



From the COSMOS Trial Directors

Dear COSMOS Participant,

We would like to offer heartfelt thanks for your dedication to COSMOS. Because of your continuing collaboration, COSMOS is well positioned to answer the question of whether taking daily supplements of cocoa flavanols or a common multivitamin reduces the risk of developing heart disease, stroke, or cancer.

If you have already completed and returned the health questionnaire that was sent to you at the end of the study pill-taking period in January 2021, thank you! If you haven't yet returned the questionnaire, please do so as soon as possible to help COSMOS answer its important scientific questions.

Also, please note that we plan to continue to send you annual health questionnaires for several more years. (You will **not** be asked to restart study pills.) You will receive your next annual health questionnaire in 2022. This questionnaire will be similar to those that you have completed in prior years. Even if there are no changes in your health since the previous questionnaire, your response is still very important. The information that you provide will allow us to build upon the wealth of data already collected to examine the longer-term effects of cocoa flavanol supplements and multivitamins and to explore other health-related topics. If you have questions about — or wish to be excluded from — this continuation of COSMOS, please contact us at the postal address, telephone number, or e-mail address in the box on page 4.

Thank you again for being part of the COSMOS community!



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Q&A

The Q&A column, a regular feature of the newsletter, takes center stage in this issue.

Thank you very much for your continued commitment to COSMOS. As you know, study pill-taking ended on December 31, 2020. COSMOS is now getting close to achieving its goal of determining whether daily cocoa flavanol or multivitamin supplementation can prevent cardiovascular disease or cancer. Here are answers to some common recent questions asked by COSMOS participants.

Q: When will you notify me of the main results of COSMOS?

A: We are now gathering and reviewing the medical records related to the key health outcomes of interest (heart disease, stroke, and cancer) reported by participants on the questionnaire filled out in January 2021. When we finish this task, we will analyze the data and submit manuscripts with the study's main findings to major medical journals. We anticipate that the main results papers will be published in late 2021. Upon publication of these results, we will notify participants. If you have shared your e-mail address with us, we will send you an e-mail that summarizes the study's main findings and/or directs you to a summary of the findings on the COSMOS website, www.COSMOStrial.org. If we don't have your e-mail address, we will send you a letter by postal mail that summarizes the study's main findings. If you would like to be added to our e-mail list, please let us know as soon as possible (our contact information is on page 4). Please be assured that we will use your e-mail address only to communicate with you about COSMOS and will not share your e-mail address with any person or group outside of COSMOS.

Q: I participated in a COSMOS substudy designed to test whether cocoa extract and multivitamins can help prevent cognitive decline. When will the results of that substudy be available?

A: Two separate COSMOS substudies are examining the relationship between the study supplements and cognitive function. In COSMOS-Mind, approximately 2,000 participants had yearly 45-minute telephone interviews to assess memory and thinking ability. In COSMOS-Web, nearly 4,000 participants completed yearly 30-minute web-based computerized cognitive assessments. In addition, a subset of approximately 600 COSMOS participants who live within driving distance to Brigham and Women's Hospital in Boston, Massachusetts completed many of these cognitive assessments in person at the beginning of the trial and again 2 years later. (Please note that the cognitive assessments in COSMOS cannot be used alone to diagnose clinical dementia or specific neurologic disorders; such diagnoses require a more comprehensive evaluation.) We expect that the results of these two substudies will be published in late 2021, around the time of the main trial results on the effects of the study supplements on heart disease,

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Participant Perspective



Clara S., of New Mexico, writes, "I believe in research to improve the health of everyone, happy to participate."



Jennifer K., of New Jersey, writes, "[A]s a biochemist, I like experiments and data. When I first heard of the trial I realized that if anyone would be compliant enough to see it through, I should fill the bill."



Penelope P., of Florida, pictured at Tampa Bay in St. Petersburg, writes, "I will miss my [study] pills in the AM!"



Marcia S., of Indiana, writes, "After losing my husband of 42 years to cancer in 2008, it felt like a chance to fight back to be a part of this study."



Ora H., of Texas, writes, "I believe Americans of African descent are underrepresented in research studies because of the Tuskegee Experiment. It is critically important that research studies include individuals who represent the variety of ethnic groups found in the population. It has been an interesting study and I am looking forward to the results."



Robert M., of Pennsylvania, writes, "In response to your question, 'Why did you join COSMOS?': I was asked. It sounded important. I thought, 'How often does an opportunity to contribute, to make a difference, fall in your lap? ... What have I got to lose? Somebody has to do it!'"



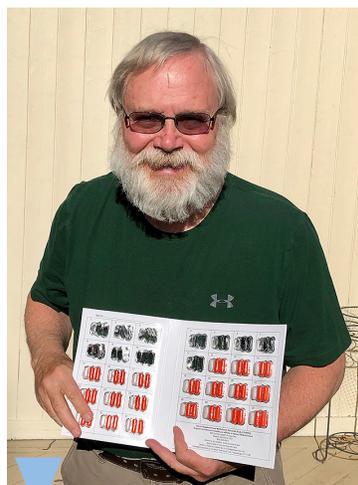
Peter Z., of Maryland, writes, "As a physician, I am aware how important research in preventing cardiovascular disease is. I am happy to participate in this trial."



Ethel H., of South Carolina, writes, "I am thankful for the opportunity to be a part of the study."



Shirley G., of North Carolina, writes, "The summer after my freshman year in college I participated in a drug study as a normal control volunteer at National Institutes of Health in Bethesda, Maryland. That experience very likely influenced my decision to participate in future research projects. I have been involved in a number of studies—the Women's Health Initiative for over 25 years, the Sister Study about breast cancer, and most recently the COSMOS Study. I appreciate the opportunity to be involved in research that furthers our understanding of possible factors that impact our health and well being."



Jim O., of New Jersey, writes, "I have done my utmost to not miss taking the pills (only 2 or 3 times in 5 years)."



Mary B., of Missouri, writes, "It's been a pleasure taking part in this study. I initially was hesitant because I didn't want to give up my daily multivitamin, but when I found out I could still take some calcium and vitamin D, that did it. Everyone has been very professional and good to work with. I'm anxious to hear the final results."

We'd like to hear from you!

Please share your thoughts about participating in COSMOS and contributing to scientific knowledge about the role of cocoa flavanol and multivitamin supplementation in human health. We also welcome your photos and stories. We will include a sampling of responses in future newsletters. Please write to us at COSMOStrial@partners.org or the postal address in the box on page 4.

Fun fact

What percentage of participants correctly guessed the type of study capsules they were assigned to during the study pill-taking period?

The COSMOS study questionnaire that you filled out in early 2021 (shortly after the study pill-taking period ended) included the following item: “At the beginning of the trial, you were randomly assigned (like a flip of a coin) to either active or placebo for each study pill. If you had to guess, for each, what do you think you were assigned to? Active/placebo/ no idea”. Based on participant responses received as of February 2021, we found the following. For the cocoa extract, about 42% of participants said that they had no idea; 19% guessed their treatment assignment correctly and 16% guessed incorrectly. For the multivitamin, 46% of study participants said they had no idea; 16% guessed correctly; and 15% guessed incorrectly. We are pleased with these numbers, as they indicate that, in general, study participants did not know whether they had been assigned to active or placebo study pills. This “blinding” of study participants is important in helping to ensure the validity of findings from randomized clinical trials such as COSMOS.

Q&A

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stroke, and cancer. Again, we will notify participants by e-mail or letter when the results are published.

Q: Will COSMOS investigators examine the effect of the study supplements on COVID-19?

A: Yes. During the spring and summer of 2020, we sent online surveys about COVID-19 to COSMOS participants who had previously provided their e-mail addresses to us. These surveys asked participants whether they had been tested for coronavirus infection, had been diagnosed with COVID-19, had experienced symptoms that may or may not have been related to the infection, and/or had been hospitalized for COVID-19. These surveys also asked about the impact of the pandemic on participants’ physical and emotional well-being. Thank you to all who participated! Questions about COVID-19 were also included on the annual questionnaire sent to all COSMOS participants in January 2021. The information that you provided on these questionnaires will allow for a detailed assessment of risk factors for, and the impact of, COVID-19 in a national sample of midlife and older adults. Such analyses are underway and we will share the results with you when they are published.

Q: Will I receive additional study questionnaires?

A: Yes. We plan to send you additional questionnaires. Please see the COSMOS Trial Directors’ Letter on page 1 for details. The supplemental information gathered on future questionnaires will be essential in addressing the long-term health effects of the COSMOS interventions and also allowing for exploration of emerging hypotheses regarding healthy aging and disease prevention.

Q: What is the active ingredient of the COSMOS cocoa extract supplement?

A: The cocoa extract supplement tested in COSMOS contained cocoa flavanols (500 mg per two capsules), as well as other natural compounds in the cocoa bean. Astute readers will note that our earlier communications stated that the amount of cocoa extract in the two capsules was 600 mg. The reason for the discrepancy is that an improved laboratory method for measuring cocoa flavanols recently became available. According to this new method, the amount of measurable cocoa flavanols in the two study capsules is 500 mg rather than the previously stated 600 mg. However, the amount of a key bioactive component of the flavanols, (-)-epicatechin, did not change.

Q: Can I buy the COSMOS supplements—or similar supplements—commercially?

A: The multivitamin tested in COSMOS was a standard Centrum Silver®. This multivitamin, which contains a comprehensive array of vitamins and minerals to help meet recommended daily intakes, is widely available for purchase. A cocoa flavanol product similar to that tested in COSMOS is also widely available for purchase. CocoaVia® is sold in capsule (225 mg of cocoa flavanols per capsule [450 mg for 2 capsules combined]) or powder packet (450 mg per packet) form.

COcocoa Supplement and
Multivitamin Outcomes Study
(COSMOS)



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**The COSMOS website has been updated with a brand-new look and new information. Please be sure to take a peek!*