Supplementary Material of "Optimal allocation strategies in platform trials"

Optimisation under unequal variances

Variance estimator of effect 1 under unequal variances

```
In[]:= w11 = 1 / s11^2 / ( 1 / s11^2 + 1 / s12^2)
```

$$\text{Out[]}= \frac{1}{s11^2 \left(\frac{1}{s11^2}+\frac{1}{s12^2}\right)}$$

```
In[]:= w12 = 1 / s12^2 / ( 1 / s11^2 + 1 / s12^2)
```

$$\text{Out[]}= \frac{1}{\left(\frac{1}{s11^2}+\frac{1}{s12^2}\right) s12^2}$$

```
In[]:= s11 = Sqrt[s0^2 * (rs10^2 / n11 + 1 / n01) ]
```

$$\text{Out[]}= \sqrt{\left(\frac{1}{n01}+\frac{rs10^2}{n11}\right) s0^2}$$

```
In[]:= s12 = Sqrt[s0^2 * (rs10^2 / n12 + 1 / n02) ]
```

$$\text{Out[]}= \sqrt{\left(\frac{1}{n02}+\frac{rs10^2}{n12}\right) s0^2}$$

```
In[]:= var1 = w11^2 * s11^2 + w12^2 * s12^2
```

$$\text{Out[]}= \frac{1}{\left(\frac{1}{n01}+\frac{rs10^2}{n11}\right)\left(\frac{1}{\left(\frac{1}{n01}+\frac{rs10^2}{n11}\right) s0^2}+\frac{1}{\left(\frac{1}{n02}+\frac{rs10^2}{n12}\right) s0^2}\right)^2 s0^2} + \frac{1}{\left(\frac{1}{n02}+\frac{rs10^2}{n12}\right)\left(\frac{1}{\left(\frac{1}{n01}+\frac{rs10^2}{n11}\right) s0^2}+\frac{1}{\left(\frac{1}{n02}+\frac{rs10^2}{n12}\right) s0^2}\right)^2 s0^2}$$

```
In[]:= FullSimplify[var1]
```

$$\text{Out[]}= \frac{\left(n11 + n01\, rs10^2\right)\left(n12 + n02\, rs10^2\right) s0^2}{(n01 + n02)\, n11\, n12 + n01\, n02\, (n11 + n12)\, rs10^2}$$

```
In[]:= 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};
example = {r1 → .2, r2 → .6, rs10 → 1.5, rs20 → 1, p02 → 0.41421356237309515`};
```

```
In[]:= invvar1 = Simplify[1 / (var1)]
```

$$\text{Out[]}= \frac{n02\, n11\, n12 + n01\, n02\, n12\, rs10^2 + n01\, n11\left(n12 + n02\, rs10^2\right)}{\left(n11 + n01\, rs10^2\right)\left(n12 + n02\, rs10^2\right) s0^2}$$

```
In[•]:= term1uneq = FullSimplify[invvar1 / (N / s0^2) /. subst /. substp ]
```

$$\text{Out[•]= } \frac{r1}{2+2\,rs10^2}-\frac{p02\,(-1+p02+p22)\,r2}{1-p22+p02\left(-1+rs10^2\right)}$$

```
In[•]:= eqvar1 = FullSimplify[var1 /. subst /. substp ]
```

$$\text{Out[•]= } -\frac{2\left(1+rs10^2\right)\left(1-p22+p02\left(-1+rs10^2\right)\right)s0^2}{N\left(2\,p02\,(-1+p02+p22)\,r2\left(1+rs10^2\right)+r1\left(-1+p02+p22-p02\,rs10^2\right)\right)}$$

```
In[•]:= (*Check case with equal variances*)
```

```
In[•]:= Simplify[term1uneq /. {rs10 → 1, N → 1, s0 → 1}]
```

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

Variance estimator of effect 2 under unequal variances

```
In[•]:= w22 = 1 / s22^2 / (1 / s22^2 + 1 / s23^2);
        w23 = 1 / s23^2 / (1 / s22^2 + 1 / s23^2);

        s22 = Sqrt[s0^2 * (rs20^2 / n22 + 1 / n02)];
        s23 = Sqrt[s0^2 * (rs20^2 / n23 + 1 / n03)];
```

```
In[•]:= var2 = w22^2 * s22^2 + w23^2 * s23^2
```

$$\text{Out[•]= } \frac{1}{\left(\frac{1}{n02}+\frac{rs20^2}{n22}\right)\left(\frac{1}{\left(\frac{1}{n02}+\frac{rs20^2}{n22}\right)s0^2}+\frac{1}{\left(\frac{1}{n03}+\frac{rs20^2}{n23}\right)s0^2}\right)^2 s0^2}+\frac{1}{\left(\frac{1}{n03}+\frac{rs20^2}{n23}\right)\left(\frac{1}{\left(\frac{1}{n02}+\frac{rs20^2}{n22}\right)s0^2}+\frac{1}{\left(\frac{1}{n03}+\frac{rs20^2}{n23}\right)s0^2}\right)^2 s0^2}$$

```
In[•]:= invvar2 = Simplify[1 / (var2)]
```

$$\text{Out[•]= } \frac{n03\,n22\,n23+n02\,n03\,n23\,rs20^2+n02\,n22\left(n23+n03\,rs20^2\right)}{\left(n22+n02\,rs20^2\right)\left(n23+n03\,rs20^2\right)s0^2}$$

```
In[•]:= term2uneq = FullSimplify[invvar2 / (N / s0^2) /. subst /. substp ]
```

$$\text{Out[•]= } -\frac{-1+r1+r2}{2\left(1+rs20^2\right)}+\frac{p02\,p22\,r2}{p22+p02\,rs20^2}$$

```
In[•]:= (*Check case equal variances*)
```

```
In[•]:= FullSimplify[term2uneq /. {rs20 → 1, N → 1, s0 → 1}]
```

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

```
In[•]:= eqvar2 = FullSimplify[var2 /. subst /. substp ]
```

$$\text{Out[•]= } -\frac{2\left(1+rs20^2\right)\left(p22+p02\,rs20^2\right)s0^2}{N\,p22\,(-1+r1+r2-2\,p02\,r2)+N\,p02\,(-1+r1+r2-2\,p22\,r2)\,rs20^2}$$

Optimisation

```
In[•]:= (*Constraint equal variances between treatment effect estimators*)
```

In[]:=
```
constr = FullSimplify[term1uneq - term2uneq]
```

Out[]=
$$\frac{r1}{2+2\,rs10^2}-\frac{p02\,(-1+p02+p22)\,r2}{1-p22+p02\left(-1+rs10^2\right)}+\frac{-1+r1+r2}{2\left(1+rs20^2\right)}-\frac{p02\,p22\,r2}{p22+p02\,rs20^2}$$

In[]:=
```
Simplify[(eqvar1 - eqvar2) * (N / s0^2)]
```

Out[]=
$$-\frac{2\left(1+rs10^2\right)\left(1-p22+p02\left(-1+rs10^2\right)\right)}{2\,p02\,(-1+p02+p22)\,r2\left(1+rs10^2\right)+r1\left(-1+p02+p22-p02\,rs10^2\right)}+\frac{2\,N\left(1+rs20^2\right)\left(p22+p02\,rs20^2\right)}{N\,p22\,(-1+r1+r2-2\,p02\,r2)+N\,p02\,(-1+r1+r2-2\,p22\,r2)\,rs20^2}$$

In[]:=
```
Solve[Simplify[term1uneq - term2uneq] == 0, p22] /. example
```

Out[]=
$$\{\{p22\to 0.136517\},\{p22\to 18.3645\}\}$$

In[]:=
```
FullSimplify[Solve[Simplify[term1uneq - term2uneq] == 0, p22][[2]]]
```

Out[]=
$$\Big\{p22\to \frac{1}{2\left((-1+r2)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)}\Big(-1+2\,r1+r2-rs10^2+r1\,rs10^2+r2\,rs10^2+r1\,rs20^2-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)\left(rs10^2+rs20^2\right)+p02\left(-1+rs10^2-rs20^2\right)\left((-1+r2)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)-\sqrt{\left((-1+r2)\left(1+rs10^2\right)-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)\left(rs10^2+rs20^2\right)+r1\left(2+rs10^2+rs20^2\right)+p02\left(-1+rs10^2-rs20^2\right)\left((-1+r2)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)\right)^2+4\,p02\,rs20^2\left((-1+r2)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)\left((-1+r2)\left(1+rs10^2\right)-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)+r1\left(2+rs10^2+rs20^2\right)+p02\,r1\left(-1+rs10^2\right)\left(2+rs10^2+rs20^2\right)+p02\left(1+rs10^2\right)\left(1-rs10^2+r2\left(1+rs10^2+2\,rs20^2\right)\right)\right)}\Big)\Big\}$$

In[]:=
```
solp22 = FullSimplify[Solve[Simplify[term1uneq - term2uneq] == 0, p22][[2]]]
```

Out[]=
$$\Big\{p22\to \frac{1}{2\left((-1+r2)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)}\Big(-1+2\,r1+r2-rs10^2+r1\,rs10^2+r2\,rs10^2+r1\,rs20^2-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)\left(rs10^2+rs20^2\right)+p02\left(-1+rs10^2-rs20^2\right)\left((-1+r2)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)-\sqrt{\left((-1+r2)\left(1+rs10^2\right)-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)\left(rs10^2+rs20^2\right)+r1\left(2+rs10^2+rs20^2\right)+p02\left(-1+rs10^2-rs20^2\right)\left((-1+r2)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)\right)^2+4\,p02\,rs20^2\left((-1+r2)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)\left((-1+r2)\left(1+rs10^2\right)-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)+r1\left(2+rs10^2+rs20^2\right)+p02\,r1\left(-1+rs10^2\right)\left(2+rs10^2+rs20^2\right)+p02\left(1+rs10^2\right)\left(1-rs10^2+r2\left(1+rs10^2+2\,rs20^2\right)\right)\right)}\Big)\Big\}$$

In[]:=
```
term1uneq
```

Out[]=
$$\frac{r1}{2+2\,rs10^2}-\frac{p02\,(-1+p02+p22)\,r2}{1-p22+p02\left(-1+rs10^2\right)}$$

In[•]:=
```
term2uneq
```

Out[•]=
$$-\frac{-1+r1+r2}{2\left(1+rs20^2\right)}+\frac{p02\,p22\,r2}{p22+p02\,rs20^2}$$

In[•]:=
```
term1subs = FullSimplify[term1uneq /. solp22]
```

Out[•]=
$$\left(-\left(\left(-1+\left(-1+r1\right)rs10^2-r1\,rs20^2\right)\left(1+p02\left(-1+rs10^2+rs20^2\right)\right)\right)+r2\left(1+rs10^2\right)\left(-1+p02\left(5-rs10^2+3\,rs20^2+2\,p02\left(1+rs20^2\right)\left(-2+rs10^2+rs20^2\right)\right)\right)+\sqrt{\left(\left(\left(-1+r2\right)\left(1+rs10^2\right)-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)\left(rs10^2+rs20^2\right)+r1\left(2+rs10^2+rs20^2\right)+p02\left(-1+rs10^2-rs20^2\right)\left(\left(-1+r2\right)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)\right)^2+4\,p02\,rs20^2\left(\left(-1+r2\right)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)\left(\left(-1+r2\right)\left(1+rs10^2\right)-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)+r1\left(2+rs10^2+rs20^2\right)+p02\,r1\left(-1+rs10^2\right)\left(2+rs10^2+rs20^2\right)+p02\left(1+rs10^2\right)\left(1-rs10^2+r2\left(1+rs10^2+2\,rs20^2\right)\right)\right)\right)}\Big/\left(4\left(1+rs10^2\right)\left(1+rs20^2\right)\left(1+p02\left(-1+rs10^2+rs20^2\right)\right)\right)$$

In[•]:=
```
term2subs = FullSimplify[term2uneq /. solp22]
```

Out[•]=
$$\left(-\left(\left(-1+\left(-1+r1\right)rs10^2-r1\,rs20^2\right)\left(1+p02\left(-1+rs10^2+rs20^2\right)\right)\right)+r2\left(1+rs10^2\right)\left(-1+p02\left(5-rs10^2+3\,rs20^2+2\,p02\left(1+rs20^2\right)\left(-2+rs10^2+rs20^2\right)\right)\right)+\sqrt{\left(\left(\left(-1+r2\right)\left(1+rs10^2\right)-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)\left(rs10^2+rs20^2\right)+r1\left(2+rs10^2+rs20^2\right)+p02\left(-1+rs10^2-rs20^2\right)\left(\left(-1+r2\right)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)\right)^2+4\,p02\,rs20^2\left(\left(-1+r2\right)\left(1+rs10^2\right)+r1\left(2+rs10^2+rs20^2\right)\right)\left(\left(-1+r2\right)\left(1+rs10^2\right)-2\,p02^2\,r2\left(1+rs10^2\right)\left(1+rs20^2\right)+r1\left(2+rs10^2+rs20^2\right)+p02\,r1\left(-1+rs10^2\right)\left(2+rs10^2+rs20^2\right)+p02\left(1+rs10^2\right)\left(1-rs10^2+r2\left(1+rs10^2+2\,rs20^2\right)\right)\right)\right)}\Big/\left(4\left(1+rs10^2\right)\left(1+rs20^2\right)\left(1+p02\left(-1+rs10^2+rs20^2\right)\right)\right)$$

In[•]:=
```
dfdp02 = D[term1uneq, p02]
```

Out[•]=
$$\frac{p02\left(-1+p02+p22\right)r2\left(-1+rs10^2\right)}{\left(1-p22+p02\left(-1+rs10^2\right)\right)^2}-\frac{p02\,r2}{1-p22+p02\left(-1+rs10^2\right)}-\frac{\left(-1+p02+p22\right)r2}{1-p22+p02\left(-1+rs10^2\right)}$$

In[•]:=
```
dfdp02s = Simplify[dfdp02]
```

Out[•]=
$$\frac{r2\left(2\,p02\left(-1+p22\right)+\left(-1+p22\right)^2-p02^2\left(-1+rs10^2\right)\right)}{\left(-1+p02+p22-p02\,rs10^2\right)^2}$$

In[•]:=
```
solp02 = Solve[dfdp02s == 0, p02]
```

Out[•]=
$$\left\{\left\{p02\to\frac{-1+p22}{-1+rs10}\right\},\left\{p02\to\frac{1-p22}{1+rs10}\right\}\right\}$$

In[•]:=
```
solp02[[2]] /. {p22 → .3, rs10 → 1}
```

Out[•]=
$$\{p02\to 0.35\}$$