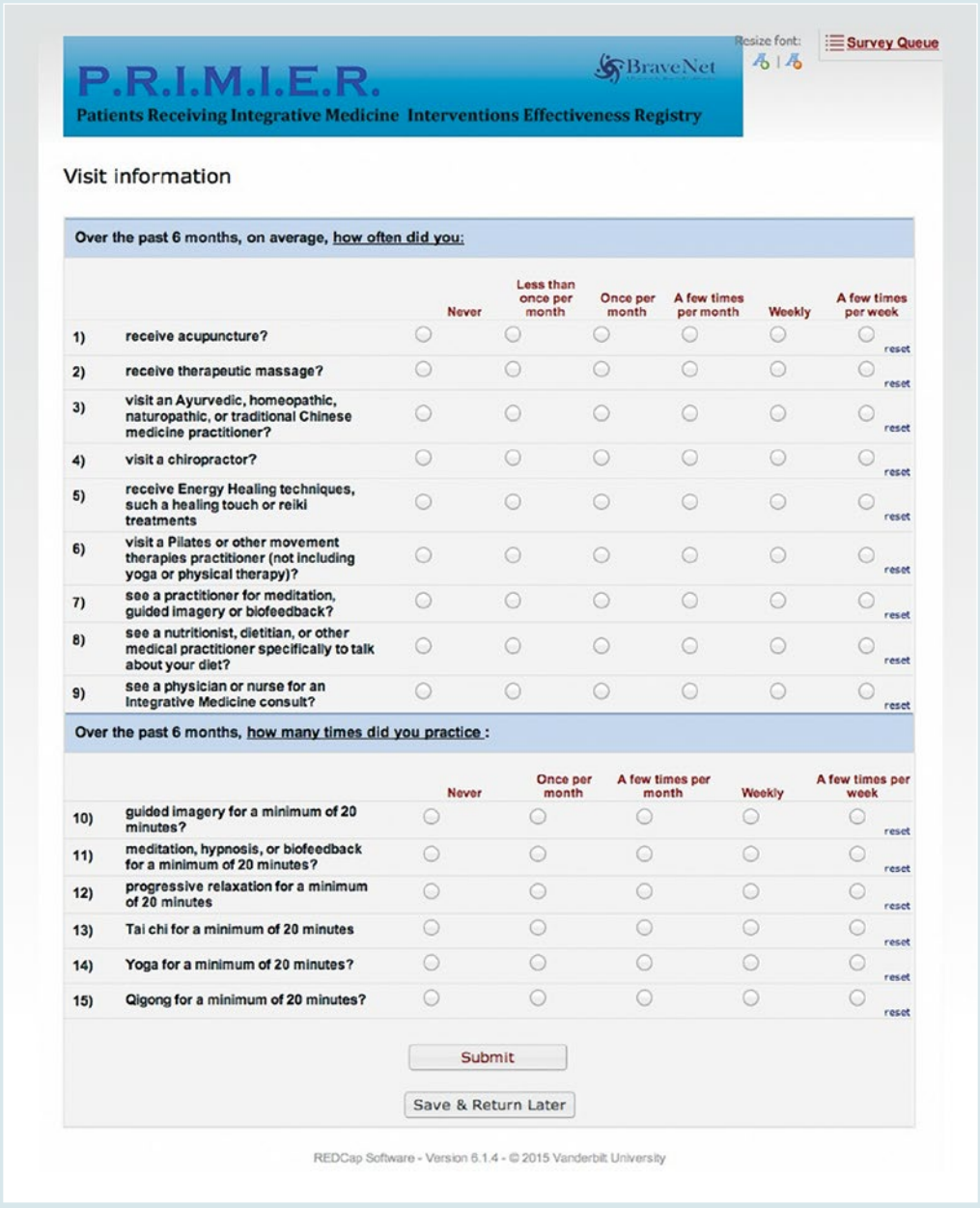


FIGURE 4: PRIMIER Survey Instrument — Visit Information



P.R.I.M.I.E.R.

Patients Receiving Integrative Medicine Interventions Effectiveness Registry

BraveNet

Resize font: A A | A A

Survey Queue

Visit information

Over the past 6 months, on average, how often did you:

		Never	Less than once per month	Once per month	A few times per month	Weekly	A few times per week	
1)	receive acupuncture?	○	○	○	○	○	○	reset
2)	receive therapeutic massage?	○	○	○	○	○	○	reset
3)	visit an Ayurvedic, homeopathic, naturopathic, or traditional Chinese medicine practitioner?	○	○	○	○	○	○	reset
4)	visit a chiropractor?	○	○	○	○	○	○	reset
5)	receive Energy Healing techniques, such a healing touch or reiki treatments	○	○	○	○	○	○	reset
6)	visit a Pilates or other movement therapies practitioner (not including yoga or physical therapy)?	○	○	○	○	○	○	reset
7)	see a practitioner for meditation, guided imagery or biofeedback?	○	○	○	○	○	○	reset
8)	see a nutritionist, dietitian, or other medical practitioner specifically to talk about your diet?	○	○	○	○	○	○	reset
9)	see a physician or nurse for an Integrative Medicine consult?	○	○	○	○	○	○	reset

Over the past 6 months, how many times did you practice :

		Never	Once per month	A few times per month	Weekly	A few times per week	
10)	guided imagery for a minimum of 20 minutes?	○	○	○	○	○	reset
11)	meditation, hypnosis, or biofeedback for a minimum of 20 minutes?	○	○	○	○	○	reset
12)	progressive relaxation for a minimum of 20 minutes	○	○	○	○	○	reset
13)	Tai chi for a minimum of 20 minutes	○	○	○	○	○	reset
14)	Yoga for a minimum of 20 minutes?	○	○	○	○	○	reset
15)	Qigong for a minimum of 20 minutes?	○	○	○	○	○	reset

Submit

Save & Return Later

REDCap Software - Version 6.1.4 - © 2015 Vanderbilt University

PROs

"Patient–Reported Outcomes (PROs)" is the term used to denote health data that is provided directly by the patient through a system of reporting. A PRO is basically a patient's feedback on their feelings or functions as they are dealing with chronic diseases or conditions.

PROMIS® PROs cover three domains: physical, mental, and social health. Examples include physical abilities, fatigue, anxiety, pain, depression, and satisfaction with social participation (or interactions). Questionnaires can be customized to measure PROs in any disease or medical condition or they can be designed to measure certain PROs that are of specific importance to one disease, such as the importance of fatigue to cancer.[2]

Common measurements across domains ensure that the PROMIS® data is comparable. Additionally, the PROMIS measures have been subjected to rounds of rigorous review and testing to ensure that the measurements are validated, precise, consistent, and accurate.

PRO measures are obtained by way of written questionnaires or computer–assisted tools.

PSS-4

The PSS-4 is a brief, validated and widely used psychological instrument for assessing a participant's perception of stress. The PSS-4 consists of four questions to measure the degree to which situations in the participant's life are perceived as stressful including questions related to perceived unpredictability and lack of control.[3]

2 Cella, D., Riley, W., Stone, A., Rothrock, N., Reeve, B., Yount, S., Amtmann, D., Bode, R., Buysse, D. J., Choi, S. W., Cook, K. F., DeVellis, R., DeWalt, D., Fries, J. F., Gershon, R., Hahn, E., Pilkonis, P., Revicki, D., Rose, M., Weinfurt, K., & Hays, R. D. on behalf of the PROMIS Cooperative Group. (2010). Initial item banks and first wave testing of the Patient–Reported Outcomes Measurement Information System (PROMIS) network: 2005–2008. *Journal of Clinical Epidemiology*, 63(11), 1179–94.

Rose, M., Bjorner, J. B., Becker, J., Fries, J. F., & Ware, J. E. (2008). Evaluation of a preliminary physical function item bank supports the expected advantages of the Patient–Reported Outcomes Measurement Information System (PROMIS). *Journal of Clinical Epidemiology*, 61(1) 17–33.

Amtmann, D. A., Cook, K. F., Jensen, M. P., Chen, W-H., Choi, S. W., Revicki, D., Cella, D., Rothrock, N., Keefe, F., Callahan, L., Lai, J-S. (2010). Development of a PROMIS item bank to measure pain interference. *Pain*, 150(1), 173–82.

Buysse, D. J., Moul, D. E., Germain, A., Yu, L., Stover, A. M., Dodds, N. E., Johnston, K. L., Shablesky–Cade, M. A., & Pilkonis, P. A. (2010). Development and validation of patient–reported outcome measures for sleep disturbance and sleep–related impairments. *Sleep*, 33(6), 781–92.

3 Cohen S, Karmarck T, Mermelstein R: A global measure of perceived stress. *Journal of Health and Social Behavior*, 1983, Vols. 24, 386–396.

PAM

The PAM is a brief, validated instrument for gauging the knowledge, skills and confidence essential to managing one's own health and healthcare. The 13-item PAM assessment segments individuals into one of four progressively higher activation levels. Each level addresses a broad array of self-care behaviors and offers deep insight into the characteristics that drive health activation.[4] Inclusion of the PAM was suggested by the BraveNet Stakeholder Advisory Group.[5]

4 Hibbard JH, Stockard J, Mahoney ER, and Tusler M. Development of the Patient Activation Measure (PAM): Conceptualizing and Measuring Activation in Patient and Consumers. *Health Services Research*. 2007; 42(4).

5 BraveNet members organized a Stakeholder Advisory Group, comprised of patients, providers and payors, in 2012. This group participates in conference calls and advises BraveNet on its research agenda.

PATIENT CARE

All patients attending a participating Integrative Medicine clinic for clinical services are invited to participate in PRIMIER, regardless of their reason for the visit or whether it is an initial or follow-up visit. The PRIMIER database tracks all medical conditions, via patient reported surveys and electronic health records, for which patients seek integrative treatment. Patient visits that are for wellness only are also included.

Integrative Healthcare is personalized to the patient and all decisions about medication use, treatments, visit frequency, assessment of tolerability, and other aspects of patient care management are left to the clinical providers' discretion.

The following is a partial list of integrative interventions that are being used in patient care by the centers participating in PRIMIER.

- Acupuncture
- Advanced Allergy Therapeutics
- Biofeedback
- Chiropractic
- Craniosacral Therapy
- Education
- Energy Therapy
- Frequency Specific Microcurrent
- Health Coaching
- Hypnotherapy
- IM Consultation
- Infusion Therapy
- Manipulation Therapy
- Massage
- Mindfulness
- Naturopathic Medicine
- Nutriceuticals
- Nutrition
- Personal Training
- Physical Therapy
- Psychotherapy
- Rolfing
- Trigger Point
- Wellness Counseling
- Yoga

PRELIMINARY FINDINGS

DEMOGRAPHICS

Patients enrolling in the PRIMIER study respond to demographic questions. *[See Table 1.]* These demographics reflect those patients enrolled from late 2013 through the beginning of 2015.

TABLE 1: Demographics

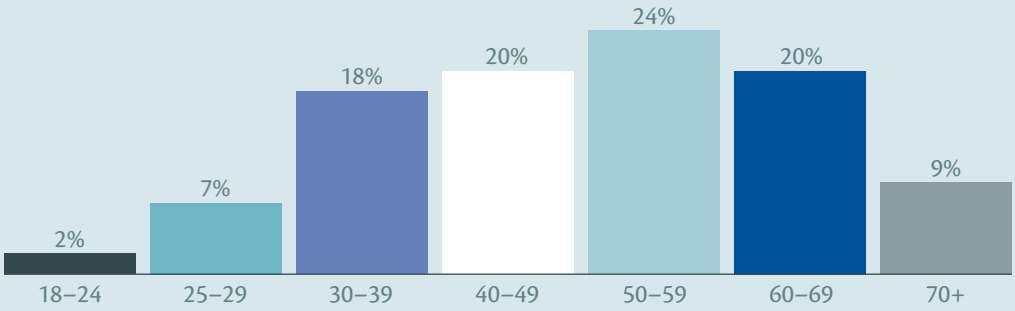
Parameter Statistic	All Patients N=1687
AGE (YEARS)	
N (Missing)	1684 (3)
Mean (SD)	50.32 (14.54)
Median (Q_1, Q_3)	50.82 (38.84, 61.51)
AGE CATEGORIES	
18–24	31/1675 (1.9%)
25–29	114/1675 (6.8%)
30–39	306/1675 (18.3%)
40–49	341/1675 (20.4%)
50–59	399/1675 (23.8%)
60–69	340/1675 (20.3%)
70+	144/1675 (8.6%)
GENDER	
Female	1306/1687 (77.4%)
Male	373/1687 (22.1%)
RACE	
White	1408/1687 (83.5%)
Black/African American	94/1687 (5.6%)
Asian	42/1687 (2.5%)
American Indian or Alaska Native	5/1687 (0.3%)
Native Hawaiian or Other Pacific Islander	5/1687 (0.3%)
Other	66/1687 (3.9%)
ETHNICITY	
Hispanic or Latino	97/1687 (5.7%)
Not Hispanic or Latino	1427/1687 (84.6%)

EDUCATION	
No HS Diploma	22/1645 (1.3%)
HS or Equivalent	49/1645 (3.0%)
Education Beyond HS; No College	242/1645 (14.7%)
College Degree	635/1645 (38.6%)
Graduate/Professional Degree	697/1645 (42.4%)
EMPLOYMENT	
Working Full-Time	874/1629 (53.7%)
Working Part-Time	228/1629 (14.0%)
Not Employed; Other Responsibilities	95/1629 (5.8%)
Retired	232/1629 (14.2%)
Medical Leave; Disabled	105/1629 (6.4%)
Unemployed; Looking for Work	51/1629 (3.1%)
Other	44/1629 (2.7%)
MARITAL STATUS	
Married, Spouse in Household	911/1626 (56.0%)
Married, Spouse not in Household	12/1626 (0.7%)
Significant Other; Partner	166/1626 (10.2%)
Widowed	41/1626 (2.5%)
Divorced	186/1626 (11.4%)
Separated	21/1626 (1.3%)
Never Married	289/1626 (17.8%)
INCOME	
< $20,000	128/1603 (8.0%)
$20,000–50,000	231/1603 (14.4%)
$50,001–$100,000	461/1603 (28.8%)
$100,001–$150,000	334/1603 (20.8%)
>$150,000	449/1603 (28.0%)
PRIMARY HEALTH INSURANCE	
Medicare	296/1635 (18.1%)
Medicaid	21/1635 (1.3%)
Other	1295/1635 (79.2%)
None	23/1635 (1.4%)
VISIT PAYMENT BY INSURANCE	
No	453/1637 (27.7%)
Yes	1095/1637 (66.9%)
Not Sure	89/1637 (5.4%)

BMI	
N (Missing)	1617 (70)
Mean (SD)	28.44 (83.50)
Median (Q_1, Q_3)	25.01 (22.11, 29.23)
BMI CATEGORIES	
Underweight (<18.5)	41/1617 (2.5%)
Normal (18.5–25)	761/1617 (47.1%)
Overweight (25–30)	458/1617 (28.3%)
Obese (>=30)	357/1617 (22.1%)
DAYS/WEEK DRINK ALCOHOL	
N (Missing)	1062 (625)
Mean (SD)	2.67 (1.86)
Median (Q_1, Q_3)	2.00 (1.00, 4.00)
# DRINKS ALCOHOL/DAY	
N (Missing)	1086 (601)
Mean (SD)	1.62 (0.94)
Median (Q_1, Q_3)	1.00 (1.00, 2.00)

The median age of PRIMIER participants is 51 years. Figure 5 shows the percentage of participants in each age category.

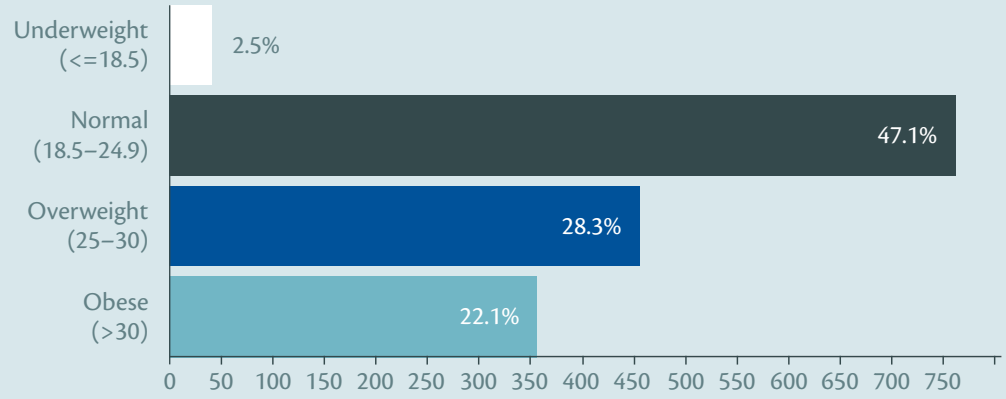
FIGURE 5: Participant Age



Fifty-six percent of the cohort is married. Eighty-one percent of enrollees have a college or graduate degree and 68% are working. Annual income is reported as under $100,000 in 51% of the participants. The majority of patients (79%) have private health insurance and 18% are covered by Medicare. Twenty-eight percent of the patients seen at the sites report that they are paying cash for their Integrative Medicine services as opposed to using their insurance. This may reflect services that are cash-based at the sites and not covered by insurance.

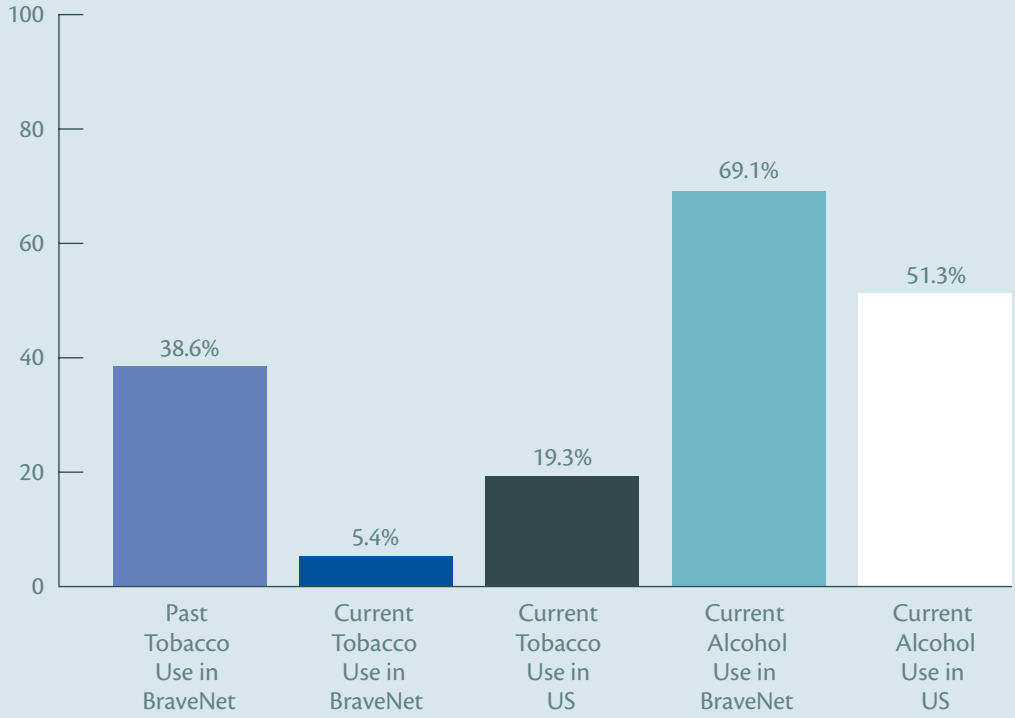
The mean Body Mass Index (BMI) of the entire cohort is 28.4, which is overweight although the median is 25.0, which is the top of the normal range. Figure 6 shows the percentage of participants in each weight category — underweight, normal, overweight and obese.

FIGURE 6: BMI



These findings suggest that our patient population overall is leaner than the US general population where 34.9% are estimated to be obese versus 22.1 % in PRIMIER (**http://www.cdc.gov/obesity/data/facts.html**). Our patients also seem to be more health conscious with regards to current tobacco use (Figure 7).

FIGURE 7: Tobacco and Alcohol Use



Although 38.6% of the participants report use of tobacco in the past, only 5.4% are currently using which is notably less than the 2010 estimate for the US population in general of 19.3% from the Centers for Disease Control. (**http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6035a5.htm**).

On the other hand, a larger percentage of our participants (69.1%) currently consume alcohol compared to the 51.3% of the general US population (**http://www.cdc.gov/nchs/fastats/alcohol.htm**). The median use of alcohol in our participants is one drink two days a week.

BraveNet continues to expand its PBRN network to include additional sites in an effort to obtain input and participation from a more diverse patient population.

CHANGES IN PATIENT ACTIVATION MEASURES

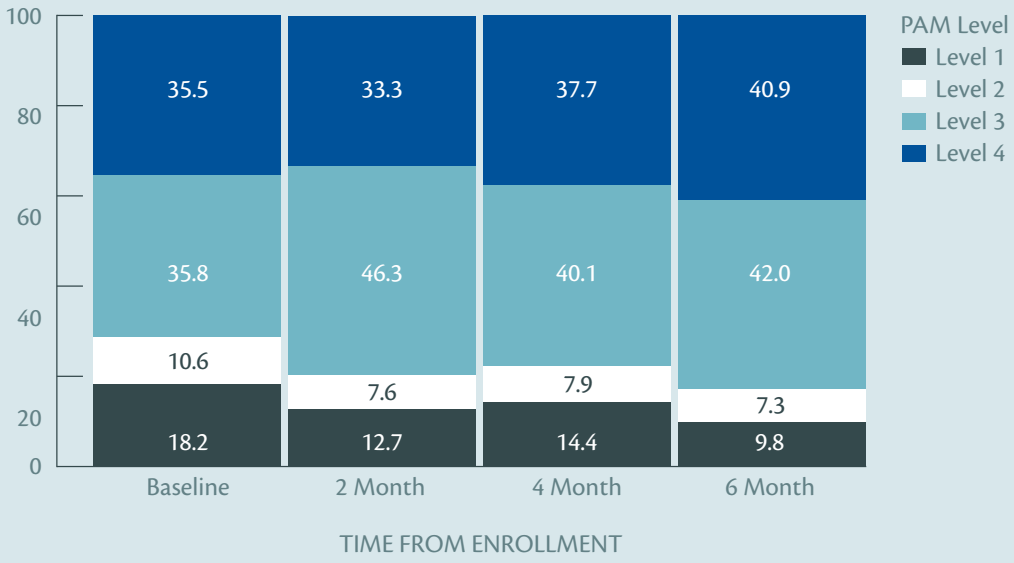
In order to determine change in the survey measures over time, we limited the following analysis to patients enrolled for at least six months who had completed at least three of the four surveys (baseline, two-month, four-month, and six-month) at the time of this writing. This resulted in a PRIMIER longitudinal cohort of 369 participants.

Preliminary findings from this PRIMIER longitudinal cohort show a statistically significant change in the four levels on the Patient Activation Measure (PAM) over six months. The four levels of patient activation are defined as:

- **LEVEL 1 –** Does not believe that he/she has an active or important role
- **LEVEL 2 –** Lacks confidence and knowledge to take action
- **LEVEL 3 –** Beginning to take action
- **LEVEL 4 –** Maintaining behavior over time

Figure 8 shows the proportion of patients at each level of patient activation at baseline, two-, four-, and six-month follow up. Over time, the proportion of patients in Level 1 and Level 2 at baseline is decreasing from 29% to 17% and the proportion of patients at Level 3 and 4 is increasing from 71% to 83% over six months (p=0.01).

FIGURE 8: Patient Activation Scores



The changes in the levels over six months are:

- **LEVEL 1 –** 46% reduction
- **LEVEL 2 –** 31% reduction
- **LEVEL 3 –** 17% increase
- **LEVEL 4 –** 15% increase

Thus BraveNet centers are transitioning patients from lower levels of knowledge, skill and confidence for managing their health, to the higher levels of understanding the importance of taking a pro-active role in managing their health with the skills and confidence to maintain behavioral changes over time. Positive changes in activation have been associated with positive changes in a variety of self-management behaviors.[6] Improvement in patient activation has also been shown to be strongly related to improvements in clinical outcomes such as less pain, an increase in utilization of prevention screenings, and a reduction in emergency room visits. [7]

6 Hibbard, Judith; Mahoney, Stock, Tusler (August 2007). **"Do increases in patient activation result in improved self-management behaviors?"**. *Health Services Research* 42 (4): 1443–1463. doi:**10.1111/j.1475-6773.2006.00669.x**. PMC **1955271**. PMID **17610432**

7 Greene, Jessica; Hibbard (November 2011). "Why Does Patient Activation Matter? An Examination of the Relationship Between Patient Activation and Health-Related Outcomes". *Journal of General Internal Medicine* 27 (5): 520–6. doi:**10.1007/s11606-011-1931-2**

IMPROVEMENT IN DEPRESSION AND STRESS

Major depressive disorder affects approximately 14.8 million American adults, or about 6.7% of the US population age 18 and older, in a given year.[8] Depression is more prevalent in women than in men[9] and as many as one in 33 children and one in eight adolescents have clinical depression.[10]

The relationship between stress and health is equally important. According to the American Psychological Association's "Findings from *Stress in America™: Missing the Health Care Connection*, which was conducted online by Harris Interactive among 2,020 US adults in 2012, people are not receiving what they need from their health care providers to manage stress and address lifestyle and behavior changes to improve their health."

By the very nature of its approach to health and healthcare — treating the whole person — Integrative Medicine addresses both stress and depression even when the patient may be seeking care for another condition.

Preliminary findings from the PRIMIER longitudinal cohort of the first 369 patients to complete six months of follow-up illustrate significant reductions in the PROMIS Depression (Figure 9, $p<0.05$) and Perceived Stress Scale (Figure 10, $p=0.001$) over six months.

8 **Ronald C. Kessler**, PhD, **Wai Tat Chiu**, AM, **Olga Demler**, MA, MS, and **Ellen E. Walters**, MS. Prevalence, Severity, and Comorbidity of Twelve-month DSM-IV Disorders in the National Comorbidity Survey Replication (NCS-R). *Archives of General Psychiatry*, 2005 Jun; 62(6): 617–27.

9 **Kessler RC**1, **Berglund P**, **Demler O**, **Jin R**, **Koretz D**, **Merikangas KR**, **Rush AJ**, **Walters EE**, **Wang PS**. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *Journal of the American Medical Association*, 2003; Jun 18; 289(23): 3095–105.

10 Center for Mental Health Services, US Dept. of Health and Human Services, 1996.

FIGURE 9: PROMIS Depression Change Score

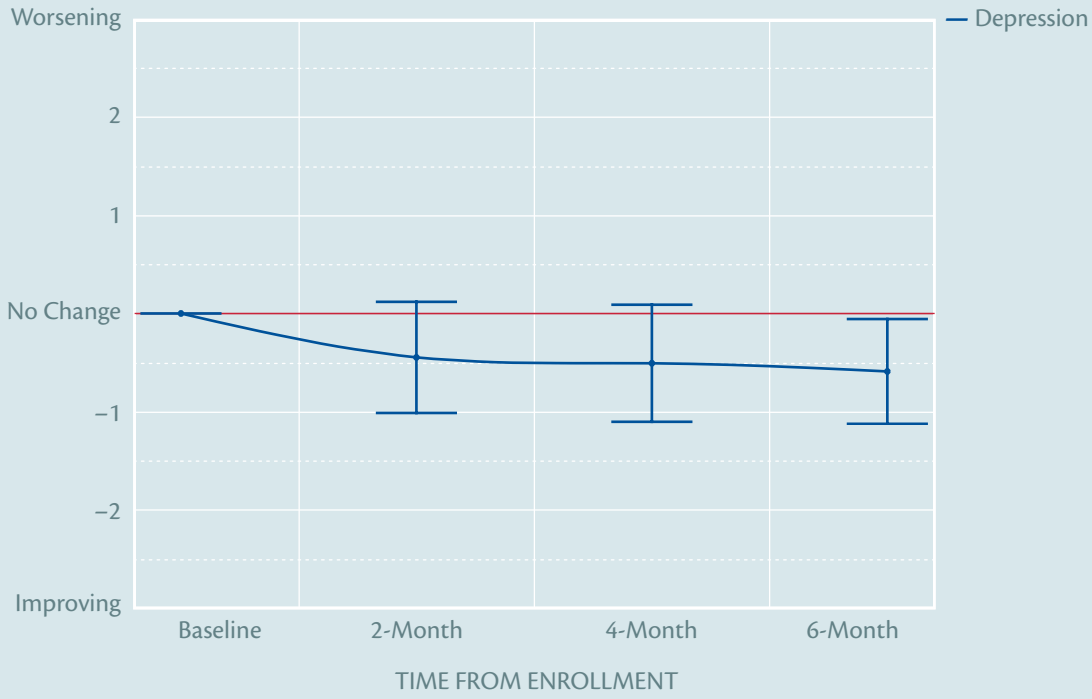
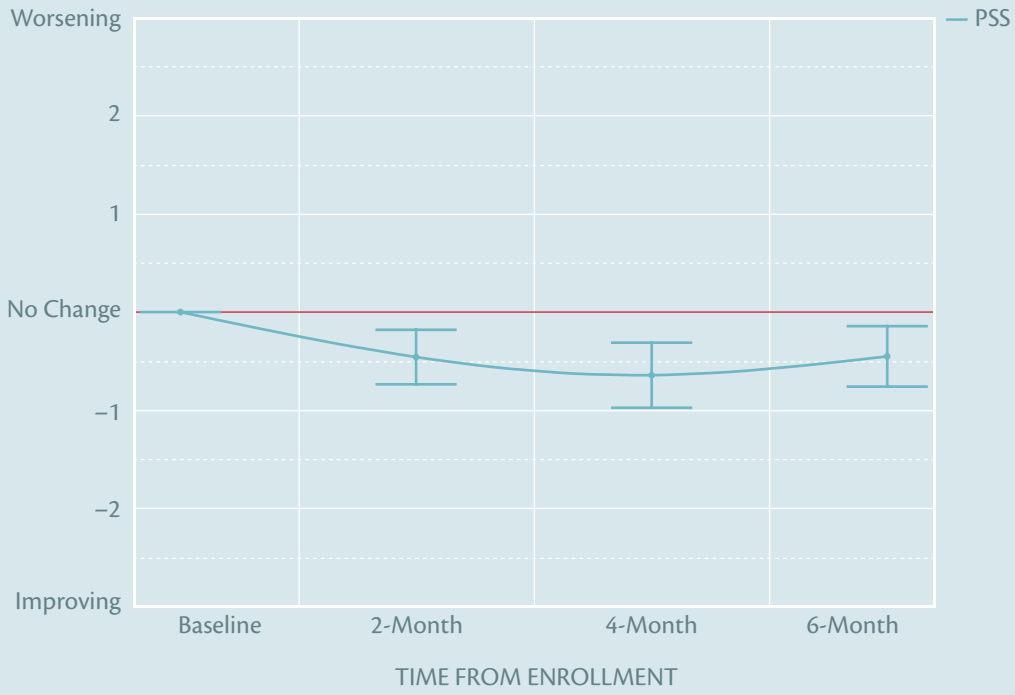


FIGURE 10: Perceived Stress Scale-4 Change Score



As shown on the previous page, integrative therapies delivered at BraveNet clinical centers improve moods and reduce the perception that life situations are stressful. These findings correspond with the results of a 2011 mapping survey sponsored by The Bravewell Collaborative that looked at how Integrative Medicine was being practiced in 29 major Integrative Healthcare clinics across the US. In this survey, Integrative Medicine center directors reported that stress and depression were two of the health challenges most successfully treated at their clinics.[11]

As PRIMIER enrollment increases, it will be possible to determine which interventions or which combination of interventions has the greatest effect on depression and stress scores and which interventions work best on which segments of the population.

11 Horrigan B, Abrams D, Lewis S, Pechura C. ***Integrative Medicine in America: How Integrative Medicine is Being Practiced in Clinics Across the US***. The Bravewell Collaborative. 2012.

IMPACT ON CHRONIC PAIN

The Institute of Medicine report, *Relieving Pain in America*, estimates that chronic pain affects nearly 116 million American adults, surpassing heart disease, cancer, and diabetes combined.[12] The 2011 report concludes that chronic pain costs between $560 billion and $635 billion annually in medical expenses and lost productivity. Many patients with chronic pain become resistant to conventional medical treatments or suffer adverse effects from widely used prescription medications with high addictive potential, such as opiates. For these reasons, patients with chronic pain frequently seek to integrate complementary therapies into their treatment regimen.[13,14,15]

In a study published in 2012, the authors reported that chronic pain was the condition for which patients sought integrative care at the BraveNet clinical sites most frequently.[16] In the prior analysis, *Integrative Medicine in America: How Integrative Medicine is Being Practiced in Clinics Across the US*, chronic pain was the condition that center directors reported having the most success treating at their sites. When asked to choose "five conditions for which you are having the most clinical success" from a menu of options, 75% chose chronic pain.[17]

Employing a personalized strategy that considers the patient's unique conditions, needs, and circumstances, Integrative Medicine uses the most appropriate interventions from an array of options to help people regain and maintain optimum health. Since Integrative Medicine is a "whole systems" approach that employs multiple modalities in concert as opposed to a sole therapy, studying outcomes is more challenging than evaluating an isolated pharmaceutical or botanical intervention. From the PRIMIER cohort, we explored if there were changes in patient self-reported pain over six months of follow-up

12 Institute of Medicine: *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*. Washington, DC: National Academies Press; 2011.

13 Nahin RL, Barnes PM, Stussman BJ, Bloom B: Costs of complementary and alternative medicine (CAM) and frequency of visits to CAM practitioners: United States, 2007. *Natl Health Stat Report* 2009, (18):1–14.

14 AARP and National Center for Complementary and Alternative Medicine: Complementary and Alternative Medicine: What People Aged 50 and Older Discuss With Their Health Care Providers. *Consumer Survey Report*; April 13, 2010. **http://nccam.nih.gov/news/camstats/2010/introduction.htm**. Accessed June 29, 2012.

15 Chou R, Huffman LH; American Pain Society; American College of Physicians: Nonpharmacologic therapies for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. *Ann Intern Med* 2007, 147(7):492–504.

16 Wolever, R, Abrams, D, Kligler, B, Dusek, J, Roberts, R, Frye, J, Edman, J, Amoils, S, Pradhan, E, Spar, M, Gaudet, T, Guarneri, M, Homel, P, Amoils, S, Lee, R, Berman, B, Monti, D and Dolor, R. Patients Seek Integrative Medicine for Preventive Approach to Optimize Health. *Explore* 2012; 8:348–352.

17 Horrigan B, Abrams D, Lewis S, Pechura C. ***Integrative Medicine in America: How Integrative Medicine is Being Practiced in Clinics Across the US***. The Bravewell Collaborative. 2012.

in our clinics. As PRIMIER participants could enroll whether they were new to the clinic or continuing in a treatment program, not all participants were in the same place on their treatment trajectory during the six months of data collection. We did not specify what particular interventions participants would or should receive to be included in the analysis, nor did we limit our exploration to a single clinical population. Whereas these are limitations of randomized controlled trials, the PRMIER study design captured real world practices where patients were offered the most appropriate treatment modalities for their conditions as assessed by the clinic practitioners.

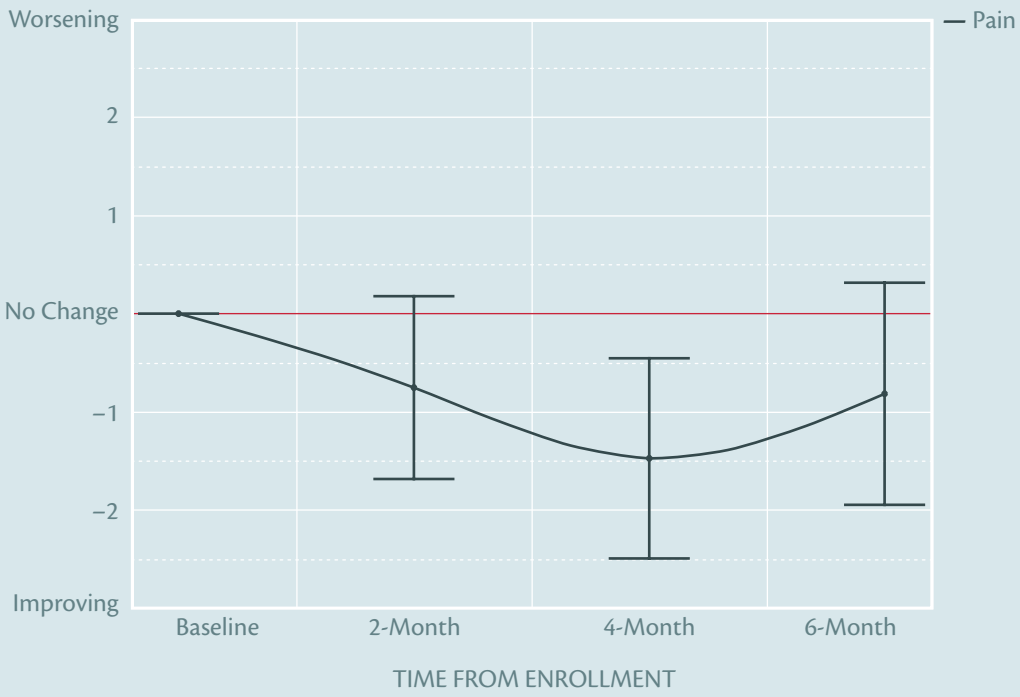
The exploration of Integrative Medicine in the real-world settings is consistent with the strategic plan of the National Institutes of Health, National Center for Complementary and Integrative Health (formerly known as National Center for Complementary and Alternative Medicine). Specifically, the most recent NCCIH Strategic Plan calls for NCCIH to "increase understanding of "Real-World" patterns and outcomes of CAM use and its integration into health care and health promotion"[18].

At present, we have six months of follow-up data on 179 patients who reported chronic pain as their reason for seeking care at our clinical sites. As Figure 11 depicts, pain scores were statistically significantly improved over time as patients continued to receive care at our centers. These findings are consistent with BraveNet's Study of Integrative Medicine Treatment Approaches to Chronic Pain (SIMTAP)[19] in which we reported significantly decreased pain severity (−23%) and interference (−28%) in chronic pain patients. We also found significant improvements in mood, stress, quality of life, fatigue, sleep and well-being. In all, the SIMTAP and preliminary PRIMIER results are consistent.

18 **https://nccih.nih.gov/about/plans/2011/objective3.htm**. Accessed Feb 18, 2015.

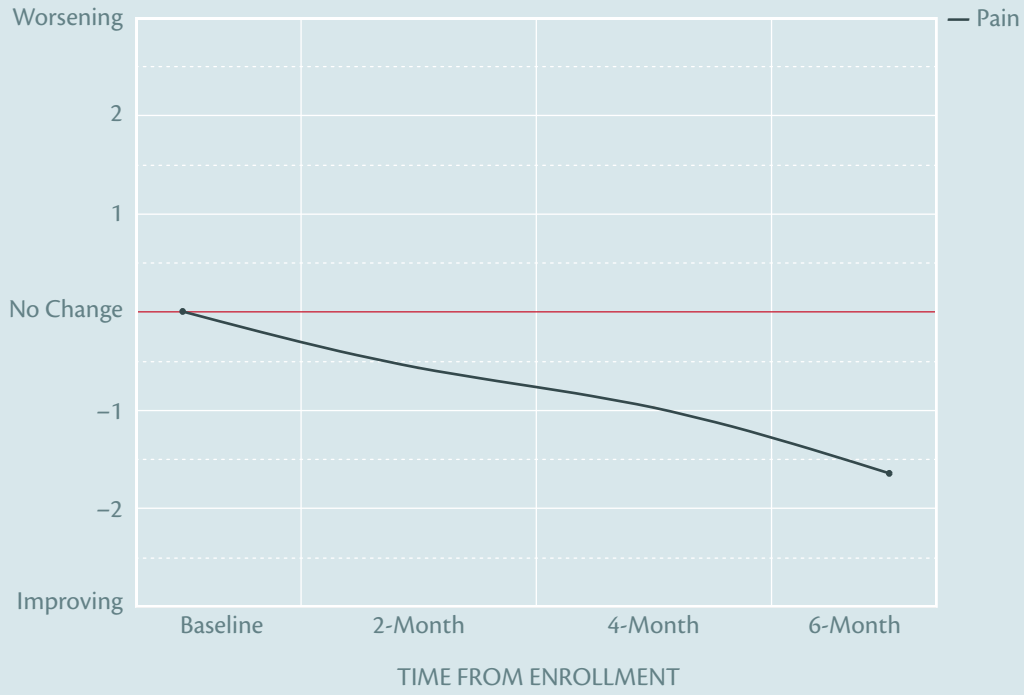
19 Abrams DI, Dolor R, Roberts R, Pechura C, Dusek J, Amoils S, Amoils S, Barrows K, Edman J, Frye J, Guarneri E, Kligler B, Monti D, Spar M, Wolever RQ. The BraveNet prospective observational study on integrative medicine treatment approaches for pain. *BMC Complementary and Alternative Medicine*. 2013, 13:146.

FIGURE 11: Change in Pain Scores



A preliminary analysis to assess whether any particular integrative intervention or combination thereof was more effective at relieving pain suggests that a combination of acupuncture, a manipulation (such as chiropractic), and an energy medicine modality (such as Reiki) yielded an impressive decrease in pain over the six months of follow-up (Figure 12).

FIGURE 12: Decrease in Pain with Acupuncture, Chiropractic, and Energy Medicine



As the number of participants increases and the proportion of those with long term follow-up also grows, we will be able to refine our analysis and further examine which modalities or combinations thereof are most promising and effective in relief of chronic pain as well as which therapies work best in certain demographic subsets.

For example, we will be able to compare the impact of Integrative Medicine on pain scores of:

- Women receiving acupuncture vs men receiving acupuncture
- Men and women receiving acupuncture only versus men and women receiving acupuncture, massage and energy healing
- Individuals receiving varying doses of acupuncture

In the end, the data in PRIMIER will help us to identify best practices and therein improve patient care and outcomes.

SUMMARY AND FUTURE DIRECTIONS

The BraveNet practice–based research network provides valuable information regarding the benefits of Integrative Medicine in real world settings. The PRIMIER registry is already demonstrating impressive changes in patient-reported outcome measures in participants receiving care at our collaborating clinical sites. As our database continues to be populated and with increased demographic diversity provided by additional sites, BraveNet is well-poised to address some of the important questions that remain as yet unanswered.

Our patients appear to be highly motivated to take their health into their own hands. The lower than average rates of obesity and tobacco use in our population reflects the fact that, on average, patients seeking care at our Integrative Medicine clinics have taken some steps to decrease health risk behaviors. Despite a mildly elevated prevalence of alcohol use in the cohort, overall alcohol consumption falls within accepted guidelines. The Patient Activation Measure results also support the impression that our patients have taken control of their health and that attendance at our clinics has moved them further along the activation continuum in a positive manner.

From our prior study of *Integrative Medicine in America*, we learned that Integrative Medicine center leaders across the country perceived that their interventions were most useful in patients coming with complains of chronic pain, depression and stress. The early findings from PRIMIER support this perception. Amongst the entire cohort of patients enrolled and followed over time, significant declines in depression and perceived stress were clearly demonstrated among PRIMIER participants. In the subset of patients coming to our sites with a chief complaint of chronic pain, pain scores decreased significantly over six months of follow-up. As additional numbers accrue, we expect to be able to ascertain which particular treatment modalities offer the greatest reduction in pain. In a preliminary investigation, a combination of acupuncture, manipulation therapy and an energy medicine intervention yielded an impressive reduction in pain.

The PRIMIER project offers a unique opportunity to assess the effectiveness of Integrative Medicine interventions in a wide variety of clinical conditions in a real-world setting. As the dataset grows and the duration of follow-up increases, we expect to derive preliminary information to develop specific research proposals to address the difficult-to-treat conditions for which patients seek our care. As our network expands with increased demographic diversity of the enrolled cohort, our results will prove to be more generalizable and robust.

ACKNOWLEDGEMENT

The analyses presented in this monograph were performed by the Duke Clinical Research Institute, which served as the Data Coordinating Center for BraveNet from 2007 to 2014. The PROMIS Assessment Center platform at Northwestern University was used to collect participant surveys in this monograph. We are most grateful to Rowena Dolor, MD, Ron Roddy, Rhonda Roberts, MSPH, Monica Prudencio and Maria Varela Diaz for their input and dedication to the project in its early phases.

CONTACT INFORMATION

Those persons wishing to inquire about joining PRIMIER or request permission to access the PRIMIER database for research purposes should contact:

Ben Kligler, MD, MPH
BKligler@chpnet.org

Diane McKee, MD, MS
Diane.Mckee@einstein.yu.edu

PRIMIER LEADERSHIP

Chair, BraveNet

Ben Kligler, MD, MPH
Vice Chair and Research Director
Mount Sinai Beth Israel Center for Health and Healing
New York, NY

Co Principal Investigators

Jeffery A. Dusek, PhD
Director of Research and Director of Integrative Health Research Center
Penny George Institute for Health and Healing, Abbott Northwestern Hospital, Allina Health
Minneapolis, MN

Donald I. Abrams, MD
Integrative Oncologist at UCSF Osher Center for Integrative Medicine
Professor of Clinical Medicine, University of California San Francisco
San Francisco, CA

Data Coordinating Center

Diane McKee, MD, MS
Co-Director of Research

Claudia Lechuga, MS
Research Coordinator
Division of Research, Department of Family and Social Medicine
Albert Einstein College of Medicine
New York, NY

APPENDIX A

ABOUT THE BRAVEWELL COLLABORATIVE

Formed in 2002, The Bravewell Collaborative is a community of philanthropists in the United States dedicated to bringing about optimal health and healing for individuals and society. An operating foundation, Bravewell develops and manages strategic initiatives that support integrative approaches to health care. Embracing rigorous research and scientific approaches in the entirety of its work, The Bravewell Collaborative's key initiatives include programs to educate the general public, change the way physicians are educated, develop leading clinical centers as models for change, acknowledge and support leaders in the field, and promote translational and outcomes-based research. Most recently, The Bravewell Collaborative established the first practice-based research network in Integrative Medicine and worked with the Institute of Medicine at the National Academies of Science to produce a National Summit on Integrative Medicine. For more information about The Bravewell Collaborative, please visit **www.bravewell.org**.

ABOUT ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY

Albert Einstein College of Medicine of Yeshiva University is one of the nation's premier centers for research, medical education and clinical investigation. During the 2014–2015 academic year, Einstein is home to 742 MD students, 212 PhD students, 102 students in the combined MD/PhD program and 292 postdoctoral research fellows. The College of Medicine has more than 2,000 full-time faculty members located on the main campus and at its clinical affiliates. In 2014, Einstein faculty received $158 million in awards from the National Institutes of Health, which also funds major research centers at Einstein in aging intellectual development disorders, diabetes, cancer, clinical and translational research, liver disease and AIDS. The college's partnership with Montefiore Medical Center, its University Hospital and academic medical center, advances clinical and translational research to accelerate the pace at which new discoveries become the treatments and therapies that benefit patients. Through its extensive affiliations with Montefiore, Jacobi Medical Center (Einstein's founding hospital) and five other hospital systems in the Bronx, Brooklyn, Long Island and Manhattan, Einstein runs one of the largest residency and fellowship training programs in the medical and dental professions in the United States.

Einstein Informatics and Research Resources

Under the leadership of Dr. McKee, Dr. Kligler and Paul Marantz, MD, MPH, associate dean for clinical research education at Einstein, BraveNet at Einstein is a collaboration between two productive and established components of Einstein research infrastructure: the Block Institute for Clinical and Translational Research at Einstein and Montefiore (ICTR) and the department of family and social medicine's division of research, home of Einstein's primary care practice-based research network, New York City Research and Improvement Networking Group (NYC RING).

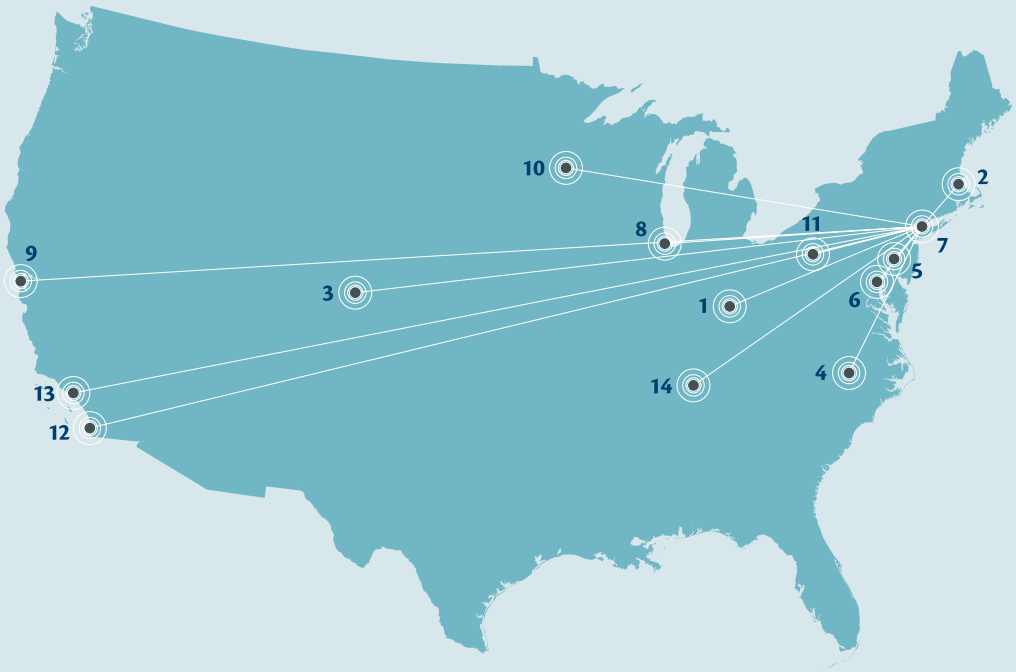
The ICTR, which Dr. Marantz co-directs, houses research cores that will provide key support. The Informatics Core, directed by Parsa Mirhaji, MD, PhD, will manage the data for PRIMIER and other BraveNet studies. The Biostatistics and Research Design Core, directed by Mimi Kim, ScD, will provide expert support for the statistics group in the department of family and social medicine. The biostatistics group will also play an important role in the development of new grant proposals for BraveNet. (The ICTR is a member of the nationwide Clinical and Translational Science Awards (CTSA) consortium, funded by the National Institutes of Health.)

The department of family and social medicine's (DFSM) division of research, which is co-led by Dr. McKee, will supply critical staffing, programmatic and administrative infrastructure for the BraveNet Coordinating Center. DFSM also sponsors NYC RING, for which Dr. McKee is director. The network consists of community-based primary care practices affiliates with Einstein and is one of only a few patient-based research networks in the United States focused exclusively on the urban underserved.

For more information, please visit **www.einstein.yu.edu**.

APPENDIX B — BRAVENET MEMBERSHIP

BraveNet consists of fourteen member clinics with the Einstein School of Medicine serving as the Coordinating Center.



MEMBERS

1 ***Alliance Institute for Integrative Medicine***
Cincinnati, Ohio
- Steve Amoils, MD, Co-Director
- Sandi Amoils, MD, Co-Director

2 ***Boston Medical Center, Boston University***
- Robert Sapier, MD, MPH, Director
- Paula Gardiner, MD, Assistant Director

3 *Integrative Medicine at the University of Colorado Denver*

- Lisa Corbin, MD, Medical Director
- Jacinda Nicklas, MD, MPH, MA, Assistant Professor

4 *Duke Integrative Medicine*

Duke University, Durham, North Carolina

- Adam Perlman, MD, Executive Director
- Ruth Quillian-Wolever, PhD, Research Director

5 *Jefferson-Myrna Brind Center for Integrative Medicine*

Thomas Jefferson Medical College, Philadelphia, Pennsylvania

- Andrew Newberg, MD, Research Director
- Nancy Wintering, Research Program Manager

6 *Center for Integrative Medicine*

University of Maryland School of Medicine, Baltimore, Maryland

- Brian Berman, MD, Executive Director
- Christopher D'Adamo, PhD, Research Director

7 *Mount Sinai Beth Israel Center for Health and Healing*

Beth Israel Medical Center, New York, New York

- Woodson Merrell MD, Executive Director
- Ben Kligler, MD, MPH, BraveNet Chair

8 *Osher Center for Integrative Medicine at Northwestern University*

Northwestern Physicians Group, Chicago, Illinois

- Melinda Ring, MD, Medical Director
- Dave Victorson, Assistant Professor, Northwestern University

9 *UCSF Osher Center for Integrative Medicine*

University of California, San Francisco, California

- Margaret Chesney, PhD, Executive Director
- Kevin Barrows, MD, Medical Director
- Donald Abrams, MD, Integrative Oncology and PRIMIER Co-PI

10 *Penny George Institute for Health and Healing,*

Allina Health, Minneapolis, Minnesota

- Courtney Baechler, MD, MS, Vice President
- Jeff Dusek, PhD, Research Director and PRIMIER Co-PI

11 *University of Pittsburgh Center for Integrative Medicine*

- Neil Ryan, MD, Director
- Carol Greco, PhD, Assistant Professor

12 *Scripps Center for Integrative Medicine*

Scripps Health, La Jolla, California

- Chris Suhar, MD, Medical Director
- Eva Stuart, RN, Research Specialist

13 *Simms/Mann Health and Wellness Center, Program in Integrative Medicine*

Venice Family Clinic, Los Angeles, California

- Myles Spar, MD, MPH, Director of Integrative Medicine
- Nancy Rodriguez, MPH, Director of Health Education and Specialty Care

14 *The Osher Center for Integrative Health at Vanderbilt University*

- Roy Elam, MD, Medical Director
- Gurjeet Birdee, MD, Director of Research

COORDINATING CENTER

Division of Research, Department of Family and Social Medicine
Albert Einstein College of Medicine

- Diane McKee, MD, MS, Co-Director of Research
- Claudia Lechuga, MS, Research Coordinator

(Previous Coordinating Center, August 2007–February 2015)

Duke Clinical Research Institute, Durham NC

- Rowena Dolor, MD, MHS, Principal Investigator
- Ronald Roddy, PA, Project Leader
- Rhonda Roberts, MSPH, Biostatistician

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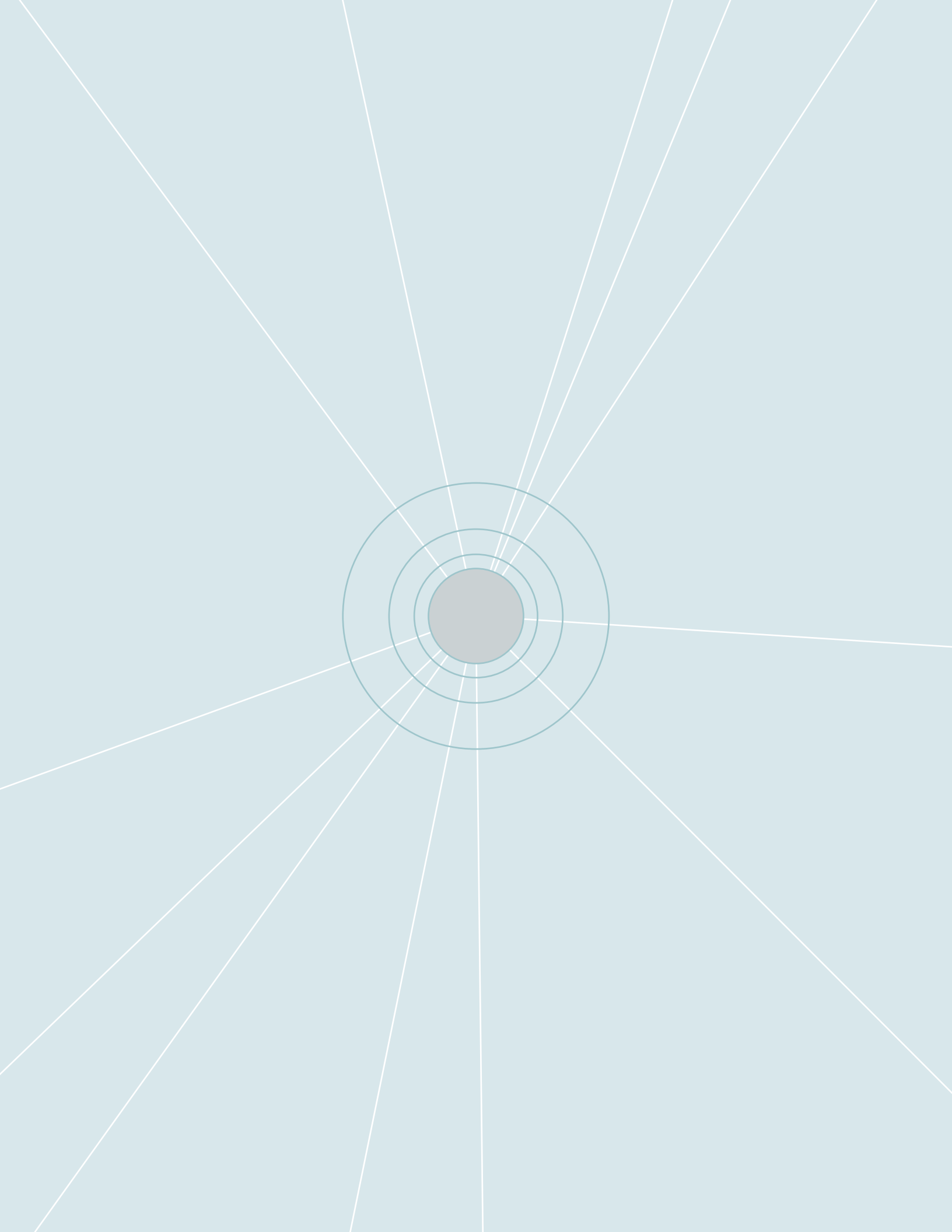

The Bravewell Collaborative

info@bravewell.org • www.bravewell.org