Supplementary Material of “Optimal allocation strategies in platform trials”

Design with concurrent and non-concurrent controls - Case 2

In this file, we provide the derivation of the optimal allocation for trials utilising concurrent and non-concurrent controls. Next, we focus on determining the optimal solutions for the Case 2 described in the paper.

For simplicity of calculation, in this file we start optimising using a different parametrization. We consider: r_{i,s} = n_{i,s} /N_s, where as before n_{i,s} is the sample size for arm i in the period s, and N_s is the total sample size in period s. At the end of the document we express the solutions in terms of p_{i,s} as in the paper.

Set conditions

```
In[∘]:= subst = {r11 → r1 / 2 , r01 → r1 / 2 , r02 → (1 - r1) - r12 - r22 };
```

```
In[∘]:= substp = {r12 → r2 p12, r22 → r2 p22, r02 → r2 p02, r3 → 1 - r1 - r2};
```

Define terms to optimise.

```
In[∘]:= term1 = FullSimplify[(r11 * r01 / (r11 + r01)) + (r12 * r02 / (r12 + r02)) /. subst]
```

Out[∘]=

$$\frac{r1}{4} + r12 + \frac{r12^2}{-1 + r1 + r22}$$

```
In[∘]:= term2 = FullSimplify[
   (1 / r22 + 1 / r02 - ((1 / r02) ^2 / (1 / r01 + 1 / r02 + 1 / r11 + 1 / r12))) ^ (-1) /. subst]
```

Out[∘]=

$$\frac{r22 \left(r1^2 + 4\, r12\, (-1 + r12 + r22) + r1\, (-1 + 4\, r12 + r22)\right)}{r1^2 + 4\, (-1 + r12)\, r12 + r1\, (-1 + 4\, r12)}$$

```
In[∘]:= sol = Solve[term1 == term2, r12] [[3]]
```

Out[∘]=

$$\left\{r12 \to \frac{1}{2} \left(1 - r1 - \sqrt{1 - r1 - 4\, r22 + 4\, r1\, r22 + 4\, r22^2}\right)\right\}$$

```
In[∘]:= term3 = Simplify[term1 /. sol]
```

Out[∘]=

$$\frac{r22 \left(-2 + 3\, r1 + 4\, r22 - 2 \sqrt{(1 - 2\, r22)^2 + r1\, (-1 + 4\, r22)}\right)}{4\, (-1 + r1 + r22)}$$

In[]:=
```
derivative = FullSimplify[D[term3, r22]]
```

Out[]=
$$\frac{1}{4\,(-1+r1+r22)^2}\left(r22\,(-1+r1+r22)\left(4-\frac{4\,(-1+r1+2\,r22)}{\sqrt{(1-2\,r22)^2+r1\,(-1+4\,r22)}}\right)-r22\left(-2+3\,r1+4\,r22-2\sqrt{(1-2\,r22)^2+r1\,(-1+4\,r22)}\right)+(-1+r1+r22)\left(-2+3\,r1+4\,r22-2\sqrt{(1-2\,r22)^2+r1\,(-1+4\,r22)}\right)\right)$$

In[]:=
```
sol2 = Solve[derivative == 0, r22];
```

Solve: There may be values of the parameters for which some or all solutions are not valid.

In[]:=
```
sol22 = Assuming[{r1 > 0, r1 < 1 / 2}, Simplify[sol2[[3]]]]
```

Out[]=
$$\left\{r22\to 1-r1+\frac{1}{4\sqrt{3}}\left(\sqrt{\left(\left((-1+r1)\left(9\,r1^2+6\,r1\left(-4+\left(8+36\,r1-108\,r1^2+27\,r1^3+6\sqrt{3}\sqrt{r1\,(16-72\,r1+108\,r1^2-27\,r1^3)}\right)^{1/3}\right)+\left(-2+\left(8+36\,r1-108\,r1^2+27\,r1^3+6\sqrt{3}\sqrt{r1\,(16-72\,r1+108\,r1^2-27\,r1^3)}\right)^{1/3}\right)^2\right)\right)\Big/\left(8+36\,r1-108\,r1^2+27\,r1^3+6\sqrt{3}\sqrt{r1\,(16-72\,r1+108\,r1^2-27\,r1^3)}\right)^{1/3}\right)}\right)-\frac{1}{2}\sqrt{\left(-\frac{22}{3}+8\,(-1+r1)^2+\frac{43\,r1}{3}-7\,r1^2-\frac{(-1+r1)\left(4-24\,r1+9\,r1^2\right)}{12\left(8+36\,r1-108\,r1^2+27\,r1^3+6\sqrt{3}\sqrt{r1\,(16-72\,r1+108\,r1^2-27\,r1^3)}\right)^{1/3}}-\frac{1}{12}\,(-1+r1)\left(8+36\,r1-108\,r1^2+27\,r1^3+6\sqrt{3}\sqrt{r1\,(16-72\,r1+108\,r1^2-27\,r1^3)}\right)^{1/3}+\left(\sqrt{3}\,(-1+r1)^2\,r1\left(8+36\,r1-108\,r1^2+27\,r1^3+6\sqrt{3}\sqrt{r1\,(16-72\,r1+108\,r1^2-27\,r1^3)}\right)^{1/6}\right)\Big/\left(\sqrt{\left((-1+r1)\left(9\,r1^2+6\,r1\left(-4+\left(8+36\,r1-108\,r1^2+27\,r1^3+6\sqrt{3}\sqrt{r1\,(16-72\,r1+108\,r1^2-27\,r1^3)}\right)^{1/3}\right)+\left(-2+\left(8+36\,r1-108\,r1^2+27\,r1^3+6\sqrt{3}\sqrt{r1\,(16-72\,r1+108\,r1^2-27\,r1^3)}\right)^{1/3}\right)^2\right)\right)}\right)\right)}\right\}$$

Next, we simplify the solution by defining terms a and b.

In[ ]:= **sol22a = FullSimplify[**

$$\mathrm{sol22}\ /.\ \left\{\left(8+36\,\mathrm{r1}-108\,\mathrm{r1}^2+27\,\mathrm{r1}^3+6\sqrt{3}\sqrt{\mathrm{r1}\left(16-72\,\mathrm{r1}+108\,\mathrm{r1}^2-27\,\mathrm{r1}^3\right)}\right)^{1/3}\to a\right\}\Big]$$

Out[ ]=

$$\Bigg\{\mathrm{r22}\to 1-\mathrm{r1}+\frac{\sqrt{\frac{(-1+\mathrm{r1})\left((-2+a)^2+6\,(-4+a)\,\mathrm{r1}+9\,\mathrm{r1}^2\right)}{\left(8+9\,\mathrm{r1}\,(4+3\,(-4+\mathrm{r1})\,\mathrm{r1})+6\sqrt{3}\sqrt{\mathrm{r1}\,(16-9\,\mathrm{r1}\,(8+3\,(-4+\mathrm{r1})\,\mathrm{r1}))}\right)^{1/3}}}}{4\sqrt{3}}-$$

$$\frac{1}{2}\sqrt{\left(-\frac{22}{3}-\frac{1}{12}\,a\,(-1+\mathrm{r1})+8\,(-1+\mathrm{r1})^2+\frac{43\,\mathrm{r1}}{3}-7\,\mathrm{r1}^2-\frac{(-1+\mathrm{r1})\,(4+3\,\mathrm{r1}\,(-8+3\,\mathrm{r1}))}{12\left(8+9\,\mathrm{r1}\,(4+3\,(-4+\mathrm{r1})\,\mathrm{r1})+6\sqrt{3}\sqrt{\mathrm{r1}\,(16-9\,\mathrm{r1}\,(8+3\,(-4+\mathrm{r1})\,\mathrm{r1}))}\right)^{1/3}}+\left(\sqrt{3}\,(-1+\mathrm{r1})^2\,\mathrm{r1}\left(8+9\,\mathrm{r1}\,(4+3\,(-4+\mathrm{r1})\,\mathrm{r1})+6\sqrt{3}\sqrt{\mathrm{r1}\,(16-9\,\mathrm{r1}\,(8+3\,(-4+\mathrm{r1})\,\mathrm{r1}))}\right)^{1/6}\right)\Big/\left(\sqrt{(-1+\mathrm{r1})\left((-2+a)^2+6\,(-4+a)\,\mathrm{r1}+9\,\mathrm{r1}^2\right)}\right)\right)}\Bigg\}$$

In[ ]:= **sol22ab = sol22a /. {(-2 + a)^2 + 6 (-4 + a) r1 + 9 r1^2 → b}**

Out[ ]=

$$\Bigg\{\mathrm{r22}\to 1-\mathrm{r1}+\frac{\sqrt{\frac{b\,(-1+\mathrm{r1})}{\left(8+9\,\mathrm{r1}\,(4+3\,(-4+\mathrm{r1})\,\mathrm{r1})+6\sqrt{3}\sqrt{\mathrm{r1}\,(16-9\,\mathrm{r1}\,(8+3\,(-4+\mathrm{r1})\,\mathrm{r1}))}\right)^{1/3}}}}{4\sqrt{3}}-$$

$$\frac{1}{2}\sqrt{\left(-\frac{22}{3}-\frac{1}{12}\,a\,(-1+\mathrm{r1})+8\,(-1+\mathrm{r1})^2+\frac{43\,\mathrm{r1}}{3}-7\,\mathrm{r1}^2-\frac{(-1+\mathrm{r1})\,(4+3\,\mathrm{r1}\,(-8+3\,\mathrm{r1}))}{12\left(8+9\,\mathrm{r1}\,(4+3\,(-4+\mathrm{r1})\,\mathrm{r1})+6\sqrt{3}\sqrt{\mathrm{r1}\,(16-9\,\mathrm{r1}\,(8+3\,(-4+\mathrm{r1})\,\mathrm{r1}))}\right)^{1/3}}+\frac{1}{\sqrt{b\,(-1+\mathrm{r1})}}\sqrt{3}\,(-1+\mathrm{r1})^2\,\mathrm{r1}\left(8+9\,\mathrm{r1}\,(4+3\,(-4+\mathrm{r1})\,\mathrm{r1})+6\sqrt{3}\sqrt{\mathrm{r1}\,(16-9\,\mathrm{r1}\,(8+3\,(-4+\mathrm{r1})\,\mathrm{r1}))}\right)^{1/6}\right)}\Bigg\}$$

We manually substitute some parts of the expression corresponding to term a

In[ ]:= **sol22ab2 =**

$$\mathrm{FullSimplify}\left[-\mathrm{r1}+\frac{\sqrt{\frac{b\,(-1+\mathrm{r1})}{a}}}{4\sqrt{3}}-\frac{1}{2}\sqrt{\left(-\frac{22}{3}-\frac{1}{12}\,a\,(-1+\mathrm{r1})+8\,(-1+\mathrm{r1})^2+\frac{43\,\mathrm{r1}}{3}-7\,\mathrm{r1}^2-\frac{(-1+\mathrm{r1})\,(4+3\,\mathrm{r1}\,(-8+3\,\mathrm{r1}))}{12\,a}+\frac{1}{\sqrt{b\,(-1+\mathrm{r1})}}\sqrt{3}\,(-1+\mathrm{r1})^2\,\mathrm{r1}\,(a)^{1/2}\right)}\right]$$

Out[ ]=

$$-\mathrm{r1}+\frac{\sqrt{\frac{b\,(-1+\mathrm{r1})}{a}}-\sqrt{-\frac{(-1+\mathrm{r1})\left(-12\sqrt{3}\,a^{3/2}\sqrt{b\,(-1+\mathrm{r1})}\,\mathrm{r1}+b\left(4+8\,a+a^2-12\,(2+a)\,\mathrm{r1}+9\,\mathrm{r1}^2\right)\right)}{a\,b}}}{4\sqrt{3}}$$

We compute the solution in terms of p22 by taking into account that p22=r22/(1-r1), as 1-r1=r2 in this case.

In[ ]:=
```
solp22 = FullSimplify[sol22ab2 / (1 - r1)]
```

Out[ ]=
$$\frac{12\,\text{r1}+\sqrt{3}\left(-\sqrt{\frac{b\,(-1+\text{r1})}{a}}+\sqrt{-\frac{(-1+\text{r1})\left(-12\sqrt{3}\,a^{3/2}\sqrt{b\,(-1+\text{r1})}\,\text{r1}+b\left(4+8\,a+a^2-12\,(2+a)\,\text{r1}+9\,\text{r1}^2\right)\right)}{a\,b}}\right)}{12\,(-1+\text{r1})}$$

Finally, to get the solution r12 (and hence p12), one needs to use the solution obtained for r22 (***sol22ab2***) and substitute it in the expression for r12 (***sol***).