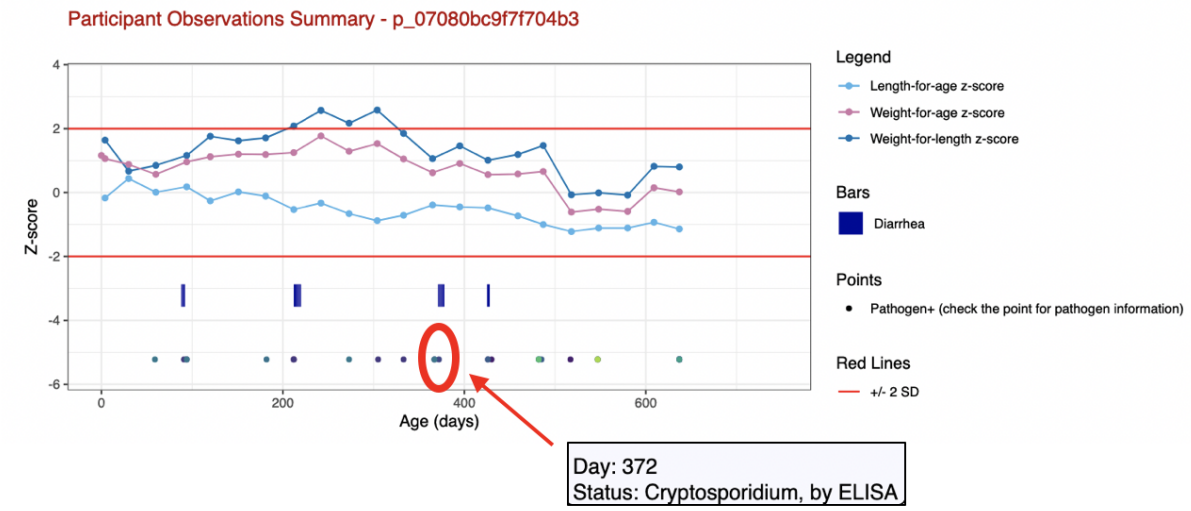
Complex Epidemiology Queries
Guided Walk-Through

Building a Search with Related Observations

In this exercise, we will go through an example together to perform a more advanced search using the "Related Observations" function. Several studies on ClinEpiDB included extensive collection of longitudinal information. The ability to search these data easily is extremely valuable. Integrating the "Related Observations" function into your searches allows you to examine data over time.

Before we start, consider the graph below. This graph plots height-for-age z-scores (light blue), weight-for-height z-scores (dark blue), and weight-for-age z-scores (pink), measured over time, for one of the participants in the MAL-ED study.



During follow-up, this participant had four episodes of diarrhea (the blue hash bars on the graph indicate diarrheal episodes). The thickness of each blue hash bar is proportional to the duration that diarrheal episode lasted. There are two diarrheal episodes that appear to be greater than a few days in length.

You can also see that this participant had multiple instances of positive laboratory test results for microbiology, indicated by the colored dots at the bottom of the graph (different colored dots represent the detection of different pathogens). One question you might want to ask is, **"Did participants tend to test positive for a certain type of pathogen before an episode of diarrhea that was five or more days in duration?"**

To explore this question, your first step might be to explore the data and see how many participants tested positive for Cryptosporidium within the 14 days before a diarrheal episode that was five or more days in duration. Then you might want to repeat the same question for any Campylobacter.

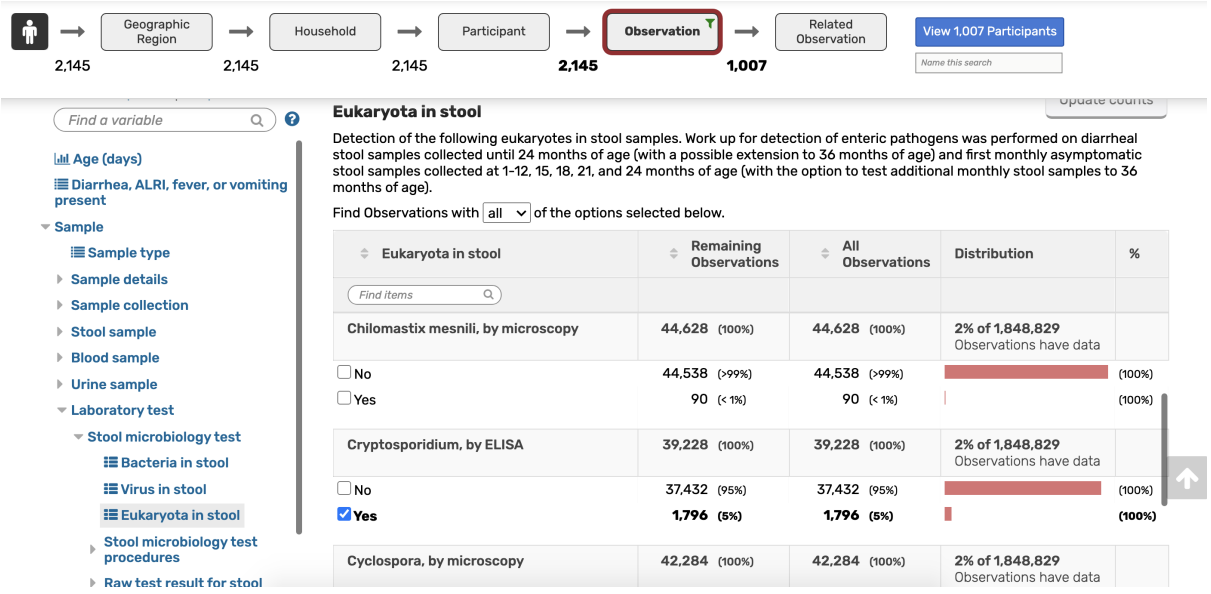
You can do this by using the Related Observations functionality! We will start with a very simple related observations query. For this exercise, to start, we will modify as few filters as possible to keep things straightforward.

Question 1: How many participants in the MAL-ED study tested positive for *Cryptosporidium* within the 14 days before a diarrheal episode that was five or more days in duration?

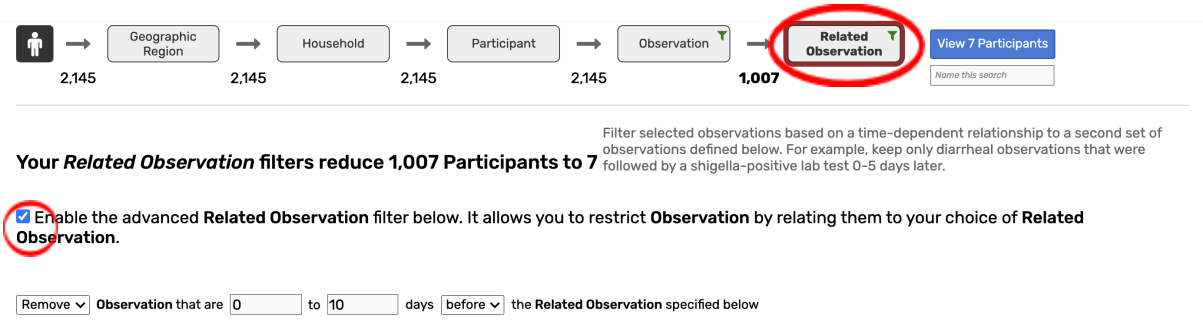
1. Start a participant-level search of the MAL-ED data. To answer this question, first select participants who tested positive for *Cryptosporidium* at any point during the study.

    - The cleaned, analytic versions of all microbiology detection results of various orgaanisms in stool samples can be found under “Bacteria in stool”, “Virus in stool”, and “Eukaryota in stool”.

    - Navigate to “Eukaryota in stool” and then select participants who had *Cryptosporidium* detected at any time in the 60 months of follow-up.



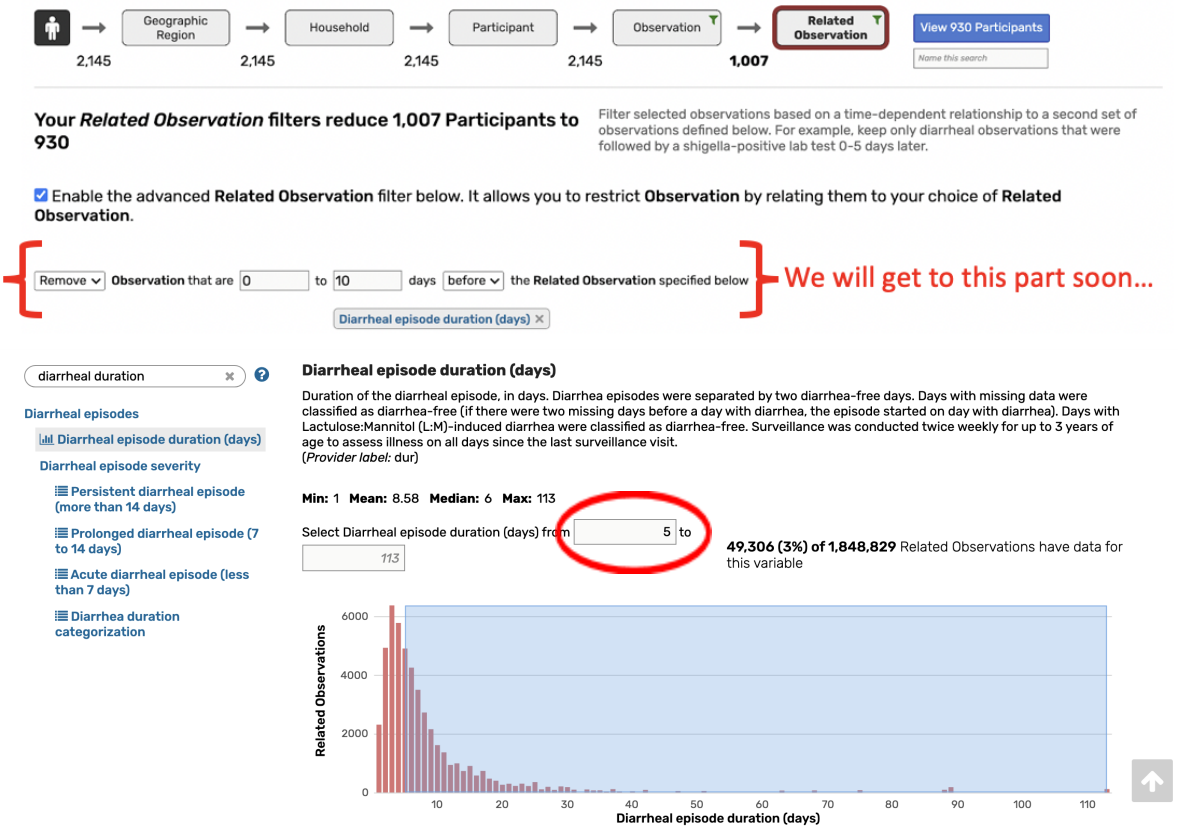
2. Now, click on the “Related Observations” box in the Search Wizard. “Related Observations” are used to narrow the dataset based on the relationship between two variables at two different points in time. Click on the small check box next to: “Enable the advanced Related observations filter below.” It allows you to restrict Observations by relating them to your choice of Related observations.”



3. After you have enabled the Related Observations filter, notice that the variables are now accessible. Take a look at the various variables and categories that appear in the variable hierarchy on the left side of the page. Do you notice anything familiar about these variables?[1]

4. Now we will want to specify that we are selecting diarrheal episodes of at least 5 days in length that occurred at any point during the study for our Related Observation. Use the "find a filter" search box to find variables related to "Diarrheal duration" and type "5" into the appropriate window to select episodes lasting at least 5 days.

    - For now, do not worry about properly completing the sentence above the variable selection panels. We will update this in the next step.



[1] The variables and categories available on the Related Observations step in the Search Wizard are duplicates of those that were available in the Observations step in the Search Wizard. The Related Observations step allows us to take the timing of different episodes, results, or data collection into account so we can select for data that occurred before (or after) something else had occurred.

6. We now want to account for the appropriate timing of the *Cryptosporidium* infections in relation to the 5+ day diarrheal episodes. We need to identify participants who tested positive for *Cryptosporidium* within the 2 weeks ***BEFORE*** a diarrheal episode lasting at least 5 days.

   Completing the sentence that we skipped over in step 4 allows us to properly account for the timing of our selections in relation to one another.

   In the Observations step in the Search Wizard, we previously selected participants who had *Cryptosporidium* detected at any point in the study period.

   In the Related Observations step, we now want to narrow down the selected participants further, and keep only the selected participants who also had a diarrheal episode lasting at least 5 days. However, we don't want to keep all selected participants who ***EVER*** had a diarrheal episode lasting at least 5 days at any point in the 5 years of follow-up. The timing of the *Cryptosporidium* test in relation to particular diarrheal episodes is important.

   Complete the 4 boxes in the sentence below to properly account for the timing of *Cryptosporidium*-positive laboratory results in relation to diarrheal episodes lasting at least 5 days.[2] *HINT: In the sentence, "Observations" refers to the observations we selected in the previous step (positive Cryptosporidium test results). "Related observations" refers to the observations we are selecting now (diarrheal episodes that lasted at least 5 days).*

7. How many participants in the MAL-ED study tested positive for Cryptosporidium within the 14 days before a diarrheal episode that was five or more days in duration?[3]

[2] The sentence should be completed to read: "**Keep** observations that are **0 to 14** days **before** the Related Observation specified below."

[3] 211 participants had a 5+ day diarrheal episode that was preceded by *Cryptosporidium* detection within the previous 2 weeks.

Your *Related Observation* filters reduce 1,007 Participants to 211

Filter selected observations based on a time-dependent relationship to a second set of observations defined below. For example, keep only diarrheal observations that were followed by a shigella-positive lab test 0-5 days later.

☑ Enable the advanced **Related Observation** filter below. It allows you to restrict **Observation** by relating them to your choice of **Related Observation**.

Keep **Observation** that are 0 to 14 days before the **Related Observation** specified below

Diarrheal episode duration (days) ×

diarrheal duration

Diarrheal episodes
- Diarrheal episode duration (days)
- Diarrheal episode severity
  - Persistent diarrheal episode (more than 14 days)
  - Prolonged diarrheal episode (7 to 14 days)
  - Acute diarrheal episode (less than 7 days)
  - Diarrhea duration categorization

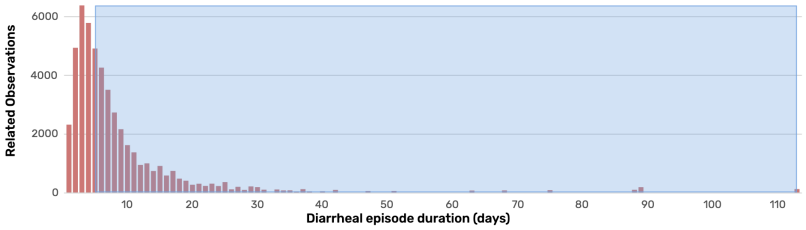
Diarrheal episode duration (days)

Duration of the diarrheal episode, in days. Diarrhea episodes were separated by two diarrhea-free days. Days with missing data were classified as diarrhea-free (if there were two missing days before a day with diarrhea, the episode started on day with diarrhea). Days with Lactulose:Mannitol (L:M)-induced diarrhea were classified as diarrhea-free. Surveillance was conducted twice weekly for up to 3 years of age to assess illness on all days since the last surveillance visit.
(*Provider label:* dur)

Min: 1 **Mean:** 8.58 **Median:** 6 **Max:** 113

Select Diarrheal episode duration (days) from 5 to 113

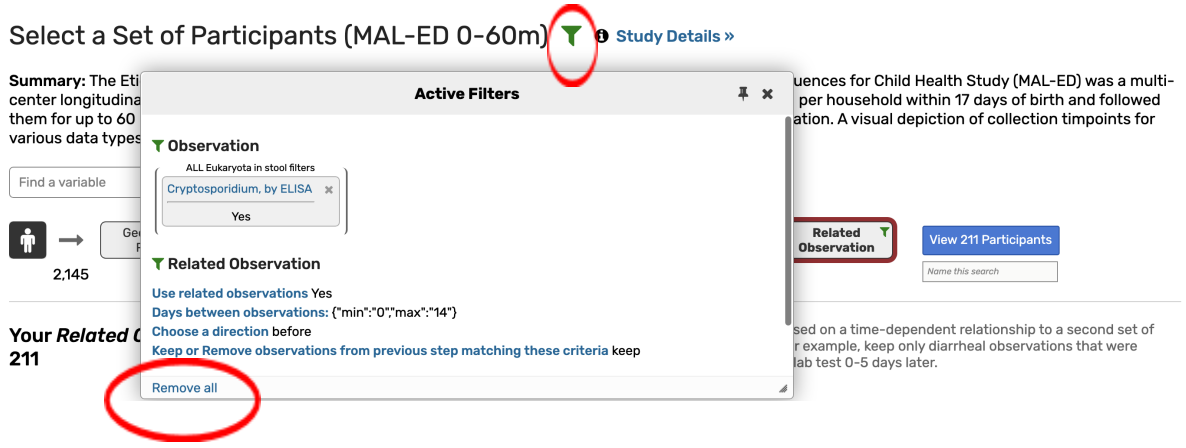
49,306 (3%) of 1,848,829 Related Observations have data for this variable



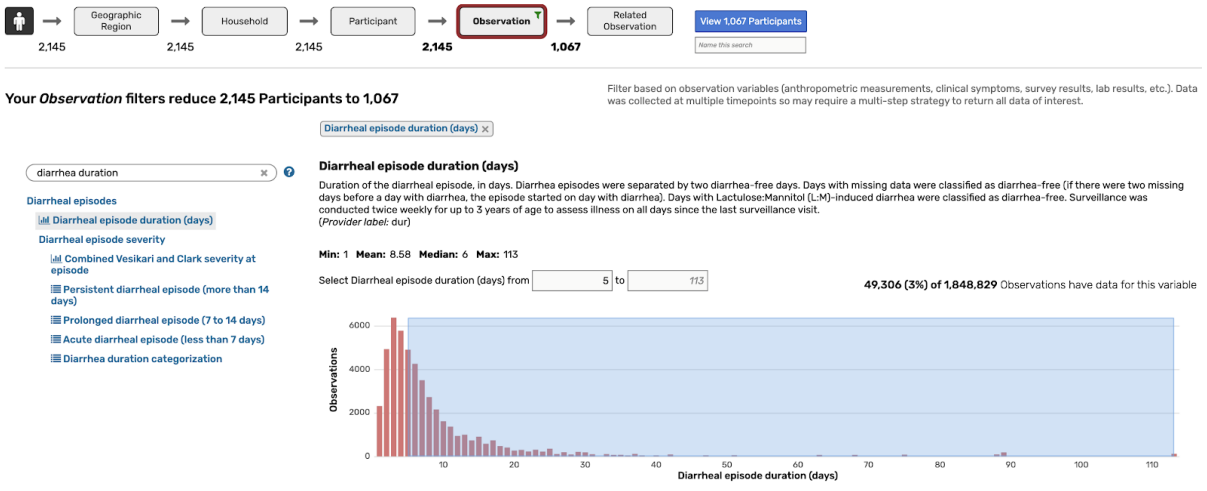
Question 2: Is there a different way we could have approached Question 1? Does this give you the same result?

What would happen if we instead selected diarrheal episodes lasting at least 5 days for our Observation and *Cryptosporidium* detection for our Related Observation? Would we get the same results? Lets try!

1. First, let's clear all of the selections we made previously. Click on the green filter icon next to "Select a set of participants (MAL-ED 0-60m)". In the popup window, click "Remove all".



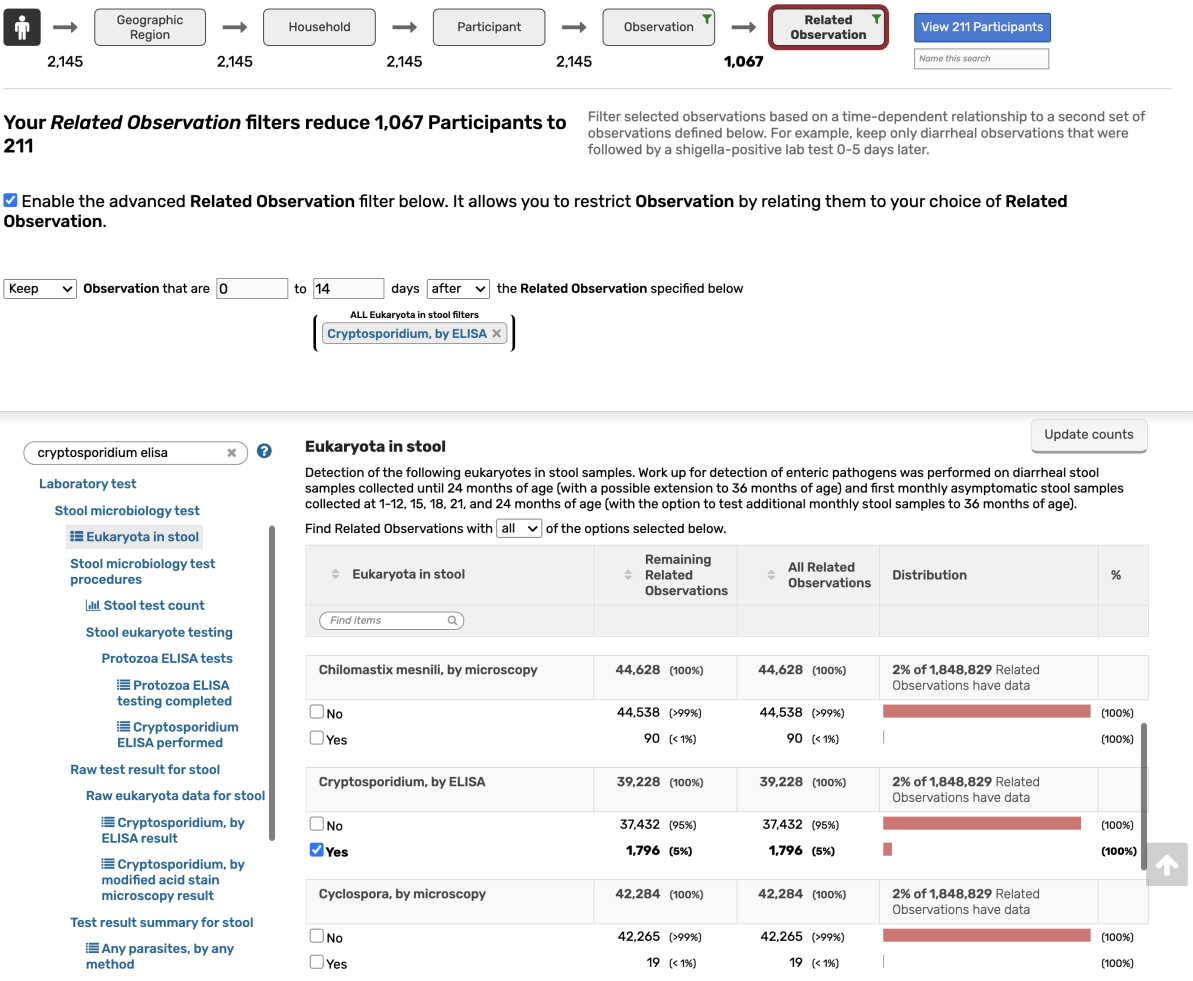
2. Now, click on the "Observations" step in the Search Wizard and select participants who had a diarrheal episode of at least 5 days in length at any point during the study.



8. Next, click on the "Related Observations" box in the Search Wizard. Click on the box to "Enable the advanced Related observations filter below." Select *Cryptosporidium*-positive observations for our Related Observation.

9. Complete the 4 boxes in the sentence below to properly account for the timing of *Cryptosporidium*-positive laboratory results in relation to diarrheal episodes lasting at least 5 days.[4] *HINT: In the sentence, "Observations" now refers to the observations we selected in the previous step (diarrheal episodes that lasted at least 5 days). "Related observations" now refers to the observations we are selecting now (positive Cryptosporidium test results).*

10. How many participants in the MAL-ED study tested positive for Cryptosporidium within the 14 days before a diarrheal episode that was five or more days in duration? Using this approach, do we return the same number of selected participants as with the approach we took to answer Question 1?[5]



[4] The sentence should be completed to read: "**Keep** observations that are **0 to 14** days **after** the Related Observation specified below."

[5] The two different approaches both returned 211 participants who met our selection criteria.

Multi-step strategies and combining searches

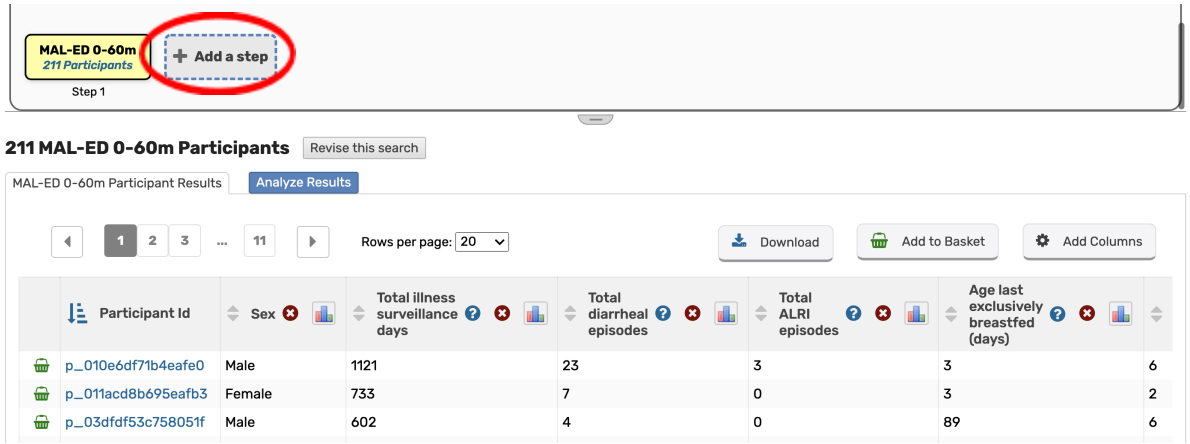
In the last search, we identified MAL-ED participants who had 1 or more episodes of diarrhea that were at least 5 days in duration and that were preceded by a detection of *Cryptosporidium* in the last 2 weeks. How many of these participants also had a reduced length-for-age z-score at 2 years of age?

To answer this question, you will need to employ a multi-step strategy. We will combine the results of our previous search, which identified all MAL-ED participants who had a *Cryptosporidium* infection followed by an episode of diarrhea lasting at least 5 days **(search 1)**, with a new search to identify all MAL-ED participants who had a length-for-age z-score of less than -2 at 2 years of age **(search 2)**.

Question 3: How many participants in the MAL-ED study tested positive for *Cryptosporidium* within the 14 days before a diarrheal episode that was five or more days in duration and also had a length-for-age z-score of less than -2 at 2 years of age?

1. Click on "View 211 participants" button on the Search Wizard to navigate to the Results Table.

2. From the Results Table of the 211 MAL-ED participants who were *Cryptosporidium*-positive within 14 days before a diarrheal episode lasting at least 5 days, navigate to the search strategy panel above the table and click the "Add a step" button. Why do we need to add a step to our search strategy instead of just applying additional filters to our original search?[6]



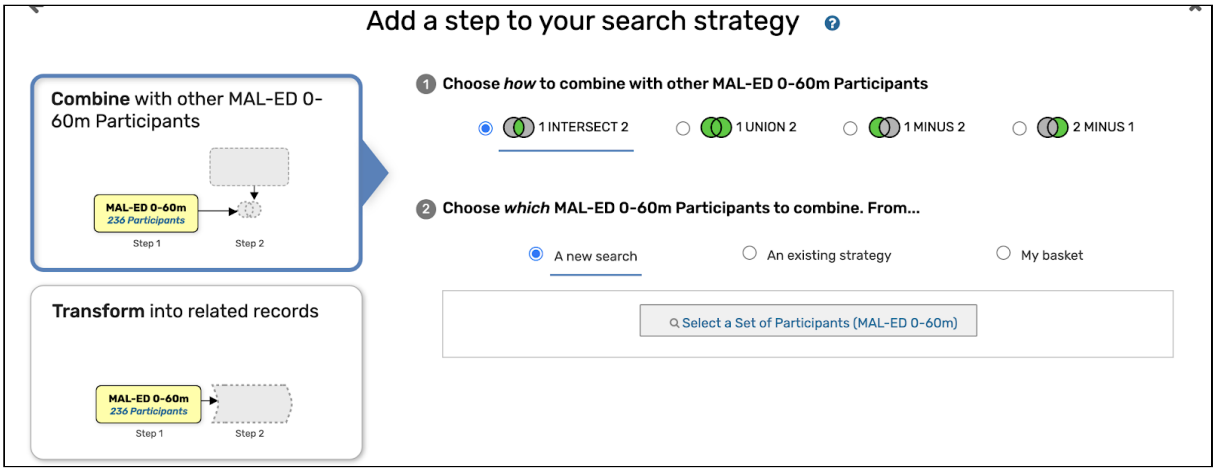
[6] In search 1, we identified all MAL-ED participants who had a *Cryptosporidium* infection followed by an episode of diarrhea lasting at least 5 days. These *Cryptosporidium* infections could have occurred at **ANY** time during follow-up. For search 2, we are being asked to identify participants who had a reduced length-for-age z-score at exactly 2 years of age. If we apply a filter to select "Age" of 2 years to search 1, we will only be selecting *Cryptosporidium* infections that occurred when the participant was 2 years old. Participants who had the *Cryptosporidium* detections occurring before and after 2 years of age would be removed from our selections.

3. In the “Add a step” popup window, click to select “Combine with other MAL-ED 0-60m Participants” and then choose how to combine this new search (search 2) with the original search (search 1).

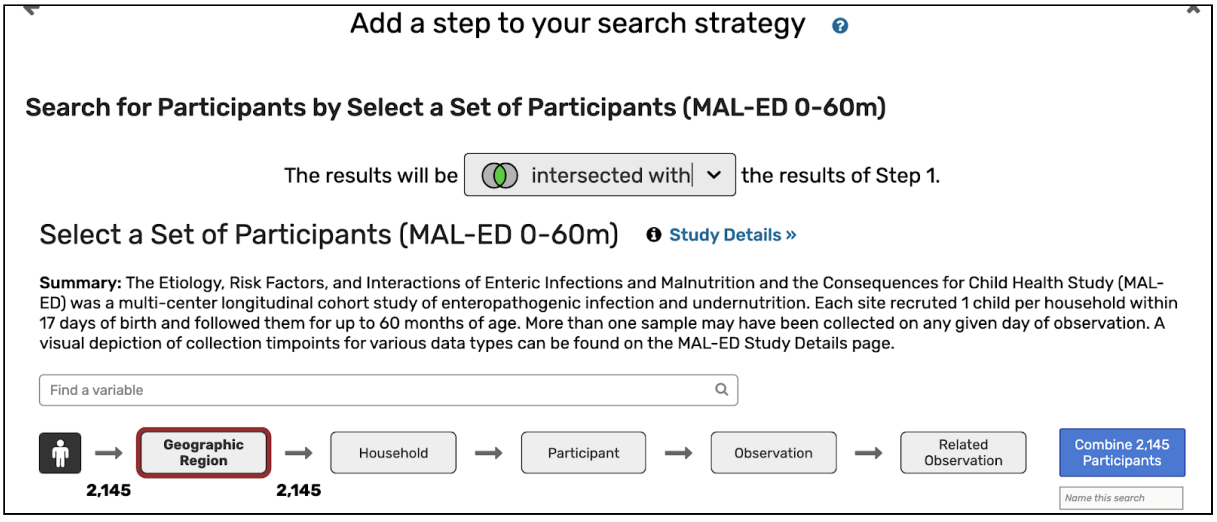
    - Since we want to identify all participants who had a length-for-age z-score less than -2 at 2 years of age (search 2) who ***ALSO*** were *Campylobacter*-positive within 14 days before a diarrheal episode lasting at least 5 days (search 1), we want to find the intersection of the two searches. Go ahead and select “1 Intersect 2.”

    - Finally, choose “A new search” to combine a new subset of MAL-ED participants with the subset of participants identified in the original search (search 1).

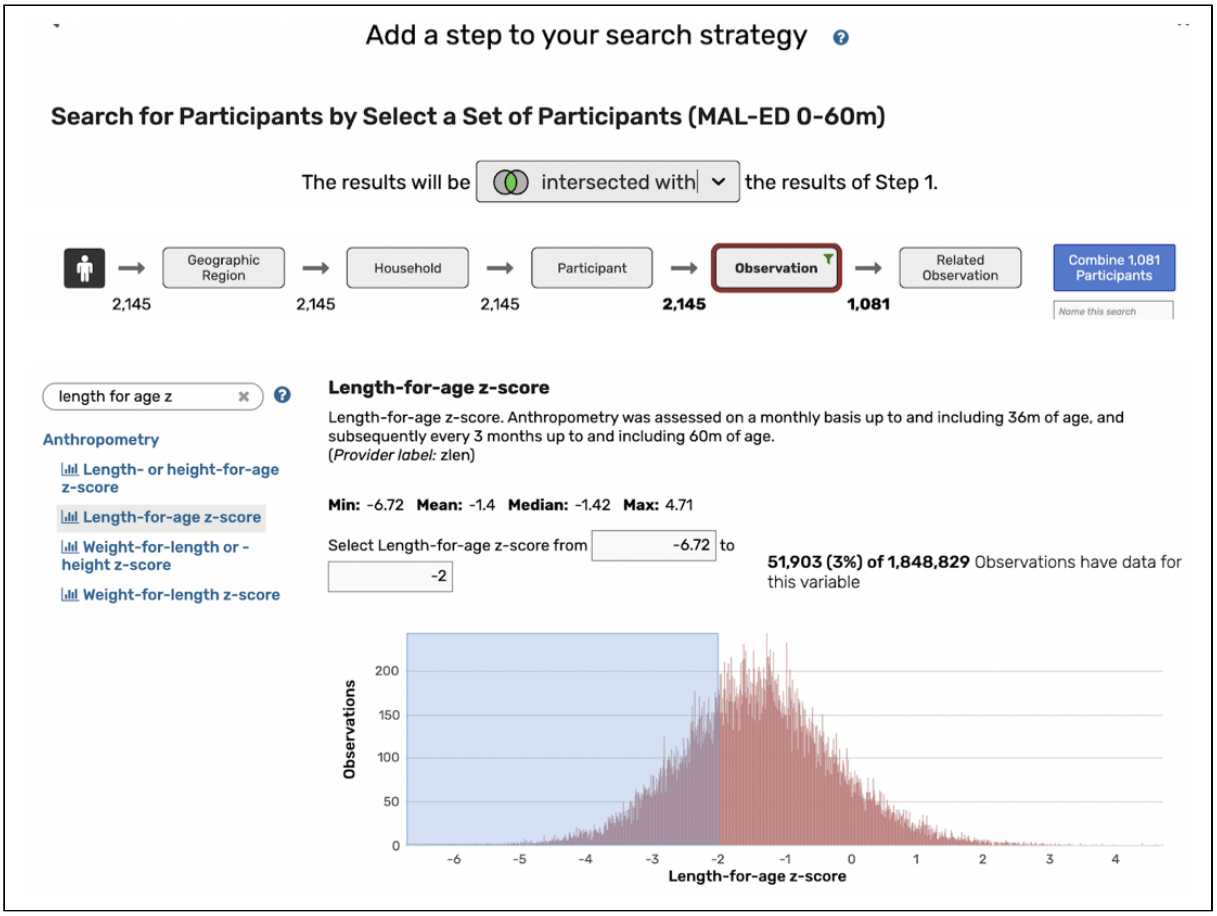
    - Click “Select a set of participants (MAL-ED 0-60m)”.



4. The “Add a step” popup window will now contain a new Search Wizard. Use this Search Wizard to obtain a list of all MAL-ED participants who had a length-for-age z-score lower than -2 at 2 years of age (search 2).

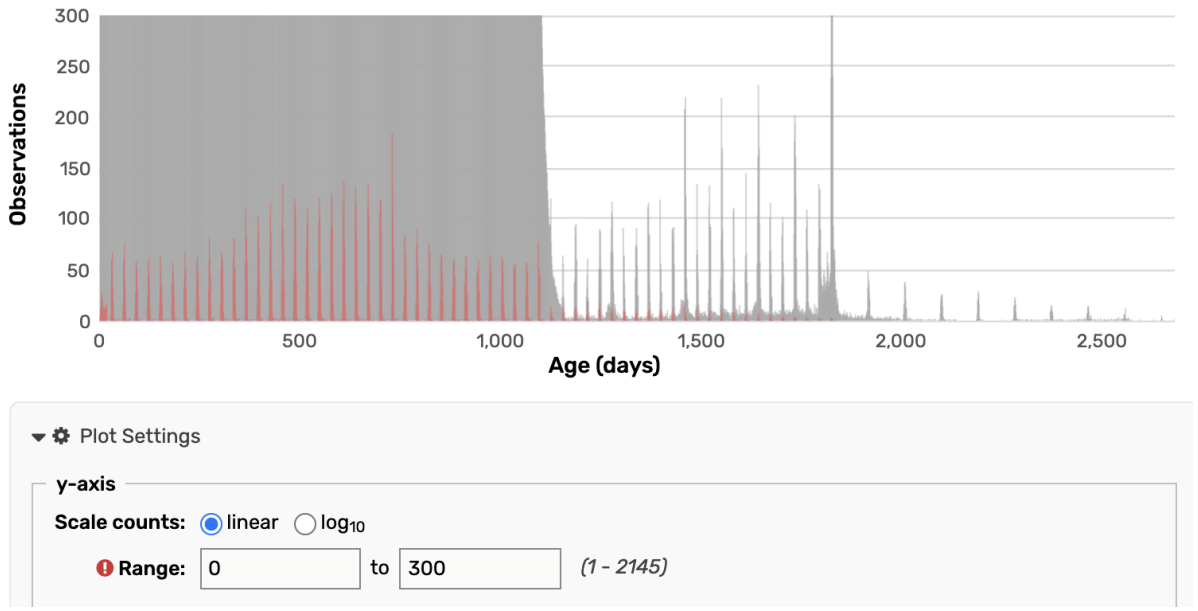


5. For search 2, we want to identify the list of participants who had a length-for-age z-score less than -2 at 2 years of age. The first step in this search is to select participants who had a length-for-age z-score less than -2 at any point during the study. Z-scores are sorted under the "Observations" step in the Search Wizard. Remember that you can use "Find a filter" to quickly search for variables of interest.

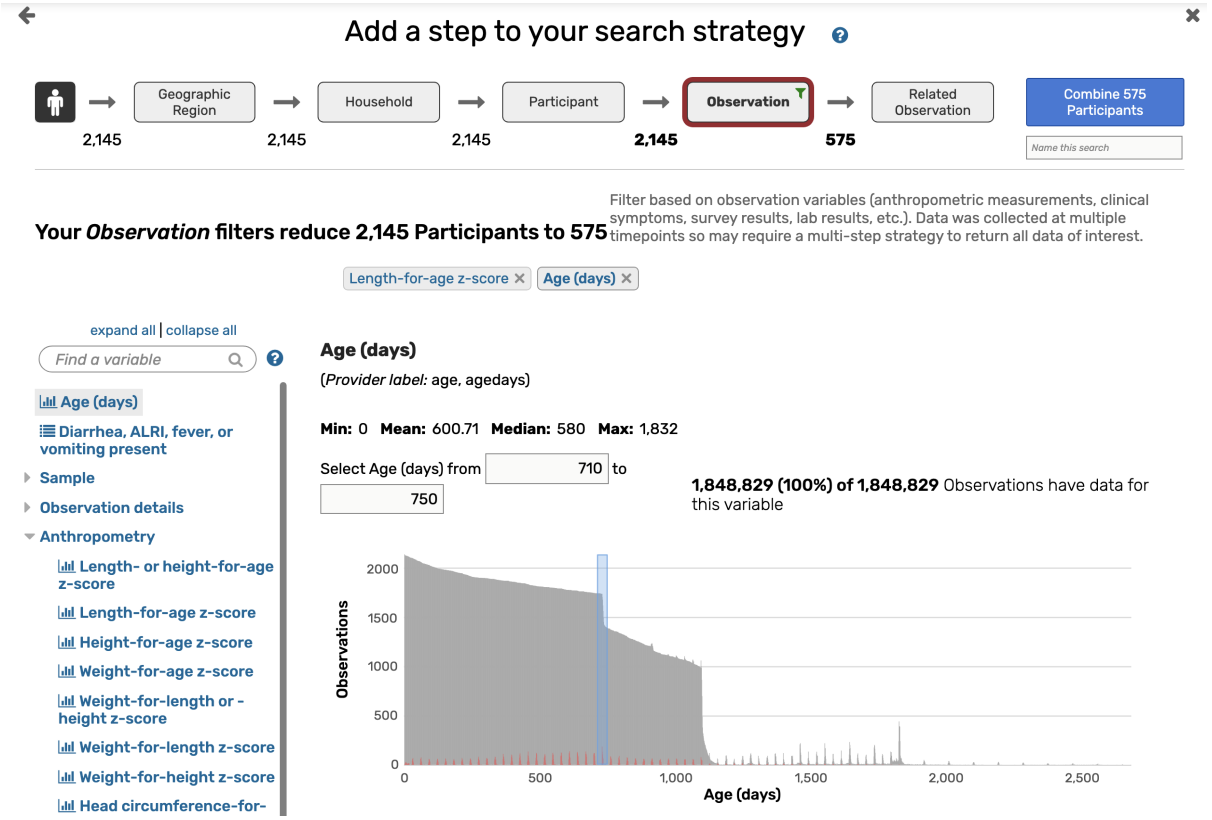


6. We still need to limit the selected length-for-age z-scores to those that were collected when the participant was 2 years of age. Navigate to the "Age (days)" variable in the "Observations" step of the Search Wizard. Use the "Plot settings" under the graph to zoom in on the data; set the y-axis to range from 0 to 300. For this variable, notice that there are a series of red peaks on a grey background. Why do you think the data looks like this?[7]

[7] From the information on the MAL-ED Data Set page, we can determine that anthropometry variables such as length-for-age z-scores were measured monthly. The peaks represent every month of anthropometry data collection, with some variation around the exact day of age when the data was collected.

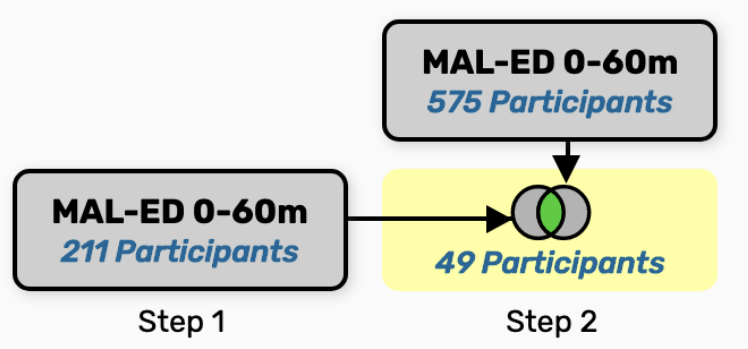


7. Select data that was collected at approximately 2 years of age. There is variation on exactly when the 2 year timepoint of anthropometry data was collected, so be sure to account for this variation by choosing 710 to 750 days for the “Age (days)” range.



8. Search 2 determined that there were 575 MAL-ED participants who had a length-for-age z-score less than -2 at 2 years of age. Click on the blue "Combine 575 Participants" box in the Search Wizard to combine the results of search 2 with search 1.

9. How many participants in the MAL-ED study tested positive for *Cryptosporidium* within the 14 days before a diarrheal episode at least five days in duration and also had a length-for-age z-score of less than -2 at 2 years of age?[8]



[8] There were 49 participants that were returned in both search 1 and search 2.