## Supplementary Material of "Optimal allocation strategies in platform trials"

## Design with concurrent and non-concurrent controls - Case 3

We first define the treatment effect for arm 2 following the expressions presented in the supplementary material (see Section A.2). To do so, we define the matrices A, B, and C, and use equation (1.b) to to obtain point estimates

```
In[*]:= nd1 = n01 + n11
    nd2 = n02 + n12 + n22
    nd3 = n03 + n23
    A = {{nd1, 0, 0}, {0, nd2, 0}, {0, 0, nd3}}
    B = {{n11, 0}, {n12, n22}, {0, n23}}
    Cm = {{n11 + n12, 0}, {0, n22 + n23}}

Out[*]:= n01 + n11

Out[*]:= n02 + n12 + n22

Out[*]:= {{n01 + n11, 0, 0}, {0, n02 + n12 + n22, 0}, {0, 0, n03 + n23}}

Out[*]:= {{n11, 0}, {n12, n22}, {0, n23}}

Out[*]:= {{n11 + n12, 0}, {0, n22 + n23}}
```

```
In[*]:= M = FullSimplify[Inverse[Cm - Transpose[B].Inverse[A].B]]
                       Nm = \{ \{ n11 * theta11 + n12 * theta12 \}, \{ n22 * theta22 + n23 * theta23 \} \} \}
                       Collect[FullSimplify[M.Nm] [2], {theta11, theta12, theta22, theta23}]
                      w11 = (n11 (n01 + n11) n12 n22 (n03 + n23)) /
                                   (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                            n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                             n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))
                      w12 = ((n01 + n11) n12^2 n22 (n03 + n23)) /
                                   (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                            n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                             n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))
                      w22 =
                             (n22 (n11 n12 (n02 + n22) + n01 (n11 n12 + n02 (n11 + n12) + (n11 + n12) n22)) (n03 + n23))
                                   (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                            n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                             n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))
                      w23 =
                              ((n11 n12 (n02 + n22) + n01 (n11 n12 + n02 (n11 + n12) + (n11 + n12) n22)) n23 (n03 + n23)) /
                                   (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                            n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                             n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))
                       sol = M.Nm
                       True ===
                            FullSimplify[sol[2][1] == w11 * theta11 + w12 * theta12 + w22 * theta22 + w23 * theta23]
Out = \{ \{ ((n01 + n11) (n03 (n02 + n12) n22 + n03 (n02 + n12) n23 + (n02 + n03 + n12) n22 n23) \} / \{ ((n01 + n11) (n03 (n02 + n12) n22 + n03 (n02 + n12) n23 + (n02 + n03 + n12) n22 n23) \} / \{ ((n01 + n11) (n03 (n02 + n12) n22 + n03 (n02 + n12) n23 + (n02 + n03 + n12) n22 + n03 (n02 + n12) n23 + (n02 + n03 + n
                                         (n01 n03 (n11 n12 + n02 (n11 + n12)) n22 +
                                                  n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23))
                                    \left( \; \left( \; \mathsf{n01} + \mathsf{n11} \right) \; \mathsf{n12} \; \mathsf{n22} \; \left( \; \mathsf{n03} + \mathsf{n23} \right) \; \right) \; / \; \left( \; \mathsf{n11} \; \mathsf{n12} \; \left( \; \mathsf{n02} \; \mathsf{n03} \; \mathsf{n22} + \mathsf{n03} \; \mathsf{n22} \; \mathsf{n23} + \mathsf{n02} \; \left( \; \mathsf{n03} + \mathsf{n22} \right) \; \mathsf{n23} \right) \; + \; \left( \; \mathsf{n03} + \mathsf{n23} \right) \; \right) \; / \; \left( \; \mathsf{n03} + \mathsf{n03} \; \mathsf{n22} + \mathsf{n03} \; \mathsf{n23} + \mathsf{n02} \; \mathsf{n03} + \mathsf{n22} \right) \; ) \; / \; \left( \; \mathsf{n03} + \mathsf{n23} \right) \; \rangle \; / \; \left( \; \mathsf{n03} + \mathsf{n23} \right) \; \rangle \; / \; \left( \; \mathsf{n03} + \mathsf{n23} \right) \; \rangle \; / \; \left( \; \mathsf{n03} + \mathsf{n23} \right) \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23} \rangle \; / \; \langle \; \mathsf{n03} + \mathsf{n23}
                                                  n01 \ (n03 \ n11 \ n12 \ n22 \ + \ (n03 \ n11 \ n12 \ + \ n11 \ n12 \ n22 \ + \ n03 \ (n11 \ + \ n12) \ n22) \ n23 \ + \ n23 \ + \ n24 \ n24 \ n24 \ + \ n24 \ n
                                                                  n02 (n11 + n12) (n22 n23 + n03 (n22 + n23)))))
                             \{ ((n01 + n11) n12 n22 (n03 + n23)) / (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) + (n01 + n11) n12 n22 (n03 + n23) \}
                                                  n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                                  n02 (n11 + n12) (n22 n23 + n03 (n22 + n23)))),
                                   ((n11 n12 (n02 + n22) + n01 (n11 n12 + n02 (n11 + n12) + (n11 + n12) n22)) (n03 + n23))
                                         (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                                  n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                                  n02 \ (n11 + n12) \ (n22 \ n23 + n03 \ (n22 + n23) \ ) \ ) \ ) \ \} \ \}
Out[*] = \{ \{ n11 \text{ theta} 11 + n12 \text{ theta} 12 \}, \{ n22 \text{ theta} 22 + n23 \text{ theta} 23 \} \}
```

```
Out[\circ] =  { (n11 (n01 + n11) n12 n22 (n03 + n23) theta11) /
                                           (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                                     n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                                      n02 (n11 + n12) (n22 n23 + n03 (n22 + n23)))) +
                                     ((n01 + n11) n12^2 n22 (n03 + n23) theta12) /
                                           (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                                     n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                                      n02 (n11 + n12) (n22 n23 + n03 (n22 + n23)))) +
                                      (\,n22\ (\,n11\ n12\ (\,n02+n22\,)\ +\ n01\ (\,n11\ n12+n02\ (\,n11+n12\,)\ +\ (\,n11+n12\,)\ n22\,)\,\,)
                                                       (n03 + n23) theta22) / (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                                     n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                                      n02 (n11 + n12) (n22 n23 + n03 (n22 + n23)))) +
                                     ((n11 n12 (n02 + n22) + n01 (n11 n12 + n02 (n11 + n12) + (n11 + n12) n22))
                                                     n23 (n03 + n23) theta23) /
                                           (\,n11\;n12\;\left(\,n02\;n03\;n22\,+\,n03\;n22\;n23\,+\,n02\;\left(\,n03\,+\,n22\right)\;n23\,\right) \;\;+
                                                     n01 \ (n03 \ n11 \ n12 \ n22 \ + \ (n03 \ n11 \ n12 \ + \ n11 \ n12 \ n22 \ + \ n03 \ (n11 \ + \ n12) \ n22) \ n23 \ + \ n23 \ + \ n24 \ n24 \ n24 \ + \ n24 \ n
                                                                      n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))
Outfe]= (n11 (n01 + n11) n12 n22 (n03 + n23))
                                (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                         n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                          n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))
n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                          n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))
(n11 \ n12 \ (n02 \ n03 \ n22 + n03 \ n22 \ n23 + n02 \ (n03 + n22) \ n23) \ +
                                          n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 + n03 (n11 + n12) n23 + n03 (n1
                                                           n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))
\textit{Out[s]} = \left( \; (\; \mathsf{n11}\; \mathsf{n12}\; (\; \mathsf{n02}\; +\; \mathsf{n22}\; )\; \; +\; \mathsf{n01}\; (\; \mathsf{n11}\; \mathsf{n12}\; +\; \mathsf{n02}\; (\; \mathsf{n11}\; +\; \mathsf{n12}\; )\; \; +\; (\; \mathsf{n11}\; +\; \mathsf{n12}\; )\; \; \mathsf{n22}\; )\; \; \mathsf{n23}\; (\; \mathsf{n03}\; +\; \mathsf{n23}\; )\; \right)\; / \; |\; \mathsf{n23}\; (\; \mathsf{n03}\; +\; \mathsf{n23}\; )\; |\; \mathsf{n23}\; )\; |\; \mathsf{n23}\; (\; \mathsf{n23}\; )\; |\; \mathsf{n23}\; )\; |\; \mathsf{n23}\; |
                                (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                         n01 (n03 n11 n12 n22 + (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22) n23 +
                                                          n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))
```

```
\textit{Out} = \text{ } \left\{ \; \left( \; \left( \; \mathsf{n01} + \mathsf{n11} \right) \; \; \left( \; \mathsf{n03} \; \; \left( \; \mathsf{n02} + \mathsf{n12} \right) \; \; \mathsf{n22} + \mathsf{n03} \; \; \left( \; \mathsf{n02} + \mathsf{n12} \right) \; \; \mathsf{n23} \; + \; \; \left( \; \mathsf{n02} + \mathsf{n03} + \mathsf{n12} \right) \; \; \mathsf{n22} \; \mathsf{n23} \right\} \right\} 
                                                                                             (n11 \; theta11 + n12 \; theta12) \; ) \; / \; (n01 \; n03 \; (n11 \; n12 + n02 \; (n11 + n12) \; ) \; n22 \; + \; (n11 \; theta11 + n12 \; theta12) \; ) \; ) \; )
                                                                                          n01 \ (n03 \ n11 \ n12 + n11 \ n12 \ n22 + n03 \ (n11 + n12) \ n22 + n02 \ (n11 + n12) \ (n03 + n22) \ ) \ n23 + n22 \ )
                                                                                          n11\;n12\;\left(\,n02\;n03\;n22\,+\,n03\;n22\;n23\,+\,n02\;\left(\,n03\,+\,n22\right)\;n23\,\right)\,\,)\,\,+
                                                                   ((n01 + n11) n12 n22 (n03 + n23) (n22 theta22 + n23 theta23)) /
                                                                           (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                                                                          n01 \ (n03 \ n11 \ n12 \ n22 \ + \ (n03 \ n11 \ n12 \ + \ n11 \ n12 \ n22 \ + \ n03 \ (n11 \ + \ n12) \ n22) \ n23 \ + \ n23 \ + \ n24 \ n24 \ + \ n
                                                                                                                     n02 (n11 + n12) (n22 n23 + n03 (n22 + n23))))),
                                                 \{ ((n01 + n11) n12 n22 (n03 + n23) (n11 theta11 + n12 theta12)) / 
                                                                           (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                                                                          n01 \ (n03 \ n11 \ n12 \ n22 \ + \ (n03 \ n11 \ n12 \ + \ n11 \ n12 \ n22 \ + \ n03 \ (n11 \ + \ n12) \ n22) \ n23 \ + \ n23 \ + \ n24 \ n24 \ + \ n
                                                                                                                     n02 \ (n11 + n12) \ (n22 \ n23 + n03 \ (n22 + n23) \ ) \ ) \ +
                                                                   \left( \; \left( \; n11\; n12 \; \left( \; n02 \; + \; n22 \right) \; + \; n01 \; \left( \; n11\; n12 \; + \; n02 \; \left( \; n11 \; + \; n12 \right) \; + \; \left( \; n11 \; + \; n12 \right) \; \; n22 \right) \; \right)
                                                                                               (n03 + n23) (n22 theta22 + n23 theta23)) /
                                                                           (n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23) +
                                                                                           n01 \ (n03 \ n11 \ n12 \ n22 + \ (n03 \ n11 \ n12 + n11 \ n12 \ n22 + n03 \ (n11 + n12) \ n22) \ n23 + n03 \ (n11 + n12) \ n22) \ n23 + n03 \ (n11 + n12) \ n23 + n03 \ (n11
                                                                                                                   n02 \ (n11 + n12) \ (n22 \ n23 + n03 \ (n22 + n23) \ ) \ ) \ ) \ \} \ \}
```

Out[\*]= True

## Variance computation

To compute the variance of treatment effect 2, first note Var(theta2) = Var(w11\*theta11+w12\*theta12+w22\*theta22+w23\*theta23)

```
lnf = l = theta11 = n01 / (n01 + n11) * (y11 - y01);
     theta12 = (n02 + n22) / (n02 + n12 + n22) * y12 -
         ((n02 / (n02 + n12 + n22)) * y02 + (n22 / (n02 + n12 + n22)) * y22);
     theta22 = (n02 + n12) / (n02 + n12 + n22) * y22 -
         ((n02 / (n02 + n12 + n22)) * y02 + (n12 / (n02 + n12 + n22)) * y12);
     theta23 = n03 / (n03 + n23) * (y23 - y03);
     expr = w11 * theta11 + w12 * theta12 + w22 * theta22 + w23 * theta23;
     Collect[FullSimplify[expr], {y01, y11, y02, y12, y22, y03, y23}];
     expr01 = FullSimplify[
         (-n01 n03 n11 n12 n22 - n01 n11 n12 n22 n23) / (n01 n03 (n11 n12 + n02 (n11 + n12)) n22 +
            n01 (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22 + n02 (n11 + n12) (n03 + n22)) n23 +
            n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23))];
     expr02 = FullSimplify[
         (-n01 n02 n03 n11 n22 - n01 n02 n03 n12 n22 - n02 n03 n11 n12 n22 - n01 n02 n11 n22 n23 -
            n01 n02 n12 n22 n23 - n02 n11 n12 n22 n23) / (n01 n03 (n11 n12 + n02 (n11 + n12)) n22 +
            n01 (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22 + n02 (n11 + n12) (n03 + n22)) n23 +
            n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23))];
     expr03 = FullSimplify[
         (-n01 n03 n11 n12 n23 - n02 n03 n11 n12 n23 - n03 n11 n12 n22 n23 - n01 n03 n11 (n02 + n22)
              n23 - n01 n03 n12 (n02 + n22) n23) / (n01 n03 (n11 n12 + n02 (n11 + n12)) n22 +
            n01 (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22 + n02 (n11 + n12) (n03 + n22)) n23 +
            n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23))];
     expr11 = FullSimplify[
         (n01 n03 n11 n12 n22 + n01 n11 n12 n22 n23) / (n01 n03 (n11 n12 + n02 (n11 + n12)) n22 +
            n01 (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22 + n02 (n11 + n12) (n03 + n22)) n23 +
            n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23))];
     expr12 = FullSimplify[
         (-n01 n03 n11 n12 n22 - n01 n11 n12 n22 n23) / (n01 n03 (n11 n12 + n02 (n11 + n12)) n22 +
            n01 (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22 + n02 (n11 + n12) (n03 + n22)) n23 +
            n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23))];
     expr22 = FullSimplify[
         (n02 n03 n11 n12 n22 + n01 n03 (n11 n12 + n02 (n11 + n12)) n22 + n01 n02 n12 n22 n23 + n02 n11
              n12 n22 n23 + n01 n11 (n02 + n12) n22 n23) / (n01 n03 (n11 n12 + n02 (n11 + n12)) n22 +
            n01 (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22 + n02 (n11 + n12) (n03 + n22)) n23 +
            n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23))];
     expr23 = FullSimplify[ (n02 n03 n11 n12 n23 + n03 n11 n12 n22 n23 +
            n01 n03 (n11 n12 + n02 (n11 + n12) + (n11 + n12) n22) n23) /
          (n01 n03 (n11 n12 + n02 (n11 + n12)) n22 +
            n01 (n03 n11 n12 + n11 n12 n22 + n03 (n11 + n12) n22 + n02 (n11 + n12) (n03 + n22)) n23 +
            n11 n12 (n02 n03 n22 + n03 n22 n23 + n02 (n03 + n22) n23))];
     FullSimplify[
       Collect[FullSimplify[expr], {y01, y11, y02, y12, y22, y03, y23}] == expr01 * y01 +
          expr02 * y02 + expr03 * y03 + expr11 * y11 + expr12 * y12 + expr22 * y22 + expr23 * y23];
```

Variance expression is then term2s\*sigma^2/N, where

```
Infa := term2f = FullSimplify[expr01^2 * y01 + expr02^2 * y02 + expr03^2 * y03 + expr11^2 * y11 +
               expr12^2 * y12 + expr22^2 * y22 + expr23^2 * y23 /. {<math>y01 \rightarrow 1 / n01, y02 \rightarrow 1 / n02,
               y03 \rightarrow 1 / n03, y11 \rightarrow 1 / n11, y12 \rightarrow 1 / n12, y22 \rightarrow 1 / n22, y23 \rightarrow 1 / n23];
       term2s =
          FullSimplify[term2f /. {n01 \rightarrow r01 * Nt, n02 \rightarrow r02 * Nt, n03 \rightarrow r03 * Nt, n11 \rightarrow r11 * Nt,
                n12 \rightarrow r12 * Nt, n22 \rightarrow r22 * Nt, n23 \rightarrow r23 * Nt \}] * Nt;
       Define terms to optimise
In[@]:= substp =
          \{r11 \rightarrow r1 p11, r12 \rightarrow r2 p12, r22 \rightarrow r2 p22, r02 \rightarrow r2 p02, r23 \rightarrow r3 p23, r3 \rightarrow 1 - r1 - r2\};
ln[*]:= subst = {r11 \rightarrow r1 / 2, r01 \rightarrow r1 / 2, r23 \rightarrow r3 / 2, r03 \rightarrow r3 / 2, r02 \rightarrow r2 - r12 - r22 };
       term1 = FullSimplify[(r11 * r01 / (r11 + r01)) + (r12 * r02 / (r12 + r02)) /. subst /. substp]
       term2 = FullSimplify[(1 / term2s) /. subst /. substp]
Out[\sigma]= (r1^2 + r1(-1 + (-4(-1 + p12) p12 + (1 - 2 p22)^2) r2) + 4 p12 r2
             (-1 + p12 + r2 + 4 (-1 + p22) p22 r2 + p12 (-1 + 4 p22) r2) / (-4 r1 + 16 (-1 + p12) p12 r2)
ln[*]:= substg = {r01 \rightarrow r1 - r11, r03 \rightarrow r3 - r23, r02 \rightarrow r2 - r12 - r22 };
       termg1 =
        FullSimplify[(r11 * r01 / (r11 + r01)) + (r12 * r02 / (r12 + r02)) /. substg /. substp]
       termg2 = FullSimplify[(1 / term2s) /. substg /. substp]
\textit{Out[*]$= p11 (r1-p11r1) } + \frac{p12 (-1+p12+p22) \ r2}{-1+p22}
```

## Numerical example: optimisation assuming balanced design in periods 1 and 3

```
ln[-]:= ex = \{r1 \rightarrow 0.1, r2 \rightarrow 0.8, r3 \rightarrow 0.1\};
       FindMinimum [\{(-term1) / . ex, term1 = term2 / . ex, p12 > 0, p22 > 0\},
        \{\{p12, r2/3/.ex\}, \{p22, r2/3/.ex\}\}\}
Out[\circ]= {-0.164091, {p12 \rightarrow 0.303787, p22 \rightarrow 0.289682}}
```

Optimisation (approach 1) - here we do not assume balanced design in periods 1 and 3 and thus also allocation rates in periods 1 and 3 are optimized

 $\frac{\text{p22 r2 } \left(- \text{ ( } \left(-1+\text{p11} \right) \text{ p11 } \left(-1+\text{p22} \right) \text{ r1} \right) \text{ } + \text{p12 } \left(-1+\text{p12}+\text{p22} \right) \text{ } \text{r2} \right)}{\left(-1+\text{p11} \right) \text{ p11 r1} + \left(-1+\text{p12} \right) \text{ p12 r2}} \text{ } + \text{p23 r3 } \left(1 + \frac{\text{p23 r3}}{-1+\text{r1}+\text{r2}} \right)$ 

```
ln[-]:= ex = \{r1 \rightarrow 0.4, r2 \rightarrow 0.4, r3 \rightarrow 0.2\};
      FindMinimum[{(-termg1) /. ex, termg1 == termg2 /. ex,
         p12 > 0, p22 > 0, p11 > 0, p23 > 0, p11 < 1, p23 < 1,
       {{p11, r1/2/. ex}, {p12, r2/3/. ex}, {p22, r2/3/. ex}, {p23, r3/2/. ex}}]
Out[*] = {-0.144071, {p11 \rightarrow 0.5, p12 \rightarrow 0.153829, p22 \rightarrow 0.457912, p23 \rightarrow 0.5}}
```

$$\begin{array}{l} \textit{In[e]} = & \text{FindMinimum} \Big[ \\ & \{-\text{termg1} \ /. \ \text{ex}, \ \text{termg1} = \text{termg2} \ /. \ \text{ex}, \ \text{p12} > \emptyset, \ \text{p22} > \emptyset, \ \text{p11} > \emptyset, \ \text{p23} > \emptyset, \ \text{p11} < 1, \ \text{p23} < 1\}, \\ & \Big\{ \Big\{ \text{p11}, \frac{\text{r1}}{2} \ /. \ \text{ex} \Big\}, \ \Big\{ \text{p12}, \frac{\text{r2}}{3} \ /. \ \text{ex} \Big\}, \ \Big\{ \text{p22}, \frac{\text{r2}}{3} \ /. \ \text{ex} \Big\}, \ \Big\{ \text{p23}, \frac{\text{r3}}{2} \ /. \ \text{ex} \Big\} \Big\} \Big] \\ & \textit{Out[e]} = \{ -\emptyset.144071, \ \{ \text{p11} \rightarrow \emptyset.5, \ \text{p12} \rightarrow \emptyset.153829, \ \text{p22} \rightarrow \emptyset.457912, \ \text{p23} \rightarrow \emptyset.5 \} \} \\ & \textit{In[e]} = \{ \text{termg2} \\ & \textit{Out[e]} = \frac{\text{p22} \ \text{r2} \ (-((-1+\text{p11}) \ \text{p11} \ (-1+\text{p22}) \ \text{r1}) + \text{p12} \ (-1+\text{p12} + \text{p22}) \ \text{r2})}{(-1+\text{p11}) \ \text{p11} \ \text{r1} + (-1+\text{p12}) \ \text{p12} \ \text{r2}} + \text{p23} \ \text{r3} \ \Big( 1 + \frac{\text{p23} \ \text{r3}}{-1+\text{r1} + \text{r2}} \Big) \\ & \textit{In[e]} = \{ \Big\{ \text{p11}, \frac{\text{r1}}{2} \ /. \ \text{ex} \Big\}, \ \Big\{ \text{p12}, \frac{\text{r2}}{3} \ /. \ \text{ex} \Big\}, \ \Big\{ \text{p22}, \frac{\text{r2}}{3} \ /. \ \text{ex} \Big\}, \ \Big\{ \text{p23}, \frac{\text{r3}}{2} \ /. \ \text{ex} \Big\} \Big\} \\ & \textit{Out[e]} = \{ \{ \text{p11}, \emptyset.2 \}, \ \{ \text{p12}, \emptyset.133333 \}, \ \{ \text{p22}, \emptyset.1333333 \}, \ \{ \text{p23}, \emptyset.1 \} \} \\ \end{aligned}$$

Note that we cannot find analytical solutions, but the numerical solutions satisfy that the optimal design follows a balanced design in periods 1 and 3.

Optimisation (approach 2) - assume balanced designs in periods 1 and 3

```
In[*]:= constr = term1 - term2;
   In[*]:= e1 = FullSimplify[Solve[D[term1, p12] == lD[constr, p12], l]]
                                      e2 = FullSimplify[Solve[D[term1, p22] == 1D[constr, p22], 1]]
                                      e3 = e1[1][1][2] = e2[1][1][2]
 Out[*]= \left\{ \left\{ 1 \rightarrow \left( (-1 + 2 p12 + p22) (r1 - 4 (-1 + p12) p12 r2)^2 \right) \right\} \right\}
                                                                         ((-1+2p12+p22) r1^2-8p12 (2p12^2+p12 (-3+p22) - (-1+p22) (1+p22^2)) r1 r2+(-1+p22) r1^2-8p12 (2p12^2+p12 (-3+p22) - (-1+p22)) r1^2-8p12 (-3+p22) r1^2-8p12 (-
                                                                                          16 p12^{2} (-1 + p12 + p22) (1 + 2 p12^{2} + p22^{2} - p12 (3 + p22)) r2^{2})
\textit{Out[*]} = \left\{ \left\{ 1 \rightarrow \left( \text{p12}^2 \ \left( -\text{r1} + 4 \ \left( -1 + \text{p12} \right) \ \text{p12} \ \text{r2} \right) \right. \right) \right. \\ \left. \left. \left( -\text{p12}^2 \ \text{r1} + \left( -1 + \text{p22} \right)^2 \ \left( -1 + 2 \ \text{p22} \right) \ \text{r1} + \left( -1 + 2 \ \text{p22} \right)^2 \right\} \right\} \right\} \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right\} \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left. \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left( -1 + 2 \ \text{p22} \right) \\ \left( -1 + 2 \ \text{p22} \right) \right] \left( -1 + 2 \ \text{p22} \right) \\ \left
                                                                                         4 p12 (-1 + p12 + p22) (1 + p12^2 - (3 + p12) p22 + 2 p22^2) r2) \}
 Out[\sigma]= ((-1 + 2 p12 + p22) (r1 - 4 (-1 + p12) p12 r2)^2)
                                                          16 p12^{2} (-1 + p12 + p22) (1 + 2 p12^{2} + p22^{2} - p12 (3 + p22)) r2^{2} =
                                                  \left(p12^{2} \left(-r1+4 \left(-1+p12\right) p12 r2\right)\right) / \left(-p12^{2} r1+\left(-1+p22\right)^{2} \left(-1+2 p22\right) r1+
                                                                         4 p12 (-1 + p12 + p22) (1 + p12^2 - (3 + p12) p22 + 2 p22^2) r2)
```

In[\*]:= sol2 = Solve[e3, {p12}];

```
In[*]:= solsim = Simplify[sol2[7]]]
```

In[\*]:= \$Assumptions = p12 > 0 && p22 > 0 && Element[p12, Reals] && Element[p22, Reals]

 $Out[\#]= p12 > 0 \&\& p22 > 0 \&\& p12 \in \mathbb{R} \&\& p22 \in \mathbb{R}$ 

In[@]:= Re[solsim]

$$\begin{array}{l} \text{Out} = \frac{1}{24 \; (-1 + \text{p22}) \; \text{r2}} \; \left( -4 \; \left( 3 - 6 \, \text{p22} + 2 \, \text{p22}^2 \right) \; \text{r2} + \left( 2 \times 2^{1/3} \; \left( 1 - i \; \sqrt{3} \; \right) \; \text{r2} \; \left( \left( 3 - 9 \, \text{p22} + 6 \, \text{p22}^2 \right) \; \text{r1} + 2 \right) \right) \right) \\ = \left( 3 - 12 \, \text{p22} + 18 \, \text{p22}^2 - 12 \, \text{p22}^3 + 4 \, \text{p22}^4 \right) \; \text{r2} \right) \right) \left/ \; \left( -9 \, \text{p22}^2 \; \text{r1} \; \text{r2}^2 + 27 \, \text{p22}^3 \; \text{r1} \; \text{r2}^2 - 18 \, \text{p22}^4 \; \text{r1} \; \text{r2}^2 + 18 \, \text{p22}^2 \; \text{r2}^3 - 72 \, \text{p22}^3 \; \text{r2}^3 + 108 \, \text{p22}^4 \; \text{r2}^3 - 72 \, \text{p22}^5 \; \text{r2}^3 + 16 \, \text{p22}^6 \; \text{r2}^3 + 2 \right) \right) \right) \\ = \left( 72^3 \; \left( -4 \; \left( \left( 3 - 9 \, \text{p22} + 6 \, \text{p22}^2 \right) \; \text{r1} + \left( 3 - 12 \, \text{p22} + 18 \, \text{p22}^2 - 12 \, \text{p22}^3 + 4 \, \text{p22}^4 \right) \; \text{r2} \right) \right)^3 + 2 \right) \\ = \left( 2 \; \left( 9 - 36 \, \text{p22} + 54 \, \text{p22}^2 - 36 \, \text{p22}^3 + 8 \, \text{p22}^4 \right) \; \text{r2} \right)^2 \right) \right)^{1/3} + 2 \\ = 2^{2/3} \; \left( 1 + i \; \sqrt{3} \; \right) \; \left( -9 \, \text{p22}^2 \; \text{r1} \; \text{r2}^2 + 27 \, \text{p22}^3 \; \text{r1} \; \text{r2}^2 - 18 \, \text{p22}^4 \; \text{r1} \; \text{r2}^2 + 18 \, \text{p22}^2 \; \text{r2}^3 - 72 \, \text{p22}^3 \; \text{r2}^3 + 108 \, \text{p22}^4 \; \text{r2}^3 - 72 \, \text{p22}^5 \; \text{r2}^3 + 16 \, \text{p22}^6 \; \text{r2}^3 + 2 \right) \\ = \left( 72^3 \; \left( -4 \; \left( \left( 3 - 9 \, \text{p22} + 6 \, \text{p22}^2 \right) \; \text{r1} + \left( 3 - 12 \, \text{p22} + 18 \, \text{p22}^2 - 12 \, \text{p22}^3 + 4 \, \text{p22}^4 \right) \; \text{r2} \right)^3 + 2 \right) \right) \right)^{1/3} + 2 \right) \\ = \left( 72^3 \; \left( -4 \; \left( \left( 3 - 9 \, \text{p22} + 6 \, \text{p22}^2 \right) \; \text{r1} + \left( 3 - 12 \, \text{p22} + 18 \, \text{p22}^2 - 12 \, \text{p22}^3 + 4 \, \text{p22}^4 \right) \; \text{r2} \right)^3 + 2 \right) \right) \right)^{1/3} + 2 \right) \\ = \left( 72^3 \; \left( -4 \; \left( \left( 3 - 9 \, \text{p22} + 6 \, \text{p22}^2 \right) \; \text{r1} + \left( 3 - 12 \, \text{p22} + 18 \, \text{p22}^2 - 12 \, \text{p22}^3 + 4 \, \text{p22}^4 \right) \; \text{r2} \right)^3 + 2 \right) \right) \right)^{1/3} + 2 \right) \\ = \left( 72^3 \; \left( -4 \; \left( \left( 3 - 9 \, \text{p22} + 6 \, \text{p22}^2 \right) \; \text{r1} + \left( 3 - 12 \, \text{p22} + 18 \, \text{p22}^2 - 12 \, \text{p22}^3 + 4 \, \text{p22}^4 \right) \; \text{r2} \right)^3 + 2 \right) \right) \right)^{1/3} + 2 \right) \right) \right) \right) \right) \right) \right) \left( -9 \; \text{p22} + 6 \; \text{p22} \right) \left( -2 \; \text{p22} + 2 \; \text{p22} \right) \left( -2 \; \text{p22} + 2 \; \text{p22} \right) \left( -2 \; \text{p22} + 2 \; \text{p22} \right) \right) \right) \right) \right) \right) \right) \right) \left( -2 \; \text{p22} + 2 \; \text{p22} \right) \right) \right) \left( -2 \; \text{p22} + 2 \; \text{p22}$$

 $ln[-]:= sol2 /. ex /. p22 \rightarrow 0.23 / 0.8$ 

$$\begin{array}{l} \text{Out[*]=} \ \left\{ \left. \{ p12 \rightarrow -0.207107 \right\} \text{, } \left\{ p12 \rightarrow 1.20711 \right\} \text{, } \left\{ p12 \rightarrow -0.196053 \right\} \text{,} \\ \\ \left\{ p12 \rightarrow 0.908553 \right\} \text{, } \left\{ p12 \rightarrow 0.866963 - 5.55112 \times 10^{-17} \ \text{i} \right\} \text{,} \\ \\ \left\{ p12 \rightarrow -0.185879 - 2.77556 \times 10^{-17} \ \text{i} \right\} \text{, } \left\{ p12 \rightarrow 0.329662 + 1.11022 \times 10^{-16} \ \text{i} \right\} \right\} \end{array}$$

```
In[@]:= eq = FullSimplify[term1 - term2]
\textit{Out[*]=} \  \  \, \frac{1}{4} \  \, \left( \texttt{r1} + \frac{4 \ \texttt{p12} \  \, \left( -1 + \texttt{p12} + \texttt{p22} \right) \  \, \texttt{r2}}{-1 + \texttt{p22}} \right. + \\
                                                                      \frac{1}{r1-4\ (-1+p12)\ p12\ r2}\left(r1^{2}+r1\ \left(-1+\left(-4\ (-1+p12)\ p12+\ (1-2\ p22)\ ^{2}\right)\ r2\right)+ \left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right)\left(-1+p12\right
                                                                                      4 p12 r2 (-1 + p12 + r2 + 4 (-1 + p22) p22 r2 + p12 (-1 + 4 p22) r2))
    In[*]:= eq3 = FullSimplify[e3]
  Out[*]= (r1-4(-1+p12) p12 r2) (p12^2/(-p12^2 r1+(-1+p22)^2(-1+2p22) r1+(-1+p22)^2) r1+(-1+p12) r1+(-
                                                                                                         4 p12 (-1 + p12 + p22) (1 + p12^2 - (3 + p12) p22 + 2 p22^2) r2) +
                                                                                ((-1+2p12+p22)(r1-4(-1+p12)p12r2))
                                                                                        ((-1+2 p12+p22) r1^2-8 p12 (2 p12^2+p12 (-3+p22) - (-1+p22) (1+p22^2)) r1 r2+p12 (-1+p22) r1^2-8 p12 (2 p12^2+p12 (-3+p22) - (-1+p22) (1+p22^2)) r1 r2+p12 (-1+p22) r1^2-8 p12 (2 p12^2+p12 (-3+p22) - (-1+p22) (1+p22^2)) r1 r2+p12 (-1+p22) r1^2-8 p12 (2 p12^2+p12 (-3+p22) - (-1+p22) (1+p22^2)) r1 r2+p12 (-1+p22) r1^2-8 p12 (2 p12^2+p12 (-3+p22) - (-1+p22) (1+p22^2)) r1 r2+p12 (-1+p22) r1^2-8 p12 (-1+p22
                                                                                                         16 p12^{2} (-1 + p12 + p22) (1 + 2 p12^{2} + p22^{2} - p12 (3 + p22)) r2^{2}) = 0
    In[@]:= NSolve[{eq == 0 /. ex, eq3 /. ex}, {p12, p22}]
  Out[\sigma]= \left\{ \left\{ p22 \rightarrow -28\,924.1 + 18\,543.2 \,\,\dot{\mathbb{1}} \,,\,\, p12 \rightarrow -0.249998 + 9.81706 \times 10^{-7} \,\,\dot{\mathbb{1}} \, \right\} \,,\,\, \right\}
                                                     \left\{\,p22\rightarrow\,-\,0.0311394\,+\,0.265623\,\,\dot{\mathbbm{1}}\,\text{, }p12\rightarrow\,-\,0.211592\,+\,0.0051594\,\,\dot{\mathbbm{1}}\,\right\} ,
                                                     \{p22 \rightarrow -0.0311394 - 0.265623 \, i, \, p12 \rightarrow -0.211592 - 0.0051594 \, i\}
                                                     \{\, p22 \rightarrow -\, 0.0311394 + 0.265623 \,\, \dot{\mathbbm{1}} \,, \, p12 \rightarrow -\, 0.211592 + 0.0051594 \,\, \dot{\mathbbm{1}} \,\} ,
                                                     \{p22 \rightarrow 0.457912, p12 \rightarrow 0.153829\}, \{p22 \rightarrow 0.457912, p12 \rightarrow 0.153829\},
                                                     \{\,p22\rightarrow0.7153+0.205041\,\,\dot{\mathbbm{1}}\,,\,\,p12\rightarrow0.151828-0.155807\,\,\dot{\mathbbm{1}}\,\} ,
                                                     \{p22 \rightarrow 0.7153 - 0.205041 i, p12 \rightarrow 0.151828 + 0.155807 i\}
                                                     \{p22 \rightarrow 1.84182, p12 \rightarrow 1.94225\}, \{p22 \rightarrow 0.5, p12 \rightarrow 0.5\}, \{p22 \rightarrow 0.5, p12 \rightarrow 0.5\},
                                                     \{p22 \rightarrow 0.117486 - 0.930047 \ \text{i}, \ p12 \rightarrow 1.17003 + 0.720353 \ \text{i} \}
                                                     \{\,p22\rightarrow0.117486\,+\,0.930047\,\,\dot{\mathbbm{1}}\,,\,\,p12\rightarrow1.17003\,-\,0.720353\,\,\dot{\mathbbm{1}}\,\} ,
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 $\{p22 \rightarrow 1.59697, p12 \rightarrow -0.816608\}$