



## Case Study: Testing Treatments for Menopause Symptoms



### Principal Investigator

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### Project

The Menopause Strategies, Finding Lasting Answers for Symptoms and Health (MsFLASH) network brought together women's health investigators from across the country to conduct randomized controlled trials quickly to test new interventions for the relief of menopause symptoms, including hot flashes, night sweats, sleep problems, mood problems, anxiety and depression, pain symptoms, and sexual problems.

The MsFLASH research network, established by the National Institutes of Health, conducted three large randomized trials that tested six different interventions. The primary outcome for all three trials was relief of hot flashes and night sweats. Secondary outcomes included improved sleep, mood, and menopause-related quality of life and relief of pain symptoms and anxiety.

- In the first trial, the researchers tested an antidepressant called escitalopram. The drug worked well for alleviating hot flashes<sup>1</sup> and helped with mood and sleep problems.

- The second trial tested yoga, aerobic exercise, and omega 3 supplements. Women were randomly assigned to practice yoga, exercise, or continue doing their usual activity; in addition, they were randomly assigned to take omega 3 supplements or a placebo.<sup>2</sup> Results showed that for sedentary menopausal women, yoga modestly improved quality of life.
- The third trial involved hormone therapy. The researchers tested a low dose of estradiol versus the antidepressant venlafaxine versus placebo. Both interventions were effective treatments for hot flashes and night sweats.<sup>3</sup>
- The researchers also conducted a fourth trial—a small pilot study with 100 women. In this trial, the researchers compared cognitive behavioral therapy for insomnia (CBT-I) delivered by phone to menopause education for alleviation of insomnia. Telephone-based CBT-I improved sleep in perimenopausal and postmenopausal women with insomnia and hot flashes.<sup>4</sup>



1. Freeman, E. W., Guthrie, K. A., Caan, B., Sternfeld, B., Cohen, L. S., Joffe, H., et al. (2011). Efficacy of escitalopram for hot flashes in healthy menopausal women: A randomized controlled trial. *JAMA*, 305(3), 267-274. PMID: 21245182.
2. Reed, S. D., Guthrie, K. A., Newton, K. M., Anderson, G. L., Booth-LaForce, C., Caan, B., et al. (2014). Menopausal quality of life: RCT of yoga, exercise, and omega-3 supplements. *American Journal of Obstetrics and Gynecology*, 210(3), 244.e1-244.e11. PMID: 24215858.
3. Joffe, H., Guthrie, K. A., LaCroix, A. Z., Reed, S. D., Ensrud, K. E., Manson, J. E., et al. (2014). Low-dose estradiol and the serotonin-norepinephrine reuptake inhibitor venlafaxine for vasomotor symptoms: A randomized clinical trial. *JAMA Internal Medicine*, 174(7), 1058-1066. PMID: 24861828.
4. McCurry, S.M., Guthrie, K.A., Morin, C.M., Woods, N.F., Landis, C.A., Ensrud, K.E., et al. (2016). Telephone-Based Cognitive Behavioral Therapy for Insomnia in Perimenopausal and Postmenopausal Women With Vasomotor Symptoms: A MsFLASH Randomized Clinical Trial. *JAMA Intern Med*, 176(7):913–920. PMID: 2522398.



## Target Population

- The MsFLASH researchers sought to include in the trials women aged 40 to 62 who lived in one of five metropolitan areas—Boston, Indianapolis, Oakland, Philadelphia, and Seattle—and represented various races and ethnic groups.
- The goal for the first trial was for 50 percent of the participants to be Black women because they suffer disproportionately from hot flashes compared with women of other races and ethnicities.

## Recruitment Approach

- The researchers used mass mailings to reach potential participants. This approach reaches anyone who can receive mail—in other words, everyone except some homeless people. In the past, mass mailing has been particularly effective for reaching minority women.
- The researchers modeled their mass mailing strategy on the methodology used in the Women’s Health Initiative—by accessing census data, which provide zip code-level information on race, ethnicity, age, and gender of residents. This information enabled the researchers to target the mailings to geographic areas in which the residents included people who were more likely to be eligible for the study, or who fulfilled particular recruitment needs.
- The MsFLASH network included five clinical research centers in Boston, Indianapolis, Oakland, Philadelphia, and Seattle and the data coordinating center at the Fred

Hutchinson Cancer Research Center in Seattle. All of the researchers were experts in women’s health who had conducted clinical trials before, but not all of them had experience in recruiting participants quickly for large-scale randomized trials.

- While many trials recruit participants over a period of years, the investigators for the MsFLASH research network needed to recruit women within a few months in order to complete several trials within the initial 5-year period of the network.
- After conducting the mailing, the researchers screened potential participants through phone interviews.
- Because the researchers needed to recruit women who had persistent hot flashes, the investigators then requested potential participants to fill out a questionnaire, including a 2-week hot flash diary. This additional step screened out women who were unwilling or unable to maintain a hot flash diary.
- The researchers subsequently published an article on the methodology and recruitment process they used within the MsFLASH network.<sup>5</sup>

## Primary Barriers

- Women in midlife can be particularly busy because they are often taking care of both children and elderly parents while also balancing work.
- Inconvenient clinic locations and lack of or difficult parking can serve as barriers to participation in clinical trials.
- Particular trials could present other barriers, such as fear of side effects or a lack of interest in learning and practicing yoga.

## Successful Recruitment Strategies

- For the first trial, each center conducted its own mailing. The research teams found that the mailing process—including acquiring mailing lists and then addressing and mailing thousands of pieces of mail—was difficult.

5. Newton, K. M., Carpenter, J. S., Guthrie, K. A., Anderson, G. L., Caan, B., Cohen, L.S., et al. (2014). Methods for the design of vasomotor symptom trials: The menopausal strategies: Finding lasting answers to symptoms and health network. *Menopause*. 21(1), 45-58. PMID: 23760428.

- Consequently, for the later trials, the mailing of postcards was centralized at the Oakland center and the initial telephone screening was centralized at a survey research center at Group Health Cooperative in Seattle. These changes reduced stress for staff at the various centers.
- The postcards featured attractive designs, including the logo of the affiliated center for each prospective study population and pictures to which the women could relate. For example, the second postcard featured photographs of midlife women exercising and looking happy.
- The researchers tracked responses to the postcards and then adjusted the rate and demographics of respondents by adjusting the number of postcards the researchers had mailed and to which zip codes. In each trial, between 0.5 percent and 1 percent of the women who received a postcard responded.
- Recruitment for the second trial was challenging because the study population needed to be women who were having hot flashes and who were not already engaging in either exercise or yoga, which excludes many midlife women. For this trial, the researchers found some participants by e-mailing members of an organization that supports breast cancer research.

### Retention Strategies

- Retention was high in these trials, probably in part because the screening process included many steps. Women who completed all of the steps in a trial's screening process may have been more likely to stay in the trial until its completion.
- Providing a good experience for participants helps with retention. Study participants appreciate well-trained staff who are friendly and welcoming, study procedures that use the participants' time well, and flexibility.

- For the exercise and yoga trial, the researchers allowed the participating women the flexibility to fit the intervention into their own lifestyle. Women in the yoga intervention were asked to come to class once a week and were each given a video and an audiotape to use for practicing yoga at home. For the exercise intervention, women were asked to come to class two or three times a week, but they could also exercise at home. More rigid instructions would have been harder for the women to adhere to.

### Lessons Learned

- Centralizing the mailing and initial telephone screening was extremely helpful and greatly reduced the burden on the individual centers.



**“It is important to do recruitment really well, but recruitment is just part of a process that is meant to be transformational in nature. We are very proud of all of the work we have done as a group. It has influenced guidelines. It has changed practice.”**

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