(1)

|  |  |
| --- | --- |
| Experimental arm (E) | Control arm (C ) |
|  |  |

* P(DC occurs, AE occurs/not occur)

(2)

. So , though defined as the prob that DC occurs ‘due to’ AE, is actually just the prob that DC and AE both occur.

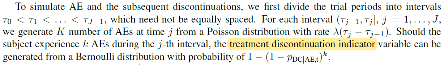
Solve for from (2)

(3)

|  |  |
| --- | --- |
| Experimental arm (E) | Control arm (C) |
| = P (discontinue due to AE in arm E)  = P (no AE occurs in arm E) | **= P (discontinue due to AE in arm C)**  0.053  **= P(no AE occurs in arm C)** |

Table

Description automatically generated



This is the Bernoulli for Indicator(DC) **conditional on the Indicator(AE)?!?**

Consider the entire trial duration (54 months) as one interval, k can be estimated by AE event rate

|  |  |
| --- | --- |
| Experimental arm (E) | Control arm (C ) |
| =0.918 ?!?! | **= 0.879 ?!?** |

………………………………………………………………………………………………………………………………………………………………….Should the

subject experience k AEs during the j-th interval, the treatment discontinuation indicator variable can be

generated from a Bernoulli distribution with probability of .

All input parameters for the AE generator are available from clinical trial summary results and publications.

From clinical trial results, it is standard protocol to list the proportion of patients that did not experience

any AE on treatment arm t, i.e. Then we have ,

which can provide an estimate for , i.e. . In assuming that the

AEs follow a Poisson process, each event is independent of the occurrence of the previous event. Given

a patient has k events, the probability of not discontinuing due to AEs during the study is

on that treatment arm. Then, on average, the corresponding discontinuation rate due to AE during the

study period is Let be the estimator for . Then

.

(is an weighted average of weighted by poisson prob.)

Left hand side

Right hand side