



From the COSMOS Trial Directors

Dear COSMOS participant,

As the end of the COSMOS pill-taking period approaches, we would like to offer heartfelt thanks for your enormous contribution to health research. Thanks to your continuing collaboration, COSMOS is well on its way to answering the question of whether taking daily supplements of cocoa flavanols (600 mg/day) or a common multivitamin reduces the risk of heart disease, stroke, or cancer.

We would also like to stress the importance of taking your study pills regularly until pill taking ends on December 31, 2020. We know that a few participants who enrolled early will hit their own personal 4-year pill-taking milestone before the official pill-taking stop date. Enrollment in COSMOS took place on a rolling basis, with some people joining the study earlier in the recruitment period and others joining later. The earliest enrollers started their study pills toward the end of 2015, while the latest enrollers did so in the fall of 2017. This means that when pill taking ends on December 31, 2020, some participants will have taken the study pills for 5 years while others will have taken them for only about 3 years—but the *average* length of time that participants will have taken the pills will be close to 4 years. An average of 4 years of pill taking is the amount of time required for COSMOS to achieve its goals. This is why we ask that all participants—even the early enrollers—continue their pills until December 31, 2020 if possible. We know that taking the study pills regularly is not an easy task, and we are grateful for each day that you are able to do so.

Thank you again for being part of the COSMOS community!



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COSMOS timeline: Final months of pill taking!

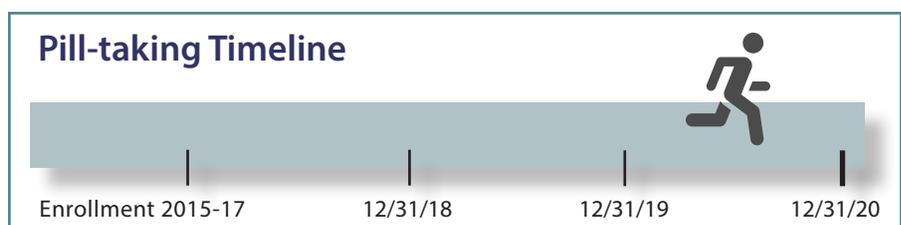
We are pleased to announce that the final stretch of pill taking in COSMOS is fast approaching. **Study pill taking will end on December 31, 2020.** On this date, COSMOS participants will have taken their study pills for an average of nearly 4 years, which is the time necessary for COSMOS to test whether cocoa flavanol supplements or multivitamins can prevent heart disease, stroke, or cancer. Thank you for your partnership as we approach this milestone—and get closer to answering these important questions. Here's what to expect next:

- Normal follow-up procedures will be in place until December 31, 2020. We will continue to mail you follow-up questionnaires to update your health information. For those who need a new supply of study pills, we will mail you enough calendar packs to last until the end of December 2020.
- Pill taking will end on December 31, 2020. In early January 2021, we will send you a questionnaire asking about new medical diagnoses, compliance, and other data necessary to address the study's key research questions and/or to explore new hypotheses regarding health promotion and disease prevention.
- After you complete and return the January 2021 questionnaire to us, we

will send you a letter notifying you whether your study pills contained active cocoa flavanols, active multivitamin, or placebo.

- We will analyze the data and submit a manuscript with the study's main findings to a major medical journal. Upon publication of the manuscript, we will send you a letter or newsletter describing the study's main findings. Although the timeline is not certain, we anticipate that the main results will most likely be available in late 2021.

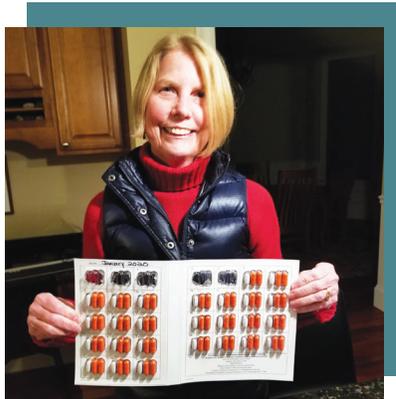
COSMOS is the only large, long-term randomized clinical trial designed to test whether cocoa flavanols can prevent heart disease and stroke. It is also one of only two large trials to test a multivitamin (Centrum Silver[®]) that contains a comprehensive array of vitamins and minerals to help meet recommended daily intakes, and the only such study to include both female and male participants, for cancer and cardiovascular disease prevention. Many patients, healthcare providers, and professional medical organizations are awaiting the trial's results. Please help COSMOS achieve its goals by continuing to take your study pills through December 31, 2020 and by completing the study questionnaires both before and after pill taking ends.



Q&A



Jeanne C., of Massachusetts, writes, "Happy to be in the study with my friends." She is pictured with **Jim G.** and **Kathy C.**, also of Massachusetts. All are COSMOS participants. Kathy is holding the calendar pack.



Claudia R., of New Hampshire, writes, "When I worked as a nurse-midwife, I so appreciated (and depended on) solid, evidence-based research to guide my practice. When I heard that Dr. Manson (whose work with the Women's Health Initiative I've long followed) was a director for the COSMOS trial, I was eager to become a study participant as a way to thank her and other clinical investigators for their vital contributions to the health and well-being of men and women."

Q. Why do you ask for consent to obtain and review medical records for certain conditions reported on the questionnaires?

A. The main reason for reviewing records is to categorize the medical reports from participants using a uniform set of diagnostic standards. By looking at actual medical records, we can, for example, use the same criteria in reviewing cardiograms to decide whether to classify reports as specific types of heart attacks. Your cooperation in providing this consent is greatly appreciated. Please be assured that any information that we receive is kept strictly confidential and is used only for the aforementioned purpose.

Q. After the COSMOS pill-taking period ends, I may want to take the cocoa flavanol or multivitamin supplements that were tested. Can these supplements be purchased?

A. Although the cocoa flavanol supplement currently is not available at the dose studied in COSMOS, a similar lower-dose preparation marketed as CocoaVia® is sold at retail stores or online. The multivitamin studied in COSMOS is Centrum Silver®, which is also widely available for purchase.

Q. Why do many clinical trials take several years to get answers to research questions?

A. COSMOS and many other clinical trials that you may have read about are *prevention trials* in generally healthy people, as opposed to *treatment trials* in those who are already ill. Testing interventions for the prevention of cardiovascular disease or cancer, which generally develop slowly over time, requires that a large group of participants be followed for a sufficient period of time to allow the agents under study—in this case, cocoa flavanol and multivitamin supplements—to exert their biological effects.



Arthur L., of California, writes, "I'm a retired scientist, so I understand how important both doing research and having good data are for progress to be made. This is especially true in the very complicated areas of heart, stroke and cancer in older adults. I am happy to do my part and hope this study provides new insights. I take my COSMOS pills each morning when I come back from the gym."



Karen C., of Massachusetts, writes, "As many members of my family have died from heart disease or stroke, I joined COSMOS to see if I could help prevent that from happening to others. Since I love dark chocolate, this seemed like the right study to try. I even took the pills to Antarctica with me."

WHY DID YOU JOIN COSMOS?

Please let us know by writing to COSMOStrial@partners.org or the postal address listed in the box to the right (and feel free to include a photo of you with your pill pack!). We will include a sampling of responses in future newsletters.

COcocoa Supplement and **Multivitamin Outcomes Study** (COSMOS)



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