Supplementary Material of “Optimal allocation strategies in platform trials”

Design with concurrent controls only

In this file, we provide the derivation of the optimal allocation for trials utilising concurrent controls only. In what follows, we focus on determining the optimal solutions for the Case 3 described in the paper.

Note that Case 2 is a particular case of Case 3 when consider r3=0. By inspection of Figure 3 in the manuscript, one can see the decrease in variance compared to separate trials with respect to r2, and that the maximum variance reduction occurs for r1+r2=1, and thus for a two-period trial.

Case 3 (Section 3.3)

Set and simplify conditions

```
In[1]:= subst = {n11 → r1 * N / 2 , n01 → r1 * N / 2 ,
           n12 → r2 * N - n02 - n22 , n03 → r3 * N / 2, n23 → r3 * N / 2};
        substp = {n12 → r2 * N * p12, n22 → r2 * N * p22, n02 → r2 * N * p02, r3 → 1 - r1 - r2};
```

Define terms to optimise.

Note: *sigma*term1^(-1)/N* is the variance of the estimator of effect 1 (analogously *sigma*term2^(-1)/N* for effect 2). But since sigma and N are fixed, we simply work on term1 and term2 expressions.

```
In[3]:= term1 =
         FullSimplify[((n11 * n01 / (n11 + n01)) + (n12 * n02 / (n12 + n02))) / N /. subst /. substp]
```

Out[3]= $$\frac{r1}{4} + \frac{p02\ (-1 + p02 + p22)\ r2}{-1 + p22}$$

```
In[4]:= term2 =
         FullSimplify[(n22 * n02 / (n22 + n02) / N) + (n23 * n03 / (n23 + n03) / N) /. subst /. substp]
```

Out[4]= $$\frac{1}{4}\ (1 - r1 - r2) + \frac{p02\ p22\ r2}{p02 + p22}$$

```
In[5]:= constr = FullSimplify[term1 - term2]
```

Out[5]= $$\frac{1}{4}\left(-1 + 2\ r1 + r2 + \frac{4\ p02\ (-1 + p02 + p22)\ r2}{-1 + p22} - \frac{4\ p02\ p22\ r2}{p02 + p22}\right)$$

In[6]:=
```
e1 = Solve[D[term2, p02] == l D[constr, p02], l]
e2 = Solve[D[term2, p22] == l D[constr, p22], l]
```

Out[6]=
$$\left\{\left\{l \to \frac{4\left(\frac{p02\,p22\,r2}{(p02+p22)^2}-\frac{p22\,r2}{p02+p22}\right)}{-\frac{4\,p02\,r2}{-1+p22}-\frac{4\,(-1+p02+p22)\,r2}{-1+p22}-\frac{4\,p02\,p22\,r2}{(p02+p22)^2}+\frac{4\,p22\,r2}{p02+p22}}\right\}\right\}$$

Out[7]=
$$\left\{\left\{l \to \frac{4\left(\frac{p02\,p22\,r2}{(p02+p22)^2}-\frac{p02\,r2}{p02+p22}\right)}{-\frac{4\,p02\,r2}{-1+p22}+\frac{4\,p02\,(-1+p02+p22)\,r2}{(-1+p22)^2}-\frac{4\,p02\,p22\,r2}{(p02+p22)^2}+\frac{4\,p02\,r2}{p02+p22}}\right\}\right\}$$

In[8]:=
```
e3 = e1[[1]][[1]][[2]] == e2[[1]][[1]][[2]]
```

Out[8]=
$$\frac{4\left(\frac{p02\,p22\,r2}{(p02+p22)^2}-\frac{p22\,r2}{p02+p22}\right)}{-\frac{4\,p02\,r2}{-1+p22}-\frac{4\,(-1+p02+p22)\,r2}{-1+p22}-\frac{4\,p02\,p22\,r2}{(p02+p22)^2}+\frac{4\,p22\,r2}{p02+p22}} == \frac{4\left(\frac{p02\,p22\,r2}{(p02+p22)^2}-\frac{p02\,r2}{p02+p22}\right)}{-\frac{4\,p02\,r2}{-1+p22}+\frac{4\,p02\,(-1+p02+p22)\,r2}{(-1+p22)^2}-\frac{4\,p02\,p22\,r2}{(p02+p22)^2}+\frac{4\,p02\,r2}{p02+p22}}$$

In[9]:=
```
sol = Solve[e3, {p02}][[3]]
```

Out[9]=
$$\left\{p02 \to \frac{-1+2\,p22-2\,p22^2}{2\,(-1+p22)}\right\}$$

The solution corresponds to the optimal allocation for p02 (Section 3.3 in the paper):

In[10]:=
```
FullSimplify[sol]
```

Out[10]=
$$\left\{p02 \to \frac{1}{2-2\,p22}-p22\right\}$$

Where the optimal solution for p22 can be obtained numerically by solving the following equation:

In[11]:=
```
eq2 = Assuming[{r2 + r3 > 1 / 2, r2 + r3 < 1, p22 > 0, p22 < 1},
  FullSimplify[(term1 - term2) /. sol]]
```

Out[11]=
$$\frac{1}{4}\left(-1+2\,r1+\frac{(-2+p22\,(11+p22\,(-29+p22\,(49-4\,p22\,(13+2\,(-4+p22)\,p22)))))\,r2}{(-1+p22)^3}\right)$$

In[12]:=
```
soleq = Assuming[{p22 > 0, p22 < 1}, FullSimplify[Solve[(eq2 == 0), r2]]]
```

Out[12]=
$$\left\{\left\{r2 \to \frac{(-1+p22)^3\,(-1+2\,r1)}{(-1+2\,p22)\,(-2+p22\,(7+p22\,(-15+p22\,(19+2\,p22\,(-7+2\,p22)))))}\right\}\right\}$$