## CTSA Program Common Metrics (CM) Operational Guideline: Median Accrual Ratio

*Revised 9-26-2019*

**Template Element** | **Description**
---|---
1. Operationalized Metric Title | Median Accrual Ratio (MAR)

### 2. Rationale

The purpose of this metric is to estimate the current accrual ratio for clinical trials in order to enhance our ability to develop performance interventions that increase actual participant accrual into clinical trials within the planned time period.

- When the ratio is close to or equal to 1, the study accrual is occurring/has occurred on time. The accrual is aligned with the projected time to complete enrollment.
- When the ratio is >1, accrual is ahead of schedule (faster than anticipated).
- When the ratio is <1, accrual is slower than planned.

**Note:** Several approaches that can help teams make sense of the Accrual metric ratio along the way:

- The information can be more actionable if teams follow the MAR during the course of recruitment to identify opportunities for course correction rather than waiting to see what the ratio is at the end of the study.
- In addition to the MAR, it is valuable to look at the range of ratios. With improved practices, the median should get lower and the variation around that lower median will narrow.
<table>
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<tr>
<th>3. Operational Specification</th>
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<td>Median accrual ratio is the median across a set of clinical trials of the following <em>within-trial ratio</em>. Thus, for each individual trial the accrual ratio would be:</td>
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<tr>
<td>% of Participants Accrued = ( \frac{# \text{ of participants accrued}}{# \text{ of participants targeted}} \times 100 )</td>
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<tr>
<td>% of Recruitment Period to Date = ( \frac{# \text{ of days elapsed since open to recruitment}}{# \text{ of days trial will be open to recruitment}} \times 100 )</td>
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<tr>
<td>Accrual Ratio = ( \frac{% \text{ of Participants Accrued}}{% \text{ of Recruitment Period to Date}} )</td>
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This metric is the ratio of the following two percentages:

- *Percent of Participants Accrued* (the number of participants accrued by December 31st or the end of actual trial recruitment, whichever comes first, divided by the number targeted by the completion of the trial, times 100).
- *Percent of Recruitment Period to Date* (the number of calendar days elapsed since the initiation of recruitment until December 31st or the end of actual trial recruitment, whichever comes first, divided by the expected total number of days the trial will be open to recruitment, times 100).

Both of these are needed to get a good picture for any trial of the accrual ratio. If we only use the first (top) one, we would know what portion of expected or targeted accrual we currently have for a trial. However, if a trial is still underway, we would not expect 100% accrual. By comparing the two percentages, we can see if accrual is ahead of or behind schedule. Note that this denominator assumes a linear rate of accrual over the recruitment period. While accrual may not happen in a linear constant manner, this is viewed as a reasonable way to approximate the current accrual ratio for a trial. An example of non-linear accrual may include trials with intermediate, planned holds on accrual for interim evaluation. The metric is a “current state” metric and describes the current accrual ratio for any given trial. Even though the trials that are eligible will likely be at different stages in their progress, the denominator adjusts for the amount of time already expended in the trial.
### 4. Technical Description

#### Key Definitions

- **Clinical Trial:** The accrual ratio metric uses the NIH revised definition of a Clinical Trial, namely a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. - See more at: [https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html#sthash.Gl7rwI4D.dpuf](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html#sthash.Gl7rwI4D.dpuf)

- **Number of Participants Accrued:** The number of participants who both signed the consent form and passed all screening requirements for the trial. Participants who subsequently withdraw from the study, or who are lost to follow-up, are considered accrued.

- **Number of Participants Targeted:** The number of participants required to satisfy the sample size for power calculation in the IRB approved protocol. In the case when there are multiple estimates, the accrual target is the lowest number of participants required.

- **Percent of Participants Accrued:** The number of participants accrued by December 31st or the end of actual trial recruitment, whichever comes first, divided by the number targeted by the completion of the trial, times 100.

- **Number of days elapsed since open to recruitment:** The number of calendar days elapsed since the initiation of recruitment until December 31st or the end of actual trial recruitment, whichever comes first.

- **Number of days trial will be open to recruitment:** The expected total number of days the trial will be open to recruitment. This is the total amount of time in days for which the trial is originally planned to be open to recruitment in order to attain the target number of evaluable participants.

- **Percent of Recruitment Period to Date:** The number of calendar days elapsed since the initiation of recruitment until December 31st or the end of actual trial recruitment, whichever comes first, divided by the expected total number of days the trial will be open to recruitment, times 100.
### Key Definitions continued

- **Accrual Ratio**: The ratio of *Percent of Participants Accrued / Percent of Recruitment Period to Date*. This ratio is computed for each trial.

- **Median Accrual Ratio**: The median of the Accrual Ratios of the sample of clinical trials for this metric.

- **Number of Clinical Trials at the primary institution that were included in calculating the median**: The total number of clinical trials that were included in computing the Median Accrual Ratio.

- **Number of clinical trials identified that were open to recruitment but had not yet accrued any participants**: The number of clinical trials included in the Median Accrual Ratio calculation that did not accrue any participants during the reporting year.

- **CTSA Program Primary institution(s)**: The intent of this metric is to generate a meaningful accrual ratio for an institution. There are hubs where there is not one, single “primary” institution. In defining the scope of the trials to be included, hubs should focus on a data source which is comprehensive and reflective of their primary institution, but which is reasonable.

### Sampling Frame

The intent of the Median Accrual Ratio metric is to apply to all clinical trials at the CTSA Program’s primary institution. However, because many institutions do not yet have a fully-functioning clinical trial management system (CTMS) or other electronic database of accrual data. During the first 2-3 years of adoption, hubs will be given flexibility in deciding the domain of trials for which data for this metric will be collected. While ideally hubs should include all eligible clinical trials, if that is not immediately feasible, they should either randomly sample from all eligible clinical trials or, secondarily, select a nonrandom targeted sample of clinical trials that can be a focus for accrual performance improvement. In summary, the order of preference for determining the sample of clinical trials on which this metric is initially collected is:

- All eligible clinical trials
- If the above is not feasible, random sampling of all eligible clinical trials
- If neither of the above is feasible, a targeted nonrandom sampling of eligible clinical trials (e.g., all NIH-supported trials or all cancer trials)
### Metric Type: Median

#### General Inclusion/Exclusion Criteria

- **Inclusion Criteria**
  - Clinical trials that meet the NIH clinical trials definition and that have been in the process of accruing participants at any point during that year. A Clinical Trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. - See more at: [https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html#sthash.Gl7rwI4D.dpuf](https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html#sthash.Gl7rwI4D.dpuf)
  - Behavioral health studies are included if they otherwise meet the definition of a clinical trial.
  - All clinical trials regardless of funding source (e.g., NIH, industry, institutionally (internally) funded).
  - Clinical trials that are on hold to recruitment but which are not yet closed to recruitment.

- **Exclusion Criteria**
  - Exclude any clinical trials for which informed consent is not required. Examples include chart review research studies, studies using research registry data that do not require consent beyond registry participation.
  - Exclude any clinical trials that have an initial targeted number of less than 5 participants at your site.
  - Exclude any clinical trials that were not open to accrual at any point during that year.
  - For multi-site trials, report only on accrual rates at your own site.
  - Exclude any multi-site trials that use competitive enrollment.
| 6. Data Sources & Methods of Data Collection | In an increasing number of institutions, it is possible to obtain some or all of the data to construct this metric directly from a Clinical Trial Management System (CTMS), at least for a subset of clinical trials. Hubs that do not have a CTMS could collect the information through a very brief annual survey of PIs (or their designated staff). If the survey method is utilized, the following questions could be asked of each PI for selected trials:

1. What is the targeted number of participants for your trial?
2. How many participants have you accrued as of the end of your recruitment period or as of December 31st if your trial is still active, whichever happened first?
3. What is/was the start date for your recruitment period?
4. If your trial is currently actively accruing, what is the anticipated recruitment period end date for your trial? If your trial is closed to recruitment, what was the date it closed to recruitment?

To minimize the burden to the investigative teams, the surveyor may be able to obtain the answers to questions 1, 3, and 4 using information already on record (e.g., by utilizing IRB or other relevant systems), in which case all that would be needed is to ask the investigative team to validate the answers and report the current number of participants accrued to date.

For hubs that undertake random sampling of the total population of eligible trials, they will need to have a list (i.e., sampling frame) of all eligible clinical trials and a mechanism for conducting the sampling. In addition, they must collect a sufficient sample size to be able to accomplish a reasonable estimate of the population, and justify this sample size in their Turn-the-Curve Plan.

For hubs that undertake a nonrandom targeted sample of eligible trials, the hub must describe and justify their choice of sample and its appropriateness for their performance improvement efforts in their Turn-the-Curve Plan.

| 7. Frequency of data collection and Reporting | This metric will be collected annually for the previous calendar year as of December 31st. The intent of this metric is to collect it for all eligible clinical trials that were open to recruitment any time during the calendar year at the primary hub institution, regardless of whether they are closed to recruitment on December 31st. The intent of this metric is also to collect the accrual ratios of the year as of December 31st of the year of the metric. If this is not possible, the best approximation of that number must be sought (e.g., use of the number in the most recent continuing review). However, for performance improvement purposes, this metric would be best if collected on an ongoing basis through a CTMS.

Data should be reported on an annual basis.

Modify the metric to be collected prospectively rather than retrospectively.

Hubs assess that prospective collection of accrual data would increase data quality and the potential usefulness for strategic management, including the ability to identify and intervene in individual trials as needed. |
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<tr>
<th>8. Unit of Analysis</th>
<th>Data will be collected within each hub at the individual clinical trial level and reported in aggregate (median) at the primary institution level.</th>
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<tr>
<td>9. Notes/Comments</td>
<td>It is generally recognized that many hub institutions are at the point of initiating or in the process of implementing Clinical Trial Management Systems (CTMS) that would make the calculation of this accrual metric more feasible. In recognition of this, for the first 2-3 years while this metric is being adopted, hubs will be afforded a degree of flexibility in defining the set of trials for which this metric will be calculated. It is expected that over that time all hubs move expeditiously towards comprehensive coverage. If that is not immediately possible, the next most preferable alternative would be random sampling of all eligible trials. Finally, if that cannot reasonably be accomplished, a hub may elect to utilize a nonrandom targeted sample of trials (e.g., all NIH-sponsored trials or all cancer trials). In either sampling case, the hub will be expected to justify their choice and provide a defense of the ultimate sample size in their Turn-the-Curve Plan. It is the intent in the next 3-5 years to include in this metric the ability to subdivide it by underrepresented minorities, gender and other less represented communities. Hubs are encouraged now to include such data where available and discuss it in connection with their Turn-the-Curve Plan. It is required that Hubs include the following in their Turn-the-Curve plans for this metric:   - A description of the sampling method utilized to determine the Median Accrual Ratio (e.g., comprehensive sampling of all eligible clinical trials, random sampling of all eligible clinical trials, targeted nonrandom sampling of eligible clinical trials. It is also recommended that Hubs include other evaluation data components that may help illuminate the key drivers for this metric, and a description of the evaluation or strategic management plan of the hub related to this data. It is recommended to collect and report additional data information such as total number of trials represented in the Median Accrual Ratio, the percentage of total eligible trials included, and the mix of clinical trials, either at a primary institution or included in the Median Accrual Ratio, impacts the ability to understand how representative the median is of the intended sample, and affects the ability to aggregate data and compare across hubs. It is also recommended to consider additional accrual metrics to augment areas not addressed by the Median Accrual Ratio. These would provide additional metrics of accrual to assist trial performance improvement, such as metrics for rare disease trials excluded by the exclusion criteria of &lt; 5 targeted participants and predictive metrics that identify trials likely to have low levels of accrual.</td>
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<td>10. References</td>
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