Bangladesh Application

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1 Variables

Table 1: Summary of the Variables

	Name	Variable Name	Data Type
Outcome Y	cognitive score	cognitive_raw	continuous
Exposure A	manganese	ln_blood_mn_conc_ugdl0	continuous
Mediator M	birth length, birth weight, head circumference	length0, weight0, head_circumference0	continuous, continuous, continuous
Pre-exposure confounder	Arsenic, Lead, protein intake, smoking, child age, education, mother age, home score, study site, sex	ln_blood_as_conc_ugdl0, ln_blood_pb_conc_ugdl0, allfood, smokenv, agedays, educcat, approxage, homescore, clinic, sex	continuous, continuous, continuous, binary, continuous, categorical, continuous, continuous, binary, binary
Post-exposure confounder	gestational age, child's haematocrit level	birthgestationalage, hematocrit2	continuous, continuous

2 Single Mediator Cases

2.1 Mediator: Birth Weight

2.1.1 DAG

```
cmdag(outcome = "cognitive_raw",
      exposure = 'ln_blood_mn_conc_ugdl0',
      mediator = 'weight0',
      postc = NULL)
```
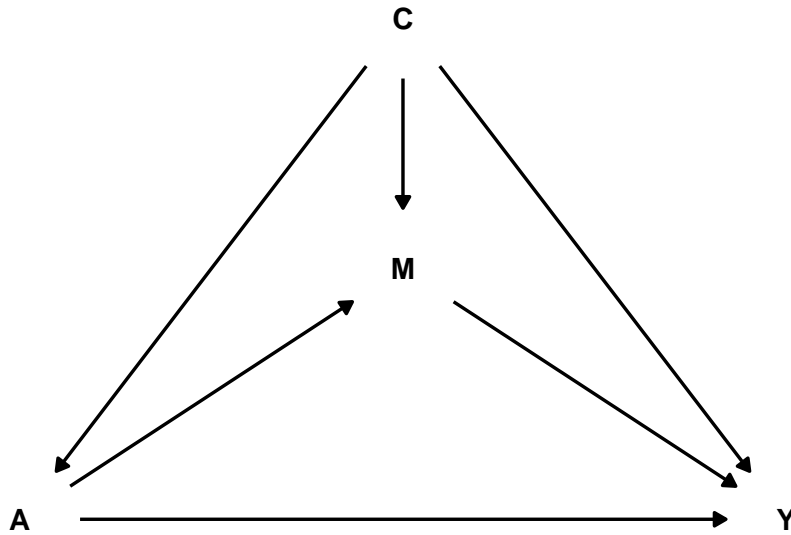
A(Exposure):ln_blood_mn_conc_ugdl0
M(Mediator):weight0
Y(Outcome):cognitive_raw
C(Pre−exposure confounders): prec

2.1.2 Causal Effects and Standard Errors Estimated By the Regression-based Approach

2.1.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```r
cmest_out <- cmest(data = bangladesh_df, model = "rb",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = 'weight0',
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "educcat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   EMint = TRUE,
                   yreg = "linear", mreg = "linear",
                   astar = log(5.84), a = log(9.5), mval = list(2.9),
                   estimation = "paramfunc", inference = "delta")

summary(cmest_out)
```

```
##           Estimate Std.error   95% CIL    95% CIU      z    pval
## cde      -0.280876  0.114696 -0.505677 -0.056076 -2.449 0.01455 *
## pnde     -0.291584  0.113848 -0.514722 -0.068447 -2.561 0.01062 *
## tnde     -0.298350  0.113462 -0.520732 -0.075969 -2.630 0.00872 **
## pnie     -0.035761  0.020814 -0.076555  0.005034 -1.718 0.08618 .
## tnie     -0.042527  0.023954 -0.089475  0.004422 -1.775 0.07623 .
## te       -0.334111  0.115341 -0.560176 -0.108046 -2.897 0.00388 **
## pm        0.067967  0.044270 -0.018801  0.154735  1.535 0.12513
```

2

```
## intref         -0.010708  0.008450 -0.027270  0.005854 -1.267 0.20546
## intmed         -0.006766  0.005634 -0.017808  0.004276 -1.201 0.23015
## pie            -0.035761  0.020814 -0.076555  0.005034 -1.718 0.08618 .
## cde_prop        0.840668  0.085177  0.673725  1.007611  9.870 < 2e-16 ***
## intref_prop     0.032049  0.028515 -0.023840  0.087938  1.124 0.26139
## intmed_prop     0.020251  0.017989 -0.015008  0.055509  1.126 0.26064
## pie_prop        0.107032  0.066472 -0.023250  0.237314  1.610 0.10777
## overall_pm      0.127283  0.077629 -0.024867  0.279433  1.640 0.10149
## overall_int     0.052300  0.041724 -0.029477  0.134077  1.253 0.21041
## overall_pe      0.159332  0.085177 -0.007611  0.326275  1.871 0.06178 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

2.1.2.2   Direct Imputation Estimation and Bootstrap Inference

```r
cmest_out <- cmest(data = bangladesh_df, model = "rb",
                outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                mediator = 'weight0',
                prec = c("ln_blood_as_conc_ugdl0",
                        "ln_blood_pb_conc_ugdl0",
                        "sex",
                        "allfood",
                        "smokenv", "educcat", "agedays", "approxage",
                        "homescore","birthgestationalage",
                        "clinic", "hematocrit2"),
                EMint = TRUE,
                yreg = "linear", mreg = "linear",
                astar = log(5.84), a = log(9.5), mval = list(2.9),
                estimation = "imputation", inference = "bootstrap",
                nboot = 200)

summary(cmest_out)
```

```
##              Estimate Std.error   95% CIL   95% CIU      z    pval
## cde          -0.280876  0.126413 -0.528641 -0.033112 -2.222 0.02658 *
## pnde         -0.293041  0.129101 -0.546075 -0.040007 -2.270 0.02349 *
## tnde         -0.299807  0.130722 -0.556018 -0.043596 -2.293 0.02209 *
## pnie         -0.035761  0.023205 -0.081242  0.009720 -1.541 0.12371
## tnie         -0.042527  0.027503 -0.096431  0.011378 -1.546 0.12245
## te           -0.335568  0.132115 -0.594508 -0.076627 -2.540 0.01128 *
## pm            0.067652  0.525339 -0.961994  1.097298  0.129 0.89757
## intref       -0.012165  0.012217 -0.036109  0.011779 -0.996 0.31969
## intmed       -0.006766  0.007055 -0.020594  0.007062 -0.959 0.33786
## pie          -0.035761  0.023205 -0.081242  0.009720 -1.541 0.12371
## cde_prop      0.837019  0.280546  0.287158  1.386879  2.984 0.00294 **
## intref_prop   0.036251  0.087943 -0.136115  0.208617  0.412 0.68030
## intmed_prop   0.020163  0.034729 -0.047905  0.088230  0.581 0.56170
## pie_prop      0.106568  0.212010 -0.308965  0.522100  0.503 0.61535
## overall_pm    0.126730  0.231185 -0.326383  0.579844  0.548 0.58373
## overall_int   0.056414  0.115820 -0.170589  0.283417  0.487 0.62634
## overall_pe    0.162981  0.280546 -0.386879  0.712842  0.581 0.56145
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

2.1.3 Causal Effects and Standard Errors Estimated By the G-formula Approach

```
cmest_out <- cmest(data = bangladesh_df, model = "g-formula",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = 'weight0',
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "educcat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   EMint = TRUE,
                   yreg = "linear", mreg = "linear",
                   astar = log(5.84), a = log(9.5), mval = list(2.9),
                   estimation = "imputation", inference = "bootstrap",
                   nboot = 200)

summary(cmest_out)
```

```
##               Estimate  Std.error      95% CIL     95% CIU      z     pval
## cde          -0.280876   0.126644   -0.529094   -0.032659 -2.218 0.02686 *
## pnde         -0.293041   0.129331   -0.546525   -0.039557 -2.266 0.02374 *
## tnde         -0.299807   0.130705   -0.555983   -0.043631 -2.294 0.02207 *
## pnie         -0.035761   0.023957   -0.082715    0.011194 -1.493 0.13592
## tnie         -0.042527   0.027448   -0.096324    0.011270 -1.549 0.12171
## te           -0.335568   0.128645   -0.587708   -0.083427 -2.608 0.00927 **
## pm            0.067652   0.309397   -0.538756    0.674060  0.219 0.82697
## intref       -0.012165   0.012098   -0.035876    0.011547 -1.006 0.31497
## intmed       -0.006766   0.008141   -0.022723    0.009191 -0.831 0.40620
## pie          -0.035761   0.023957   -0.082715    0.011194 -1.493 0.13592
## cde_prop      0.837019   9.760484  -18.293178   19.967215  0.086 0.93168
## intref_prop   0.036251   1.758018   -3.409402    3.481904  0.021 0.98355
## intmed_prop   0.020163   0.837877   -1.622047    1.662372  0.024 0.98081
## pie_prop      0.106568   7.175874  -13.957887   14.171022  0.015 0.98816
## overall_pm    0.126730   8.010623  -15.573801   15.827262  0.016 0.98738
## overall_int   0.056414   2.595146   -5.029980    5.142807  0.022 0.98266
## overall_pe    0.162981   9.760484  -18.967215   19.293178  0.017 0.98668
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

2.2 Mediator: Birth Length

2.2.1 DAG

```
cmdag(outcome = "cognitive_raw",
      exposure = 'ln_blood_mn_conc_ugdl0',
      mediator = 'length0',
      postc = NULL)
```

A(Exposure):ln_blood_mn_conc_ugdl0
M(Mediator):length0
Y(Outcome):cognitive_raw
C(Pre−exposure confounders): prec
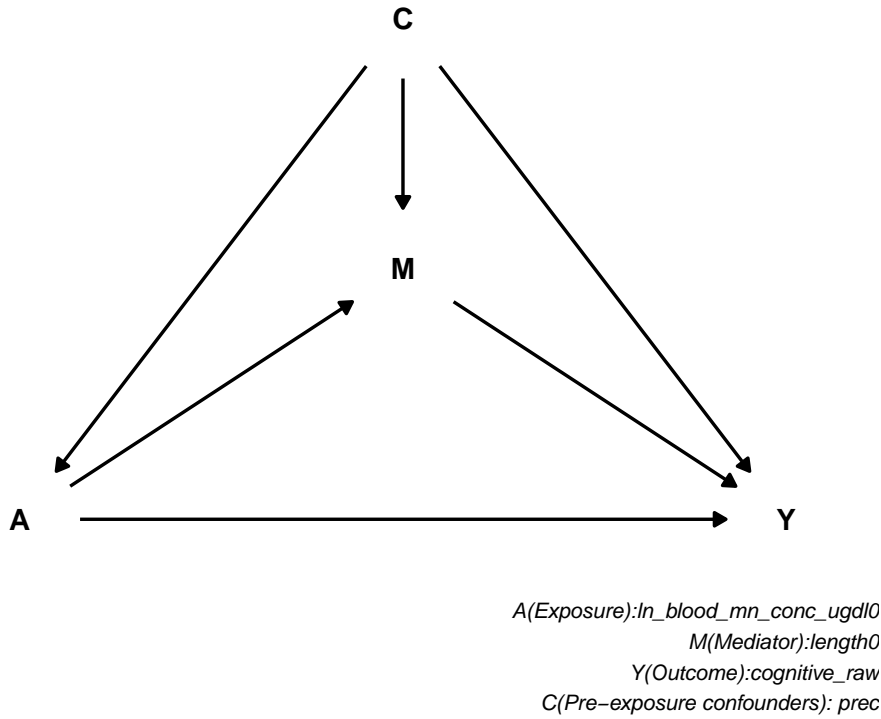
2.2.2 Causal Effects and Standard Errors Estimated By the Regression-based Approach

2.2.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```r
cmest_out <- cmest(data = bangladesh_df, model = "rb",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = 'length0',
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "educcat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   EMint = TRUE,
                   yreg = "linear", mreg = "linear",
                   astar = log(5.84), a = log(9.5), mval = list(47),
                   estimation = "paramfunc", inference = "delta")

summary(cmest_out)
```

```
##              Estimate Std.error   95% CIL   95% CIU      z      pval
## cde         -0.199932  0.112685 -0.420791  0.020927 -1.774 0.076417 .
## pnde        -0.253442  0.112467 -0.473874 -0.033010 -2.253 0.024511 *
## tnde        -0.288941  0.112666 -0.509763 -0.068119 -2.565 0.010519 *
## pnie        -0.072365  0.026589 -0.124477 -0.020252 -2.722 0.006643 **
## tnie        -0.107864  0.036800 -0.179991 -0.035737 -2.931 0.003478 **
## te          -0.361306  0.115238 -0.587169 -0.135442 -3.135 0.001782 **
## pm           0.175461  0.084331  0.010174  0.340747  2.081 0.037800 *
```

```
## intref       -0.053510  0.020765 -0.094208 -0.012811 -2.577 0.010153 *
## intmed       -0.035499  0.014543 -0.064004 -0.006995 -2.441 0.014874 *
## pie          -0.072365  0.026589 -0.124477 -0.020252 -2.722 0.006643 **
## cde_prop      0.553360  0.158432  0.242839  0.863880  3.493 0.000505 ***
## intref_prop   0.148101  0.072848  0.005321  0.290881  2.033 0.042395 *
## intmed_prop   0.098253  0.045623  0.008834  0.187672  2.154 0.031582 *
## pie_prop      0.200286  0.086673  0.030410  0.370163  2.311 0.021107 *
## overall_pm    0.298539  0.122068  0.059290  0.537789  2.446 0.014681 *
## overall_int   0.246354  0.102838  0.044794  0.447914  2.396 0.016834 *
## overall_pe    0.446640  0.158432  0.136120  0.757161  2.819 0.004939 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

2.2.2.2 Direct Imputation Estimation and Bootstrap Inference

```r
cmest_out <- cmest(data = bangladesh_df, model = "rb",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = 'length0',
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "eduecat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   EMint = TRUE,
                   yreg = "linear", mreg = "linear",
                   astar = log(5.84), a = log(9.5), mval = list(47),
                   estimation = "imputation", inference = "bootstrap",
                   nboot = 200)

summary(cmest_out)
```

```
##               Estimate Std.error   95% CIL   95% CIU      z    pval
## cde          -0.199932  0.120221 -0.435562  0.035698 -1.663 0.09671 .
## pnde         -0.248867  0.119691 -0.483458 -0.014277 -2.079 0.03793 *
## tnde         -0.284367  0.122710 -0.524874 -0.043860 -2.317 0.02074 *
## pnie         -0.072365  0.026166 -0.123648 -0.021081 -2.766 0.00582 **
## tnie         -0.107864  0.033710 -0.173934 -0.041794 -3.200 0.00143 **
## te           -0.356731  0.131261 -0.613998 -0.099464 -2.718 0.00672 **
## pm            0.178111  2.909414 -5.524236  5.880458  0.061 0.95120
## intref       -0.048935  0.023025 -0.094063 -0.003808 -2.125 0.03388 *
## intmed       -0.035499  0.014877 -0.064657 -0.006342 -2.386 0.01726 *
## pie          -0.072365  0.026166 -0.123648 -0.021081 -2.766 0.00582 **
## cde_prop      0.560455  0.415306 -0.253530  1.374441  1.349 0.17757
## intref_prop   0.137177  0.218089 -0.290269  0.564623  0.629 0.52954
## intmed_prop   0.099513  0.098064 -0.092688  0.291714  1.015 0.31053
## pie_prop      0.202855  0.147527 -0.086292  0.492002  1.375 0.16952
## overall_pm    0.302367  0.233626 -0.155532  0.760266  1.294 0.19597
## overall_int   0.236690  0.298317 -0.348002  0.821381  0.793 0.42778
## overall_pe    0.439545  0.415306 -0.374441  1.253530  1.058 0.29022
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

2.2.3 Causal Effects and Standard Errors Estimated By the G-formula Approach

```
cmest_out <- cmest(data = bangladesh_df, model = "g-formula",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = 'length0',
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "educcat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   EMint = TRUE,
                   yreg = "linear", mreg = "linear",
                   astar = log(5.84), a = log(9.5), mval = list(47),
                   estimation = "imputation", inference = "bootstrap",
                   nboot = 200)

summary(cmest_out)
```

```
##              Estimate Std.error   95% CIL   95% CIU      z     pval
## cde         -0.199932  0.107201 -0.410043  0.010179 -1.865 0.06256 .
## pnde        -0.248867  0.106148 -0.456913 -0.040822 -2.345 0.01930 *
## tnde        -0.284367  0.107642 -0.495341 -0.073392 -2.642 0.00841 **
## pnie        -0.072365  0.029444 -0.130075 -0.014655 -2.458 0.01420 *
## tnie        -0.107864  0.035842 -0.178112 -0.037616 -3.009 0.00270 **
## te          -0.356731  0.111428 -0.575126 -0.138337 -3.201 0.00142 **
## pm           0.178111  0.177249 -0.169291  0.525514  1.005 0.31528
## intref      -0.048935  0.019534 -0.087221 -0.010650 -2.505 0.01244 *
## intmed      -0.035499  0.015528 -0.065934 -0.005064 -2.286 0.02252 *
## pie         -0.072365  0.029444 -0.130075 -0.014655 -2.458 0.01420 *
## cde_prop     0.560455  0.311384 -0.049846  1.170757  1.800 0.07227 .
## intref_prop  0.137177  0.203124 -0.260939  0.535294  0.675 0.49967
## intmed_prop  0.099513  0.057204 -0.012604  0.211630  1.740 0.08232 .
## pie_prop     0.202855  0.135122 -0.061979  0.467688  1.501 0.13369
## overall_pm   0.302367  0.172755 -0.036226  0.640961  1.750 0.08047 .
## overall_int  0.236690  0.228177 -0.210529  0.683909  1.037 0.29992
## overall_pe   0.439545  0.311384 -0.170757  1.049846  1.412 0.15848
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

2.3 Mediator: Head Circumference

2.3.1 DAG

```
cmdag(outcome = "cognitive_raw",
      exposure = 'ln_blood_mn_conc_ugdl0',
      mediator = 'head_circumference0',
      postc = NULL)
```
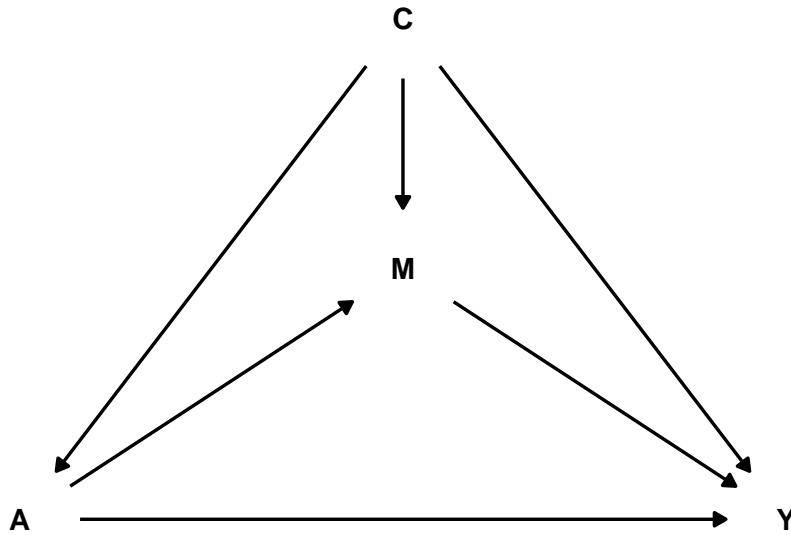
A(Exposure):ln_blood_mn_conc_ugdl0
M(Mediator):head_circumference0
Y(Outcome):cognitive_raw
C(Pre−exposure confounders): prec

2.3.2 Causal Effects and Standard Errors Estimated By the Regression-based Approach

2.3.2.1 Closed-form Parameter Function Estimation and Delta Method Inference

```r
cmest_out <- cmest(data = bangladesh_df, model = "rb",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = 'head_circumference0',
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "educcat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   EMint = TRUE,
                   yreg = "linear", mreg = "linear",
                   astar = log(5.84), a = log(9.5), mval = list(33),
                   estimation = "paramfunc", inference = "delta")

summary(cmest_out)
```

```
##              Estimate  Std.error     95% CIL     95% CIU      z     pval
## cde        -0.3390325  0.1169034  -0.5681589  -0.1099060  -2.900  0.00384 **
## pnde       -0.3384610  0.1150130  -0.5638825  -0.1130396  -2.943  0.00335 **
## tnde       -0.3383468  0.1148361  -0.5634214  -0.1132721  -2.946  0.00331 **
## pnie       -0.0135033  0.0119751  -0.0369739   0.0099674  -1.128  0.25983
## tnie       -0.0133890  0.0117278  -0.0363751   0.0095971  -1.142  0.25396
## te         -0.3518500  0.1152877  -0.5778097  -0.1258904  -3.052  0.00235 **
## pm          0.0193956  0.0180345  -0.0159515   0.0547427   1.075  0.28250
```

```
## intref          0.0005715  0.0139954 -0.0268591   0.0280020   0.041 0.96744
## intmed          0.0001143  0.0027996 -0.0053728   0.0056013   0.041 0.96746
## pie            -0.0135033  0.0119751 -0.0369739   0.0099674  -1.128 0.25983
## cde_prop         0.9635710  0.0547831  0.8561982   1.0709439  17.589 < 2e-16 ***
## intref_prop    -0.0016241  0.0397435 -0.0795200   0.0762717  -0.041 0.96741
## intmed_prop    -0.0003247  0.0079498 -0.0159060   0.0152565  -0.041 0.96743
## pie_prop         0.0383779  0.0352110 -0.0306344   0.1073901   1.090 0.27608
## overall_pm       0.0380531  0.0347096 -0.0299765   0.1060827   1.096 0.27328
## overall_int    -0.0019489  0.0476892 -0.0954180   0.0915203  -0.041 0.96741
## overall_pe       0.0364290  0.0547831 -0.0709439   0.1438018   0.665 0.50627
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

2.3.2.2 Direct Imputation Estimation and Bootstrap Inference

```r
cmest_out <- cmest(data = bangladesh_df, model = "rb",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = 'head_circumference0',
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "educcat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   EMint = TRUE,
                   yreg = "linear", mreg = "linear",
                   astar = log(5.84), a = log(9.5), mval = list(33),
                   estimation = "imputation", inference = "bootstrap",
                   nboot = 200)

summary(cmest_out)
```

```
##                Estimate  Std.error     95% CIL     95% CIU      z     pval
## cde          -0.3390325  0.1306447 -0.5950915  -0.0829735 -2.595  0.00964
## pnde         -0.3385052  0.1323435 -0.5978937  -0.0791168 -2.558  0.01072
## tnde         -0.3383910  0.1331492 -0.5993587  -0.0774233 -2.541  0.01123
## pnie         -0.0135033  0.0132338 -0.0394410   0.0124345 -1.020  0.30788
## tnie         -0.0133890  0.0134300 -0.0397112   0.0129332 -0.997  0.31910
## te           -0.3518942  0.1330138 -0.6125964  -0.0911921 -2.646  0.00832
## pm            0.0193931  0.0541031 -0.0866471   0.1254333  0.358  0.72011
## intref        0.0005272  0.0230130 -0.0445774   0.0456319  0.023  0.98173
## intmed        0.0001143  0.0061053 -0.0118519   0.0120804  0.019  0.98507
## pie          -0.0135033  0.0132338 -0.0394410   0.0124345 -1.020  0.30788
## cde_prop      0.9634499  0.1678475  0.6344748   1.2924251  5.740 1.36e-08
## intref_prop  -0.0014983  0.1545537 -0.3044181   0.3014215 -0.010  0.99227
## intmed_prop  -0.0003247  0.0619675 -0.1217788   0.1211294 -0.005  0.99582
## pie_prop      0.0383730  0.3450280 -0.6378695   0.7146156  0.111  0.91147
## overall_pm    0.0380483  0.2860067 -0.5225144   0.5986111  0.133  0.89420
## overall_int  -0.0018230  0.2130566 -0.4194062   0.4157603 -0.009  0.99318
## overall_pe    0.0365501  0.1678475 -0.2924251   0.3655252  0.218  0.82768
##
## cde          **
## pnde          *
```

```
## tnde         *
## pnie
## tnie
## te           **
## pm
## intref
## intmed
## pie
## cde_prop     ***
## intref_prop
## intmed_prop
## pie_prop
## overall_pm
## overall_int
## overall_pe
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

2.3.3 Causal Effects and Standard Errors Estimated By the G-formula Approach

```r
cmest_out <- cmest(data = bangladesh_df, model = "g-formula",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = 'head_circumference0',
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "educcat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   EMint = TRUE,
                   yreg = "linear", mreg = "linear",
                   astar = log(5.84), a = log(9.5), mval = list(33),
                   estimation = "imputation", inference = "bootstrap",
                   nboot = 200)

summary(cmest_out)
```

```
##                Estimate  Std.error     95% CIL     95% CIU       z     pval
## cde          -0.3390325  0.1319453  -0.5976405  -0.0804245  -2.569  0.01037 *
## pnde         -0.3385052  0.1328641  -0.5989142  -0.0780963  -2.548  0.01104 *
## tnde         -0.3383910  0.1334342  -0.5999173  -0.0768647  -2.536  0.01141 *
## pnie         -0.0135033  0.0115529  -0.0361465   0.0091400  -1.169  0.24284
## tnie         -0.0133890  0.0127424  -0.0383636   0.0115856  -1.051  0.29371
## te           -0.3518942  0.1337682  -0.6140751  -0.0897134  -2.631  0.00869 **
## pm            0.0193931  0.0358792  -0.0509288   0.0897150   0.541  0.58900
## intref        0.0005272  0.0225954  -0.0437589   0.0448134   0.023  0.98139
## intmed        0.0001143  0.0056744  -0.0110073   0.0112359   0.020  0.98394
## pie          -0.0135033  0.0115529  -0.0361465   0.0091400  -1.169  0.24284
## cde_prop      0.9634499  0.1022381   0.7630670   1.1638328   9.424  < 2e-16 ***
## intref_prop  -0.0014983  0.0755082  -0.1494917   0.1464951  -0.020  0.98417
## intmed_prop  -0.0003247  0.0193584  -0.0382665   0.0376171  -0.017  0.98662
## pie_prop      0.0383730  0.0835020  -0.1252879   0.2020339   0.460  0.64597
```

10

```
## overall_pm    0.0380483   0.0815031 -0.1216949   0.1977916   0.467 0.64075
## overall_int -0.0018230   0.0900721 -0.1783611   0.1747152  -0.020 0.98386
## overall_pe    0.0365501   0.1022381 -0.1638328   0.2369330   0.357 0.72082
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

3   Multiple Mediator Case

3.1   DAG

```
cmdag(outcome = "cognitive_raw",
      exposure = 'ln_blood_mn_conc_ugdl0',
      mediator = c("weight0","length0",'head_circumference0'),
      postc = NULL)
```
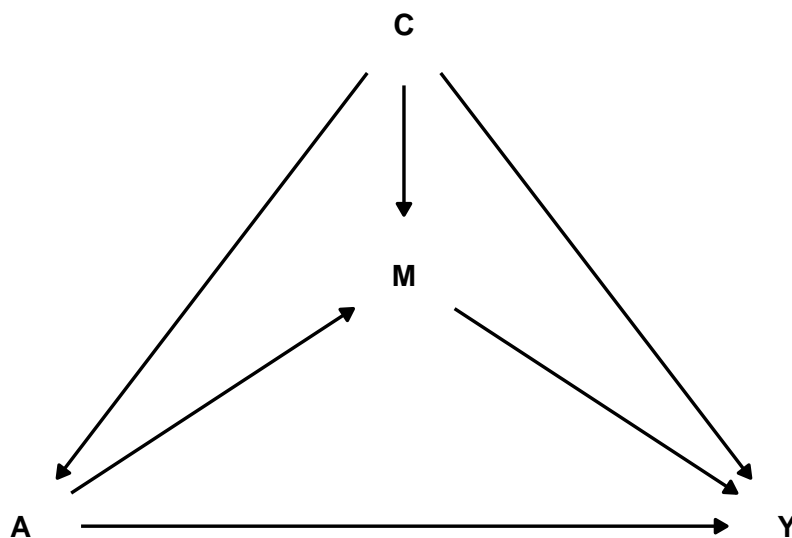

A(Exposure):ln_blood_mn_conc_ugdl0
M(Mediator):weight0, length0, head_circumference0
Y(Outcome):cognitive_raw
C(Pre−exposure confounders): prec

3.2   Causal Effects and Standard Errors Estimated By the Regression-based Approach

```
cmest_out <- cmest(data = bangladesh_df, model = "rb",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = c("weight0","length0",'head_circumference0'),
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
```

```
                          "smokenv", "educcat", "agedays", "approxage",
                          "homescore","birthgestationalage",
                          "clinic", "hematocrit2"),
                  EMint = TRUE,
                  yreg = "linear", mreg = c("linear", "linear", "linear"),
                  astar = log(5.84), a = log(9.5), mval = list(2.9,47,33),
                  estimation = "imputation", inference = "bootstrap",
                  nboot = 200)

summary(cmest_out)
```

```
##                 Estimate Std.error    95% CIL    95% CIU      z    pval
## cde            -0.212917  0.107327 -0.423274 -0.002560 -1.984 0.04763 *
## pnde           -0.247038  0.107631 -0.457991 -0.036085 -2.295 0.02199 *
## tnde           -0.279741  0.107127 -0.489706 -0.069775 -2.611 0.00920 **
## pnie           -0.084662  0.032851 -0.149048 -0.020275 -2.577 0.01015 *
## tnie           -0.117364  0.039629 -0.195035 -0.039693 -2.962 0.00315 **
## te             -0.364402  0.111841 -0.583607 -0.145197 -3.258 0.00117 **
## pm              0.191947  0.683614 -1.147912  1.531806  0.281 0.77895
## intref         -0.034122  0.022662 -0.078539  0.010295 -1.506 0.13256
## intmed         -0.032702  0.015193 -0.062480 -0.002924 -2.152 0.03167 *
## pie            -0.084662  0.032851 -0.149048 -0.020275 -2.577 0.01015 *
## cde_prop        0.584290  0.221435  0.150286  1.018294  2.639 0.00849 **
## intref_prop     0.093637  0.090041 -0.082841  0.270115  1.040 0.29870
## intmed_prop     0.089742  0.065088 -0.037827  0.217312  1.379 0.16836
## pie_prop        0.232330  0.134749 -0.031772  0.496432  1.724 0.08508 .
## overall_pm      0.322073  0.179915 -0.030555  0.674700  1.790 0.07383 .
## overall_int     0.183380  0.130271 -0.071946  0.438705  1.408 0.15963
## overall_pe      0.415710  0.221435 -0.018294  0.849714  1.877 0.06085 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

3.3 Causal Effects and Standard Errors Estimated By the G-formula Approach

```
cmest_out <- cmest(data = bangladesh_df, model = "g-formula",
                  outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                  mediator = c("weight0","length0",'head_circumference0'),
                  prec = c("ln_blood_as_conc_ugdl0",
                          "ln_blood_pb_conc_ugdl0",
                          "sex",
                          "allfood",
                          "smokenv", "educcat", "agedays", "approxage",
                          "homescore","birthgestationalage",
                          "clinic", "hematocrit2"),
                  EMint = TRUE,
                  yreg = "linear", mreg = c("linear", "linear", "linear"),
                  astar = log(5.84), a = log(9.5), mval = list(2.9,47,33),
                  estimation = "imputation", inference = "bootstrap",
                  nboot = 200)

summary(cmest_out)
```

```
##                 Estimate Std.error    95% CIL    95% CIU      z    pval
```

```
## cde         -0.212917  0.110819 -0.430118  0.004285 -1.921 0.05506 .
## pnde        -0.247038  0.112434 -0.467405 -0.026671 -2.197 0.02831 *
## tnde        -0.279741  0.114843 -0.504828 -0.054653 -2.436 0.01508 *
## pnie        -0.084662  0.031121 -0.145657 -0.023666 -2.720 0.00667 **
## tnie        -0.117364  0.035969 -0.187861 -0.046867 -3.263 0.00115 **
## te          -0.364402  0.118864 -0.597371 -0.131434 -3.066 0.00225 **
## pm           0.191947  0.213826 -0.227145  0.611039  0.898 0.36964
## intref      -0.034122  0.024930 -0.082983  0.014739 -1.369 0.17149
## intmed      -0.032702  0.014182 -0.060498 -0.004906 -2.306 0.02138 *
## pie         -0.084662  0.031121 -0.145657 -0.023666 -2.720 0.00667 **
## cde_prop     0.584290  0.494958 -0.385809  1.554390  1.180 0.23817
## intref_prop  0.093637  0.137015 -0.174907  0.362181  0.683 0.49455
## intmed_prop  0.089742  0.184517 -0.271904  0.451389  0.486 0.62685
## pie_prop     0.232330  0.217060 -0.193099  0.657759  1.070 0.28480
## overall_pm   0.322073  0.386063 -0.434597  1.078743  0.834 0.40440
## overall_int  0.183380  0.302838 -0.410172  0.776931  0.606 0.54500
## overall_pe   0.415710  0.494958 -0.554390  1.385809  0.840 0.40123
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
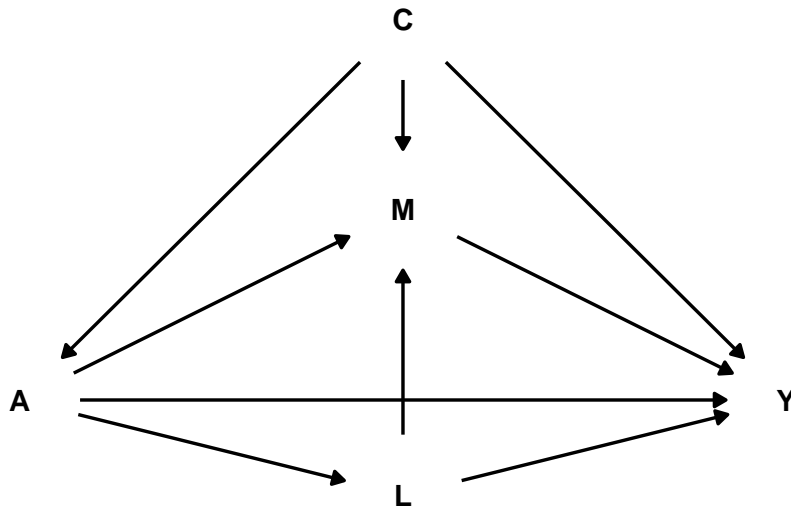
4 Multiple Mediator with Time-dependent Confounding Case

4.1 Variables and DAG

```
cmdag(outcome = "cognitive_raw",
      exposure = 'ln_blood_mn_conc_ugdl0',
      mediator = c("weight0","length0",'head_circumference0'),
      postc = c("birthgestationalage","hematocrit2"))
```

13

A(Exposure):ln_blood_mn_conc_ugdl0
M(Mediator):weight0, length0, head_circumference0
Y(Outcome):cognitive_raw
C(Pre−exposure confounders): prec
L(Post−exposure confounders):birthgestationalage, hematocrit2

4.2 Methods Can Be Used

4.2.1 G-formula approach

```r
cmest_out <- cmest(data = bangladesh_df, model = "g-formula",
                   outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = c("weight0","length0",'head_circumference0'),
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "educcat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   postc = c("birthgestationalage","hematocrit2"),
                   postcreg = c("linear", "linear"),
                   EMint = TRUE,
                   yreg = "linear", mreg = c("linear", "linear", "linear"),
                   astar = log(5.84), a = log(9.5), mval = list(2.9,47,33),
                   estimation = "imputation", inference = "bootstrap",
                   nboot = 200)

summary(cmest_out)
```

```
##           Estimate Std.error   95% CIL   95% CIU      z    pval
## cde      -0.212917  0.122580 -0.453170  0.027337 -1.737 0.08280 .
## rpnde    -0.247038  0.123023 -0.488158 -0.005918 -2.008 0.04499 *
## rtnde    -0.279741  0.124886 -0.524512 -0.034969 -2.240 0.02538 *
```

14

```
## rpnie       -0.084662  0.031274 -0.145957 -0.023366 -2.707 0.00694 **
## rtnie       -0.117364  0.037335 -0.190539 -0.044189 -3.144 0.00173 **
## rte         -0.364402  0.129204 -0.617637 -0.111167 -2.820 0.00492 **
## pm           0.191947  0.875643 -1.524281  1.908175  0.219 0.82655
## intref      -0.034122  0.025553 -0.084205  0.015962 -1.335 0.18217
## intmed      -0.032702  0.014426 -0.060977 -0.004428 -2.267 0.02367 *
## pie         -0.084662  0.031274 -0.145957 -0.023366 -2.707 0.00694 **
## cde_prop     0.584290  0.268728  0.057593  1.110987  2.174 0.02999 *
## intref_prop  0.093637  0.099282 -0.100952  0.288226  0.943 0.34590
## intmed_prop  0.089742  0.062192 -0.032151  0.211636  1.443 0.14943
## pie_prop     0.232330  0.167972 -0.096889  0.561549  1.383 0.16702
## overall_pm   0.322073  0.210963 -0.091407  0.735552  1.527 0.12725
## overall_int  0.183380  0.142924 -0.096747  0.463506  1.283 0.19986
## overall_pe   0.415710  0.268728 -0.110987  0.942407  1.547 0.12229
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

5 Sensitivity Analysis

5.1 Sensitivity Analysis For Unmeasured Confounding

```r
cmest_out <- cmest(data = bangladesh_df, model = "rb",
                   outcome = "cognitive_raw",
                   exposure = 'ln_blood_mn_conc_ugdl0',
                   mediator = c("weight0","length0",'head_circumference0'),
                   prec = c("ln_blood_as_conc_ugdl0",
                            "ln_blood_pb_conc_ugdl0",
                            "sex",
                            "allfood",
                            "smokenv", "educcat", "agedays", "approxage",
                            "homescore","birthgestationalage",
                            "clinic", "hematocrit2"),
                   EMint = TRUE,
                   yreg = "linear", mreg = c("linear", "linear", "linear"),
                   astar = log(5.84), a = log(9.5), mval = list(2.9,47,33),
                   estimation = "imputation", inference = "bootstrap",
                   nboot = 200)

cmsens_out <- cmsens(cmest_out, sens = "uc",
                     data = bangladesh_df, model = "rb",
                     outcome = "cognitive_raw",
                     yreg = "linear",
                     mreg = c("linear", "linear", "linear"))

cmsens_out
```

```
##        Point       CI
## cde  1.249382 1.000000
## pnde 1.273329 1.061757
## tnde 1.295454 1.107734
## pnie 1.144997 1.080957
## tnie 1.174907 1.104277
```

```
## te   1.350010 1.182487
```

5.2 Sensitivity Analysis For Measurement Error

5.2.1 Exposure Measured With Error

```r
cmsens_out <- cmsens(sens = "me", MEvariable = "ln_blood_mn_conc_ugdl0",
                     MEvariable.type="continuous",
                     measurement.error=c(0.1, 0.3,0.5),
                     data = bangladesh_df, model = "rb",
                     outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                     mediator = c("weight0","length0",'head_circumference0'),
                     prec = c("ln_blood_as_conc_ugdl0",
                              "ln_blood_pb_conc_ugdl0",
                              "sex",
                              "allfood",
                              "smokenv", "educcat", "agedays", "approxage",
                              "homescore","birthgestationalage",
                              "clinic", "hematocrit2"),
                     EMint = TRUE,
                     yreg = "linear", mreg = c("linear", "linear", "linear"),
                     astar = log(5.84), a = log(9.5), mval = list(2.9,47,33),
                     estimation = "imputation", inference = "bootstrap",
                     nboot = 200)

cmsens_out
```

```
##
##   measurement.error =  0.1
##               Estimate   Std.error    95% CIL    95% CIU          z
## cde          -2.133e-01  2.578e-15 -2.133e-01 -2.133e-01 -8.274e+13
## pnde         -2.482e-01  4.636e-03 -2.573e-01 -2.391e-01 -5.353e+01
## tnde         -2.825e-01  4.636e-03 -2.916e-01 -2.734e-01 -6.093e+01
## pnie         -8.686e-02  2.676e-15 -8.686e-02 -8.686e-02 -3.246e+13
## tnie         -1.211e-01  2.611e-15 -1.211e-01 -1.211e-01 -4.639e+13
## te           -3.693e-01  4.636e-03 -3.784e-01 -3.603e-01 -7.966e+01
## pm            1.962e-01  2.946e-03  1.904e-01  2.019e-01  6.658e+01
## intref       -3.490e-02  4.636e-03 -4.399e-02 -2.581e-02 -7.528e+00
## intmed       -3.428e-02  3.769e-15 -3.428e-02 -3.428e-02 -9.097e+12
## pie          -8.686e-02  2.676e-15 -8.686e-02 -8.686e-02 -3.246e+13
## cde_prop      5.775e-01  7.250e-03  5.633e-01  5.917e-01  7.966e+01
## intref_prop   9.450e-02  1.137e-02  7.222e-02  1.168e-01  8.313e+00
## intmed_prop   9.282e-02  1.165e-03  9.054e-02  9.511e-02  7.966e+01
## pie_prop      2.352e-01  2.952e-03  2.294e-01  2.409e-01  7.966e+01
## overall_pm    3.280e-01  4.118e-03  3.199e-01  3.361e-01  7.966e+01
## overall_int   1.873e-01  1.020e-02  1.673e-01  2.073e-01  1.836e+01
## overall_pe    4.225e-01  7.250e-03  4.083e-01  4.367e-01  5.827e+01
##                  pval
## cde           < 2e-16 ***
## pnde          < 2e-16 ***
## tnde          < 2e-16 ***
## pnie          < 2e-16 ***
## tnie          < 2e-16 ***
```

```
## te          < 2e-16 ***
## pm          < 2e-16 ***
## intref      1.45e-13 ***
## intmed      < 2e-16 ***
## pie         < 2e-16 ***
## cde_prop    < 2e-16 ***
## intref_prop 4.22e-16 ***
## intmed_prop < 2e-16 ***
## pie_prop    < 2e-16 ***
## overall_pm  < 2e-16 ***
## overall_int < 2e-16 ***
## overall_pe  < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## -------------------------------------------------------------
##
## measurement.error =  0.3
##              Estimate  Std.error    95% CIL    95% CIU          z
## cde        -2.687e-01  3.398e-15 -2.687e-01 -2.687e-01 -7.909e+13
## pnde       -3.064e-01  5.735e-03 -3.176e-01 -2.952e-01 -5.342e+01
## tnde       -3.582e-01  5.735e-03 -3.694e-01 -3.469e-01 -6.245e+01
## pnie       -9.869e-02  2.707e-15 -9.869e-02 -9.869e-02 -3.646e+13
## tnie       -1.504e-01  3.560e-15 -1.504e-01 -1.504e-01 -4.226e+13
## te         -4.568e-01  5.735e-03 -4.681e-01 -4.456e-01 -7.965e+01
## pm          1.971e-01  2.960e-03  1.913e-01  2.029e-01  6.659e+01
## intref     -3.770e-02  5.735e-03 -4.894e-02 -2.646e-02 -6.573e+00
## intmed     -5.175e-02  4.414e-15 -5.175e-02 -5.175e-02 -1.173e+13
## pie        -9.869e-02  2.707e-15 -9.869e-02 -9.869e-02 -3.646e+13
## cde_prop    5.882e-01  7.378e-03  5.737e-01  6.026e-01  7.972e+01
## intref_prop 8.252e-02  1.151e-02  5.996e-02  1.051e-01  7.170e+00
## intmed_prop 1.133e-01  1.421e-03  1.105e-01  1.161e-01  7.972e+01
## pie_prop    2.160e-01  2.710e-03  2.107e-01  2.213e-01  7.972e+01
## overall_pm  3.293e-01  4.131e-03  3.212e-01  3.374e-01  7.972e+01
## overall_int 1.958e-01  1.009e-02  1.760e-01  2.156e-01  1.941e+01
## overall_pe  4.118e-01  7.378e-03  3.974e-01  4.263e-01  5.582e+01
##                  pval
## cde         < 2e-16 ***
## pnde        < 2e-16 ***
## tnde        < 2e-16 ***
## pnie        < 2e-16 ***
## tnie        < 2e-16 ***
## te          < 2e-16 ***
## pm          < 2e-16 ***
## intref      9.12e-11 ***
## intmed      < 2e-16 ***
## pie         < 2e-16 ***
## cde_prop    < 2e-16 ***
## intref_prop 1.77e-12 ***
## intmed_prop < 2e-16 ***
## pie_prop    < 2e-16 ***
## overall_pm  < 2e-16 ***
## overall_int < 2e-16 ***
## overall_pe  < 2e-16 ***
## ---
```

```
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## ----------------------------------------------------------------
##
##   measurement.error =  0.5
##                 Estimate  Std.error      95% CIL     95% CIU          z
## cde          -3.808e-01  1.876e-15  -3.808e-01  -3.808e-01  -2.030e+14
## pnde         -4.171e-01  8.239e-03  -4.333e-01  -4.010e-01  -5.063e+01
## tnde         -4.965e-01  8.239e-03  -5.127e-01  -4.804e-01  -6.027e+01
## pnie         -1.132e-01  3.280e-15  -1.132e-01  -1.132e-01  -3.453e+13
## tnie         -1.926e-01  2.315e-15  -1.926e-01  -1.926e-01  -8.321e+13
## te           -6.098e-01  8.239e-03  -6.259e-01  -5.936e-01  -7.401e+01
## pm            1.876e-01  2.990e-03   1.817e-01   1.934e-01   6.274e+01
## intref       -3.632e-02  8.239e-03  -5.247e-02  -2.017e-02  -4.408e+00
## intmed       -7.938e-02  4.119e-15  -7.938e-02  -7.938e-02  -1.927e+13
## pie          -1.132e-01  3.280e-15  -1.132e-01  -1.132e-01  -3.453e+13
## cde_prop      6.245e-01  8.390e-03   6.081e-01   6.410e-01   7.444e+01
## intref_prop   5.956e-02  1.263e-02   3.480e-02   8.432e-02   4.715e+00
## intmed_prop   1.302e-01  1.749e-03   1.268e-01   1.336e-01   7.444e+01
## pie_prop      1.857e-01  2.495e-03   1.808e-01   1.906e-01   7.444e+01
## overall_pm    3.159e-01  4.244e-03   3.076e-01   3.242e-01   7.444e+01
## overall_int   1.897e-01  1.088e-02   1.684e-01   2.111e-01   1.743e+01
## overall_pe    3.755e-01  8.390e-03   3.590e-01   3.919e-01   4.475e+01
##                    pval
## cde           < 2e-16 ***
## pnde          < 2e-16 ***
## tnde          < 2e-16 ***
## pnie          < 2e-16 ***
## tnie          < 2e-16 ***
## te            < 2e-16 ***
## pm            < 2e-16 ***
## intref        1.19e-05 ***
## intmed        < 2e-16 ***
## pie           < 2e-16 ***
## cde_prop      < 2e-16 ***
## intref_prop   2.87e-06 ***
## intmed_prop   < 2e-16 ***
## pie_prop      < 2e-16 ***
## overall_pm    < 2e-16 ***
## overall_int   < 2e-16 ***
## overall_pe    < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## ----------------------------------------------------------------
```

5.2.2 A Mediator Measured With Error

```
cmsens_out <- cmsens(sens = "me", MEvariable = "weight0",
                MEvariable.type="continuous",
                measurement.error=c(0.1, 0.3,0.5),
                data = bangladesh_df, model = "rb",
                outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                mediator = c("weight0","length0",'head_circumference0'),
                prec = c("ln_blood_as_conc_ugdl0",
```

```
                              "ln_blood_pb_conc_ugdl0",
                              "sex",
                              "allfood",
                              "smokenv", "educcat", "agedays", "approxage",
                              "homescore","birthgestationalage",
                              "clinic", "hematocrit2"),
                      EMint = TRUE,
                      yreg = "linear", mreg = c("linear", "linear", "linear"),
                      astar = log(5.84), a = log(9.5), mval = list(2.9,47,33),
                      estimation = "imputation", inference = "bootstrap",
                      nboot = 200)

cmsens_out
```

```
##
##   measurement.error =  0.1
##                Estimate  Std.error    95% CIL     95% CIU            z
## cde          -2.136e-01  3.557e-15 -2.136e-01 -2.136e-01 -6.005e+13
## pnde         -2.474e-01  1.570e-02 -2.782e-01 -2.166e-01 -1.576e+01
## tnde         -2.800e-01  1.449e-02 -3.084e-01 -2.516e-01 -1.933e+01
## pnie         -8.605e-02  1.748e-02 -1.203e-01 -5.178e-02 -4.922e+00
## tnie         -1.186e-01  2.604e-02 -1.697e-01 -6.761e-02 -4.556e+00
## te           -3.660e-01  2.444e-02 -4.139e-01 -3.181e-01 -1.498e+01
## pm            1.934e-01  3.919e-02  1.166e-01  2.702e-01  4.935e+00
## intref       -3.379e-02  1.570e-02 -6.457e-02 -3.021e-03 -2.152e+00
## intmed       -3.260e-02  9.034e-03 -5.030e-02 -1.489e-02 -3.609e+00
## pie          -8.605e-02  1.748e-02 -1.203e-01 -5.178e-02 -4.922e+00
## cde_prop      5.835e-01  3.938e-02  5.064e-01  6.607e-01  1.482e+01
## intref_prop   9.233e-02  4.222e-02  9.568e-03  1.751e-01  2.187e+00
## intmed_prop   8.906e-02  2.083e-02  4.824e-02  1.299e-01  4.276e+00
## pie_prop      2.351e-01  3.670e-02  1.631e-01  3.070e-01  6.405e+00
## overall_pm    3.241e-01  5.597e-02  2.144e-01  4.338e-01  5.791e+00
## overall_int   1.814e-01  3.219e-02  1.183e-01  2.445e-01  5.636e+00
## overall_pe    4.165e-01  3.938e-02  3.393e-01  4.936e-01  1.058e+01
##                   pval
## cde           < 2e-16 ***
## pnde          < 2e-16 ***
## tnde          < 2e-16 ***
## pnie         1.05e-06 ***
## tnie         6.05e-06 ***
## te            < 2e-16 ***
## pm           9.82e-07 ***
## intref       0.031677 *
## intmed       0.000328 ***
## pie          1.05e-06 ***
## cde_prop      < 2e-16 ***
## intref_prop  0.029075 *
## intmed_prop  2.14e-05 ***
## pie_prop     2.62e-10 ***
## overall_pm   1.02e-08 ***
## overall_int  2.45e-08 ***
## overall_pe    < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
## ------------------------------------------------------------------
##
## measurement.error = 0.3
##               Estimate  Std.error   95% CIL   95% CIU          z
## cde          -2.057e-01  1.121e-15 -2.057e-01 -2.057e-01 -1.835e+14
## pnde         -2.390e-01  1.453e-02 -2.675e-01 -2.105e-01 -1.645e+01
## tnde         -2.694e-01  1.285e-02 -2.946e-01 -2.443e-01 -2.097e+01
## pnie         -8.440e-02  1.622e-02 -1.162e-01 -5.261e-02 -5.203e+00
## tnie         -1.148e-01  2.474e-02 -1.633e-01 -6.636e-02 -4.643e+00
## te           -3.538e-01  2.150e-02 -3.960e-01 -3.117e-01 -1.645e+01
## pm            1.937e-01  3.930e-02  1.167e-01  2.707e-01  4.929e+00
## intref       -3.330e-02  1.453e-02 -6.178e-02 -4.820e-03 -2.292e+00
## intmed       -3.044e-02  8.718e-03 -4.753e-02 -1.336e-02 -3.492e+00
## pie          -8.440e-02  1.622e-02 -1.162e-01 -5.261e-02 -5.203e+00
## cde_prop      5.813e-01  3.562e-02  5.115e-01  6.511e-01  1.632e+01
## intref_prop   9.411e-02  4.136e-02  1.305e-02  1.752e-01  2.275e+00
## intmed_prop   8.604e-02  2.092e-02  4.503e-02  1.270e-01  4.113e+00
## pie_prop      2.385e-01  3.549e-02  1.690e-01  3.081e-01  6.721e+00
## overall_pm    3.246e-01  5.561e-02  2.156e-01  4.336e-01  5.836e+00
## overall_int   1.802e-01  3.052e-02  1.203e-01  2.400e-01  5.902e+00
## overall_pe    4.187e-01  3.562e-02  3.489e-01  4.885e-01  1.175e+01
##                   pval
## cde            < 2e-16 ***
## pnde           < 2e-16 ***
## tnde           < 2e-16 ***
## pnie          2.52e-07 ***
## tnie          4.04e-06 ***
## te             < 2e-16 ***
## pm            1.01e-06 ***
## intref        0.022195 *
## intmed        0.000507 ***
## pie           2.52e-07 ***
## cde_prop       < 2e-16 ***
## intref_prop   0.023156 *
## intmed_prop   4.33e-05 ***
## pie_prop      3.52e-11 ***
## overall_pm    7.86e-09 ***
## overall_int   5.38e-09 ***
## overall_pe     < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## ------------------------------------------------------------------
##
## measurement.error = 0.5
##               Estimate  Std.error   95% CIL   95% CIU          z
## cde          -1.981e-01  2.876e-15 -1.981e-01 -1.981e-01 -6.888e+13
## pnde         -2.306e-01  1.388e-02 -2.578e-01 -2.034e-01 -1.661e+01
## tnde         -2.587e-01  1.244e-02 -2.831e-01 -2.343e-01 -2.080e+01
## pnie         -7.830e-02  1.364e-02 -1.050e-01 -5.157e-02 -5.741e+00
## tnie         -1.064e-01  2.119e-02 -1.479e-01 -6.488e-02 -5.022e+00
## te           -3.370e-01  1.927e-02 -3.748e-01 -2.993e-01 -1.749e+01
## pm            1.875e-01  3.543e-02  1.180e-01  2.569e-01  5.291e+00
## intref       -3.255e-02  1.388e-02 -5.976e-02 -5.335e-03 -2.344e+00
## intmed       -2.811e-02  7.665e-03 -4.313e-02 -1.309e-02 -3.667e+00
```

```
## pie       -7.830e-02  1.364e-02 -1.050e-01 -5.157e-02 -5.741e+00
## cde_prop   5.877e-01  3.338e-02  5.223e-01  6.531e-01  1.761e+01
## intref_prop 9.657e-02 4.025e-02  1.769e-02  1.754e-01  2.399e+00
## intmed_prop 8.340e-02 1.935e-02  4.547e-02  1.213e-01  4.310e+00
## pie_prop    2.323e-01  3.144e-02  1.707e-01  2.940e-01  7.389e+00
## overall_pm  3.157e-01  5.030e-02  2.171e-01  4.143e-01  6.277e+00
## overall_int 1.800e-01  3.028e-02  1.206e-01  2.393e-01  5.943e+00
## overall_pe  4.123e-01  3.338e-02  3.469e-01  4.777e-01  1.235e+01
##                   pval
## cde          < 2e-16 ***
## pnde         < 2e-16 ***
## tnde         < 2e-16 ***
## pnie        1.36e-08 ***
## tnie        6.35e-07 ***
## te           < 2e-16 ***
## pm          1.59e-07 ***
## intref      0.019320 *
## intmed      0.000262 ***
## pie         1.36e-08 ***
## cde_prop     < 2e-16 ***
## intref_prop 0.016657 *
## intmed_prop 1.85e-05 ***
## pie_prop    3.87e-13 ***
## overall_pm  5.76e-10 ***
## overall_int 4.23e-09 ***
## overall_pe   < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## --------------------------------------------------------------
```

5.2.3 Outcome Measured With Error

```r
cmsens_out <- cmsens(sens = "me", MEvariable = "cognitive_raw",
                     MEvariable.type="continuous",
                     measurement.error=c(0.1, 0.3,0.5),
                     data = bangladesh_df, model = "rb",
                     outcome = "cognitive_raw", exposure = 'ln_blood_mn_conc_ugdl0',
                     mediator = c("weight0","length0",'head_circumference0'),
                     prec = c("ln_blood_as_conc_ugdl0",
                              "ln_blood_pb_conc_ugdl0",
                              "sex",
                              "allfood",
                              "smokenv", "educcat", "agedays", "approxage",
                              "homescore","birthgestationalage",
                              "clinic", "hematocrit2"),
                     EMint = TRUE,
                     yreg = "linear", mreg = c("linear", "linear", "linear"),
                     astar = log(5.84), a = log(9.5), mval = list(2.9,47,33),
                     estimation = "imputation", inference = "bootstrap",
                     nboot = 200)

cmsens_out
```

```
## 
##   measurement.error =  0.1
##               Estimate  Std.error    95% CIL    95% CIU          z
## cde         -2.122e-01  3.516e-15 -2.122e-01 -2.122e-01 -6.036e+13
## pnde        -2.464e-01  1.627e-02 -2.783e-01 -2.145e-01 -1.514e+01
## tnde        -2.790e-01  1.416e-02 -3.068e-01 -2.513e-01 -1.971e+01
## pnie        -8.481e-02  2.475e-02 -1.333e-01 -3.630e-02 -3.427e+00
## tnie        -1.175e-01  3.368e-02 -1.835e-01 -5.146e-02 -3.488e+00
## te          -3.638e-01  3.019e-02 -4.230e-01 -3.047e-01 -1.205e+01
## pm           1.925e-01  5.001e-02  9.446e-02  2.905e-01  3.849e+00
## intref      -3.418e-02  1.627e-02 -6.607e-02 -2.279e-03 -2.100e+00
## intmed      -3.265e-02  9.842e-03 -5.194e-02 -1.336e-02 -3.318e+00
## pie         -8.481e-02  2.475e-02 -1.333e-01 -3.630e-02 -3.427e+00
## cde_prop     5.832e-01  4.896e-02  4.873e-01  6.792e-01  1.191e+01
## intref_prop  9.393e-02  4.465e-02  6.419e-03  1.814e-01  2.104e+00
## intmed_prop  8.974e-02  2.185e-02  4.692e-02  1.326e-01  4.108e+00
## pie_prop     2.331e-01  5.130e-02  1.325e-01  3.336e-01  4.544e+00
## overall_pm   3.228e-01  6.993e-02  1.858e-01  4.599e-01  4.616e+00
## overall_int  1.837e-01  3.259e-02  1.198e-01  2.475e-01  5.637e+00
## overall_pe   4.168e-01  4.896e-02  3.208e-01  5.127e-01  8.512e+00
##                  pval
## cde          < 2e-16 ***
## pnde         < 2e-16 ***
## tnde         < 2e-16 ***
## pnie        0.000643 ***
## tnie        0.000514 ***
## te           < 2e-16 ***
## pm          0.000129 ***
## intref      0.036053 *
## intmed      0.000950 ***
## pie         0.000643 ***
## cde_prop     < 2e-16 ***
## intref_prop 0.035727 *
## intmed_prop 4.43e-05 ***
## pie_prop    6.41e-06 ***
## overall_pm  4.58e-06 ***
## overall_int 2.43e-08 ***
## overall_pe   < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## -------------------------------------------------------------
## 
##   measurement.error =  0.3
##               Estimate  Std.error    95% CIL    95% CIU          z
## cde         -2.136e-01  3.521e-15 -2.136e-01 -2.136e-01 -6.067e+13
## pnde        -2.474e-01  1.533e-02 -2.774e-01 -2.173e-01 -1.614e+01
## tnde        -2.799e-01  1.399e-02 -3.073e-01 -2.525e-01 -2.001e+01
## pnie        -8.476e-02  2.478e-02 -1.333e-01 -3.619e-02 -3.420e+00
## tnie        -1.173e-01  3.371e-02 -1.833e-01 -5.120e-02 -3.479e+00
## te          -3.646e-01  3.096e-02 -4.253e-01 -3.040e-01 -1.178e+01
## pm           1.916e-01  4.911e-02  9.535e-02  2.879e-01  3.901e+00
## intref      -3.373e-02  1.533e-02 -6.377e-02 -3.681e-03 -2.200e+00
## intmed      -3.251e-02  1.005e-02 -5.222e-02 -1.281e-02 -3.234e+00
## pie         -8.476e-02  2.478e-02 -1.333e-01 -3.619e-02 -3.420e+00
```

```
## cde_prop     5.859e-01  5.030e-02  4.873e-01  6.845e-01  1.165e+01
## intref_prop  9.249e-02  4.234e-02  9.508e-03  1.755e-01  2.185e+00
## intmed_prop  8.916e-02  2.231e-02  4.544e-02  1.329e-01  3.997e+00
## pie_prop     2.324e-01  5.134e-02  1.318e-01  3.331e-01  4.527e+00
## overall_pm   3.216e-01  6.952e-02  1.853e-01  4.579e-01  4.626e+00
## overall_int  1.817e-01  3.098e-02  1.209e-01  2.424e-01  5.864e+00
## overall_pe   4.141e-01  5.030e-02  3.155e-01  5.127e-01  8.232e+00
##                      pval
## cde          < 2e-16 ***
## pnde         < 2e-16 ***
## tnde         < 2e-16 ***
## pnie        0.000658 ***
## tnie        0.000532 ***
## te           < 2e-16 ***
## pm          0.000104 ***
## intref      0.028097 *
## intmed      0.001275 **
## pie         0.000658 ***
## cde_prop     < 2e-16 ***
## intref_prop 0.029225 *
## intmed_prop 7.04e-05 ***
## pie_prop    6.92e-06 ***
## overall_pm  4.38e-06 ***
## overall_int 6.72e-09 ***
## overall_pe  7.87e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## --------------------------------------------------------------
##
##  measurement.error =  0.5
##               Estimate  Std.error     95% CIL     95% CIU           z
## cde         -2.082e-01  3.562e-15  -2.082e-01  -2.082e-01  -5.845e+13
## pnde        -2.434e-01  1.776e-02  -2.782e-01  -2.085e-01  -1.370e+01
## tnde        -2.769e-01  1.529e-02  -3.069e-01  -2.469e-01  -1.811e+01
## pnie        -8.461e-02  2.725e-02  -1.380e-01  -3.119e-02  -3.104e+00
## tnie        -1.182e-01  3.677e-02  -1.902e-01  -4.609e-02  -3.213e+00
## te          -3.615e-01  3.291e-02  -4.260e-01  -2.970e-01  -1.098e+01
## pm           1.954e-01  5.508e-02   8.741e-02   3.033e-01   3.547e+00
## intref      -3.516e-02  1.776e-02  -6.996e-02  -3.518e-04  -1.980e+00
## intmed      -3.356e-02  1.060e-02  -5.433e-02  -1.279e-02  -3.167e+00
## pie         -8.461e-02  2.725e-02  -1.380e-01  -3.119e-02  -3.104e+00
## cde_prop     5.759e-01  5.264e-02   4.727e-01   6.791e-01   1.094e+01
## intref_prop  9.725e-02  5.047e-02  -1.667e-03   1.962e-01   1.927e+00
## intmed_prop  9.282e-02  2.399e-02   4.581e-02   1.398e-01   3.870e+00
## pie_prop     2.340e-01  5.813e-02   1.201e-01   3.480e-01   4.026e+00
## overall_pm   3.269e-01  7.819e-02   1.736e-01   4.801e-01   4.180e+00
## overall_int  1.901e-01  3.595e-02   1.196e-01   2.605e-01   5.287e+00
## overall_pe   4.241e-01  5.264e-02   3.209e-01   5.273e-01   8.057e+00
##                      pval
## cde          < 2e-16 ***
## pnde         < 2e-16 ***
## tnde         < 2e-16 ***
## pnie        0.001977 **
## tnie        0.001367 **
```

```
## te           < 2e-16 ***
## pm          0.000413 ***
## intref      0.048085 *
## intmed      0.001604 **
## pie         0.001977 **
## cde_prop     < 2e-16 ***
## intref_prop 0.054356 .
## intmed_prop 0.000118 ***
## pie_prop    6.23e-05 ***
## overall_pm  3.24e-05 ***
## overall_int 1.62e-07 ***
## overall_pe  2.99e-15 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
## ----------------------------------------------------------------
```