Development of a Composite Site Performance Score: Optimizing Site Selection and Trial Methodology

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1 – Developing a Composite Site Performance Score

- Site performance traditionally has focused on operational metrics, including speed and volume of enrollment. PK data, when available at trial completion, are used as a snapshot of dose adherence.
- Datasets tend to be relatively small and proprietary to a single sponsor or CRO. Different metrics, scoring systems and infrequent updates to the underlying data make it difficult to compare site performance across the industry and to leverage the most up-to-date information.
- The emphasis on enrollment, has, in part, derived from the need to increase patient enrollment in order to account for a possible reduction in treatment effect due to non-adherence.
- More precise measures of participant and site performance collected on electronic platforms offer the opportunity to identify adherence-based variance and other drivers of site performance that can be used to quantify, and benchmark site performance based on a single score, potentially enhancing site selection during the design and execution of clinical trials.
- A Composite Site Performance Score prototype, based on four factors, was developed to quantify and normalize site performance across 52 studies.

2 – Methodology

- Dose adherence and participant status data were collected across 52 trials, 701 sites, and 6,132 participants.
- 370/701 (52.0%) of sites were enrolled in 1-2 trials; 19/701 (2.7%) were enrolled in > 4 trials.
- 36/52 trials (69.2%) are in CNS, across 18 unique sponsors.

AiCure metrics were calculated for each site:

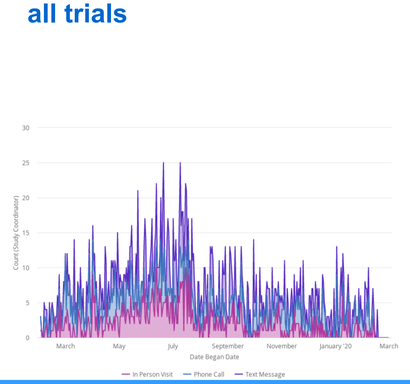
- AiCure Adherence: average subject adherence rate (20% quantiles)
- AiCure study completion rate: average of (active AiCure dosing days)/(expected total dosing days) (20% quantiles)
- AiCure early term rate: (number of AiCure early term subjects/(total subjects enrolled) (33% quantiles)
- AiCure Alert Rate: (number of subjects with 20% or more of their doses flagged as alerts)/(total subjects enrolled) (50% quantiles)

Note: metrics were categorized before modelling based on percentile groups to minimize non-linear inter-relationships and facilitate interpretation.

Scoring Analysis:

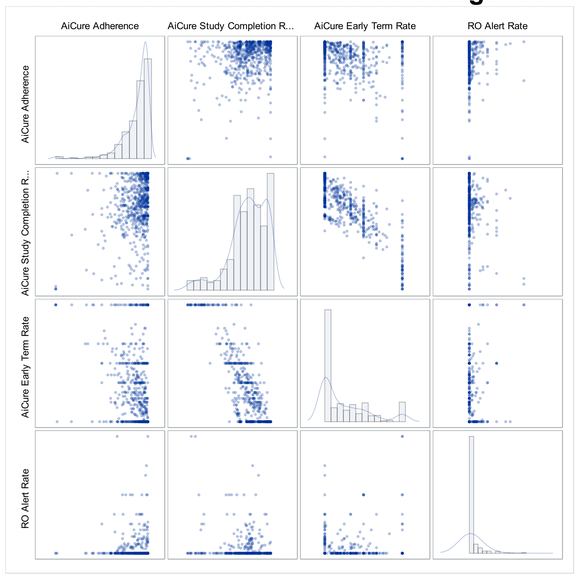
Principal Component Analysis was conducted across the 4 AiCure metrics to identify factors corresponding to maximal variance or information across the site level metric categories.

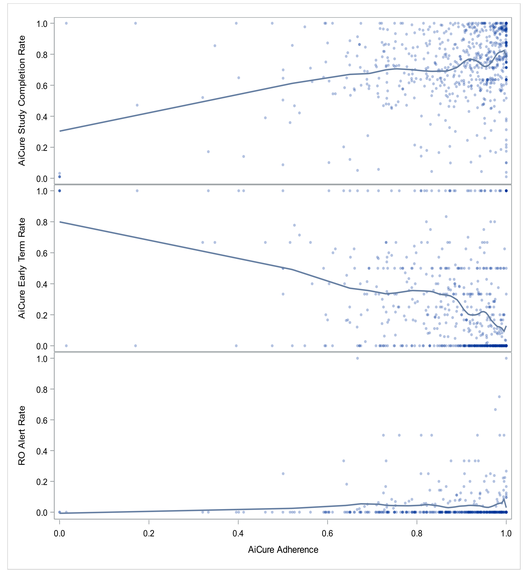
3 – AI platform (AiCure®): structured participant and site data are captured across all trials



4 – Findings from the Principal Component Analysis

Matrix Plots of AiCure Metrics Categories:





PCA Analyses:

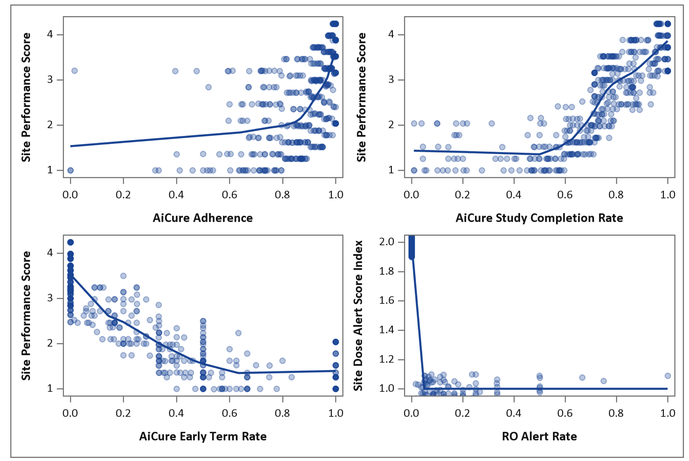
Two factors were identified that accounted for 75% of the total variance measured across the 4 metrics. Based on the factor loadings given in the table below, the two factors can be interpreted as “Composite Site Performance Score” and “Site Dosing Alerts Score”.

Factor Loadings	Factor1		Factor2	
AiCure Adherence	63	*	2	
AiCure Study Completion	86	*	13	
RO Alert Rate	5		100	*
AiCure Early Term Rate	93	*	-3	

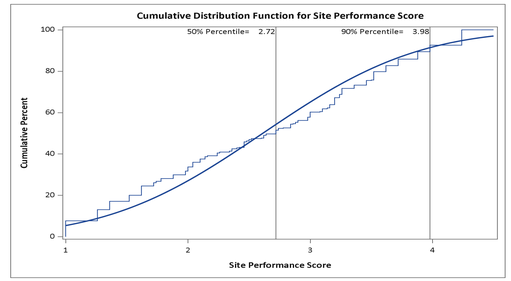
Composite Site Performance Score =	
	0.26 x AiCure Adherence Category
+	0.36 x AiCure Study Completion Category
+	0.38 x AiCure Early Term Category
Site Dosing Alert Score = AiCure RO Alert Category	

5 – Score Performance

Plot of score by underlying AiCure metrics



Cumulative Distribution of Site Performance Score



6 – Conclusion

- Historical data from 701 sites, across 52 trials were used as inputs for the development of a novel Composite Site Performance Score.
- Based on a Principal Component Analysis incorporating 4 metrics, ‘study completion’ and ‘intentional non-adherence’ accounted for 75% of total composite site performance variance between sites. Ranking or Prioritization or exclusion of sites above/below a pre-defined percentile-based on Score. Combined with historical data across sponsors, this scoring may contribute to a substantial reduction in site selection risk associated new metrics.
- Future work to refine the framework includes adding new metrics and refining input variables.
- To our knowledge, this is the first attempt at developing a Composite Site Performance Score based on technological advances and acceleration of data availability to quantify and reduce operational risk in drug development.