Debiasing Probability of Success Estimates for Clinical Trials

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The time-series probability of success (PoS) is defined as the probability of success of the clinical trial in the time window \( (t - \Delta t : t) \). Since clinical trials take multiple years to complete, the time-series PoS can be defined in two different ways, using its start date or its end date:

\[
PoS_{t,\text{start}} = \frac{\text{Number of successful trials starting in } t - \Delta t : t}{\text{Total number of trials starting in } t - \Delta t : t}
\]

\[
PoS_{t,\text{end}} = \frac{\text{Number of successful trials ending in } t - \Delta t : t}{\text{Total number of trials ending in } t - \Delta t : t}
\]

Both \( PoS_{t,\text{start}} \) and \( PoS_{t,\text{end}} \) may be important to an application, depending on its basis. In particular, the \( PoS_{t,\text{start}} \) is necessary to estimate the feasibility of a drug project portfolio when the projects start in the window \( (t - \Delta t : t) \). In our analysis, we use a value for \( \Delta t \) of 3 years.

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The $\text{PoS}_{\text{start}}$ values are plotted in Figure 1. We observe that the $\text{PoS}_{\text{start}}$ values are larger in recent years. This is possibly due to a completion bias: given the current date in our estimate of the $\text{PoS}_{t,\text{start}}$, a large number of clinical trials are incomplete, and their results are unknown. Only those trials that are successfully finished will contribute to the PoS. Hence, the PoS values are biased, and the large number of unfinished trials contribute to larger lower and upper bounds on the PoS.

To debias the $\text{PoS}_{\text{start}}$ for the most recent period, we compute a debiasing factor. This debiasing factor is computed by estimating the bias in the historical data. To compute the debiasing factor for the time $\text{present} - t1$, we use the following methodology.

At time $t$ in our history, we censor the trials after $t + t1$. This censoring is performed by dropping all trials with a start date after $t + t1$, changing the status of trials with an end date after $t + t1$ to “open,” and changing the values of the end date to “not available.” The PoS is then computed for the censored data at time $t$. This value will correspond to the biased PoS. We also compute the PoS at time $t$ for the uncensored data. The debiasing factor will be $\frac{\text{PoS}_{\text{unbiased}}}{\text{PoS}_{\text{biased}}}$.

For $t1 = 0$, the PoS for censored and uncensored data over time $t$ is given in Figure 2. The bottom plots in Figure 2 present the ratio between the debiased and biased PoS. The ratio is averaged over time to compute the debiasing factor. Similarly, we can compute the
Figure 2: PoS calculated for different phase transitions on censored (for $t_1 = 0$) and uncensored data (top plots). The bottom plots correspond to the ratio between the debiased and biased PoS. The ratio can be averaged over time (here, 2006 to 2016) to compute the debiasing factor.

debiasing factor for different values of $t_1$.

Figure 3: The debiasing ratio for phase transitions for the most recent four-year period.

In the present sample, we use the 2006 to 2016 period to compute the debiasing ratio. A
two-year buffer window is used between 2016 and 2018 when debiasing the PoS for 2018 to 2022. The debiasing factor is given in Figure 3.

In Figure 4, we present both the biased and the debiased $\text{PoS}_{\text{start}}$ against the $\text{PoS}_{\text{end}}$, along with their upper and lower bounds. Compared to the $\text{PoS}_{\text{start}}$, the $\text{PoS}_{\text{end}}$ has larger values in the earlier years and smaller values in the recent years. The debiased $\text{PoS}_{\text{start}}$ values are more reasonable in recent years compared to the biased values. The $\text{PoS}_{\text{end}}$ values show a sharp elbow pattern in the most recent period, but its upper and lower bounds also increase, implying that many trials that ended most recently have unknown results.\footnote{The end dates of the trials are updated prior to updating the trial results, with the possibility that the...}
Notes:

- The debiasing ratios may not be completely accurate due to data backfilling.

- The accuracy of the $P_{oS_{start}}$ and $P_{oS_{end}}$ depends on the accuracy of the clinical trial start date and end date. However, the time of "transition: enndate" and "start date" may not be correctly specified in the dataset.