

Appendix A: Derivation of the probability of having an event before calendar time t .

Assume subjects are accrued over an accrual period of length t_a , with an additional follow-up time t_f , so that the study duration $\tau = t_a + t_f$, and that the entry time Y is uniformly distributed with $H(t)$ over $[0, t_a]$. With no patient loss to follow-up or drop out, the censoring distribution $G(t) = H(\tau - t)$ is a uniform distribution over interval $[t_f, t_a + t_f]$, that is, $G(x) = 1$ if $x \leq t_f$; $= (t_a + t_f - x)/t_a$ if $t_f \leq x \leq t_a + t_f$; $= 0$ otherwise. Let T be the event time with survival distribution $S_i(x)$ under the alternative for $i = 1, 2$. The probability of a subject in the i^{th} group having an event before calendar time t can be calculated by

$$\begin{aligned} p_i(t) &= P(T_i + Y \leq t) = \int_0^\infty P(T_i + Y \leq t | Y = x) dH(x) \\ &= \int_0^\infty P(T_i \leq t - x) dH(x) = \frac{1}{t_a} \int_0^{t \wedge t_a} \{1 - S_i(t - x)\} dx \\ &= (t \wedge t_a)/t_a - \frac{1}{t_a} \int_{(t-t_a)^+}^t S_i(x) dx. \end{aligned}$$

By letting $t = \tau$, we have the equation (9).

Appendix B: Formulae for calculating expected sample size, number of events, and study time for sequential tests with information time for survival data

For a group sequential test with information time for survival data, let \hat{s} be the stopping time for the calendar time t over $[0, \tau]$, and let \hat{s}^* be the corresponding stopping time for the corresponding information time t^* over $[0, 1]$. Let $N_a(t)$ be the number of patients enrolled by calendar time t , then for a study with uniform enrollment over $[0, t_a]$, $N_a(t) = (t/t_a)N_{max}$ for $0 < t < t_a$ and $N_a(t) = N_{max}$ for $t_a \leq t \leq \tau$, where N_{max} is the maximum sample size for the group sequential trial. For a group sequential test with K looks, assume t_1, \dots, t_K are calendar times and t_1^*, \dots, t_K^* are the corresponding information times. Assume the probability that the sequential test statistic W_t on information time stops at time t_k^* is denoted as $P_{t_k^*} = P(\hat{s}^* = t_k^*)$, which is usually available from the distribution of W_t . Under the alternative hypothesis, the expected sample size is $E[N_a(\hat{s})] = \sum_{k=1}^K N_a(t_k)P_{t_k^*}$; and the expected study duration is $E(\hat{s}) = \sum_{k=1}^K t_k P_{t_k^*}$. For the traditional method, the expected number of events is $E[d(\hat{s})] = d_{max}E_{t^*}$ with $E_{t^*} = \sum_{k=1}^K t_k^* P_{t_k^*}$, where d_{max} is the maximum number of events for the group sequential design. For the new method, the expected number of events is $E[d(\hat{s})] = \sum_{k=1}^K d_a(t_k)P_{t_k^*}$ with $d_a(t_k) = N_a(t_k)P(t_k)$, where $P(t_k) = \omega_1 p_1(t_k) + \omega_2 p_2(t_k)$ with $p_i(t_k)$ by (14).

Appendix C: R code for sample size and information time calculation

```

SIZEinfTime=function(s1, s2, x, pi, ta, tf, alpha, beta, t)
{
  ### s1 and s2 are the survival probabilities at x for groups 1 and 2 ####
  ### pi is the proportion of patients assign to group 1 #####
  ### ta and tf are the accrual time and follow-up time #####
  ### alpha and beta are the type I and II error, study power=1-beta #####
  ### for a two-sided test, input half of alpha as alpha in this function ##
  ### t is the calendar time at which to calculate the information time####
  ### one can calculate the sample size and information time for any #####
  ### distribution by change S1 and S2 to the corresponding distributions###

  z0=qnorm(1-alpha); z1=qnorm(1-beta)
  lambda1=-log(s1)/x; HR=log(s1)/log(s2)
  S1=function(t){ans=exp(-lambda1*t); return(ans)}
  S2=function(t){ans=S1(t)^(1/HR);return(ans)}
  dSC=ceiling((z0+z1)^2/(pi*(1-pi)*(log(HR))^2))##expected total number of events#
  p1=1-integrate(S1, tf, ta+tf)$value/ta
  p2=1-integrate(S2, tf, ta+tf)$value/ta
  P0=pi*p1+(1-pi)*p2
  NSC=ceiling((z0+z1)^2/(pi*(1-pi)*(log(HR))^2*P0))##Schoenfeld formula (6)#
  NXW=ceiling((z0+z1)^2*P0/(pi*(1-pi)*(log(HR))^2*p1*p2))##New formula (7)##
  dXW=ceiling(NXW*P0)
  a=t-min(t,ta); b=min(t,ta)
  pt1=b/ta-integrate(S1, a, t)$value/ta
  pt2=b/ta-integrate(S2, a, t)$value/ta
  dt=NSC*(pi*pt1+(1-pi)*pt2)
  dtau=(z0+z1)^2/(pi*(1-pi)*log(HR)^2)
  Dt=NXW*(1/(pi*pt1)+1/((1-pi)*pt2))^(-1)
  Dtau=(z0+z1)^2/log(HR)^2

```

```

td=round(dt/dtau,3) ### information time td based on traditional method #
tD=round(Dt/Dtau,3) ### information time tD based on new method #
ans=data.frame(dSC=dSC, NSC=NSC, dXW=dXW, NXW=NXW, td=td, tD=tD)
return(ans)
}
SIZEinfTime(s1=0.5, s2=0.6, x=3, pi=0.3, ta=5, tf=3, alpha=0.05, beta=0.1, t=2)
dSC NSC dXW NXW    td    tD
438 697 413 656 0.106 0.109

```