**Two Treatment Two-period Crossover Design for Recurring Disease**

Let, K = A, B; KK’ = AB, BA

Let, Xk = # recurrence of a chronic disease with treatment K in the first period.

Xkk’ = # recurrence of a chronic disease with treatment K’ in the second period, provided treatment K(≠K’) was applied in first period.

Let, U : prognostic variant or covariate, assumed to remain same for a patient in both periods, like age, sex, some genotype etc.

Also suppose U assumes G+1 ordinal categories with scores 0, 1,….., G; i.e. U is assumed to be ordinal categorical variable with, P[ U = u ] = πu say, such that,

Assuming that higher value (level) of U restricts a treatment to perform satisfactorily, i.e. higher value (level) of U reduces effect of a treatment we propose probability models as,

1. Xk|U = u ~ Poisson with, E(Xk|U = u) = λk *a*G - u , where *a* is a known prognostic index, 0<*a*<1.
2. Xkk’|Xk = xk, U = u ~ Poisson with,

Some realizations about these probability models:

1. E(Xk) = E E(Xk|U) = λk π where, π = E[*a*G - u] =

=>E(Xkk’) = λkk’π

1. If Nk patients are assigned to treatment k in first period, k=A,B

Then, NA + NB = N, N : prefixed number

|  |
| --- |
| 1 if ith patient is assigned to treatment k  0 if else |

Define, δki =

Then the joint distribution will be,

, θ = λA,λB,λAB,λBA

Define, Sk = and Skk’ =

Also, note that, Nk =

Now, E(Sk|*ḓ*k) = = λk π = λk π Nk

Var(Sk|*ḓ*k) = =

E(Skk’) = = λkk’ π = λkk’ π Nk

Var(Skk’) = = E Var(Xkk’|Xk,U) + Var E(Xkk’|Xk,U)

Again,

are the consistent estimators of λk and λkk’ respectively.

To avoid their estimates to be 0, we adjust the estimates as follows:

, where, and Nk

,

where, and Nk

Now,

Again,

where, Nk

So, where,

Since, this asymptotic distribution does not depend on allocation (n), we describe the procedures under NA = NB = n i.e. N/2 = n.

Define:-

log and log , k=A,B and k=AB,BA where is the main effect due to treatment k and is the period effect. No carryover effect is present in the model by assuming sufficiently large washout.