Heterogeneity

Sarah Medland & Hermine Maes

Mike, Liz, Brad, Dave, Baptiste, Rob, Mike, Jose, Daniel, Philip, Luis, Dan

Heterogeneity

2-group **10 min**
oneADEvca
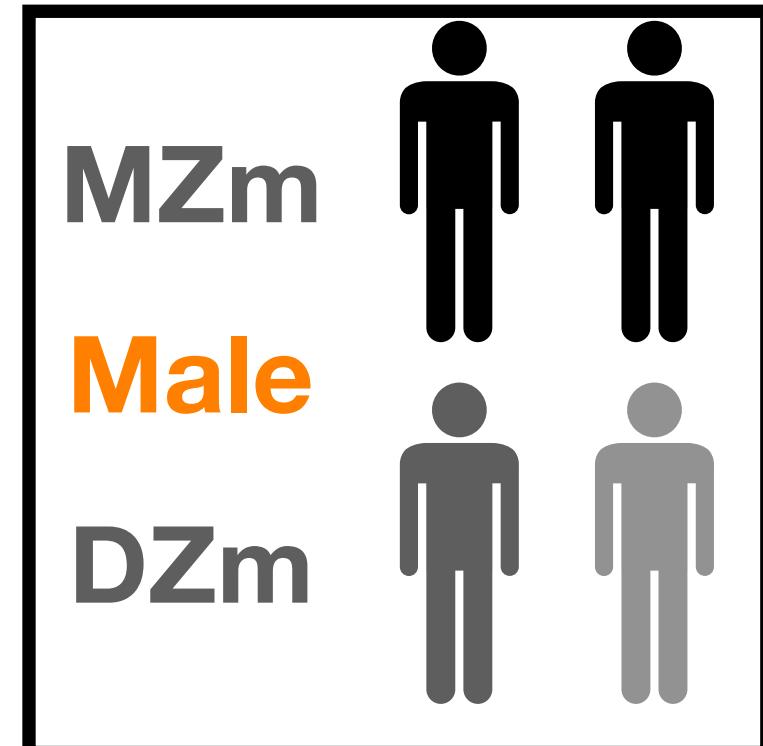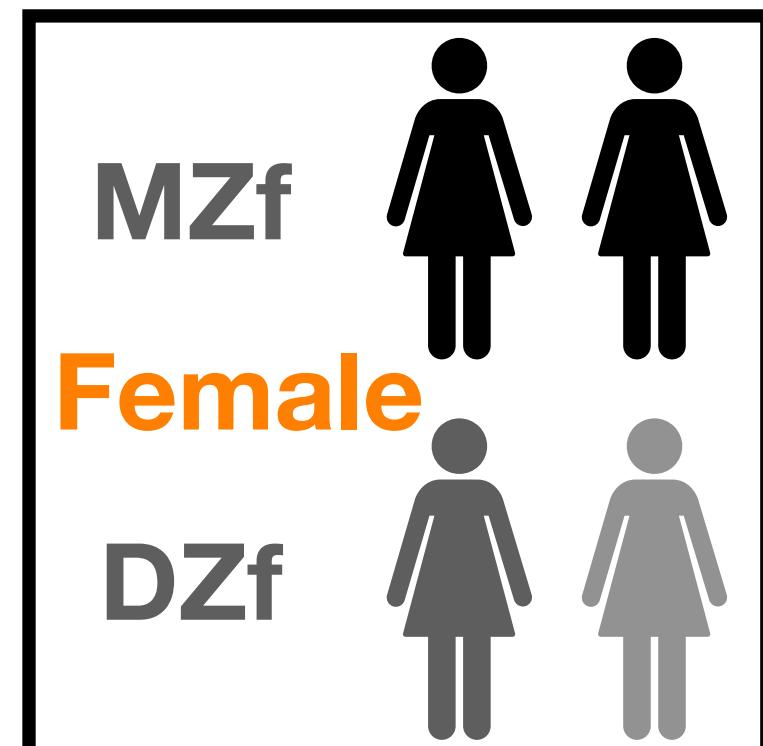
**4-group** **15 min**
oneADE4vca
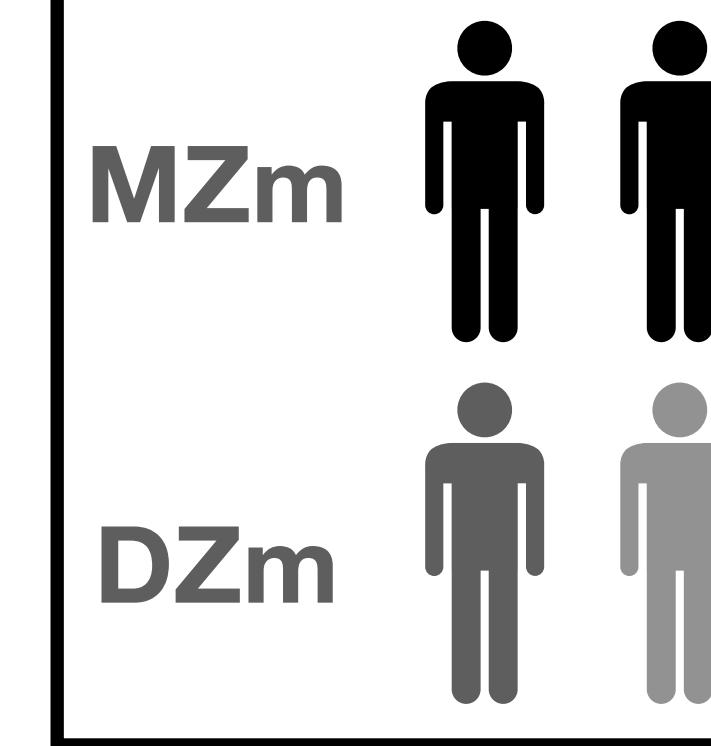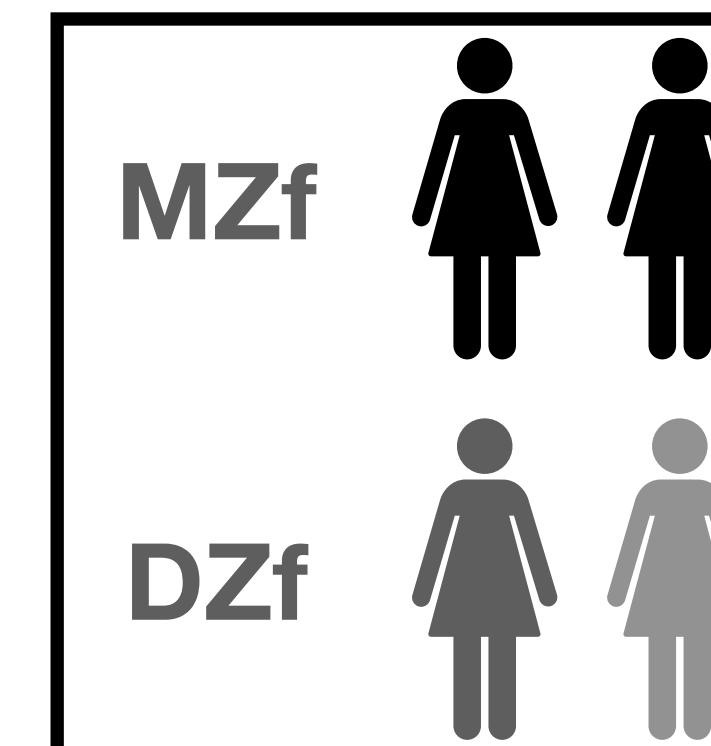
5-group **15 min**
oneADE5vca
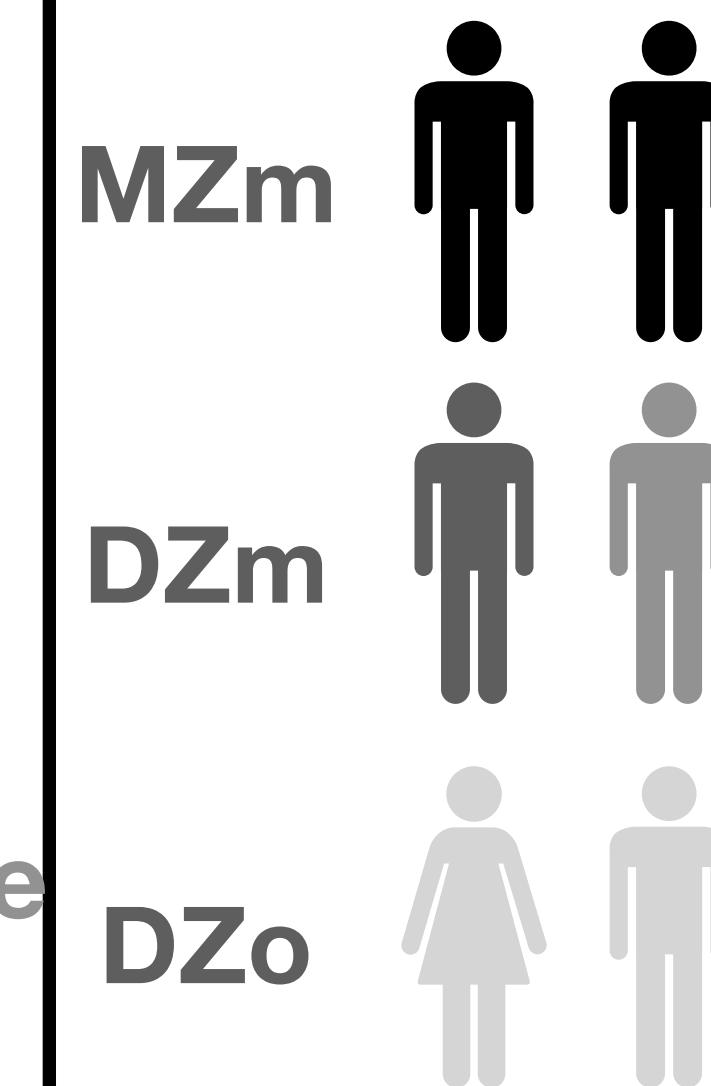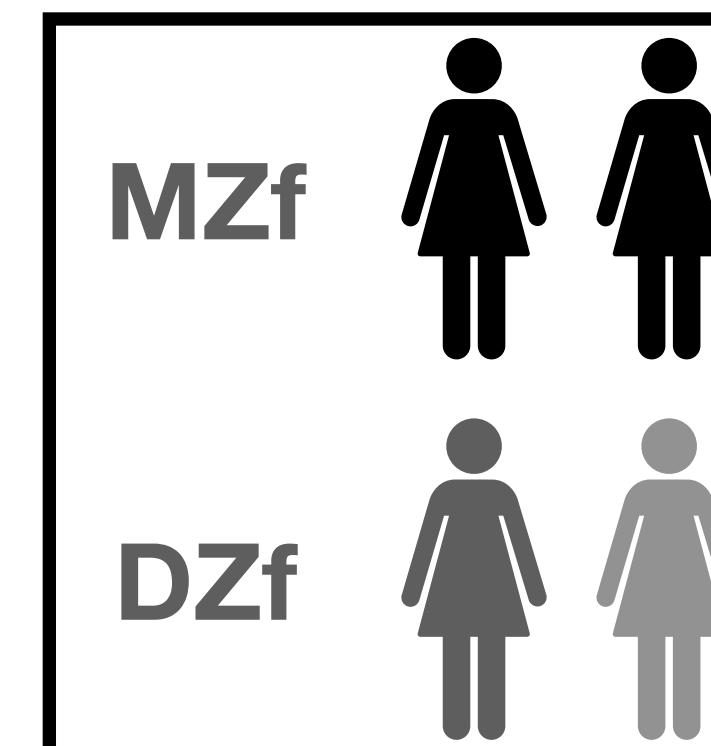
interaction **20 min**
oneADEcal
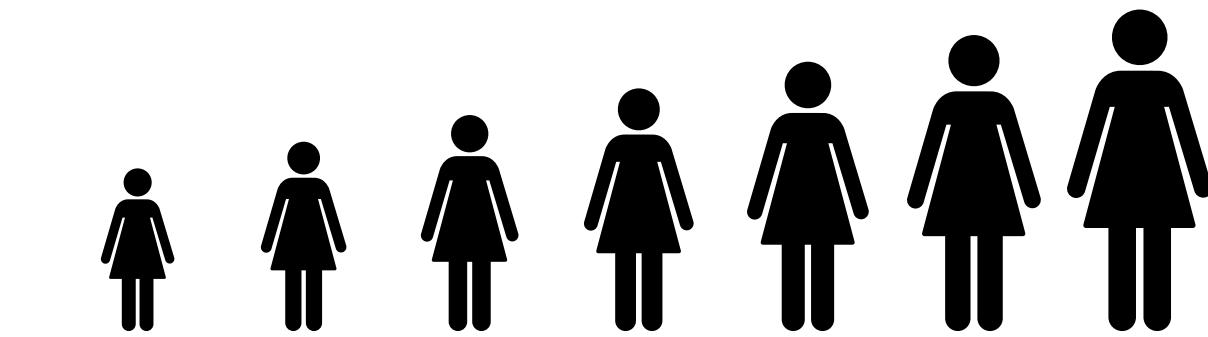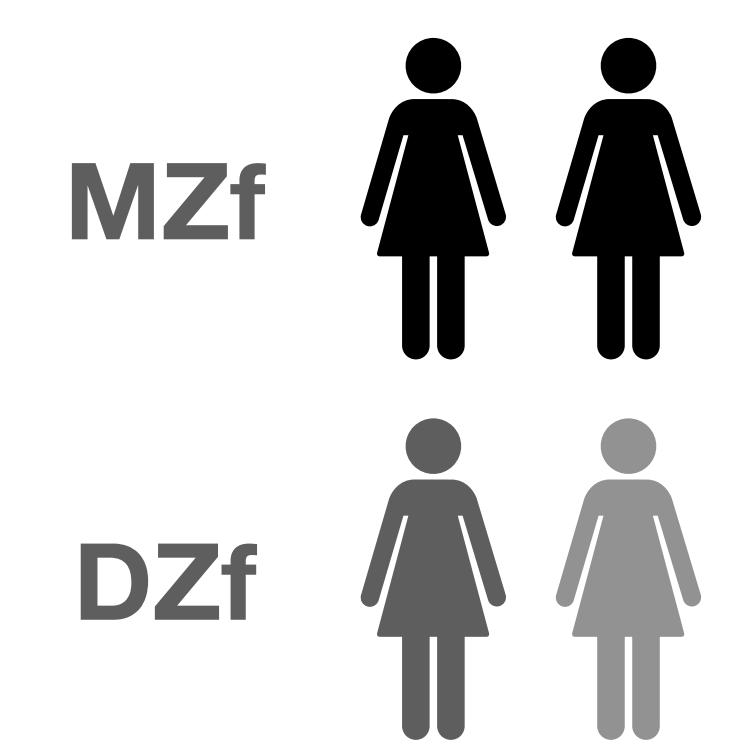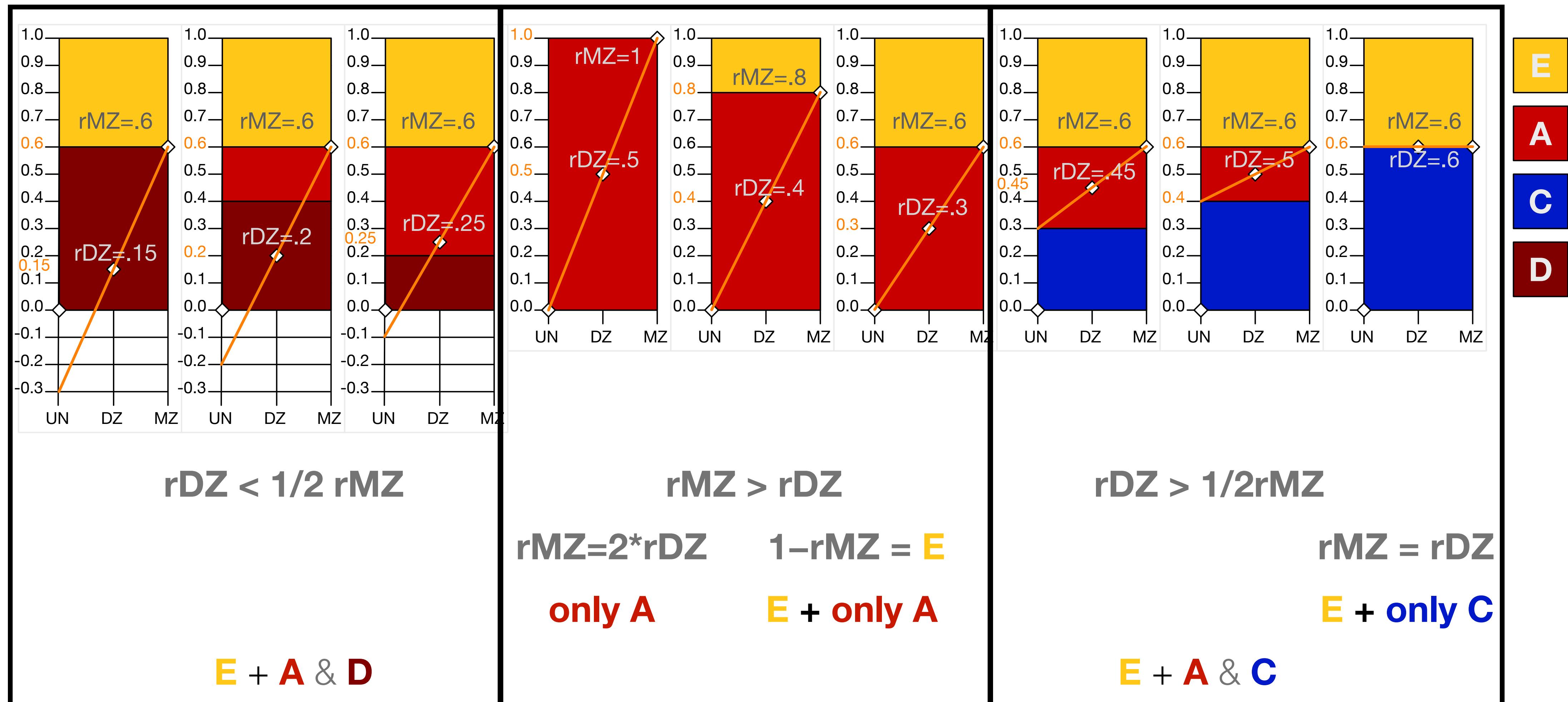
From twin correlations to sources of variance

rDZ < 1/2 rMZ

E + **A** & **D**

rMZ > rDZ

rMZ=2*rDZ   **1–rMZ = E**

only A   **E** + **only A**

rDZ > 1/2rMZ

rMZ = rDZ

E + **only C**

E + **A** & **C**

rMZ: monozygotic twin correlation; rDZ: dizygotic twin correlation;
A: additive genetic factors; E: unique environment: C: common environment; D: dominance

Lindon:
'Look at the bloody data'
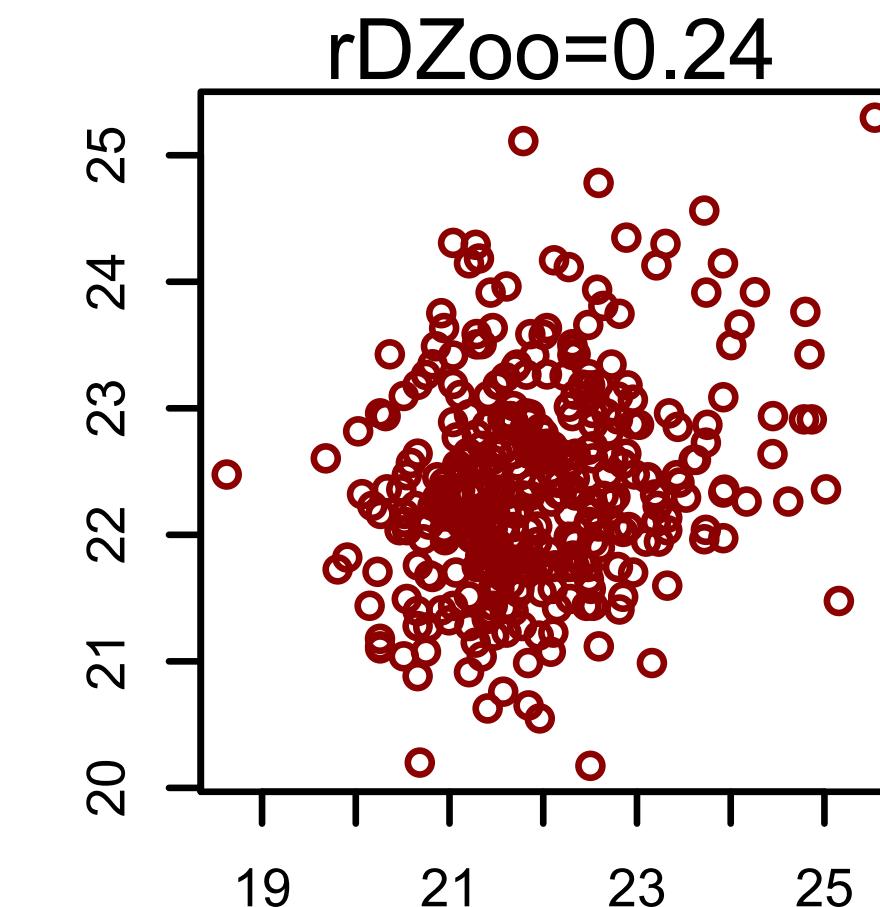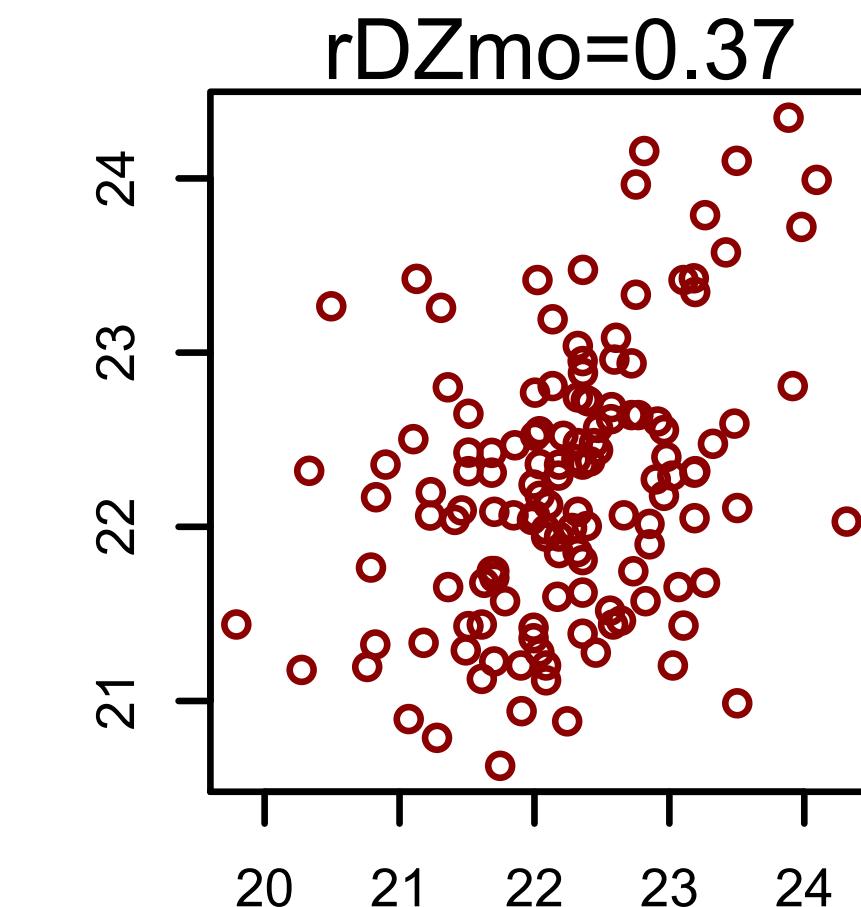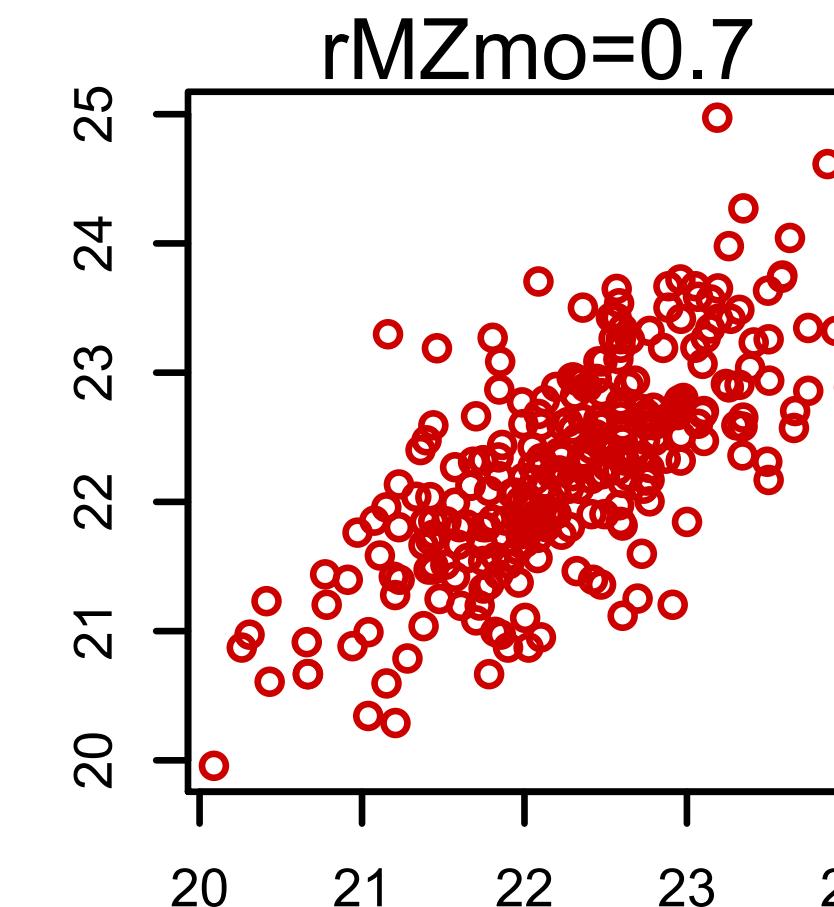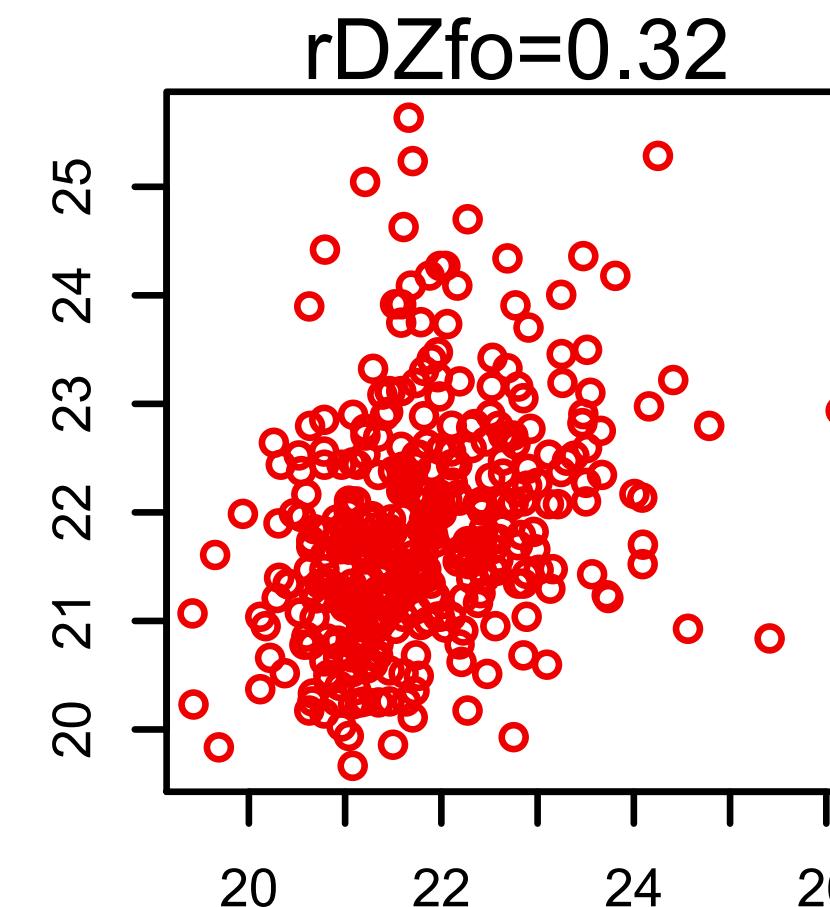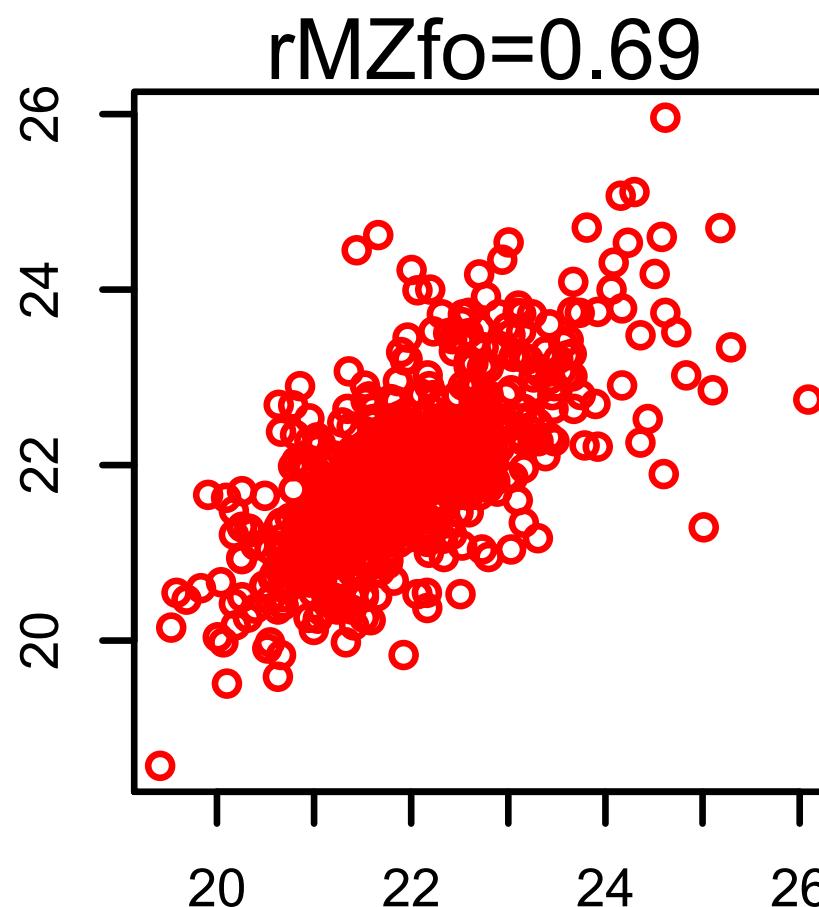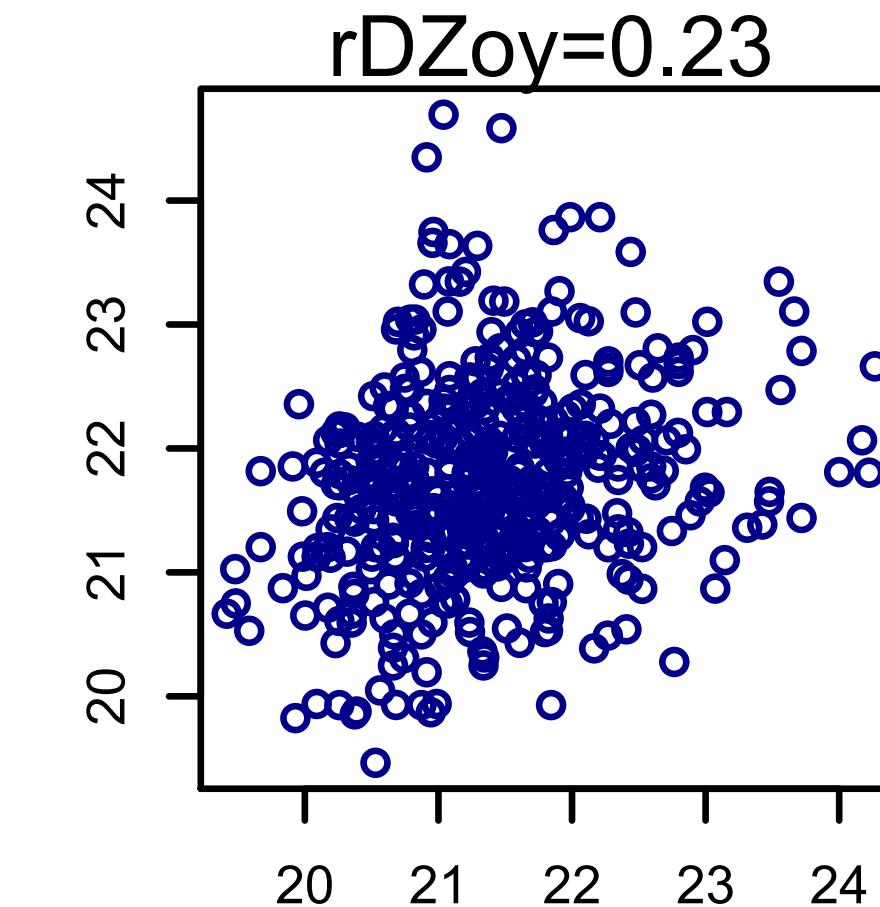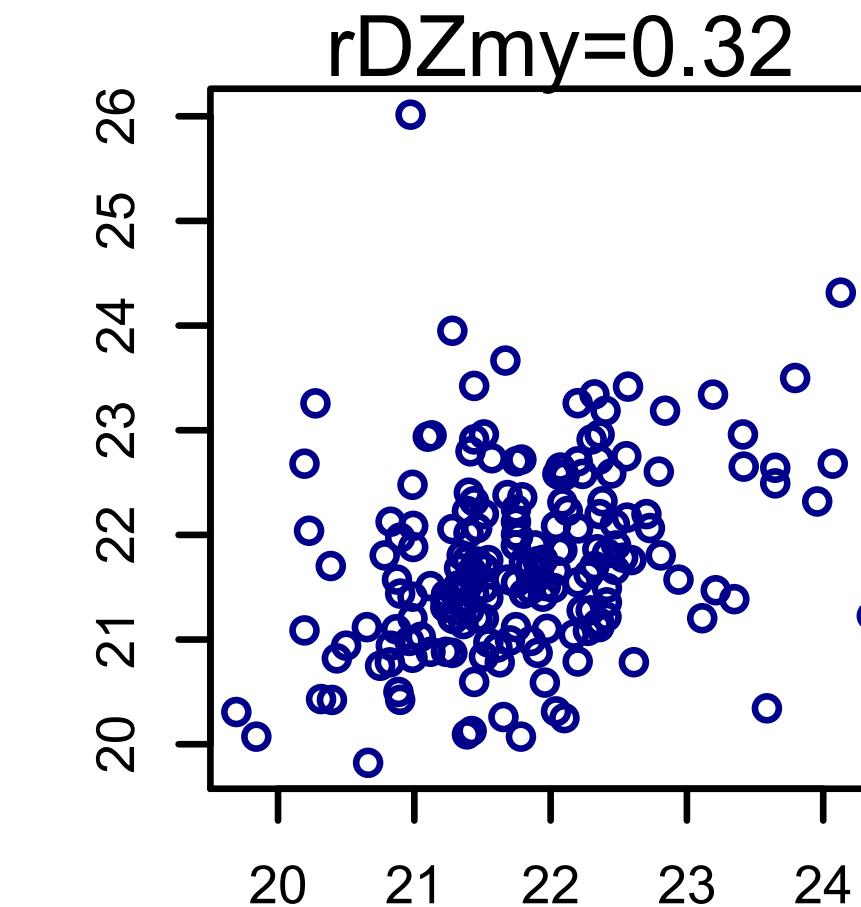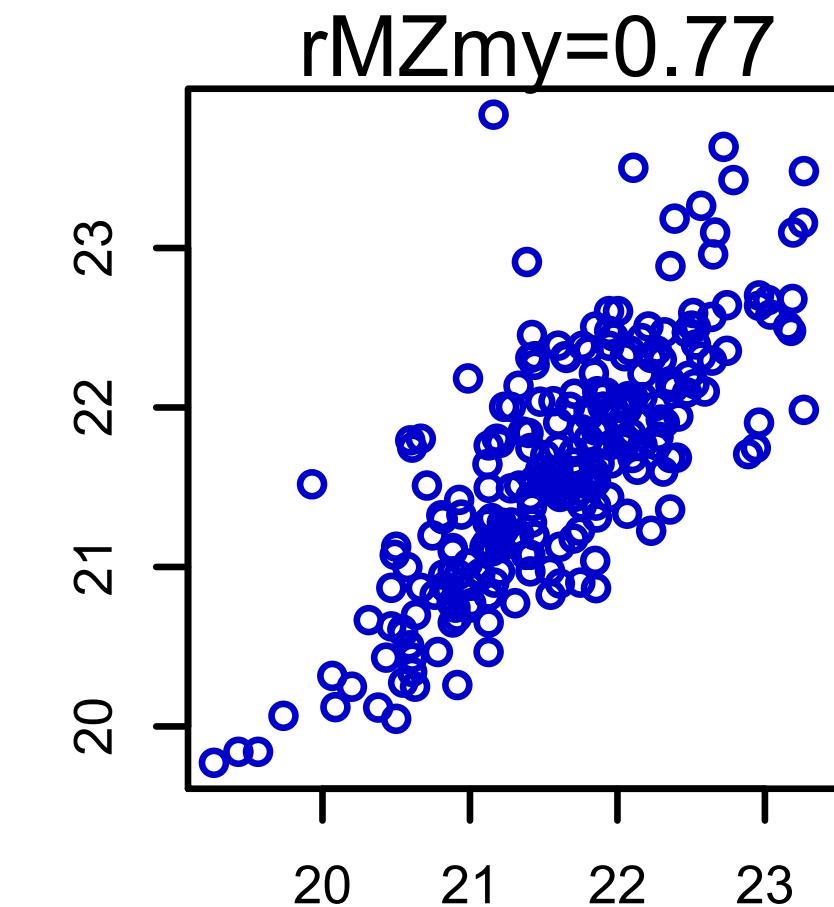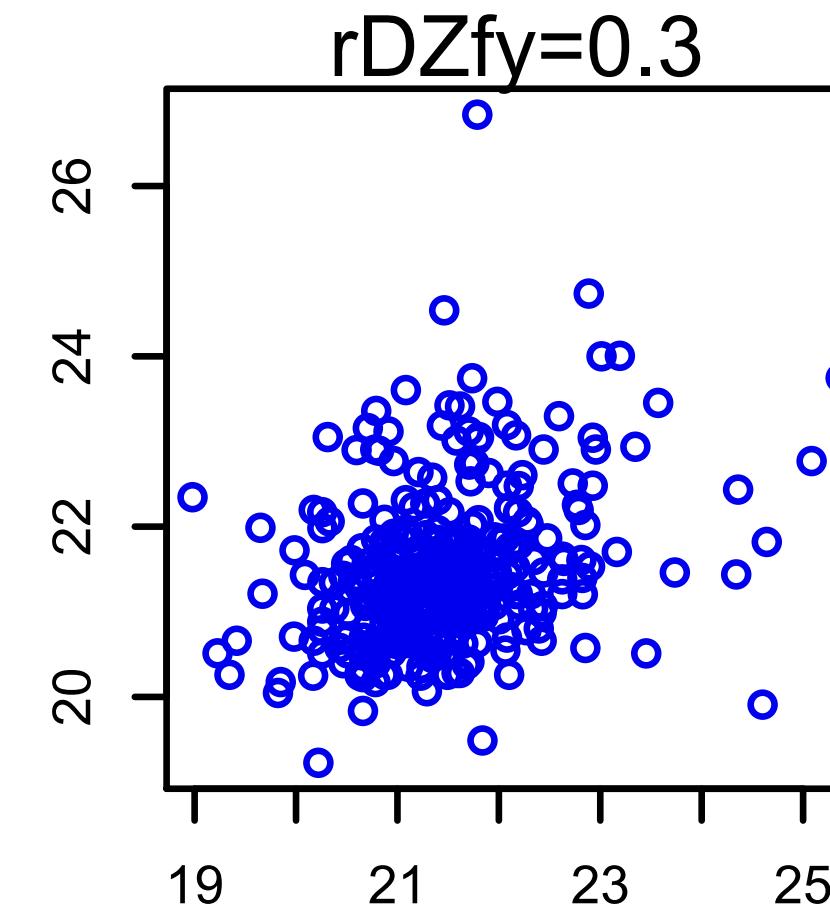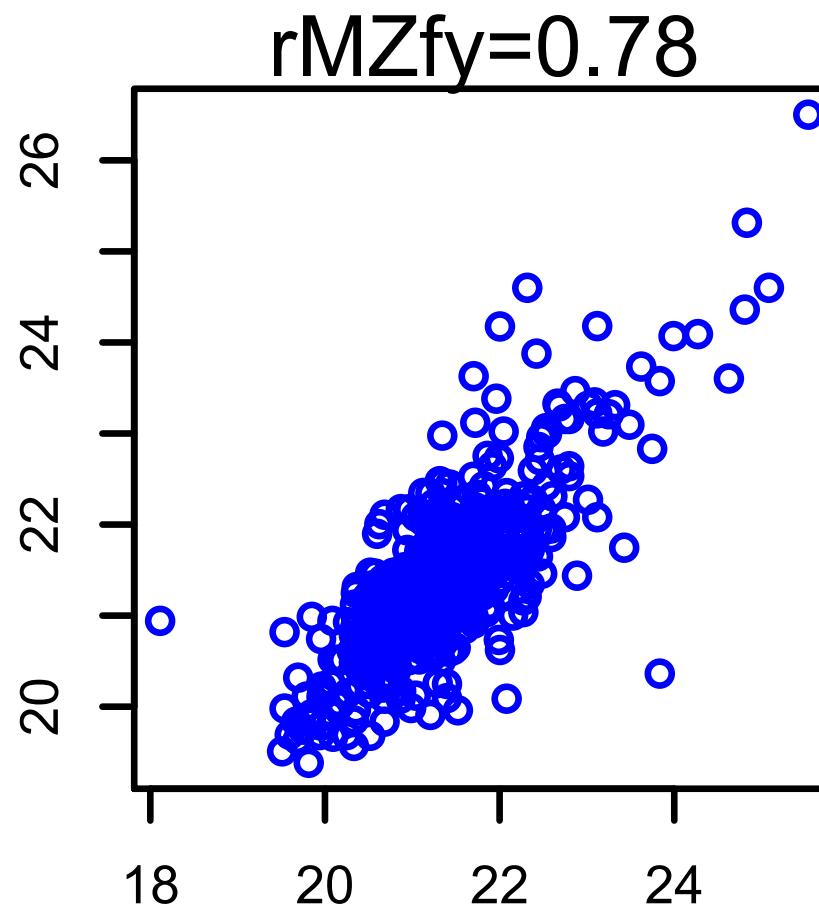
2-group multi-group
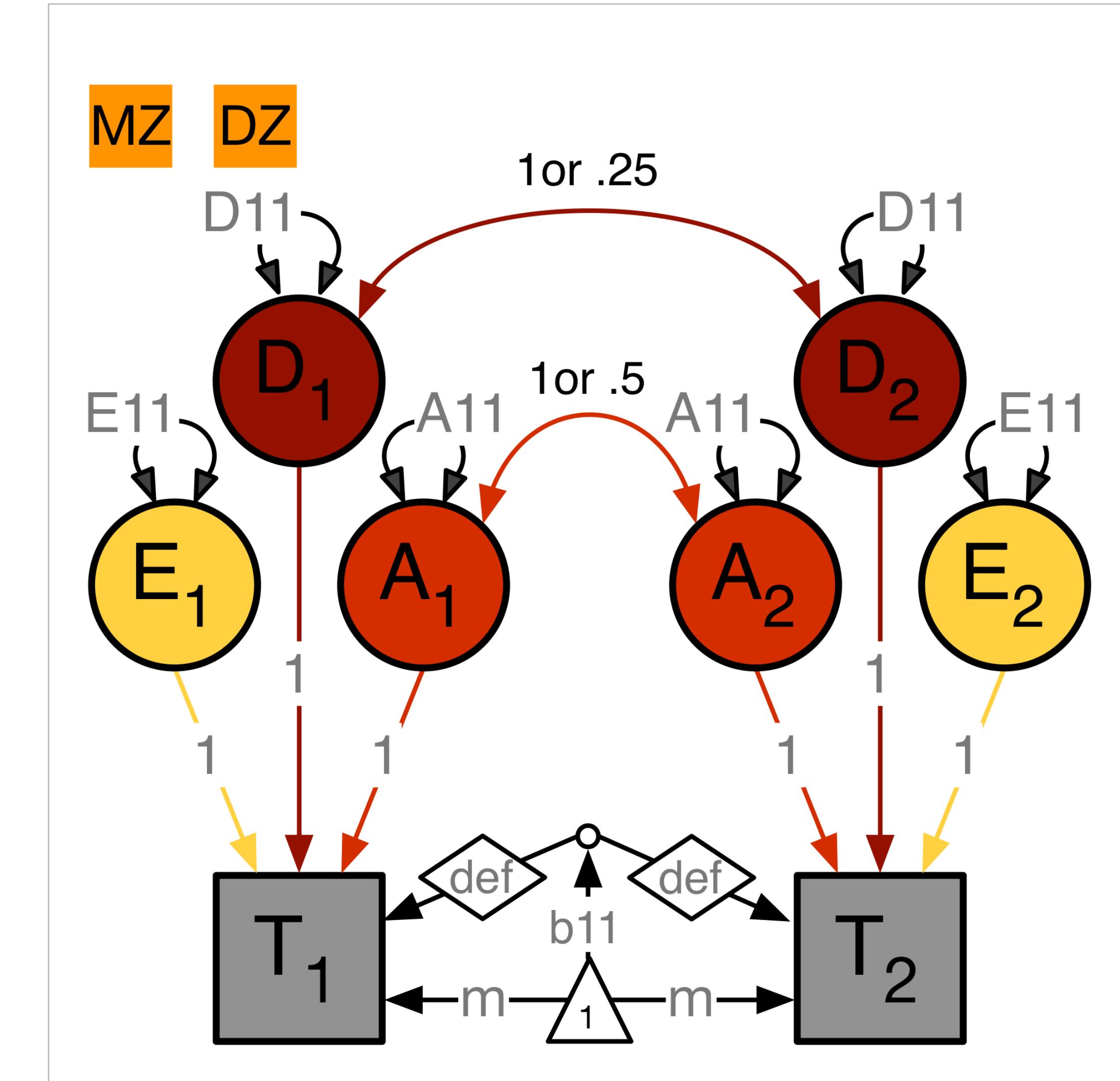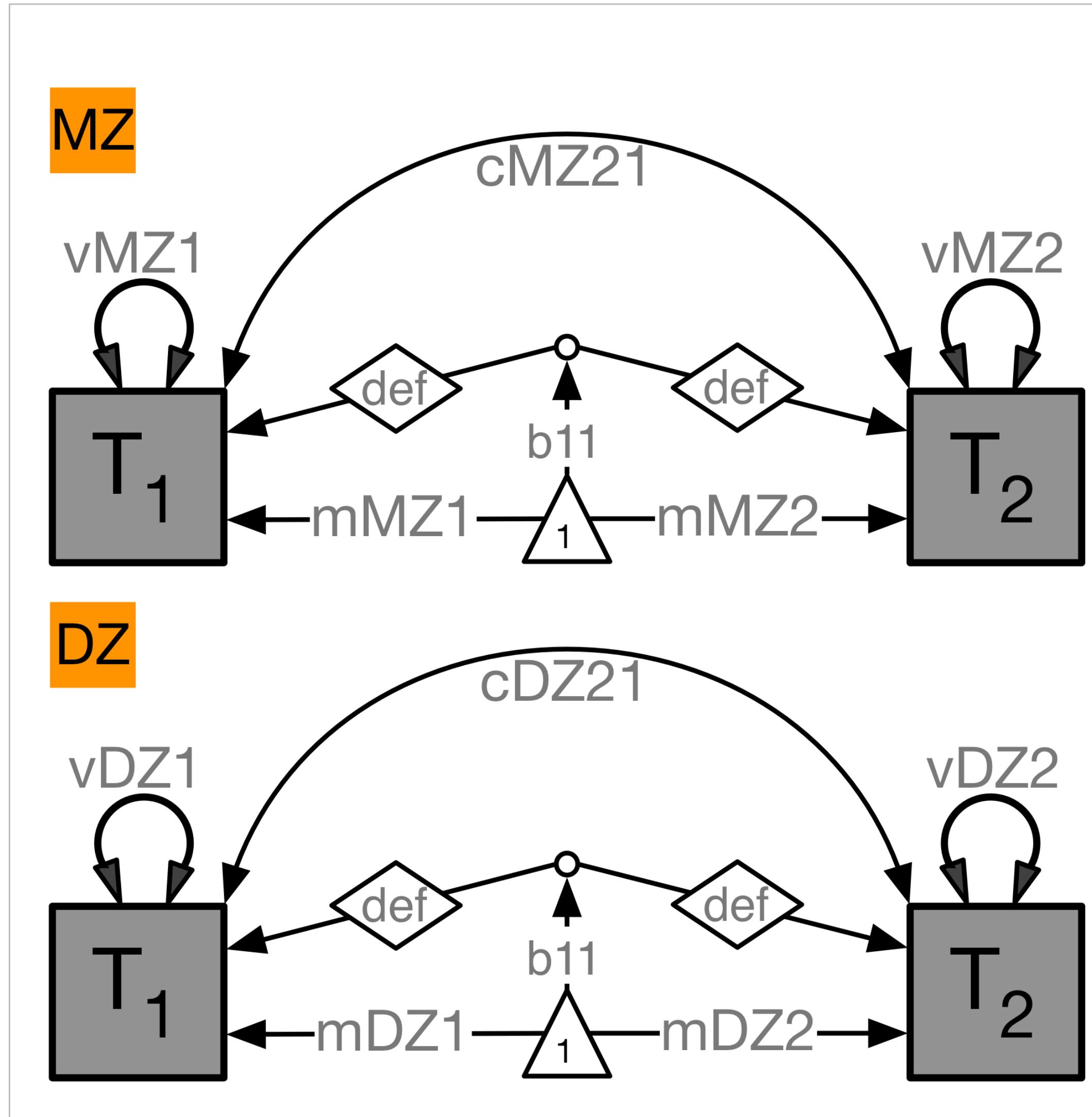
2-group
Females

```
Mx:oneSATc   os=1775   ns=919   ep=11   co=0   df=1764   ll=4015.1185   cpu=0.1924   opt=NPSOL   ver=2.19.5.1   stc=0

    b11     mMZ1     mMZ2     vMZ1     cMZ21     vMZ2     mDZ1     mDZ2     vDZ1     cDZ21     vDZ2
 2.7532  20.6888  20.6936   0.7214   0.5841   0.7843  20.7835  20.8082   0.7281   0.2415   0.8030
```

```
      base  comparison ep  minus2LL   df       AIC      diffLL diffdf          p
1 oneSATc        <NA> 11 4015.1185 1764 4037.1185        NA     NA         NA
2 oneSATc     oneEMOc  9 4015.3493 1766 4033.3493 0.2308120      2 0.89100432
3 oneSATc    oneEMVOc  7 4018.6107 1768 4032.6107 3.4922277      4 0.47906112
4 oneSATc    oneEMVZc  5 4022.7885 1770 4032.7885 7.6700423      6 0.26328698
```

```
      base  comparison ep  minus2LL   df       AIC      diffLL diffdf          p
1 oneSATc        <NA> 11 4015.1185 1764 4037.1185        NA     NA         NA
2 oneSATc    oneADEvc  5 4022.7885 1770 4032.7885 7.6700423      6 0.26328698
```

```
Mx:oneADEvc   os=1775   ns=919   ep=5   co=0   df=1770   ll=4022.7885   cpu=0.324   opt=NPSOL   ver=2.19.5.1   stc=0

    b11     mean     VA11     VD11     VE11
 2.7678  20.7346   0.3674   0.2250   0.1690
                  lbound estimate ubound
oneADEvc.US[1,1]   0.0681    0.3674 0.6530
oneADEvc.US[1,2]  -0.0459    0.2250 0.5244
oneADEvc.US[1,3]   0.1503    0.1690 0.1910
```

```
      base  comparison ep  minus2LL   df       AIC      diffLL diffdf          p
1 oneADEvc       <NA>  5 4022.7885 1770 4032.7885        NA     NA         NA
2 oneADEvc    oneAEvc  4 4025.4093 1771 4033.4093 2.6208252      1 1.0546958e-01
3 oneADEvc     oneEvc  3 4549.6129 1772 4555.6129 526.8243890      2 3.9951902e-115
```

```
        VA     VD     VE       SA     SD     SE
US  0.3674 0.225 0.1690   0.4825 0.2956 0.2220
US  0.5976 0.000 0.1719   0.7766 0.0000 0.2234
US  0.0000 0.000 0.7598   0.0000 0.0000 1.0000
```

2-group
Males

```
Mx:oneSATc   os=910   ns=479   ep=11   co=0   df=899   ll=1883.7212   cpu=0.1162   opt=NPSOL   ver=2.19.5.1   stc=0

     b11    mMZ1    mMZ2    vMZ1    cMZ21   vMZ2    mDZ1    mDZ2    vDZ1    cDZ21   vDZ2
  6.5889 20.0568 20.0704  0.5456  0.3924  0.5085 20.2591 20.2294  0.6485  0.1692  0.7148

         base comparison ep  minus2LL  df       AIC      diffLL diffdf           p
1 oneSATc         <NA> 11 1883.7212 899 1905.7212         NA     NA          NA
2 oneSATc      oneEMOc  9 1884.0599 901 1902.0599  0.33875227      2 0.844191312
3 oneSATc     oneEMVOc  7 1885.2538 903 1899.2538  1.53260364      4 0.820850873
4 oneSATc     oneEMVZc  5 1899.3977 905 1909.3977 15.67656595      6 0.015599373

         base comparison ep  minus2LL  df       AIC      diffLL diffdf           p
1 oneSATc         <NA> 11 1883.7212 899 1905.7212         NA     NA          NA
2 oneSATc      oneADEvc  5 1899.3977 905 1909.3977  15.676566      6 0.015599373

Mx:oneADEvc   os=910   ns=479   ep=5   co=0   df=905   ll=1899.3977   cpu=0.2982   opt=NPSOL   ver=2.19.5.1   stc=0

     b11    mean    VA11    VD11    VE11
  6.5518 20.1644  0.1032  0.3758  0.1375
                  lbound estimate ubound
oneADEvc.US[1,1] -0.2054   0.1032 0.3965
oneADEvc.US[1,2]  0.0929   0.3758 0.6960
oneADEvc.US[1,3]  0.1157   0.1375 0.1650

         base comparison ep  minus2LL  df       AIC      diffLL diffdf           p
1 oneADEvc         <NA>  5 1899.3977 905 1909.3977         NA     NA          NA
2 oneADEvc      oneAEvc  4 1906.4279 906 1914.4279  7.0302024      1 8.0146294e-03
3 oneADEvc       oneEvc  3 2121.8315 907 2127.8315 222.4337643      2 5.0017479e-49

        VA     VD     VE      SA     SD     SE
US  0.1032 0.3758 0.1375  0.1675 0.6096 0.2230
US  0.4854 0.0000 0.1446  0.7705 0.0000 0.2295
US  0.0000 0.0000 0.6028  0.0000 0.0000 1.0000
```

4-group multigroup - quantitative differences
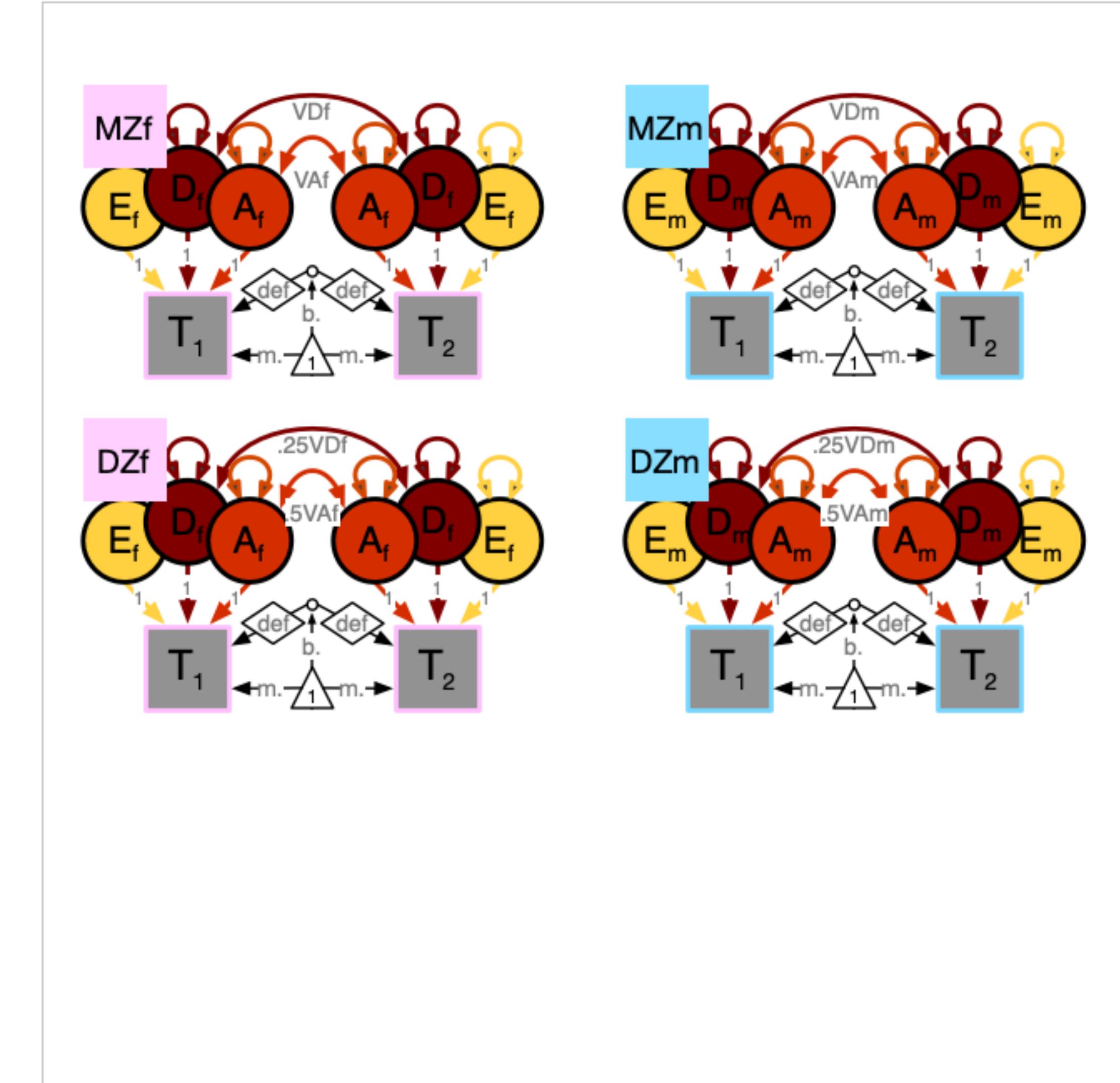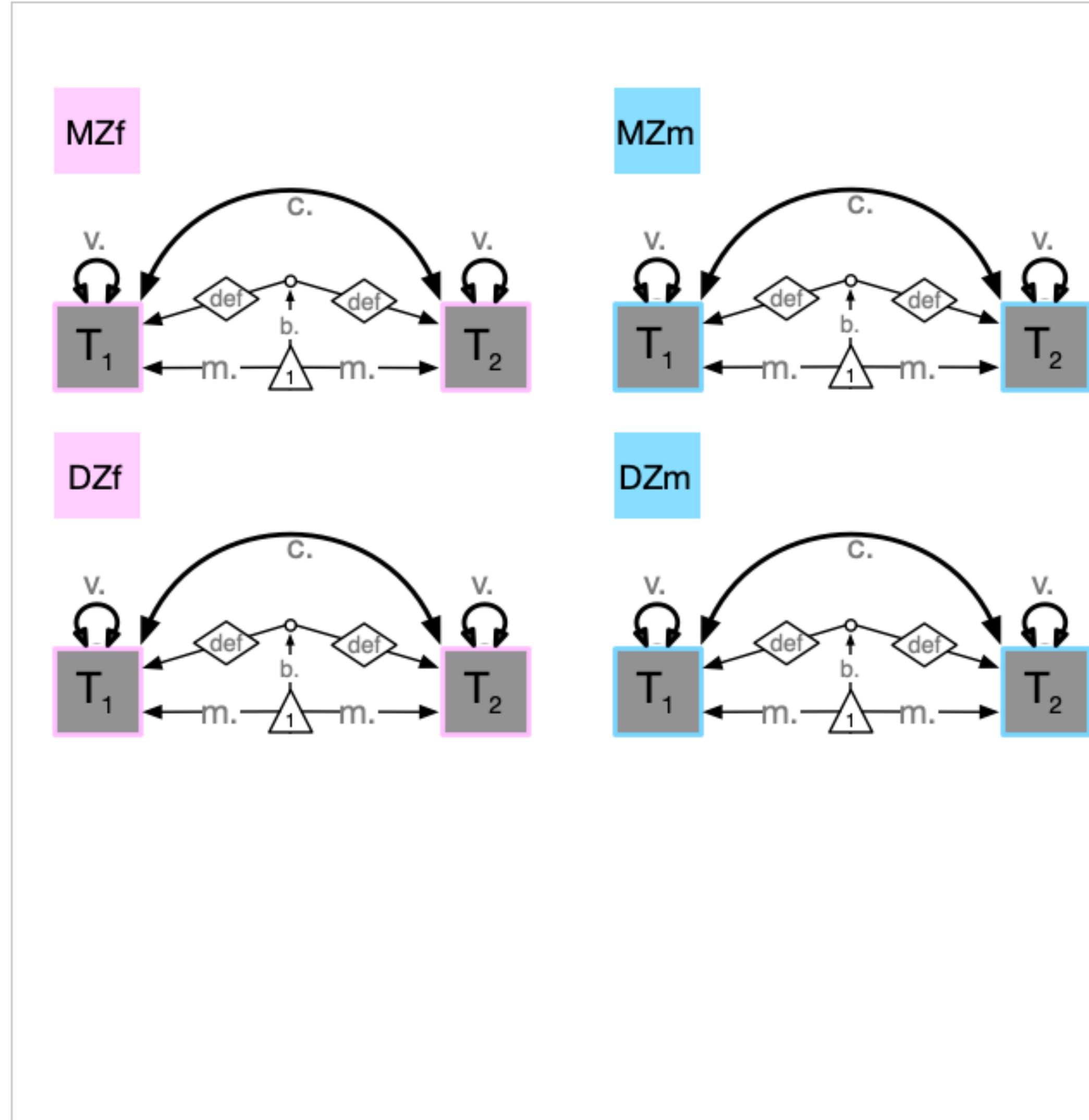
4-group

```
Mx:oneSAT4ca  os=2685   ns=1398    ep=22    co=0   df=2663  ll=5898.8396   cpu=12.175   opt=NPSOL   ver=2.19.5.1   stc=0
    bf11     bm11    mMZf1    mMZf2    vMZf1   cMZf21    vMZf2    mDZf1    mDZf2    vDZf1   cDZf21    vDZf2    mMZm1    mMZm2    vMZm1
  2.7537   6.5888  20.6887  20.6935   0.7214   0.5841   0.7843  20.7834  20.8081   0.7281   0.2415   0.8030  20.0568  20.0704   0.5456
   cMZm21    vMZm2    mDZm1    mDZm2    vDZm1   cDZm21    vDZm2
   0.3924   0.5085  20.2591  20.2294   0.6486   0.1692   0.7148


Mx:oneADEq4vca  os=2685   ns=1398    ep=10    co=0   df=2675  ll=5922.1862   cpu=1.6431   opt=NPSOL   ver=2.19.5.1   stc=0
    bf11    VAf11    VDf11    VEf11     bm11    VAm11    VDm11    VEm11     mZf      mZm
  2.7677   0.3674   0.2250   0.1690   6.5515   0.1033   0.3758   0.1375  20.7346  20.1645
                    lbound estimate ubound
oneADEq4vca.US[1,1]   0.0681    0.3674 0.6530
oneADEq4vca.US[1,2]  -0.0459    0.2250 0.5244
oneADEq4vca.US[1,3]   0.1503    0.1690 0.1910
oneADEq4vca.US[1,7]  -0.2054    0.1033 0.3965
oneADEq4vca.US[1,8]   0.0929    0.3758 0.6960
oneADEq4vca.US[1,9]   0.1157    0.1375 0.1650


Mx:oneADE4vca  os=2685   ns=1398    ep=7     co=0   df=2678  ll=5935.0138   cpu=1.3796   opt=NPSOL   ver=2.19.5.1   stc=0
    bf11     VA11     VD11     VE11     bm11      mZf      mZm
  2.7736   0.2664   0.2861   0.1588   6.5383  20.7337  20.1656


        base comparison ep  minus2LL    df       AIC     diffLL diffdf          p
1 oneADEq4vca         <NA> 10 5922.1862 2675 5942.1862      NA      NA         NA
2 oneADEq4vca oneADE4vca  7 5935.0138 2678 5949.0138 12.827571       3 0.0050247266


      VAf     VDf     VEf     SAf     SDf     SEf     VAm     VDm     VEm     SAm     SDm     SEm
US 0.3674  0.2250  0.1690  0.4825  0.2956  0.2220  0.1033  0.3758  0.1375  0.1675  0.6096  0.2230
US 0.2664  0.2861  0.1588  0.3745  0.4022  0.2233  0.2664  0.2861  0.1588  0.3745  0.4022  0.2233
```

5-group multigroup qualitative & quantitative
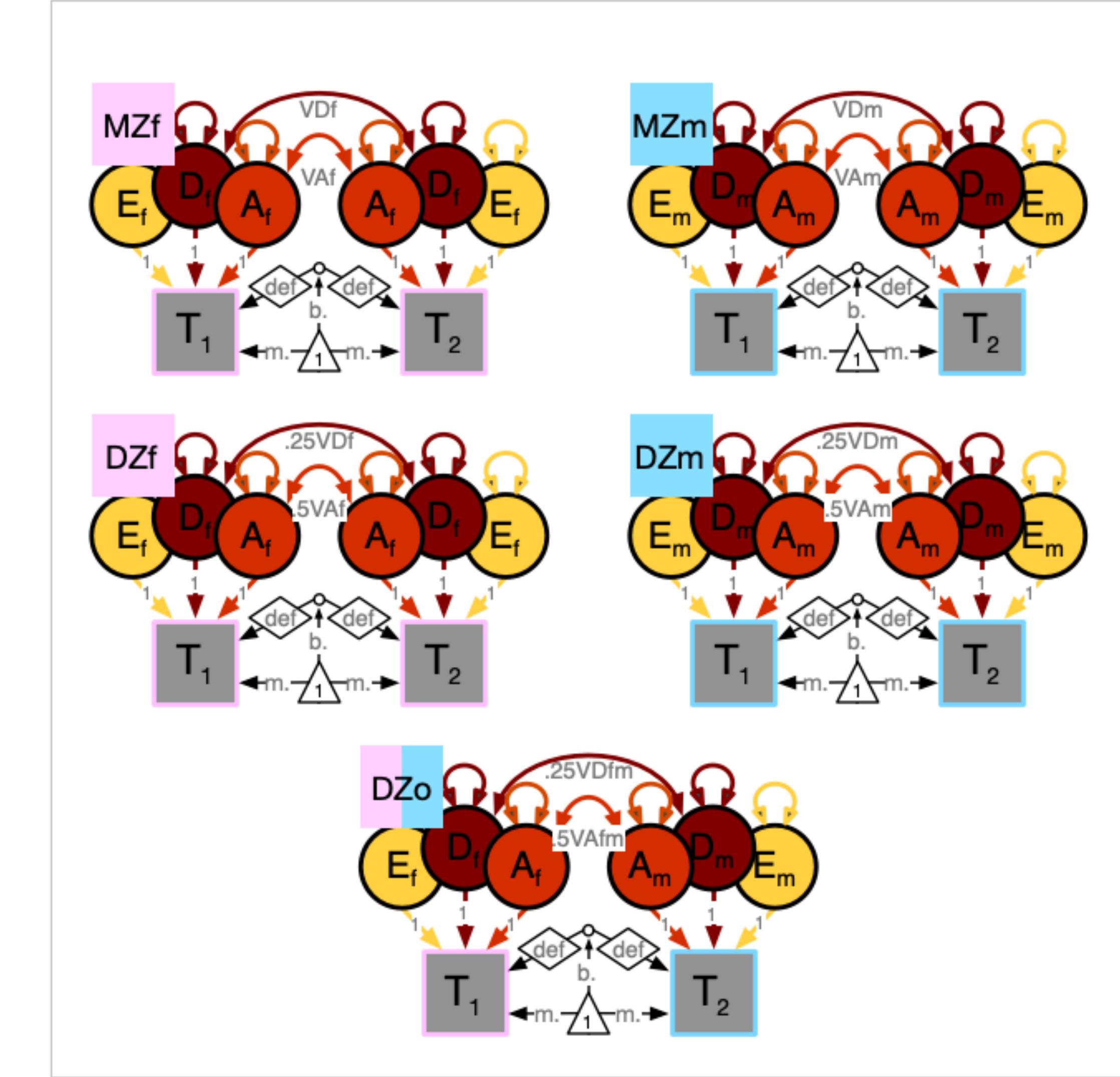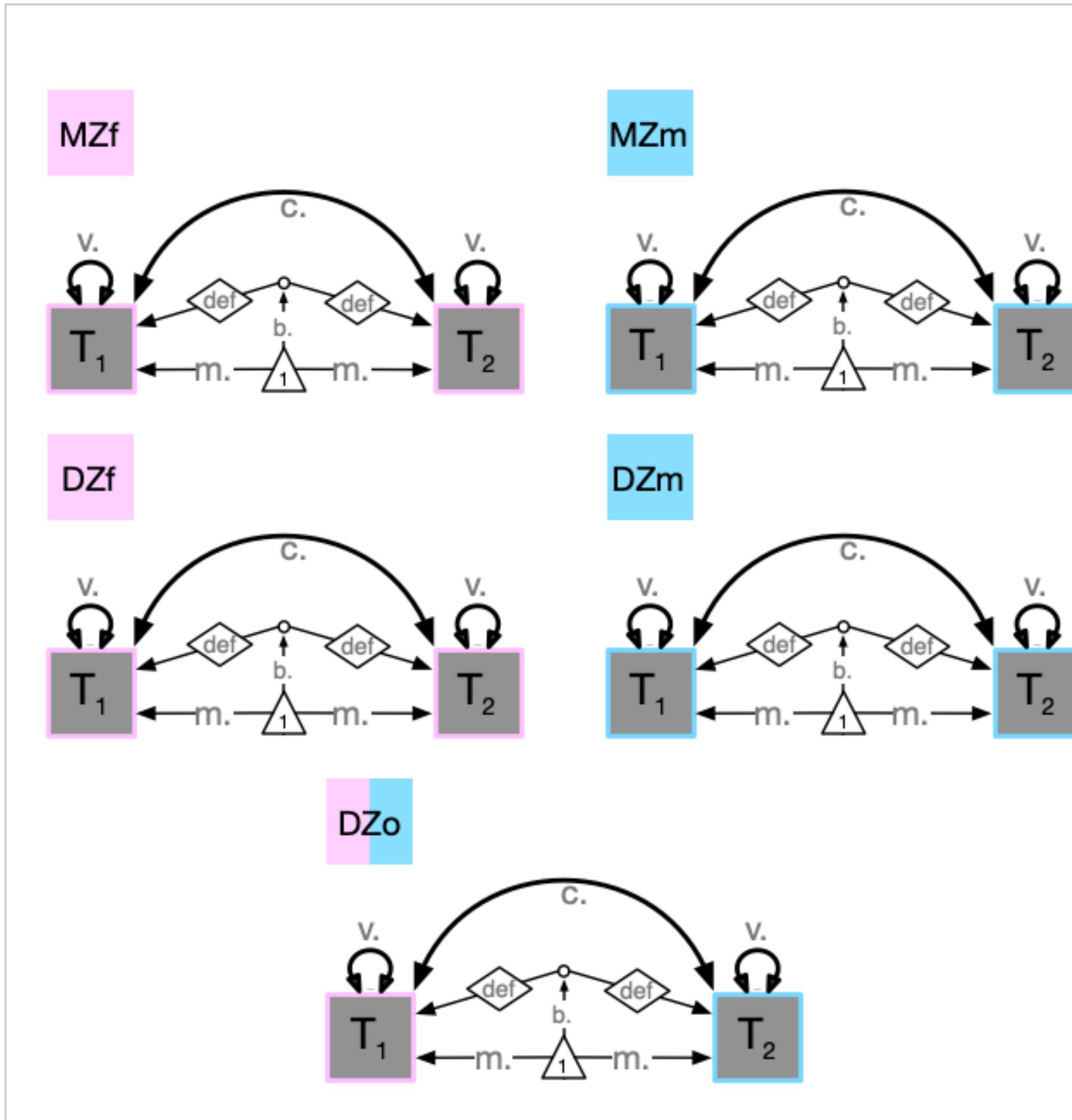
5-group

```
Mx:oneADEra5vca   os=3654   ns=1907     ep=11     co=0   df=3643   ll=8219.2209   cpu=3.8965   opt=NPSOL   ver=2.19.5.1   stc=0

   bf11     VAf11    VDf11    VEf11     bm11    VAm11    VDm11    VEm11   VAms11      mZf      mZm
 2.7703   0.3389   0.2307   0.1683   5.5588   0.0771   0.3792   0.1373   0.0209  20.7291  20.4263

                       lbound estimate ubound
oneADEra5vca.US[1,1]       NA    0.3389      NA
oneADEra5vca.US[1,2]   0.0000    0.2307      NA
oneADEra5vca.US[1,3]   0.1497    0.1683  0.1900
oneADEra5vca.US[1,7]       NA    0.0980  0.3838
oneADEra5vca.US[1,8]   0.0977    0.3792      NA
oneADEra5vca.US[1,9]   0.1156    0.1373  0.1647
oneADEra5vca.US[1,13]      NA    0.8872      NA
oneADEra5vca.US[1,14]  1.0000    1.0000  1.0000
```

```
          base     comparison ep   minus2LL   df       AIC         diffLL diffdf          p
1 oneADEra5vca           <NA> 11  8219.2209 3643 8241.2209            NA     NA         NA
2 oneADEra5vca oneADErd5vca   11  8219.2209 3643 8241.2209  -2.1827691e-07      0         NA
3 oneADEra5vca  oneADEq5vca   10  8219.2444 3644 8239.2444   2.3513966e-02      1 0.8781280748
4 oneADEra5vca    oneADE5vca   7  8234.7876 3647 8248.7876   1.5566673e+01      4 0.0036593125
```

```
                      VAf     VDf     VEf     SAf     SDf     SEf     VAm     VDm     VEm     SAm     SDm     SEm     rg     rd
US oneADEra5vca    0.3389  0.2307  0.1683  0.4592  0.3127  0.2281   0.098  0.3792  0.1373  0.1595  0.6171  0.2234  0.8872  1
US oneADErd5vca    0.3389  0.2307  0.1683  0.4592  0.3127  0.2281   0.098  0.3792  0.1373  0.1594  0.6172  0.2234  1       0.8613
US oneADEq5vca     0.3409  0.2288  0.1683  0.4619  0.31    0.2281  0.0772  0.4     0.1371  0.1256  0.6512  0.2232  1       1
US oneADE5vca      0.1909  0.3405  0.1581  0.2769  0.4938  0.2293  0.1909  0.3405  0.1581  0.2769  0.4938  0.2293  1       1
```

2-group interaction x age
means & covariances
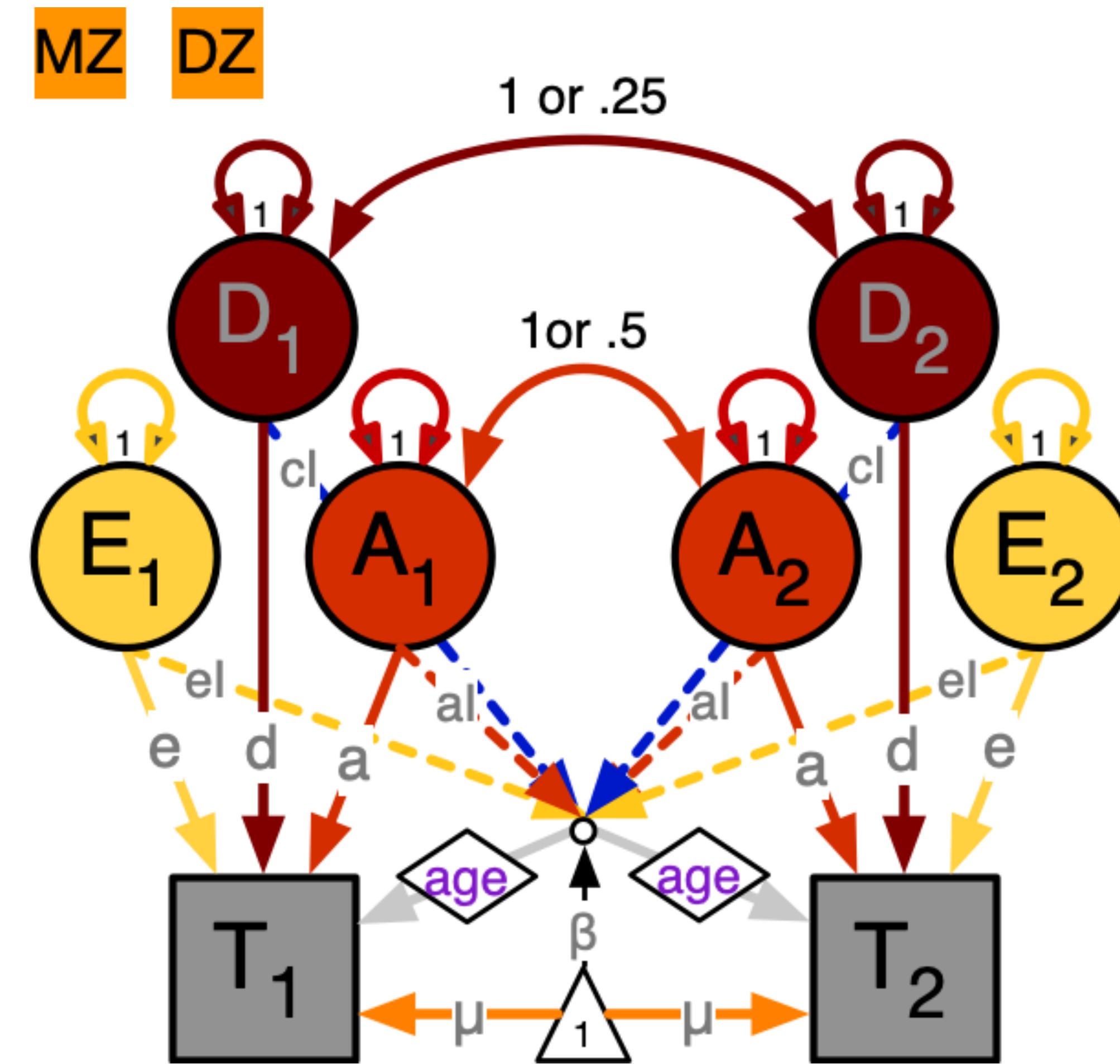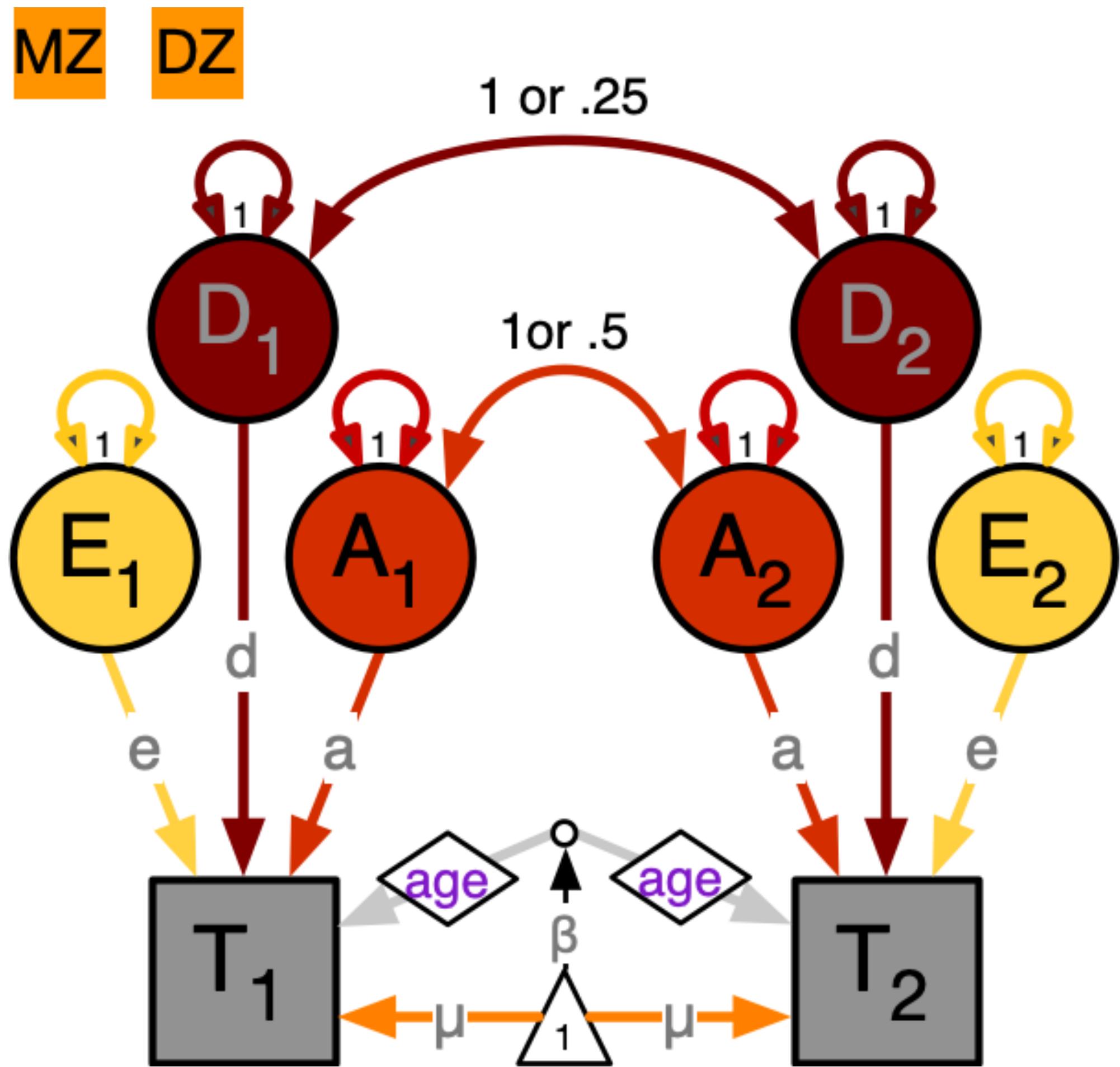
2-group age x ADE interaction
Females

```
Mx:oneADEcaI   os=3853   ns=1982   ep=9   co=0   df=3844   ll=9316.5572   cpu=51.7077   opt=NPSOL   ver=2.19.5.1   stc=1

        l11      q11 meanbmi       a11      d11      e11      aI11     dI11     eI11
     3.8278  -2.0909 20.5932    0.6546  -0.2978  -0.2931  -0.0352  -0.3819  -0.5442

       agevalues        MI          AI          DI          EI          VI
Age15         15 21.120358  0.42166997  0.12607553  0.14044989  0.68819539
Age25         25 21.419506  0.41710835  0.15465499  0.18419682  0.75596015
Age35         35 21.676836  0.41257153  0.18615151  0.23386577  0.83258881
Age45         45 21.892349  0.40805952  0.22056512  0.28945673  0.91808137
Age55         55 22.066046  0.40357232  0.25789580  0.35096970  1.01243782
Age65         65 22.197924  0.39910993  0.29814356  0.41840468  1.11565817
Age75         75 22.287986  0.39467235  0.34130839  0.49176167  1.22774241
> fitADElqi$SxAge$result
       agevalues        MI          AI          DI          EI          VI
Age15         15 21.120358  0.61271839  0.18319729  0.20408432  0.68819539
Age25         25 21.419506  0.55175970  0.20458087  0.24365943  0.75596015
Age35         35 21.676836  0.49552855  0.22358157  0.28088988  0.83258881
Age45         45 21.892349  0.44446989  0.24024572  0.31528439  0.91808137
Age55         55 22.066046  0.39861443  0.25472754  0.34665803  1.01243782
Age65         65 22.197924  0.35773496  0.26723558  0.37502946  1.11565817
Age75         75 22.287986  0.32146185  0.27799674  0.40054141  1.22774241

        base comparison ep    minus2LL   df       AIC      diffLL diffdf            p
1 oneADEcaI        <NA>  9  9316.5572 3844 9334.5572          NA     NA           NA
2 oneADEcaI oneADEcaI2   6  9382.8512 3847 9394.8512   66.2940104      3 2.6517015e-14
3 oneADEcaI oneADEcaI3   8  9322.6262 3845 9338.6262    6.0690704      1 1.3756934e-02
4 oneADEcaI oneADEcaI4   7  9551.0273 3846 9565.0273  234.4701786      2 1.2174402e-51
```

Age x ADE interaction

Unstandardized

Standardized

Age Moderation – unstandardized variance components

Legend: VA, VD, VE, VT

Age Moderation – standardized variance components

Legend: SVA, SVD, SVE
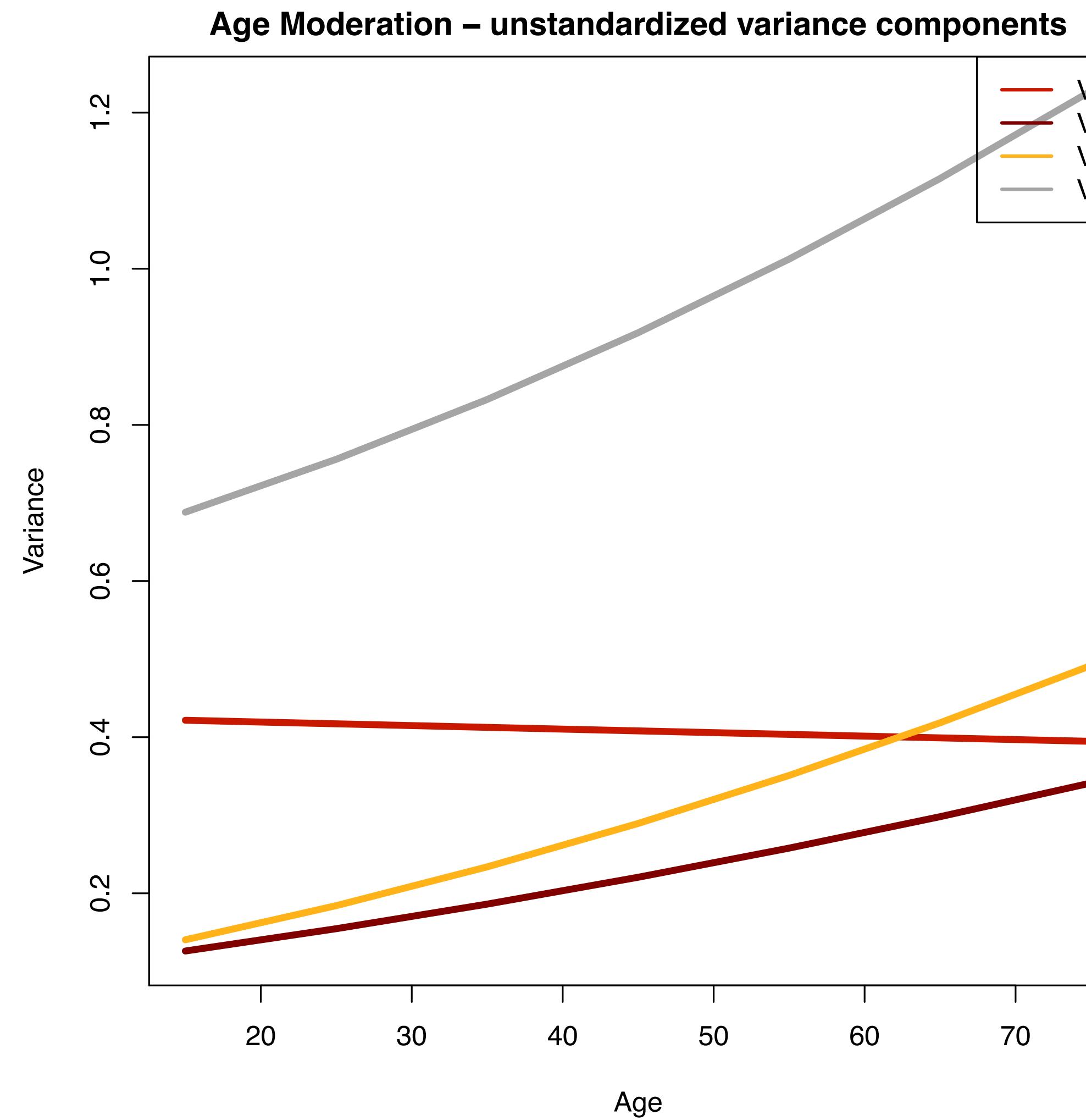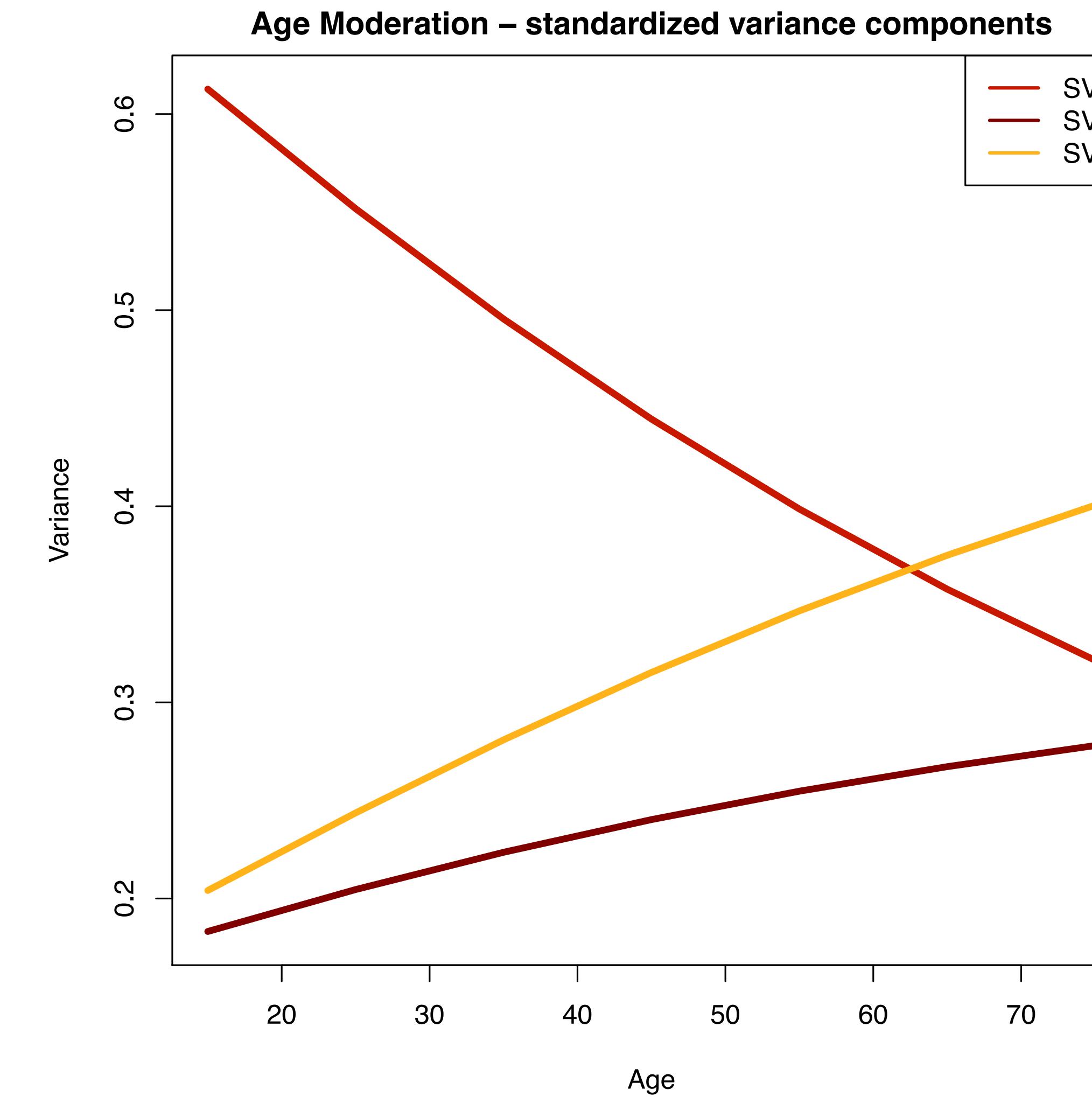
Age x ADE interaction

VA

VD

VE

Unstandardized VA variance components +CIs
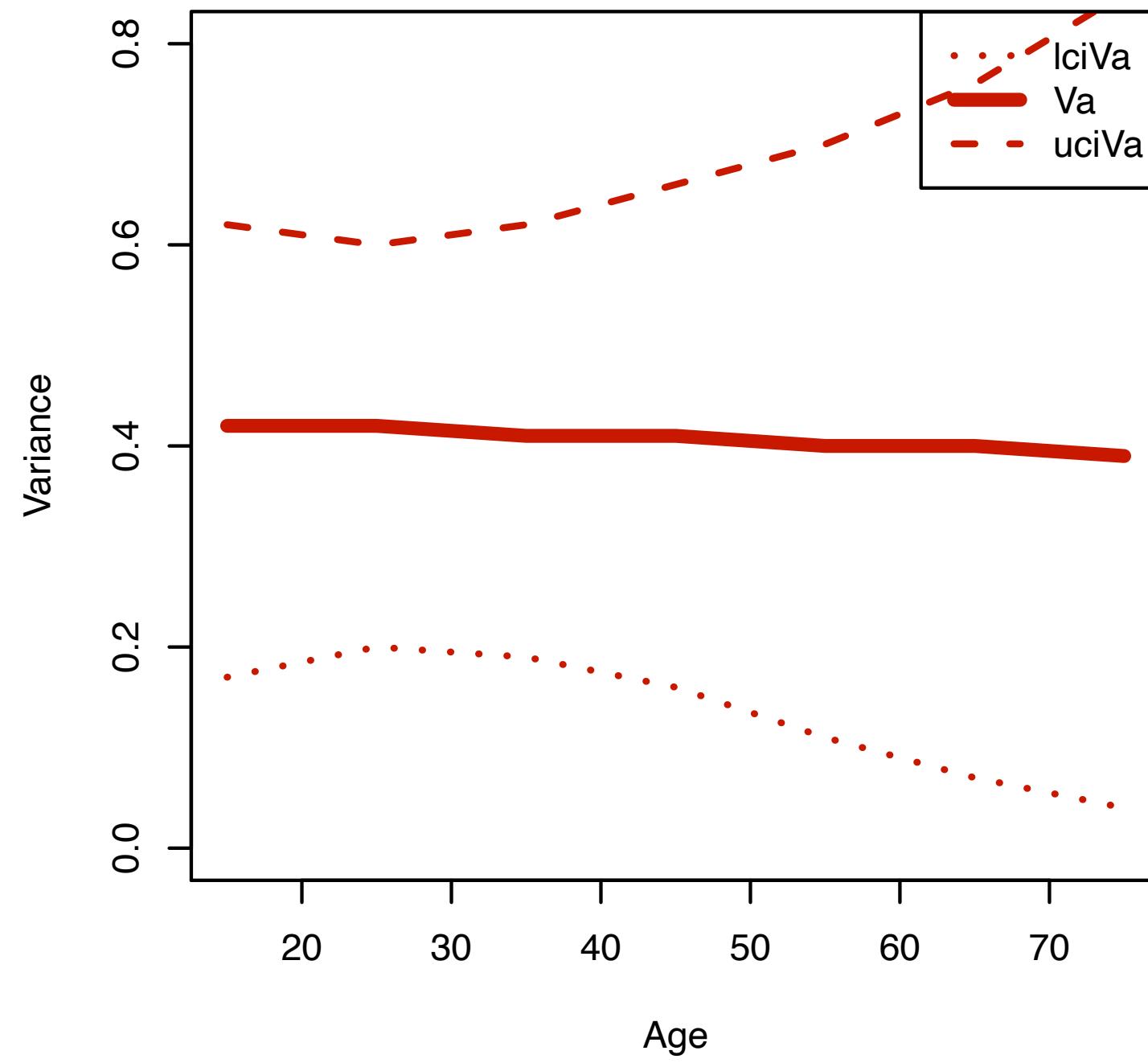
Unstandardized VD variance components +CIs
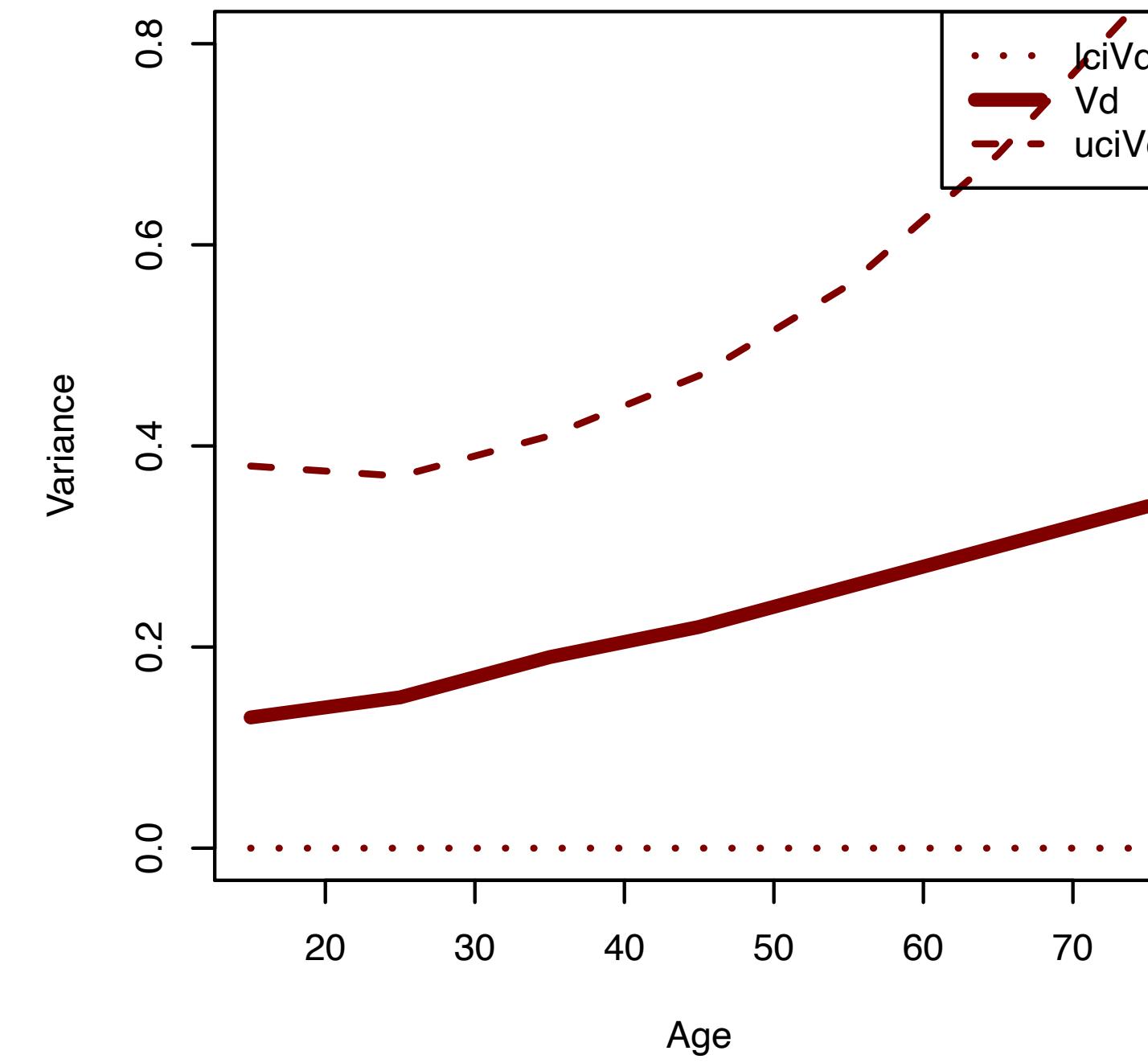
Unstandardized VE variance components +CIs

https://hermine-maes.squarespace.com/pubs/

hermine-maes.squarespace.com
Hermine Maes: hermine.maes@vcuhealth.org

From twin correlations to sources of variance

rDZ < 1/2 rMZ   **rMZ > rDZ**   **rDZ > 1/2rMZ**

rMZ=2*rDZ   **1–rMZ = E**   **rMZ = rDZ**

only A   **E + only A**   **E + only C**

E + **A** & **D**   **E** + **A** & **C**
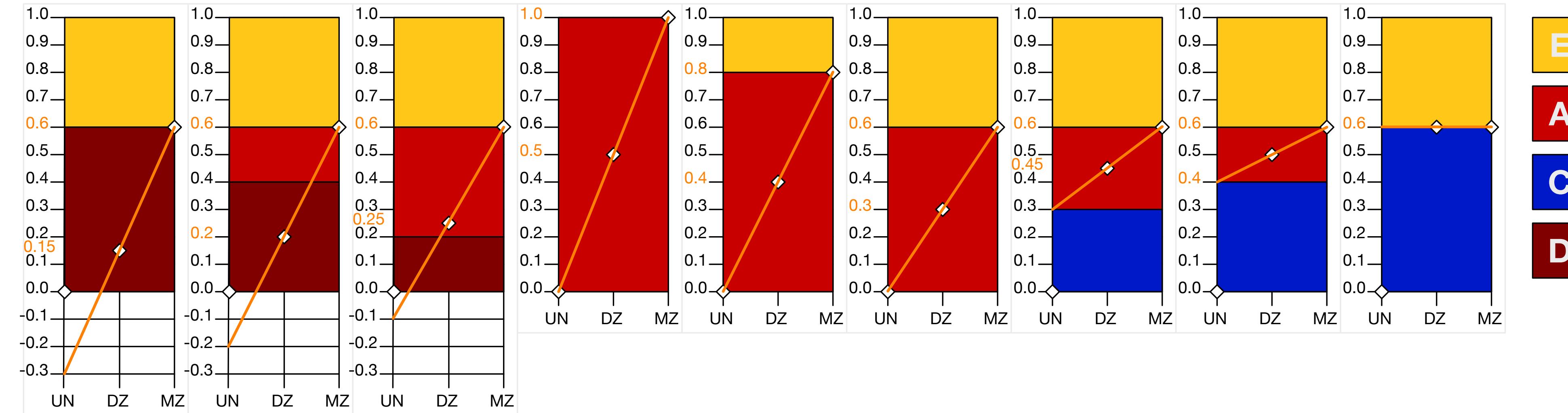
D= **-2*C**   **A'**= **A+3C**   **C**= **-1/2*D**   **A'**= **A +3/2D**

rMZ: monozygotic twin correlation; rDZ: dizygotic twin correlation;
A: additive genetic factors; E: unique environment: C: common environment; D: dominance