Practical 3: Inconsistency in network meta-analysis

R packages

We will use the package **readxl** to import excel data and the packages **netmeta** to run network meta-analyses.

```
library(readxl)
library(netmeta)
```

Datasets

We will again use the Acute mania and Schizophrenia datasets; see the Practical 6-8 for more information on these datasets. You only have to re-run the following commands if the R objects *AcuteMania* and *Leucht* do no longer exist.

```
AcuteMania = read_excel("AcuteMania.xls")
AcuteMania = as.data.frame(AcuteMania)

Leucht = read_excel("Leucht.xls")
Leucht = as.data.frame(Leucht)
```

Network meta-analyses

Re-run the following R commands if the R object *net1* and *net3* do no longer exist.

```
AcuteManiaPair = pairwise(treat = treatment, event = r, n = n,
                          data = AcuteMania, studlab = studyid, sm = "OR")
net1 = netmeta(AcuteManiaPair, ref = "PLA", comb.fixed = FALSE)

net3 = netmeta(effect, se, treat1, treat2, study, data = Leucht,
               sm = "SMD", ref = "PBO", comb.fixed = FALSE,
               tol.multiarm = 0.075)
```

Inconsistency evaluation in acute mania dataset

First, we print the number of designs

```
net1$d
```

```
## [1] 30
```

and the list of all designs (to see how many designs have two and three studies)

```
unique(net1$designs)
```

```
##  [1] "ARI:HAL"    "CARB:DIV"    "CARB:HAL"    "DIV:LITH"
##  [5] "DIV:OLA"    "HAL:OLA"     "LAM:LITH"    "LITH:OLA"
##  [9] "LITH:QUE"   "OLA:RIS"     "PLA:ARI"     "PLA:CARB"
```

```
## [13] "PLA:DIV"      "PLA:OLA"      "PLA:PAL"      "PLA:QUE"
## [17] "PLA:RIS"      "PLA:TOP"      "PLA:ZIP"      "PLA:ARI:HAL"
## [21] "PLA:ARI:LITH" "PLA:ASE:OLA"  "PLA:DIV:LITH" "PLA:DIV:OLA"
## [25] "PLA:HAL:OLA"  "PLA:HAL:QUE"  "PLA:HAL:RIS"  "PLA:HAL:ZIP"
## [29] "PLA:LITH:QUE" "PLA:PAL:QUE"
```

We see that the acute mania dataset contains 30 designs of which 11 are three-arm designs.

Next, we apply the SIDE method and print the results for the random effects model.

```
split1 = netsplit(net1)
print(split1, show = "both", digits = 2)

## Back-calculation method to split direct and indirect evidence
##
## Random effects model:
##
##  comparison k prop  nma direct indir.  RoR     z p-value
##     ARI:HAL 2 0.46 0.88   1.16   0.70 1.65  1.48  0.1398
##    ARI:LITH 1 0.34 1.13   1.09   1.15 0.95 -0.12  0.9044
##     ARI:PLA 6 0.83 1.99   1.77   3.55 0.50 -1.93  0.0534
##     ASE:OLA 1 0.82 0.78   0.69   1.37 0.50 -0.85  0.3938
##     ASE:PLA 1 0.67 1.69   2.04   1.15 1.78  0.85  0.3938
##    CARB:DIV 1 0.16 1.25   0.42   1.55 0.27 -1.46  0.1455
##    CARB:HAL 1 0.11 1.10   0.80   1.14 0.70 -0.33  0.7415
##    CARB:PLA 1 0.78 2.47   3.10   1.10 2.83  1.41  0.1579
##    DIV:LITH 2 0.25 1.12   0.78   1.25 0.62 -0.90  0.3704
##     DIV:OLA 2 0.48 0.91   0.77   1.06 0.73 -0.89  0.3712
##     DIV:PLA 5 0.70 1.98   2.16   1.60 1.35  0.85  0.3955
##     HAL:OLA 2 0.31 1.03   1.21   0.97 1.25  0.62  0.5363
##     HAL:PLA 5 0.57 2.25   2.26   2.24 1.01  0.03  0.9753
##     HAL:QUE 1 0.23 1.16   1.72   1.03 1.66  1.12  0.2612
##     HAL:RIS 1 0.31 0.95   0.95   0.96 0.99 -0.01  0.9902
##     HAL:ZIP 1 0.32 1.64   2.05   1.48 1.38  0.76  0.4468
##    LITH:OLA 2 0.20 0.81   0.62   0.87 0.72 -0.67  0.5050
##    LITH:PLA 3 0.56 1.77   2.28   1.28 1.78  1.60  0.1100
##    LITH:QUE 2 0.47 0.91   0.70   1.15 0.61 -1.22  0.2242
##     OLA:PLA 8 0.67 2.18   1.90   2.89 0.66 -1.66  0.0971
##     OLA:RIS 1 0.28 0.92   1.20   0.83 1.45  0.89  0.3750
##     PAL:PLA 2 0.85 1.72   1.57   2.85 0.55 -0.92  0.3601
##     PAL:QUE 1 0.53 0.89   1.25   0.60 2.08  1.47  0.1426
##     QUE:PLA 6 0.83 1.94   1.98   1.77 1.12  0.29  0.7724
##     RIS:PLA 4 0.74 2.36   2.51   1.99 1.26  0.60  0.5503
##     ZIP:PLA 5 0.91 1.37   1.48   0.63 2.33  1.46  0.1447
##
## Legend:
##  comparison - Treatment comparison
##  k          - Number of studies providing direct evidence
##  prop       - Direct evidence proportion
##  nma        - Estimated treatment effect (OR) in network meta-analysis
##  direct     - Estimated treatment effect (OR) derived from direct evidence
```

```
##  indir.      - Estimated treatment effect (OR) derived from indirect
evidence
##  RoR        - Ratio of Ratios (direct versus indirect)
##  z          - z-value of test for disagreement (direct versus indirect)
##  p-value    - p-value of test for disagreement (direct versus indirect)
```

How do you interpret the results? Are there any large discrepancies between the direct and indirect estimates?

As the columns 'RoR', 'z', and 'p-value' indicate there is no single pairwise comparison showing large inconsisteny between direct and indirect evidence.

Finally, we look at the design-by-treatment interaction model.

```
decomp.design(net1)

## Q statistics to assess homogeneity / consistency
##
##                      Q df p-value
## Total           88.39 45  0.0001
## Within designs  33.62 17  0.0094
## Between designs 54.77 28  0.0018
##
## Design-specific decomposition of within-designs Q statistic
##
##     Design    Q df p-value
##   LITH:OLA 2.71  1  0.0995
##    PLA:ARI 7.32  3  0.0623
##    PLA:DIV 3.38  2  0.1842
##    PLA:OLA 6.88  4  0.1426
##    PLA:QUE 1.66  2  0.4350
##    PLA:RIS 6.73  2  0.0345
##    PLA:ZIP 4.93  3  0.1771
##
## Between-designs Q statistic after detaching of single designs
##
##   Detached design     Q df p-value
##           ARI:HAL 48.70 27  0.0064
##          CARB:DIV 51.94 27  0.0027
##          CARB:HAL 54.51 27  0.0013
##          DIV:LITH 51.82 27  0.0028
##           DIV:OLA 51.67 27  0.0029
##           HAL:OLA 54.68 27  0.0013
##          LITH:OLA 54.11 27  0.0015
##          LITH:QUE 49.78 27  0.0048
##           OLA:RIS 52.71 27  0.0022
##           PLA:ARI 54.23 27  0.0014
##          PLA:CARB 51.97 27  0.0027
##           PLA:DIV 54.18 27  0.0014
##           PLA:OLA 54.27 27  0.0014
##           PLA:PAL 48.07 27  0.0075
```

```
##          PLA:QUE 54.33 27  0.0014
##          PLA:RIS 51.38 27  0.0031
##          PLA:ZIP 54.77 27  0.0012
##      PLA:ARI:HAL 51.92 26  0.0018
##     PLA:ARI:LITH 54.34 26  0.0009
##      PLA:ASE:OLA 53.23 27  0.0019
##     PLA:DIV:LITH 51.82 26  0.0019
##      PLA:DIV:OLA 52.20 26  0.0017
##      PLA:HAL:OLA 50.78 26  0.0025
##      PLA:HAL:QUE 52.09 26  0.0018
##      PLA:HAL:RIS 53.82 26  0.0011
##      PLA:HAL:ZIP 47.87 26  0.0056
##     PLA:LITH:QUE 49.80 26  0.0033
##      PLA:PAL:QUE 47.93 26  0.0055
##
## Q statistic to assess consistency under the assumption of
## a full design-by-treatment interaction random effects model
##
##                      Q df p-value tau.within tau2.within
## Between designs 28.27 28  0.4503     0.2861      0.0819
```

How do you interpret the overall results (Q statistics)?

The overall Q statistics show that both within-design heterogeneity and between-design inconsistency exists.

Which individual comparison contributes most to the within-design heterogeneity?

The comparison 'PLA:RIS' contributes most to the within-design heterogenity.

Which designs show the largest between-design inconsistency?

The designs 'ARI:HAL' and 'PLA:PAL' have the largest p-values for the between-designs Q statistic after detaching a single design. Accordingly, these two designs contribute most to the inconsistency in the network.

Is any residual inconsistency left after allowing for a full design by treatment interaction model?

No residual inconsistency remains after allowing for a full design by treatment interaction model.

Inconsistency evaluation in schizophrenia dataset

Again, we print the number of designs

```
net3$d
```

```
## [1] 63
```

and the list of all designs (to see how many designs have two, three, and four studies)

```
unique(net3$designs)
```

```
##  [1] "AMI:HAL"        "AMI:OLA"        "AMI:RIS"
##  [4] "ARI:HAL"        "ARI:OLA"        "ARI:RIS"
```

```
##  [7] "ARI:ZIP"           "ASE:OLA"          "CLO:CPZ"
## [10] "CLO:HAL"           "CLO:OLA"          "CLO:RIS"
## [13] "CLO:ZOT"           "CPZ:QUE"          "HAL:ILO"
## [16] "HAL:OLA"           "HAL:QUE"          "HAL:RIS"
## [19] "HAL:SER"           "HAL:ZIP"          "HAL:ZOT"
## [22] "OLA:QUE"           "OLA:RIS"          "OLA:SER"
## [25] "OLA:ZIP"           "PBO:ARI"          "PBO:CPZ"
## [28] "PBO:HAL"           "PBO:LURA"         "PBO:OLA"
## [31] "PBO:pal"           "PBO:QUE"          "PBO:RIS"
## [34] "PBO:SER"           "PBO:ZIP"          "PBO:ZOT"
## [37] "QUE:RIS"           "RIS:SER"          "RIS:ZIP"
## [40] "ARI:OLA:QUE:RIS" "CLO:HAL:OLA"      "CLO:HAL:RIS"
## [43] "OLA:QUE:RIS"       "OLA:QUE:RIS:ZIP" "PBO:ARI:HAL"
## [46] "PBO:ARI:RIS"       "PBO:ASE:HAL"      "PBO:ASE:OLA"
## [49] "PBO:ASE:RIS"       "PBO:CLO:CPZ"      "PBO:CPZ:HAL"
## [52] "PBO:CPZ:ZOT"       "PBO:HAL:ILO"      "PBO:HAL:LURA"
## [55] "PBO:HAL:QUE"       "PBO:HAL:RIS"      "PBO:HAL:SER"
## [58] "PBO:HAL:ZIP"       "PBO:ILO:RIS"      "PBO:ILO:ZIP"
## [61] "PBO:LURA:OLA"      "PBO:LURA:QUE"     "PBO:OLA:pal"
```

We see that the schizophrenia dataset contains 63 designs of which 22 are three-arm designs and 2 are four-arm designs.

Next, we apply the SIDE method and print the results for the random effects model.

```
split3 = netsplit(net3)
print(split3, show = "both", digits = 2)

## Back-calculation method to split direct and indirect evidence
##
## Random effects model:
##
##  comparison  k prop   nma direct indir.  Diff     z p-value
##     AMI:HAL  6 0.40 -0.21  -0.30  -0.14 -0.16 -1.33  0.1827
##     AMI:OLA  5 0.37 -0.07  -0.01  -0.10  0.09  0.75  0.4558
##     AMI:RIS  4 0.35 -0.10  -0.05  -0.13  0.08  0.64  0.5253
##     ARI:HAL  4 0.34  0.02  -0.01   0.04 -0.05 -0.48  0.6278
##     ARI:OLA  4 0.36  0.16   0.23   0.11  0.12  1.17  0.2418
##     ARI:PBO  6 0.42 -0.43  -0.44  -0.42 -0.03 -0.28  0.7825
##     ARI:QUE  1 0.03  0.00   0.38  -0.01  0.39  1.14  0.2530
##     ARI:RIS  3 0.17  0.13   0.10   0.13 -0.04 -0.25  0.7990
##     ARI:ZIP  1 0.14 -0.04  -0.16  -0.02 -0.14 -0.80  0.4244
##     ASE:HAL  1 0.18  0.07  -0.02   0.09 -0.11 -0.64  0.5205
##     ASE:OLA  3 0.57  0.21   0.13   0.32 -0.19 -1.43  0.1538
##     ASE:PBO  4 0.58 -0.37  -0.18  -0.64  0.46  3.43  0.0006
##     ASE:RIS  1 0.10  0.18  -0.15   0.22 -0.37 -1.61  0.1078
##     CLO:CPZ  5 0.49 -0.48  -0.42  -0.53  0.11  0.61  0.5421
##     CLO:HAL  8 0.51 -0.40  -0.48  -0.32 -0.16 -1.02  0.3057
##     CLO:OLA  2 0.15 -0.26   0.07  -0.32  0.39  1.71  0.0879
##     CLO:PBO  1 0.02 -0.85  -1.64  -0.83 -0.81 -1.51  0.1299
##     CLO:RIS  2 0.13 -0.29  -0.36  -0.28 -0.08 -0.33  0.7401
```

```
##      CLO:ZOT   2 0.27 -0.36  -0.43  -0.33 -0.10 -0.40  0.6868
##      CPZ:HAL   1 0.04  0.08  -0.29   0.09 -0.39 -0.91  0.3640
##      CPZ:PBO  11 0.53 -0.37  -0.39  -0.34 -0.04 -0.26  0.7945
##      CPZ:QUE   1 0.24  0.06   0.05   0.07 -0.02 -0.08  0.9380
##      CPZ:ZOT   1 0.25  0.12   0.76  -0.09  0.85  3.28  0.0011
##      HAL:ILO   4 0.51 -0.12  -0.08  -0.18  0.10  0.94  0.3494
##     HAL:LURA   1 0.13 -0.12  -0.28  -0.10 -0.18 -0.94  0.3468
##      HAL:OLA  11 0.31  0.14   0.14   0.14  0.00  0.04  0.9679
##      HAL:PBO  21 0.42 -0.45  -0.50  -0.41 -0.09 -1.44  0.1491
##      HAL:QUE   4 0.22 -0.02  -0.07  -0.00 -0.07 -0.63  0.5302
##      HAL:RIS  17 0.37  0.11   0.16   0.07  0.09  1.25  0.2111
##      HAL:SER   3 0.53 -0.06  -0.12   0.01 -0.13 -0.95  0.3396
##      HAL:ZIP   3 0.23 -0.05  -0.13  -0.03 -0.09 -0.77  0.4413
##      HAL:ZOT   4 0.45  0.04  -0.09   0.15 -0.24 -1.31  0.1892
##      ILO:PBO   4 0.51 -0.32  -0.26  -0.39  0.13  1.15  0.2493
##      ILO:RIS   2 0.29  0.23   0.29   0.21  0.09  0.69  0.4932
##      ILO:ZIP   1 0.21  0.07   0.02   0.08 -0.06 -0.38  0.7004
##     LURA:OLA   1 0.19  0.26   0.16   0.28 -0.12 -0.71  0.4758
##     LURA:PBO   6 0.82 -0.33  -0.34  -0.29 -0.05 -0.30  0.7621
##     LURA:QUE   1 0.22  0.10   0.17   0.08  0.09  0.50  0.6145
##      OLA:pal   4 0.51 -0.09  -0.06  -0.13  0.07  0.60  0.5514
##      OLA:PBO  14 0.40 -0.58  -0.58  -0.59  0.01  0.16  0.8728
##      OLA:QUE   7 0.29 -0.15  -0.08  -0.19  0.10  1.00  0.3164
##      OLA:RIS  10 0.31 -0.03  -0.05  -0.02 -0.04 -0.44  0.6591
##      OLA:SER   1 0.22 -0.20  -0.23  -0.19 -0.04 -0.26  0.7928
##      OLA:ZIP   5 0.42 -0.19  -0.14  -0.23  0.09  0.84  0.3988
##      pal:PBO   8 0.85 -0.49  -0.50  -0.46 -0.04 -0.25  0.7990
##      QUE:PBO   7 0.44 -0.43  -0.42  -0.43  0.01  0.14  0.8874
##      RIS:PBO  12 0.42 -0.55  -0.58  -0.53 -0.05 -0.76  0.4483
##      SER:PBO   3 0.39 -0.39  -0.35  -0.41  0.06  0.43  0.6704
##      ZIP:PBO   4 0.30 -0.39  -0.40  -0.39 -0.01 -0.10  0.9212
##      ZOT:PBO   2 0.37 -0.49  -0.54  -0.46 -0.08 -0.42  0.6737
##      QUE:RIS   6 0.39  0.12   0.06   0.17 -0.11 -1.13  0.2586
##      QUE:ZIP   1 0.19 -0.04  -0.02  -0.04  0.02  0.14  0.8876
##      RIS:SER   1 0.15 -0.17   0.15  -0.22  0.37  1.87  0.0612
##      RIS:ZIP   2 0.26 -0.16  -0.09  -0.19  0.10  0.85  0.3941
##
## Legend:
##   comparison - Treatment comparison
##   k          - Number of studies providing direct evidence
##   prop       - Direct evidence proportion
##   nma        - Estimated treatment effect (SMD) in network meta-analysis
##   direct     - Estimated treatment effect (SMD) derived from direct
## evidence
##   indir.     - Estimated treatment effect (SMD) derived from indirect
## evidence
##   Diff       - Difference between direct and indirect treatment estimates
##   z          - z-value of test for disagreement (direct versus indirect)
##   p-value    - p-value of test for disagreement (direct versus indirect)
```

How do you interpret the results? Are there any large discrepancies between the direct and indirect estimates?

Taking into account the large number of 54 pairwise comparisons, only the p-value from the comparison 'ASE:PBO' indicates that direct and indirect evidence differs substantially (p = 0.0006 < 0.05 / 54).

Finally, we look at the design-by-treatment interaction model.

```
decomp.design(net3)

## Q statistics to assess homogeneity / consistency
##
##                      Q  df  p-value
## Total          279.59 192 < 0.0001
## Within designs 139.67 118   0.0846
## Between designs 139.93  74 < 0.0001
##
## Design-specific decomposition of within-designs Q statistic
##
##        Design     Q df p-value
##       AMI:HAL  2.15  5  0.8287
##       AMI:OLA 14.48  4  0.0059
##       AMI:RIS  1.92  3  0.5897
##       ARI:OLA  0.14  2  0.9320
##       CLO:CPZ  5.93  3  0.1151
##       CLO:HAL  8.03  5  0.1549
##       CLO:ZOT  3.06  1  0.0804
##       HAL:ILO  0.19  2  0.9109
##       HAL:OLA  8.85  9  0.4510
##       HAL:QUE  0.76  2  0.6844
##       HAL:RIS 24.26 12  0.0187
##       HAL:ZIP  0.03  1  0.8619
##       HAL:ZOT  6.39  3  0.0942
##       OLA:QUE  0.31  1  0.5781
##       OLA:RIS  0.04  4  0.9998
##       OLA:ZIP  2.23  3  0.5269
##       PBO:ARI  0.27  1  0.6027
##       PBO:CPZ  2.87  7  0.8968
##       PBO:HAL  8.52  6  0.2025
##      PBO:LURA  3.89  2  0.1432
##       PBO:OLA 13.24  6  0.0394
##       PBO:pal  2.86  3  0.4136
##       PBO:QUE  5.03  4  0.2844
##       PBO:RIS  3.27  4  0.5143
##       PBO:ZIP  0.02  1  0.8806
##   OLA:QUE:RIS  2.69  4  0.6102
##   PBO:ARI:HAL  3.66  4  0.4537
##   PBO:ASE:OLA  4.44  2  0.1087
##   PBO:HAL:RIS  4.16  4  0.3850
##   PBO:HAL:SER  1.24  2  0.5377
##   PBO:ILO:RIS  0.77  2  0.6796
```

```
##   PBO:OLA:pal  3.99  6  0.6774
##
## Between-designs Q statistic after detaching of single designs
##
##   Detached design      Q df  p-value
##           AMI:HAL 137.90 73 < 0.0001
##           AMI:OLA 139.51 73 < 0.0001
##           AMI:RIS 139.32 73 < 0.0001
##           ARI:HAL 139.35 73 < 0.0001
##           ARI:OLA 138.16 73 < 0.0001
##           ARI:RIS 139.89 73 < 0.0001
##           ARI:ZIP 138.79 73 < 0.0001
##           ASE:OLA 134.81 73 < 0.0001
##           CLO:CPZ 137.81 73 < 0.0001
##           CLO:HAL 138.95 73 < 0.0001
##           CLO:OLA 139.93 73 < 0.0001
##           CLO:RIS 139.79 73 < 0.0001
##           CLO:ZOT 139.50 73 < 0.0001
##           CPZ:QUE 139.89 73 < 0.0001
##           HAL:ILO 137.71 73 < 0.0001
##           HAL:OLA 139.75 73 < 0.0001
##           HAL:QUE 138.57 73 < 0.0001
##           HAL:RIS 139.74 73 < 0.0001
##           HAL:SER 139.86 73 < 0.0001
##           HAL:ZIP 139.92 73 < 0.0001
##           HAL:ZOT 137.86 73 < 0.0001
##           OLA:QUE 139.36 73 < 0.0001
##           OLA:RIS 139.69 73 < 0.0001
##           OLA:SER 139.85 73 < 0.0001
##           OLA:ZIP 139.91 73 < 0.0001
##           PBO:ARI 139.83 73 < 0.0001
##           PBO:CPZ 138.83 73 < 0.0001
##           PBO:HAL 136.40 73 < 0.0001
##          PBO:LURA 139.93 73 < 0.0001
##           PBO:OLA 137.62 73 < 0.0001
##           PBO:pal 133.19 73 < 0.0001
##           PBO:QUE 134.12 73 < 0.0001
##           PBO:RIS 139.50 73 < 0.0001
##           PBO:SER 139.52 73 < 0.0001
##           PBO:ZIP 139.07 73 < 0.0001
##           PBO:ZOT 139.05 73 < 0.0001
##           QUE:RIS 139.93 73 < 0.0001
##           RIS:SER 134.82 73 < 0.0001
##           RIS:ZIP 139.72 73 < 0.0001
##   ARI:OLA:QUE:RIS 137.29 71 < 0.0001
##       CLO:HAL:OLA 135.71 72 < 0.0001
##       CLO:HAL:RIS 132.96 72 < 0.0001
##       OLA:QUE:RIS 139.58 72 < 0.0001
##   OLA:QUE:RIS:ZIP 133.26 71 < 0.0001
##       PBO:ARI:HAL 139.18 72 < 0.0001
```

```
##       PBO:ARI:RIS 139.62 72 < 0.0001
##       PBO:ASE:HAL 138.94 72 < 0.0001
##       PBO:ASE:OLA 116.83 72   0.0007
##       PBO:ASE:RIS 137.26 72 < 0.0001
##       PBO:CLO:CPZ 137.10 72 < 0.0001
##       PBO:CPZ:HAL 136.48 72 < 0.0001
##       PBO:CPZ:ZOT 124.04 72   0.0001
##       PBO:HAL:ILO 139.08 72 < 0.0001
##      PBO:HAL:LURA 131.62 72 < 0.0001
##       PBO:HAL:QUE 138.66 72 < 0.0001
##       PBO:HAL:RIS 131.06 72 < 0.0001
##       PBO:HAL:SER 137.11 72 < 0.0001
##       PBO:HAL:ZIP 138.36 72 < 0.0001
##       PBO:ILO:RIS 138.59 72 < 0.0001
##       PBO:ILO:ZIP 139.30 72 < 0.0001
##      PBO:LURA:OLA 138.41 72 < 0.0001
##      PBO:LURA:QUE 124.26 72   0.0001
##       PBO:OLA:pal 130.89 72 < 0.0001
##
## Q statistic to assess consistency under the assumption of
## a full design-by-treatment interaction random effects model
##
##                      Q df p-value tau.within tau2.within
## Between designs 113.70 74  0.0021     0.0728      0.0053
```

How do you interpret the overall results (Q statistics)?

The overall Q statistics shows that large between-design inconsistency exists, however, that results within-designs do - in total - not differ substantially.

Which individual comparisons contribute most to the within-design heterogeneity?

The comparisons 'AMI:OLA' and 'HAL:RIS' contribute most to the (non-significant) within-study heterogeneity.

Which designs show the largest between-design inconsistency?

Looking at the Q statistics and noticing that the degrees of freedom are very similar, we see that the designs 'PBO:ASE:OLA', 'PBO:CPZ:ZOT', and 'PBO:LURA:QUE' contribute most to the between-study inconsistency.

Is any residual inconsistency left after allowing for a full design by treatment interaction model?

Substantial residual inconsistency remains in a full design by treatment interaction model.